FIG. 8

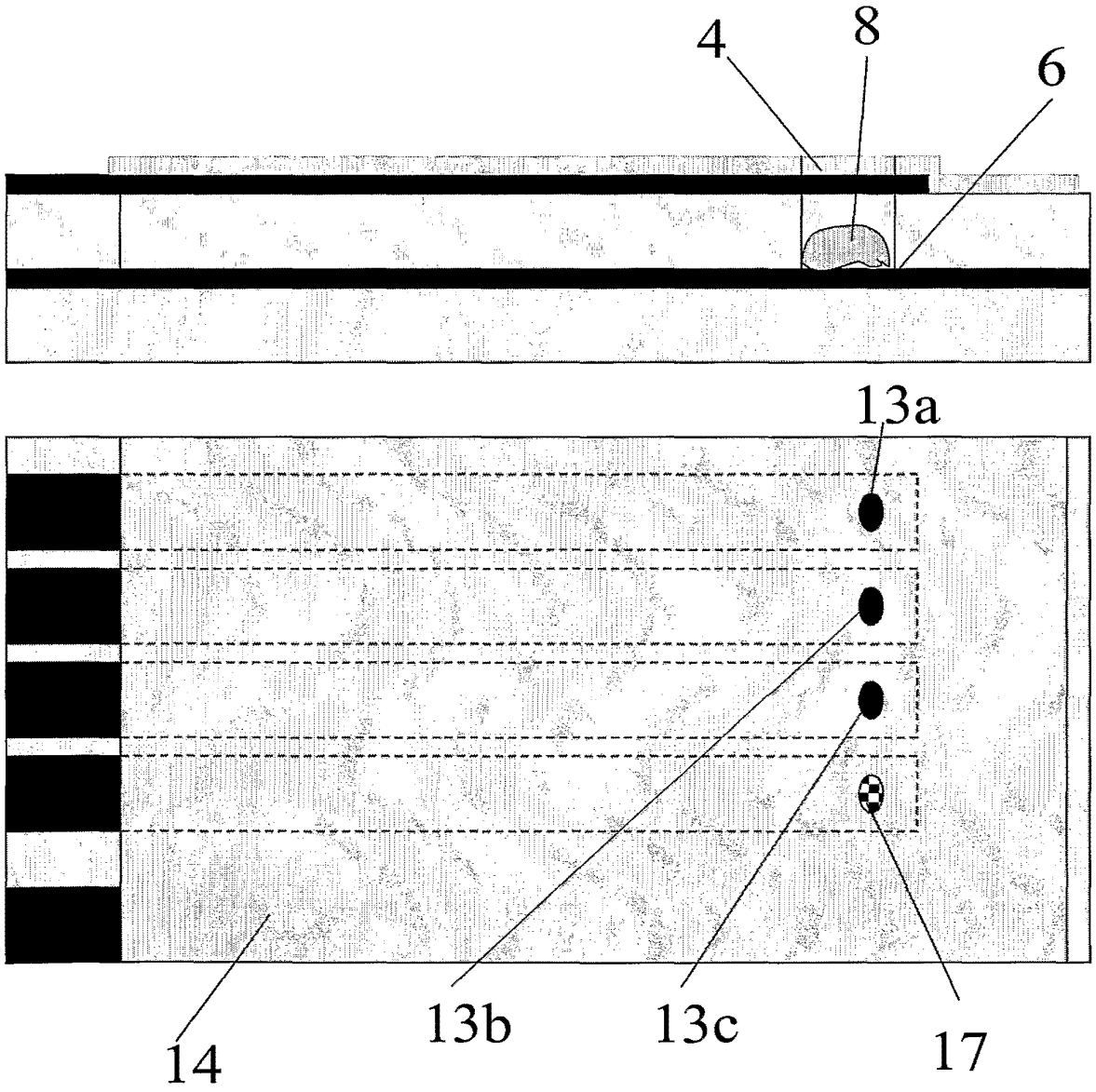


FIG. 9

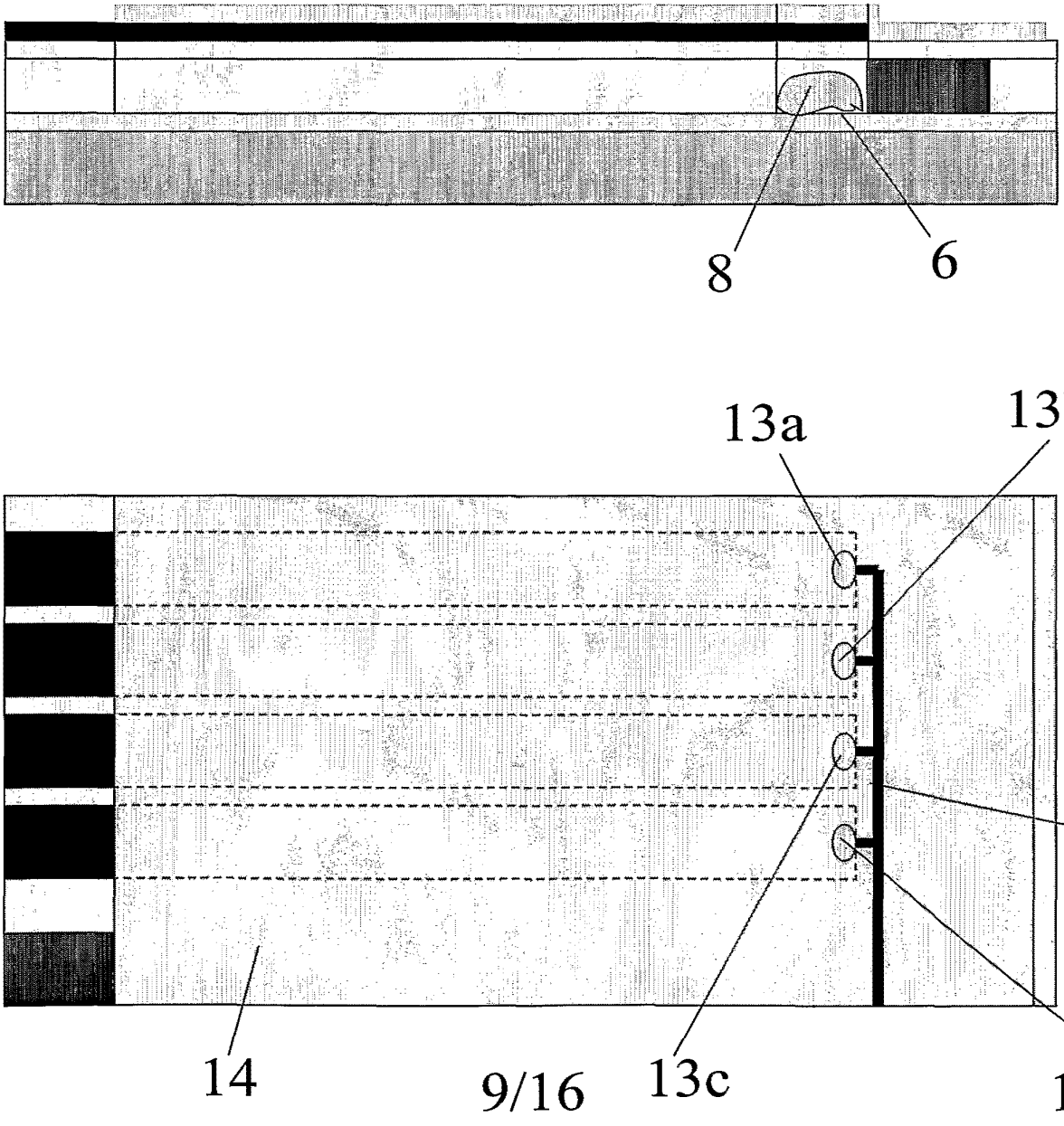


FIG. 10

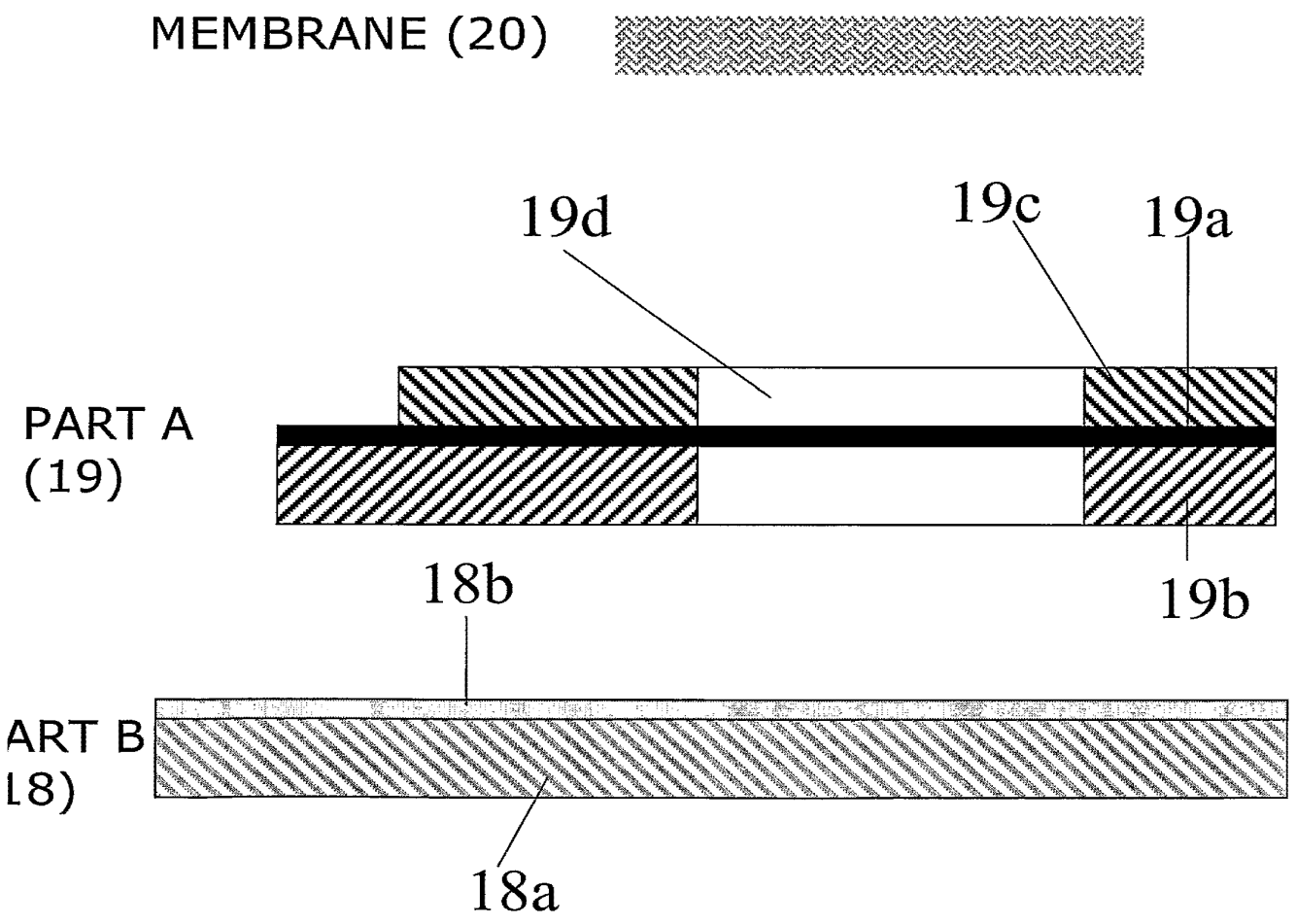
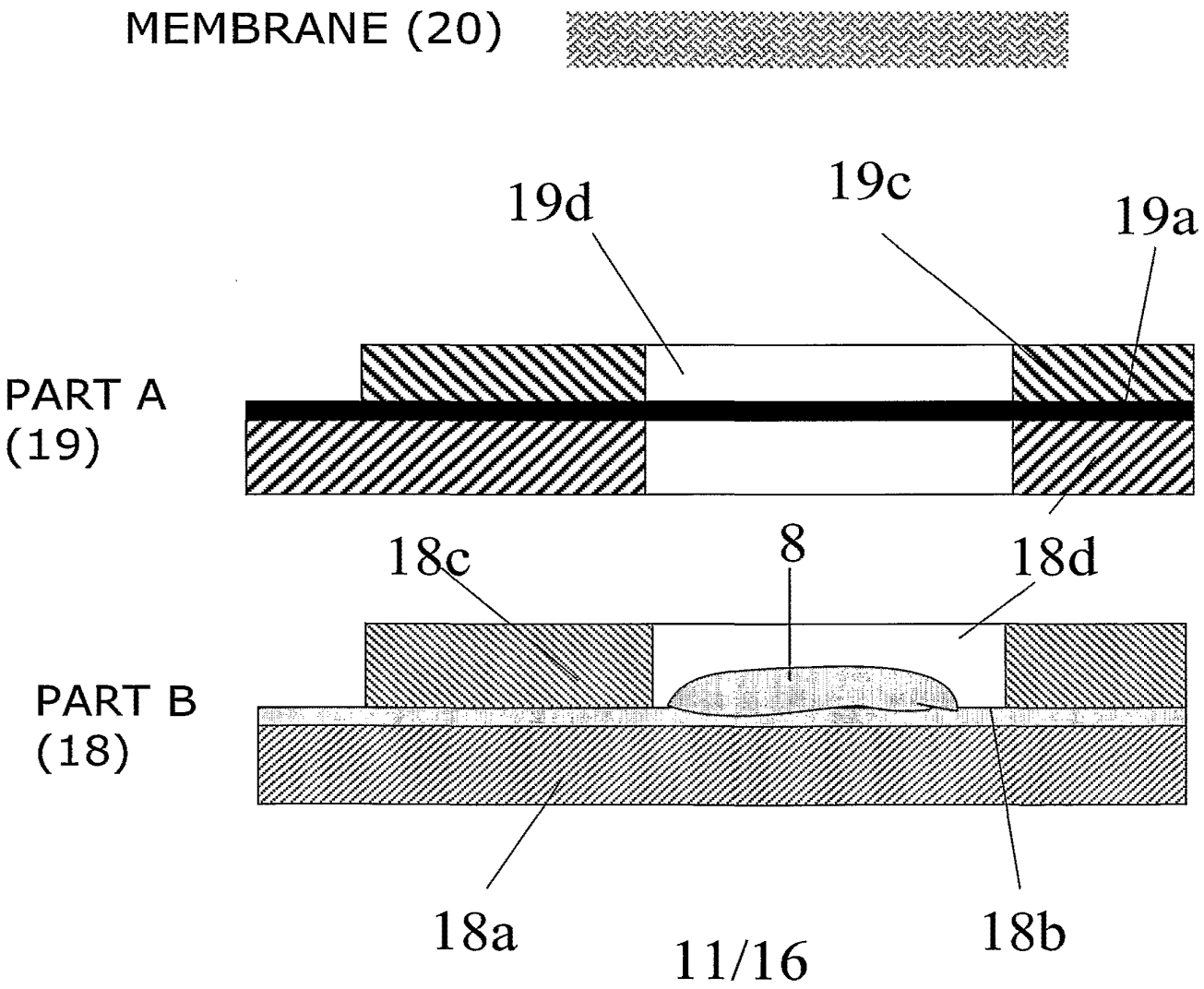


FIG. 11



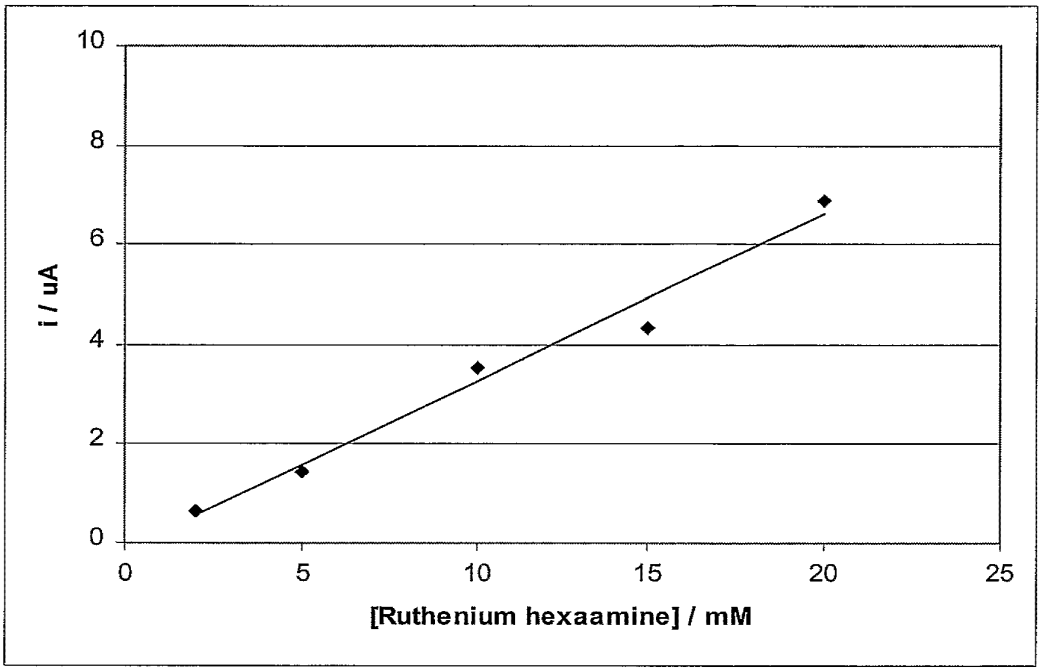


Figure 12

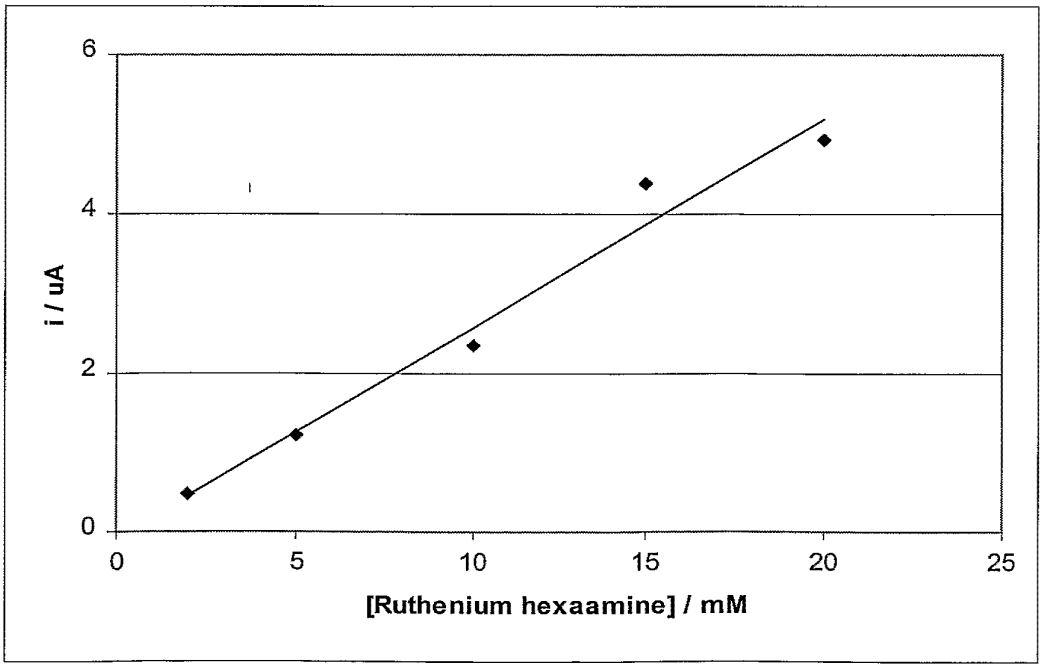


Figure 13

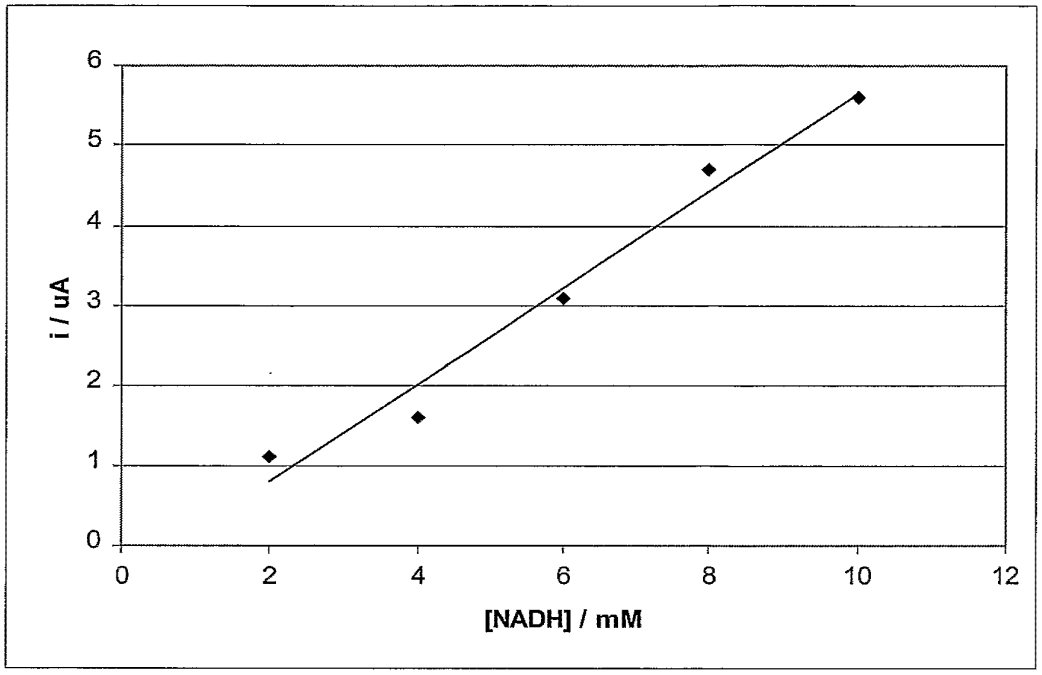


Figure 14

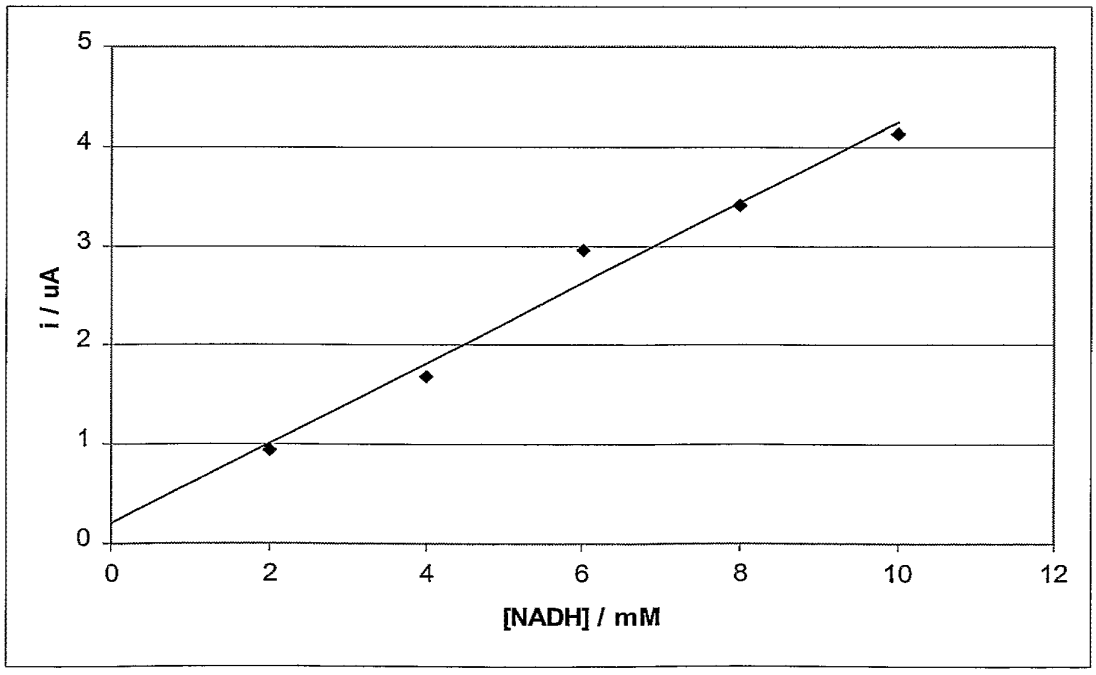


Figure 15

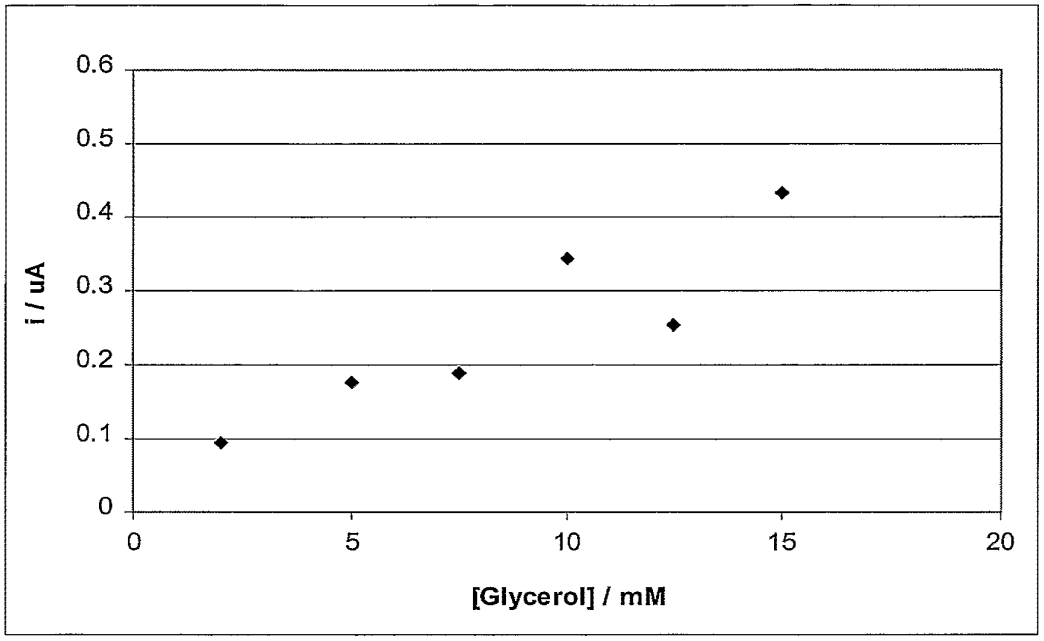


Figure 16

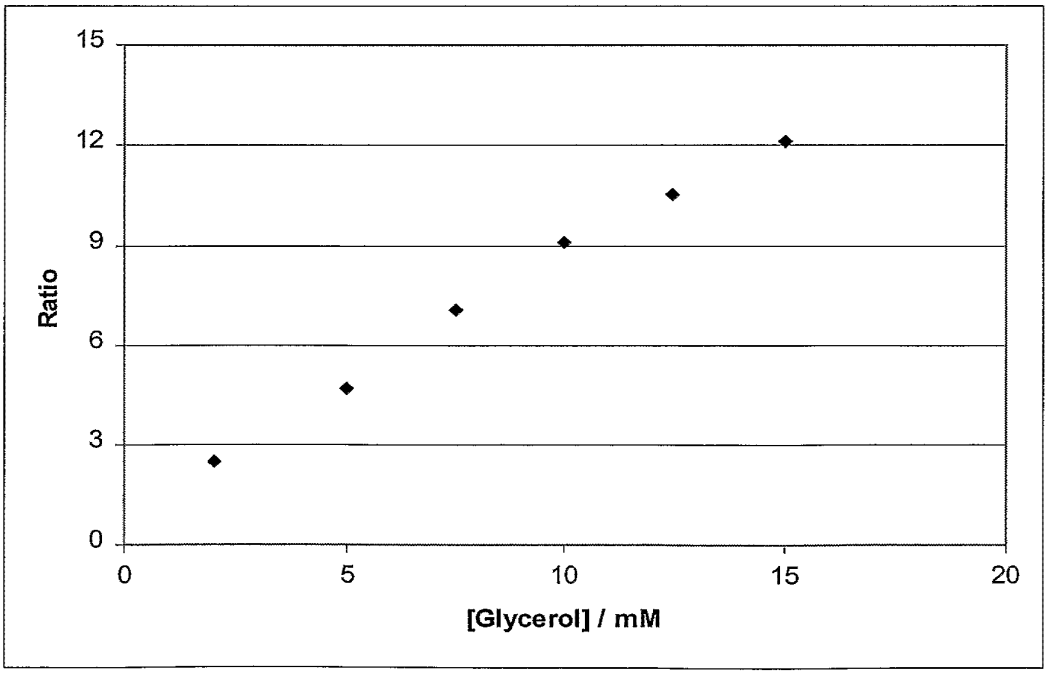


Figure 17

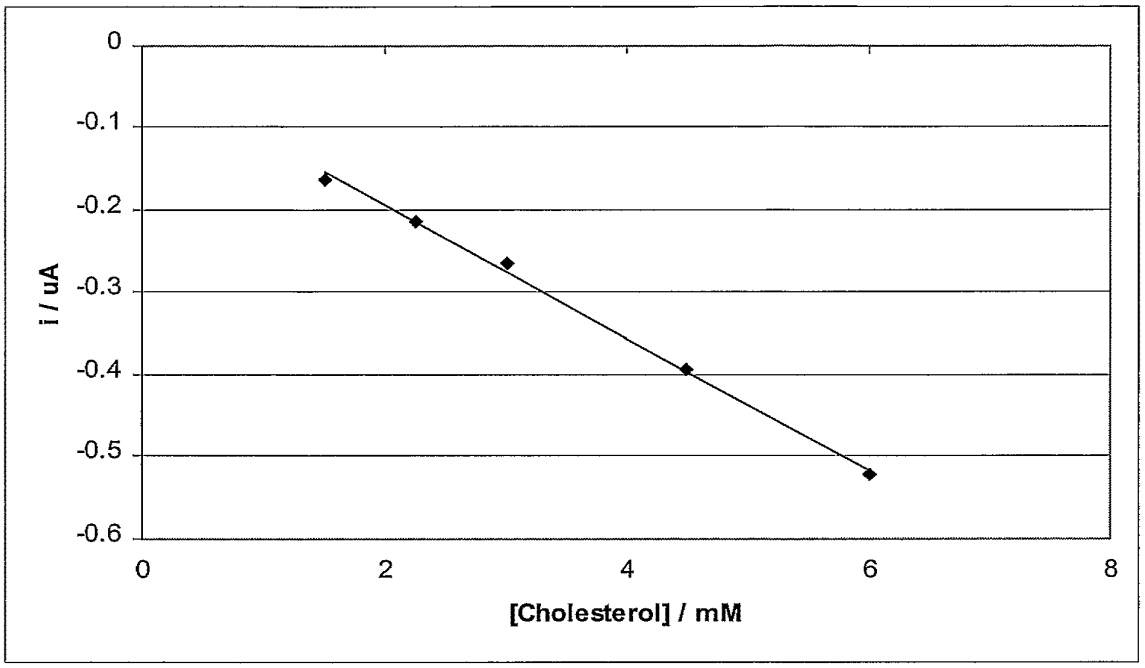


Figure 18

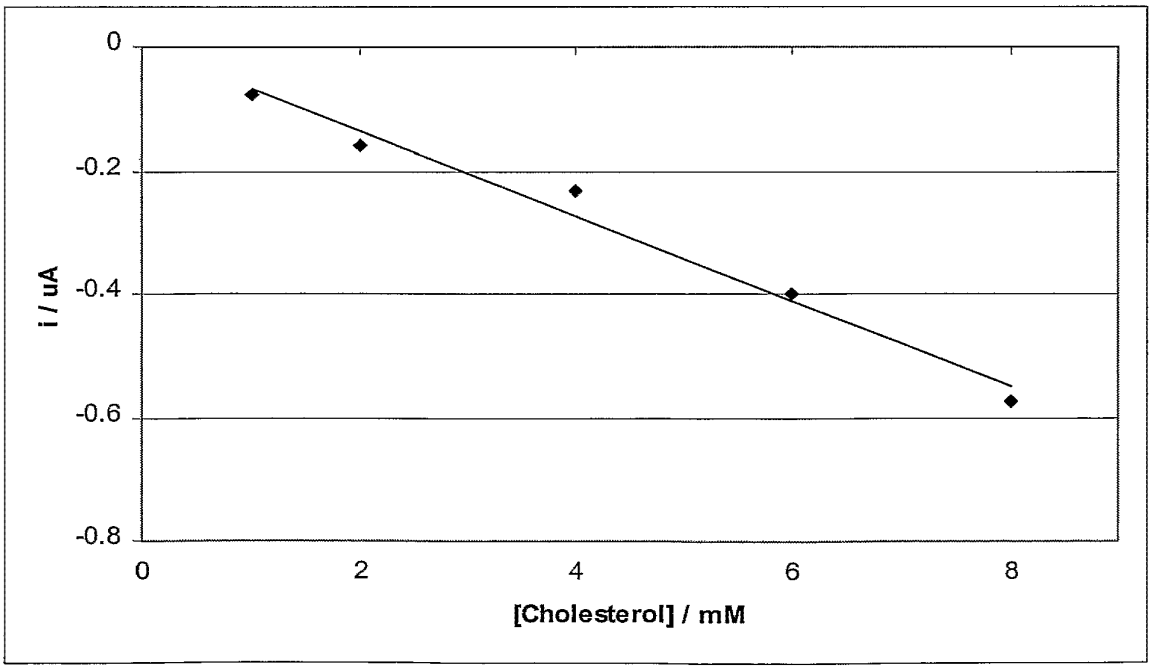


Figure 19

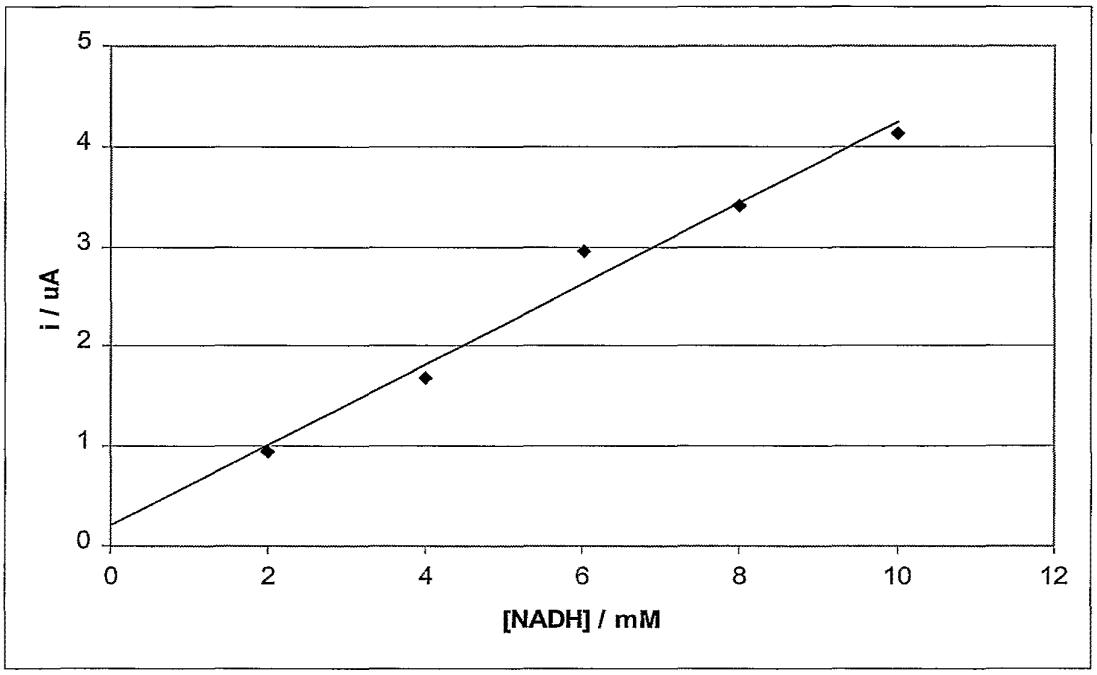


Figure 20

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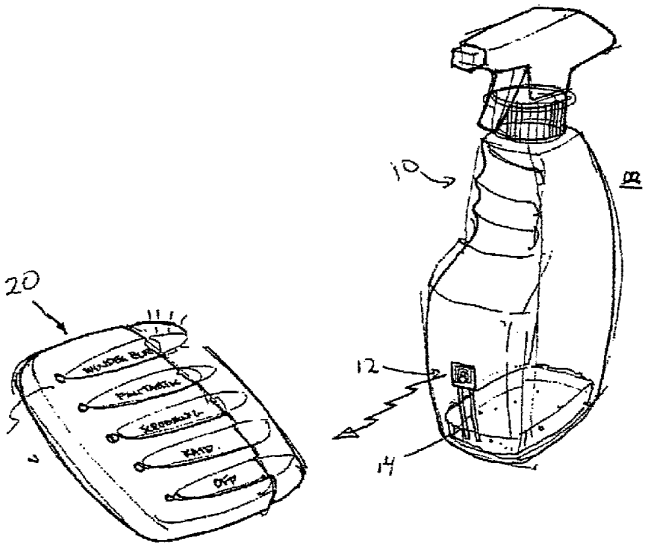
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(54) Title: PRODUCTS HAVING RFID TAGS TO PROVIDE INFORMATION TO PRODUCT CONSUMERS



(57) Abstract: RFID tags attached to a product contain information regarding the product and communicate this information to a reader. This information can include the age of the product, the amount of product left and preparation or care instructions for the product. To record the age of a product, a timer is initiated in the RFID tag. Thereafter, the elapsed time on the timer can be read and displayed by the reader. For other products, the RFID tag can have contacts monitoring the level of remaining product. Once the contacts sense that the amount of product is low, this information can be transmitted and communicated by the reader. Preparation and care instructions are prerecorded on the tag. Instructions can also be communicated between a product and a base, such as a heater.

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PRODUCTS HAVING RFID TAGS TO PROVIDE INFORMATION TO PRODUCT CONSUMERS

[0001] The instant application is based upon U.S. Provisional Patent Applications Serial No. 60/427,934, filed November 21, 2002, Serial No. 60/430,101, filed December 2, 2002, Serial No. 60/430,102, filed December 2, 2002 and Serial No. 60/482,867.

BACKGROUND OF THE INVENTION

[0002] Consumers often desire to know information regarding the many products in the household but the large number of consumer products makes keeping track of the condition of all products infeasible. Conditions that consumers often wish to know include age and time before replacement is necessary. At present, consumers often need to write a date on a product to keep track of its age of or continually check the amount remaining to estimate the time before replacement.

[0003] Many devices designed to dispense actives (also variously called dispensers) use refillable cartridges. Such devices include air fragrance dispensers. One problem encountered with such dispensers is that the cartridges are relatively long-lasting and when they finally do run out of product, the consumer is caught unprepared to replace the cartridge or they forget. Other products are used out of plain sight of the consumer. These devices include insect baits and traps. The consumer places them in hidden locations and may be unaware of whether they are being effective in controlling insects.

[0004] Consumers can place dates on products to know their age. Many freezer bags are provided with an area for marking the contents of the bag. To retrieve this information, the user needs to remove the bag from the freezer and read the information that has been imprinted on the bag and back compute the age from the date marked on the bag.

[0005] There is a need in the prior art for a single system able to track all products in a household and give information regarding the condition of the products, including age and amount of time before replacement.

[0006] It is an object of the invention to provide consumer items able to record and communicate condition of the product.

[0007] It is another object of the invention to provide products with RFID tags and a reader for storing information regarding the products and a reader for communicating this information to the consumer.

[0008] It is another object of the invention to provide a system for recording and communicating condition of a large number of items.

[0009] It is still another object of the invention to display information to the user by placing a reader in proximity to the item.

[0010] It is yet another object of the invention to use an RFID tag on a product to provide instructions to a recharger.

[0011] It is another object of the invention to provide consumers with information regarding products within the household.

[0012] These and other objects of the invention will become apparent to one of ordinary skill in the art after reviewing the disclosure of the invention.

SUMMARY OF THE INVENTION

[0013] RFID tags attached to a product contain information regarding the product and communicate this information to a reader. This information can include the age of the product, the amount of product left and preparation or care instructions for the product. To record the age of an product, a timer is initiated in the RFID reader once the RFID tag is recognized by the reader. Thereafter, the elapsed time on the timer can be read and displayed by the reader every time the RFID tag is passed in proximity to the reader. For other products, the RFID

tag can have contacts monitoring the level of remaining product. Once the contacts sense that the amount of product is low, this information can be transmitted and communicated by the reader. Preparation and care instructions are prerecorded on the tag or within the reader depending on the type of tag (read only or read-write). Instructions can also be communicated between a product and a base, such as a heater.

[0014] A monitoring system alerts a consumer when a cartridge is near empty or when a device, such as an insect bait/trap, is being effective in controlling pests. An automated triggering and signaling device is applied to the dispenser or bait/trap to signal the consumer when the cartridge is near empty or the trap is being used. Simple electrical or electromechanical mechanisms trigger the signaling device and communicate the status to the consumer via a hand-held PDA or other capable device. When the designated time period of the refill is known, a countdown can be started when the refill is installed, and an automated status of near empty can be signaled after a predetermined time.

[0015] Another use for RFID tags is for initiating instructions within the reader when an item having the RFID tag is brought in proximity to reader. An item needing to be heated or recharged, for instance, has an RFID tag. When the item is placed in the heater or recharger, the reader on the heater or charger senses the proximity of the RFID tag and can initiate the appropriate reheating or recharging cycle, which can be initiated by the RFID tag. Conversely, the RFID tag can contain information on it to communicate to the reader and initiate a series of instructions or commands. The tag can be preprogrammed with specific instructions in the manufacturing process or can be programmable. In this case a read-write RFID tag would be used where instructions or data is written to the tag or previous instructions unwritten.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] **FIGURE 1a** depicts a trigger spray container having a near-empty indicator;

[0017] **FIGURE 1b** depicts a trigger spray container having an alternative near-empty indicator;

[0018] **FIGURE 2** depicts an aerosol can having a functional label incorporating a near-empty indicator;

[0019] **FIGURE 3** depicts containers having near-empty indicators communicating with a central base station;

[0020] **FIGURE 4a** depicts a dispenser having an active refill incorporating a near-empty indicator;

[0021] **FIGURE 4b** shows a dispenser having an alternative refill incorporating a near-empty indicator;

[0022] **FIGURE 5** depicts a bottle having an RFID tag that mates with a holder;

[0023] **FIGURE 5a** depicts a heater and container for flowable products;

[0024] **FIGURE 6** depicts a multiple fragrance dispenser responsive to a key fob controller;

[0025] **FIGURE 7** depicts a fragrance dispenser responsive to a light sequence;

[0026] **FIGURE 8** depicts a reader for an RFID tag recording elapsed time;

[0027] **FIGURE 9** depicts bags incorporating an RFID tag;

[0028] **FIGURE 10** depicts a clip having an RFID tag; and

[0029] **FIGURE 11** depicts an insect trap incorporating an effectiveness indicator.

DETAILED DESCRIPTION OF THE INVENTION

[0030] RFID is a type of automatic identification technology, similar to bar code technology, except that RFID uses radio frequency instead of optical signals. The reader (or reader/writer) produces a low-level radio frequency magnetic field, typically either at 125 KHz or at 13.56 MHz. It must be noted that other frequencies can be used depending on the application. This magnetic field emanates from the reader (or reader/writer) by means of a transmitting antenna, typically in the form of a coil. Meanwhile, an RFID tag, typically including an antenna and an integrated surface, can be placed on any product.

[0031] The RFID system can be either read-only or read/write. Read-only systems, as their name suggests, permit the reader to receive information from the tag, but not vice-versa. Read/write systems, on the other hand, permit two-way communication between the tag and the reader/writer, and each of these components typically include an electronic memory for storing information received from the other component.

[0032] Figure 1a depicts a trigger spray container **10** having a near-empty indicator. The near-empty indicator consists of an RFID (radio frequency identification) tag **12** attached to the interior of the container. The RFID tag **12** has a pair of contacts **14** extending downwardly from the tag. When the contents of the container reach a level below the end of the contacts **14**, an electrical circuit is broken, causing the RFID tag to send a signal to a monitoring unit **20**. Power for the RFID tag to signal the reader is provided by a printed battery. The monitoring unit **20** has a series of LED lights, each LED light designating a particular product being monitored. In response to a signal from the RFID tag **12**, the LED light will illuminate to indicate to the

user or the consumer that the product will soon be in need of replacement. The signal may be audible.

[0033] Figure 1b depicts an alternative near-empty indicator. The trigger spray container **10** has a flexible printed circuit board **16** mounted thereon with a pair of contacts extending downwardly inside of the container. In a manner similar to the embodiment shown in Figure 1a, the reduction in level of product below the terminal ends of the contacts **18** causes the printed circuit board **16** to display a message on a display, such as e-paper attached to the container. Power for the printed circuit board and display is provided by a printed battery **25** adhered to the container exterior.

[0034] Figure 2 depicts the incorporation of a near-empty indicator on an aerosol can **30**. A functional label **32** is attached to the can. The functional label **32** includes a refill sensor **34**. When the contents of the container fall below a certain level, the refill sensor **34** sends a signal to a base monitor **38**. The base monitor **38** is able to display a printed message to the user indicating the need to replace the product in the very near future. The refill sensor is provided power by a printable battery **36** incorporated into the label.

[0035] Figure 3 depicts the ability for a plurality of containers to interact with a single central base station. The trigger spray container **10** has an RFID tag **12**. In this instance, the contacts **114** are molded into the container. The spray can **30** has a near-empty indicator attached to the interior of the can during manufacturing. Both of these containers communicate with a base monitor to alert the consumer that the level of product remaining in either respective container has reached a certain, predetermined low level.

[0036] Figure 4a shows a plug-in appliance for discharging fragrances, insecticides or similar actives. The actives are contained in a replaceable cartridge **42** received by the plug-in appliance **40** and having an RFID tag **44**. Contacts from the RFID tag extend downwardly from the tag and a reduction in the amount of liquid or gel contained in the refill breaks the electrical

circuit when the product falls below a certain level. The signal sent from the RFID tag alerts the consumer of this condition. In this instance, the RFID tag causes indicator light **45** at the top of the plug-in appliance to illuminate. The plug-in appliance can also have an audible message in response to a signal from the RFID tag. An additional embodiment would have the RFID tag signal a timer in the heater **40** to start. When the timer reaches a set time limit a signal is activated indicating that the refill is near empty.

[0037] Figure 4b shows a similar plug-in appliance **46** having a different type of cartridge **48** incorporating an RFID tag **49** having contacts extending downwardly into the container that break an electrical circuit when the product falls below a certain level. In the same manner, after such an event occurs, the RFID tag causes an indicator light **45** to illuminate. An additional embodiment would have the RFID tag signal a timer in the heater **46** to start. When the timer reaches a set time limit a signal is activated indicating that the refill is near empty.

[0038] Some actives and other products are not plugged directly into an outlet but are heated by a base unit, or charging device. Figure 5 shows a charging device comprising a coil **50** for generator a magnetic field, a control device **52** such as a circuit board for controlling the coil to selectively generate the magnetic field, a switch **53** for manually activating the charging device to generate the magnetic field, a heatable element **51** and a detection device **58** such as a reader writer. The heat storage unit has a radio frequency identification device **59** storing information about the heat storage unit. The detection device of the charging device reads the information stored by the RFID tag on the heat storage unit. The charging device is automatically activated to generate the magnetic field when the heat storage unit is placed in proximity to the charging device. With a heat storage unit and charging device, a proximity between tag and reader of 0.1 to six inches is preferred.

[0039] The RFID reader/writer **58** is connected to control device **52**. The heat storage unit has RFID tag **59** including an antenna. Preferably, the RFID tag is affixed to the outside of the heat storage unit or formed integrally with the heat storage unit. The tag signals reader/writer **58** when an appropriate heat storage unit is placed in proximity to the charging device causing control dervice **52** to activate coil **50**. The heatable element **51** generates heat in the presence of the generated magnetic field. Any device not having an RFID tag will not activate the charging device.

[0040] More than signaling the proximity of a container to activate the charger, in a more advanced embodiment, RFID tag **59** can transmit information to reader/writer **58** regarding preferred heating conditions for the particular heat storage unit. This can include both heating durations and peak temperatures. Additionally, the RFID tag can be used to transmit information to the reader/writer **58** regarding the product placed in the charger element. The reader recognizes the unique signature of the tag and accesses a stored regimen corresponding to that signature. Or the tag may store the heating regimen and transmit this information to the reader. In this manner, a single recharger can be used for a variety of different products such as different fragrances, insecticides, sanitizers, odor counteractant, liquid cleaning solution, shaving cream, lotion, or dispensing devices each having a different heating regimen.

[0041] Optionally, the RFID tag could have a writable electronic memory. The electronic memory contains stored information which may be updated by transmissions from the reader/writer **58**, including the heating history of the heat storage unit. The heating history of the bottle can be transmitted to the charge so that the charging device raises the peak temperature each time the charging device cycles on. This incrementally increases the evaporation rate of a fragrance to overcome any possible desensitizing problem. Transmitting the history of the bottle, a signal may be sent to the user to

replace the bottle with a new one based on the known duration of the contents of the bottle.

[0042] A real time clock connected to the control circuit can keep track of how long a particular heat storage unit has been heated and how recently. The control circuit therefore prevents overheating of the heat storage unit in such instances as when the heat storage unit has been recently heated and again plugged into the charging device. The RFID tag may also have a temperature sensor detecting the temperature of the heat storage unit to prevent overheating.

[0043] In addition to heating volatiles, a bottle containing flowable products may be placed in the charging device. The RFID tag on the bottle transmits information to the charging unit that a bottle has been placed in proximity and, optionally, to transmit information regarding the heating regimen of the particular flowable product. A charger and container for heating flowable consumer products is shown in Figure 5a. Similar to the system of Figure 5, the charger has a control device **52**, a detection device, reader/writer **58**, and a magnetic field generator **50**. The charger also has a manual switch **53** and indicator light **54**.

[0044] The container mating with the charger has a housing **140** accommodating a pressurized container **130** having a valve stem **134**. The valve stem leads to the inlet **116** of a reservoir **120**. The reservoir is sized to hold one to five doses of the flowable product dispensed by the pressurized container by an actuator **136**. The reservoir is surrounded by a heatable element **151** generating heat in the presence of the generated magnetic field and a heat retentive body **180**. An RFID tag **59** controls the heating of the heating element. Similar to the embodiment of Figure 5, the tag may simply signal the presence of a suitable container to initiate the magnetic field generator, or initiate a specific heating regimen by accessing a regimen stored in the charger or transmitting the regimen to the charger. As is true with both chargers shown in Figure 5 and 5a, any type of

conventional heating, such as resistive heating, can be used in place of magnetic heating.

[0045] Figure 6 depicts a fragrance dispenser **60** activated by a controller. The controller can be a key fob **62** having a printed circuit board and RFID chip to signal the dispenser. The signals can be controlled by the user by a button to allow the user dispense the fragrance in the dispenser.

[0046] Figure 7 discloses a multi-fragrance dispenser **70** responsive to controls to dispense a particular fragrance. Each fragrance has a corresponding and specific RFID tag. The fragrance to be dispensed in response to specific signals is programmed via a RFID chip. In addition to dispensing a fragrance, the controller causes the RFID chip to illuminate various colored lights, such as LEDs. The dispenser has several LEDs of various colors which illuminate, singly or in combinations. In this manner, visual stimulation is provided to accompany the olfactory stimulation. In addition or place of visual signals, specific audio signals can be generated along with the dispensing of a particular fragrance.

[0047] Figure 8 depicts a reader **60** having a display **62** for visually displaying information transmitted from an RFID tag, such as age and time. In addition, the reader may be provided with a speaker to audibly transmit information. The display has a target area **64** indicating the position of the antenna on the circuit board housed within the reader for receiving information from the RFID tag. A hook **66** may be provided on the reader for allowing the reader to hang from a refrigerator door or other similar device. In place of a hook, other mounting devices, such as magnets, adhesive or Velcro may be used. The reader has a start button **68** used to initialize a timer relating to the RFID tag and reset the timer, if desired.

[0048] RFID tags can be attached to rigid or flexible containers, such as bags. Figure 9 depicts a bag **90** having an RFID tag **92**. The RFID tag **92** is initialized by the depression of a start button **68** on the reader **60**. Once initialized by a particular RFID tag, the timing sequence begins recording elapsed

time since initialization. With a single reader, a plurality of RFID tags on reclosable bags or any other types of containers can be monitored. The tags may be applied by the manufacturer or may be sold separately to be applied by the consumer. If applied by the consumer, the RFID tags may be disposable or reusable with limited number of uses and be attached on multiple bags or containers. In this instance, when the RFID tag is switched from one container to another, it is reinitialized by the reader to again, monitor elapsed time since initialization. A variety of attachment means can be used to attach and remove the reusable version of the tag. In addition to containers, such as bags, RFID tags **92** can be applied to clips **93** used to reclose bags, as seen in Figure 10. After initially opening the bag, the clip **93** is used to reclose or reseal the bag with the RFID tag being initialized. This gives the consumer information about elapsed time since the bag was opened. The clip, being reusable, has an RFID tag reset each time it is applied to a bag for the first time. If the tag is disposable or has a limited number of uses, the clip can have a provision to nest the tag in a pocket or recess.

[0049] The use of RFID tags to monitor elapsed time can be used for a whole host of applications. Any device needing routine maintenance can have an RFID tag to record elapsed time since the last maintenance cycle. Common devices which require routine, timed maintenance include HVAC systems, horticultural items and various items on automobiles.

[0050] Figure 11 depicts an insect trap **94** having an RFID tag **95** measuring insect presence. Activity of insects activates the RFID tag and sends a signal to a monitor **96.** The monitor may have an indicator light **97** or LCD readout **98** to alert the consumer that the trap has been activated by the presence of insects. A reset button **99** adds to the effectiveness of the monitor in assessing the effectiveness of the trap. The insect can trigger a low power electrical trigger to signal the device. Alternatively, pheromone sensors can be used to trigger insect presence.

[0051] Besides elapsed time, prerecorded information can be placed on an RFID tag appropriate for the item to which the tag is attached. For example, such an application is clothes. Clothes may be provided with tags having care instructions. Whether dry cleaning is necessary, the best method for removing stains and the type of wash cycle to allow sorting of laundry into like articles of clothing for washing purposes, can be placed on an RFID tag. As an educational tool, tags may be provided with information allowing children to match clothes together. If the tags are applied by the manufacturer, the tags can be used to store information regarding a sweepstakes or other promotional activity. Also, the tags can be used as a simple means to track inventory of food in a household.

[0052] Other types of information that may be stored on RFID tags is cooking instructions. The packaging of food items may contain RFID tags with cooking instructions. By bringing the package within proximity of a reader, the RFID tag can initiate an audio message providing cooking instructions, or a visual display on a screen.

[0053] Because a reader senses proximity of an RFID tag, tags may be incorporated into items such as keys, pet collars, or any other item that is often lost. Using the portable reader, the user can receive an audio or visual signal through the reader display whenever the reader comes within proximity of an RFID tag. At present, a proximity of two meters is envisioned. However, greater read distances are feasible depending on power requirements. The use of active tags, those having their own power source, enables greater distances. However, one of ordinary skill in the art is able to adjust proximity requirements to suit the particular application.

[0054] The RFID tag may be made small enough that the tag may be added to bait and ingested by rodents or other animals. Once ingested, the tag may be tracked by using the reader to indicate the proximity of the tag.

[0055] Although specific components, materials, configurations, arrangements, etc. have been shown and described

with reference to several preferred embodiments, our invention is not limited to these specific embodiments. One of ordinary skill in the art will realize that various modifications and variations are possible within the spirit and scope of our invention which is intended to be limited in scope only by the accompanying claims.

WHAT IS CLAIMED IS:

1. A system for signaling level of product in a container, comprising:

a container having a sensor affixed to one portion thereof,

contacts extending downwardly from said sensor;

an electrical circuit broken when the level of product in said container falls below said contacts, and

a device for generating a signal from said sensor when said electrical circuit is broken for alerting a user that the level of product is low, and

a remote receiver separate from said container for communicating said signal for alerting the user.

2. The system of claim 1, wherein said sensor comprises an RFID chip.

3. The system of claim 1, wherein said sensor comprises an RFID chip that signals a timer in a primary device, base station or similar device to countdown a present time to refill.

4. The system of claim 2, wherein said sensor comprises an RFID chip that signals a timer in a primary device, base station or similar device to countdown a present time to refill.

5. The unit, comprising:

a base,

a container having an RFID tag, said container fitting in said base, wherein

said RFID tag signals the presence of the container to said base when the container is placed in proximity to said base.

6. The unit of claim 5, wherein said base is a heater.

7. The unit of claim 5, wherein said container contains a flowable product.

8. The unit of claim 5, wherein said container contains a fragrance.

9. The unit of claim 5, wherein said container is a dispensing device.

10. The unit of claim 5, wherein said RFID tag communicates a heating regimen to said base.

11. The unit of claim 5, wherein said RFID tag communicates a heating history for said container to said base.

12. The unit of claim 5, wherein said RFID tag is attached to said container,

Said base having a radio frequency identification reader/writer in operable connection with a microprocessor-based control circuit, said reader/writer transmitting updated information for storage in an electronic memory associated with said RFID tag,

13. A volatile dispensing system, comprising:

at least one container having a volatile,

a holder retaining said at least one container, and

an RFID tag controlling dispensing of said volatile.

14. The system of claim 13, wherein said volatile is a air freshener.

15. The system of claim 13, wherein said volatile is a fragrance.

16. The system of claim 13, wherein said at least one container is a plurality of containers, each container having an RFID tag, and further comprising a controller, said controller controlling which one of said plurality of containers is dispensed.

17. The system of claim 13, wherein said holder is a heater, said RFID tag is connected to said at least one container, and said RFID tag controls dispensing by initiating heating of said container.

18. The system of claim 17, wherein said RFID tag controls dispensing by communicating heating instructions to said heater.

19. A system for monitoring the age of an item, comprising

an RFID tag associated with said item,

a reader having a timer, said reader initializing said timer and displaying elapsed time since initiation when said RFID tag is in proximity to said reader.

20. The system of claim 19, wherein said item is a container, said RFID attached to said container.

21. The system of claim 19, wherein said item is a container, said RFID tag attached to a device designed for closing said container.

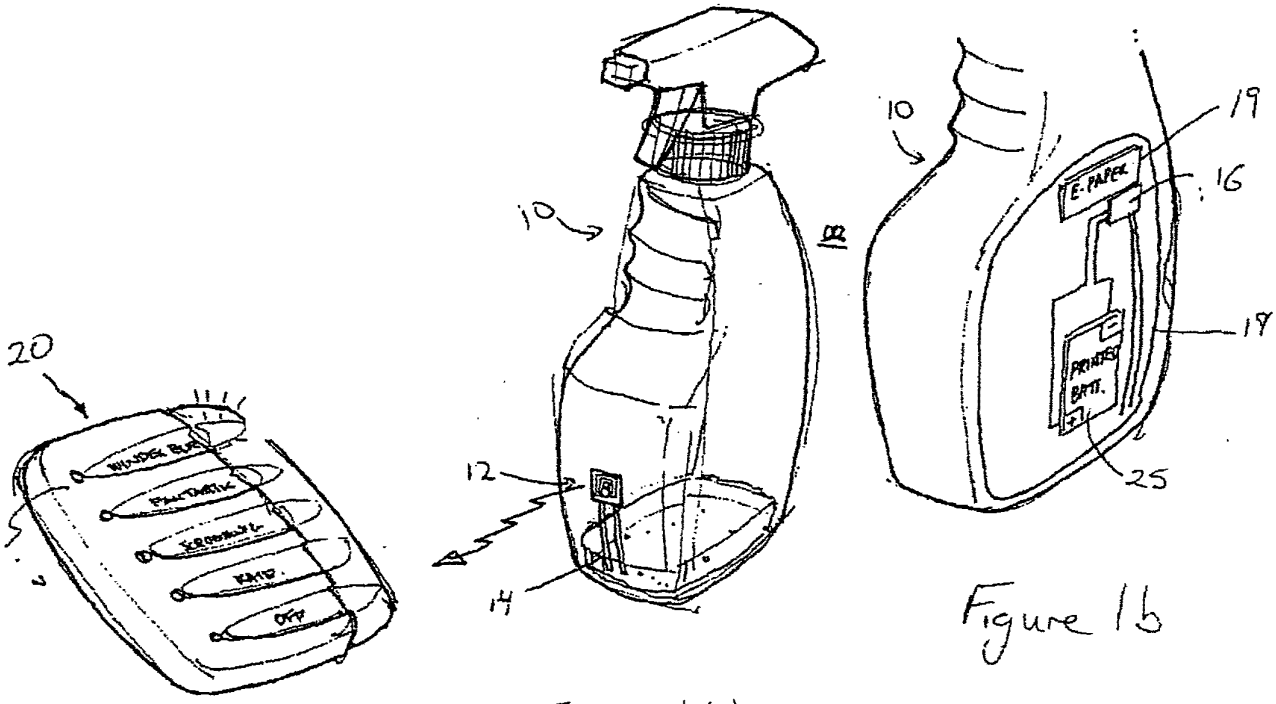


Figure 1(a)

Figure 1b

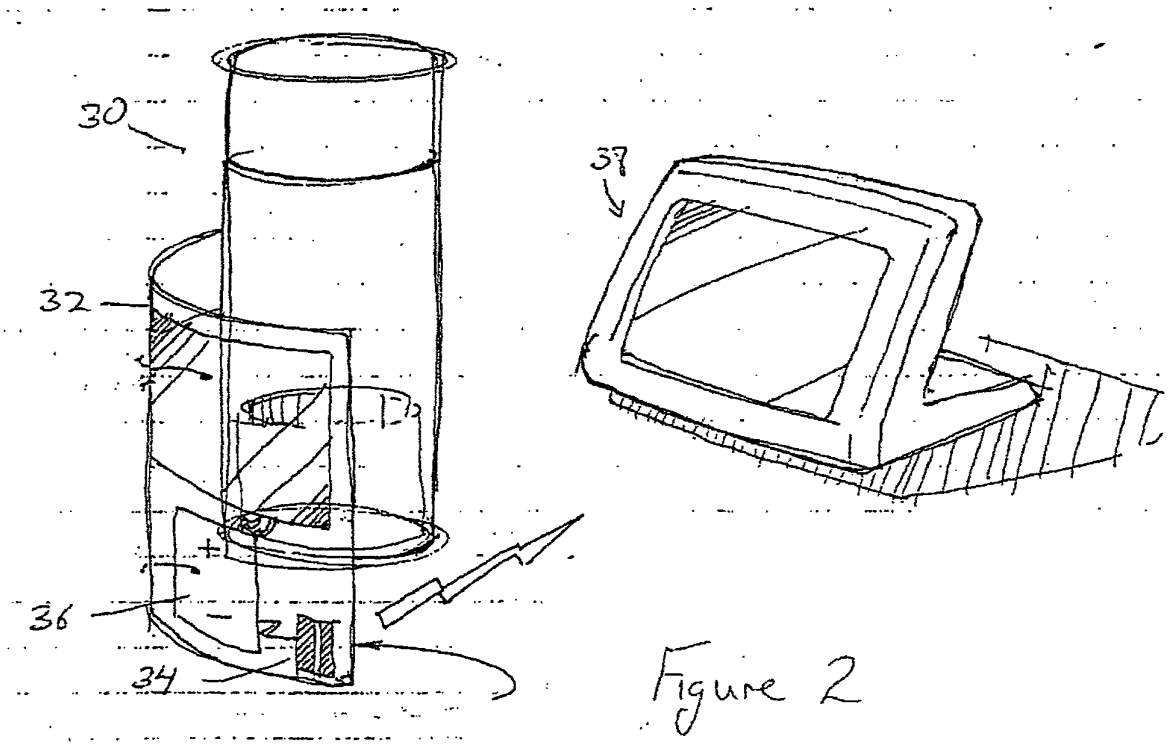


Figure 2

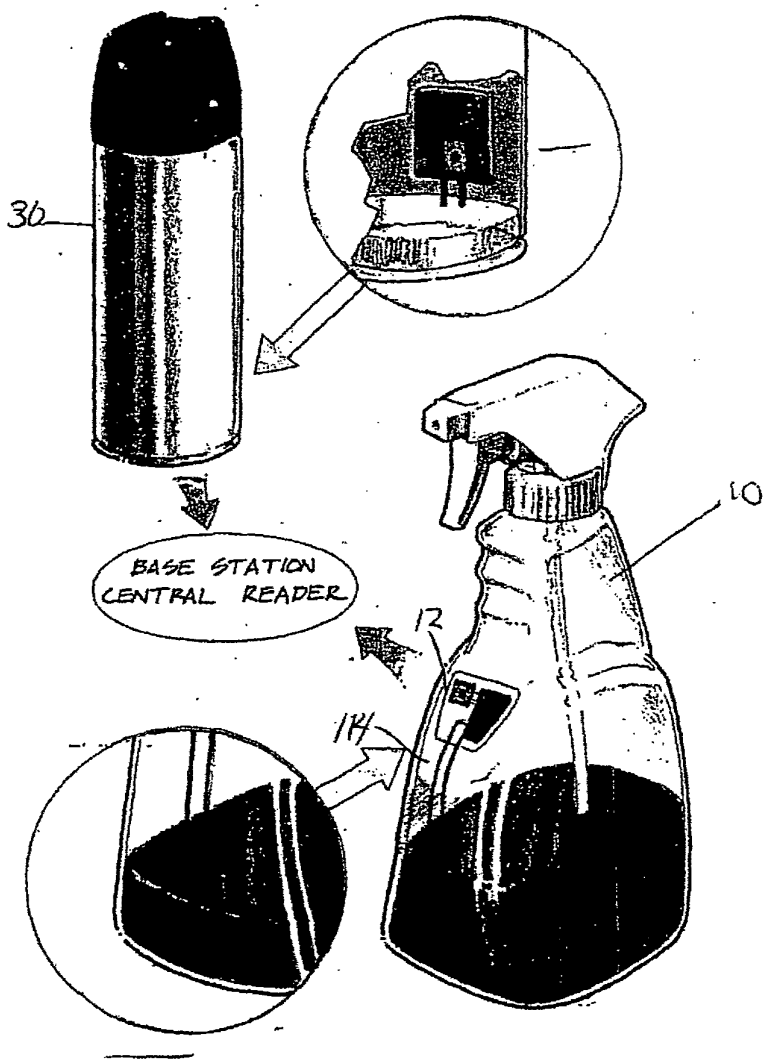


Figure 3

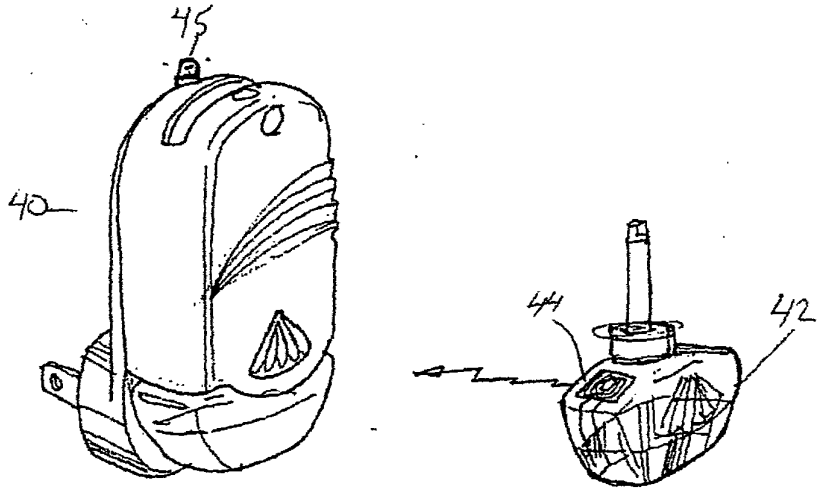


Figure 4a

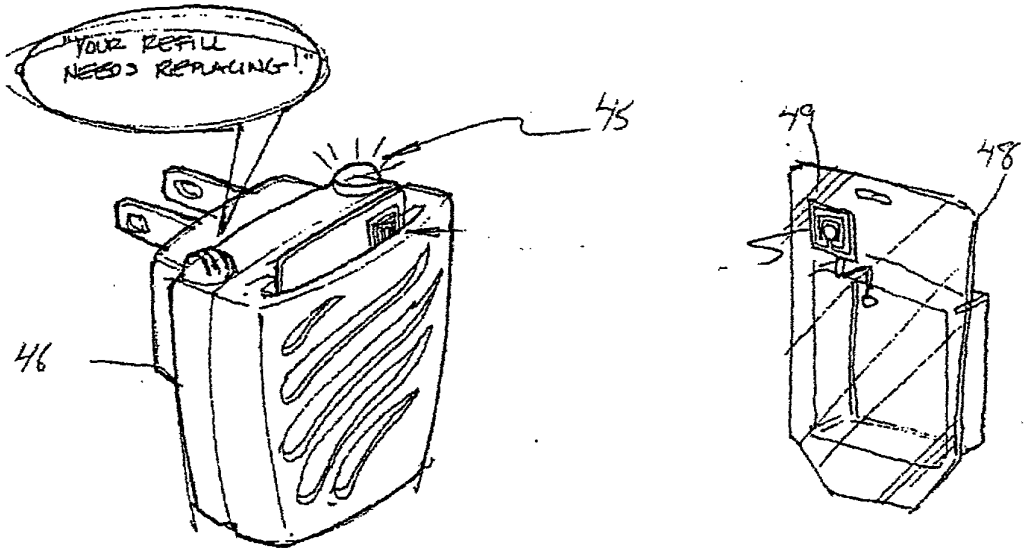


Figure 4b

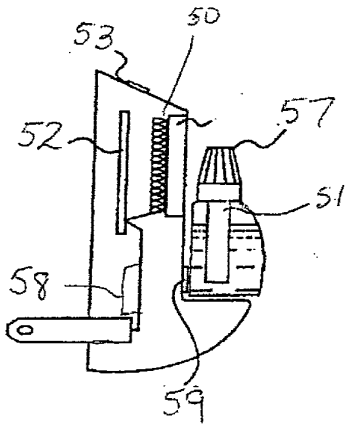


FIG. 5

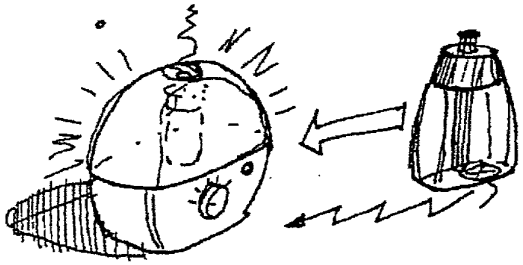


Figure 7

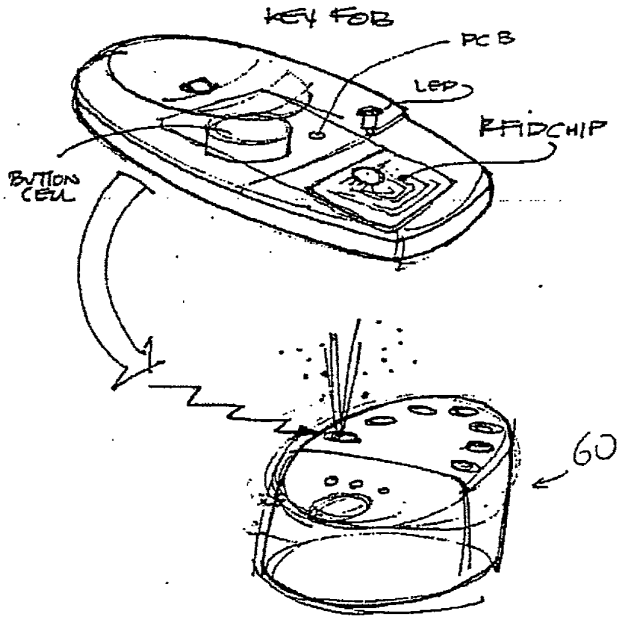


Figure 6

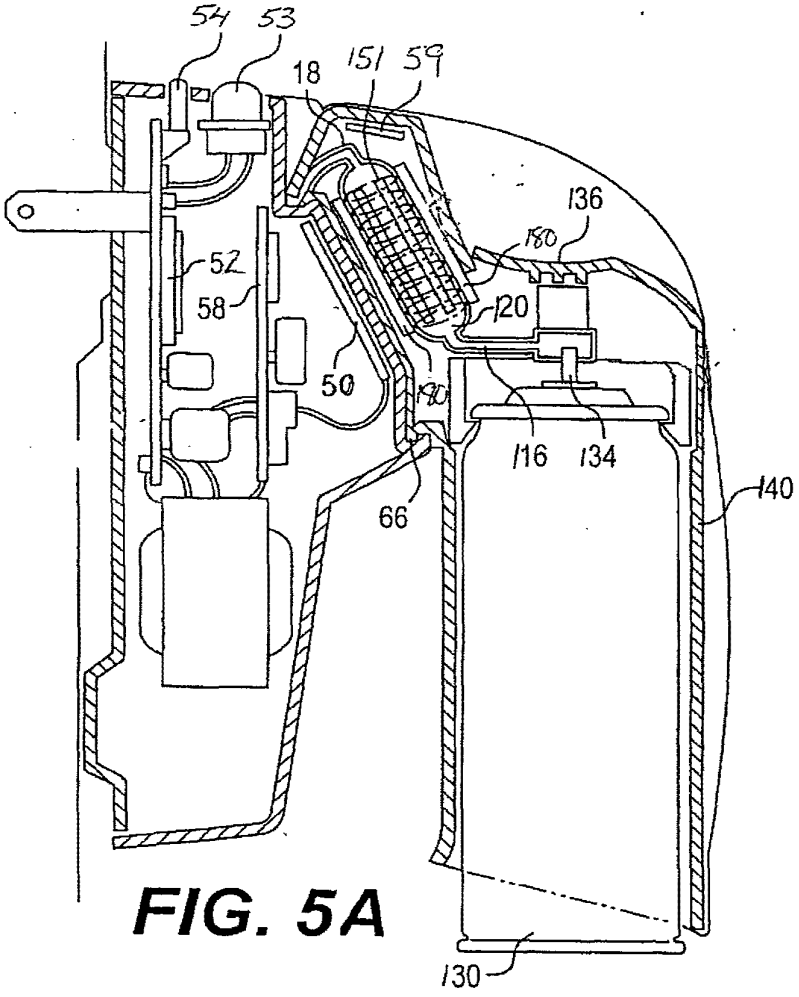


FIG. 5A

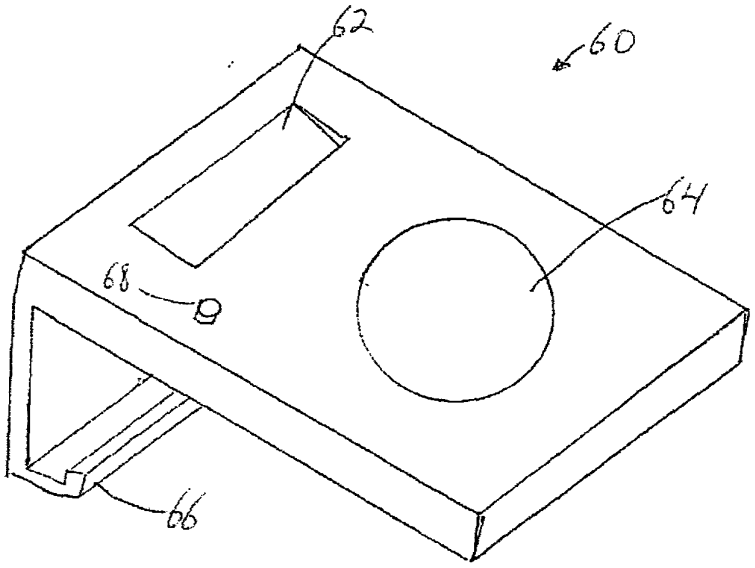


Figure 8

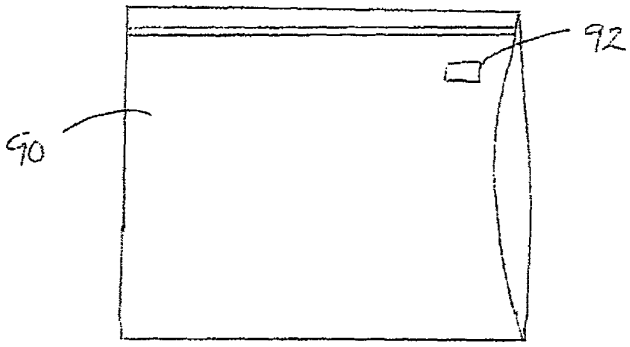


Figure 9

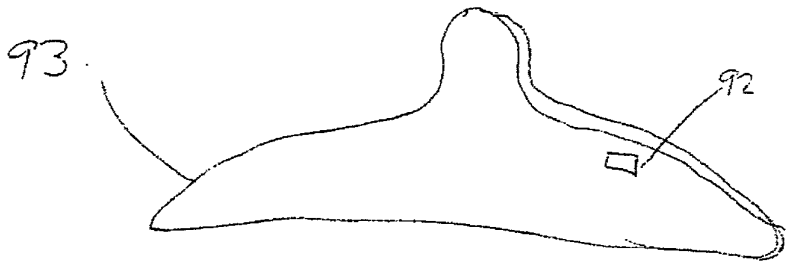


Figure 10

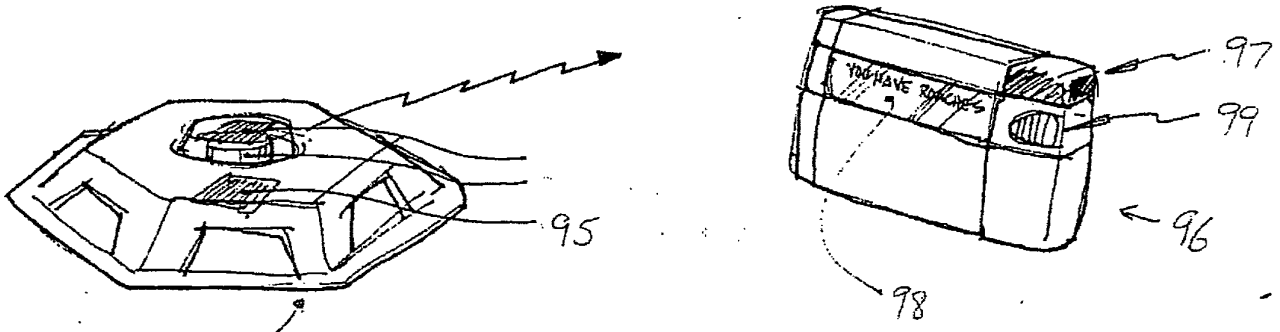


Figure 11

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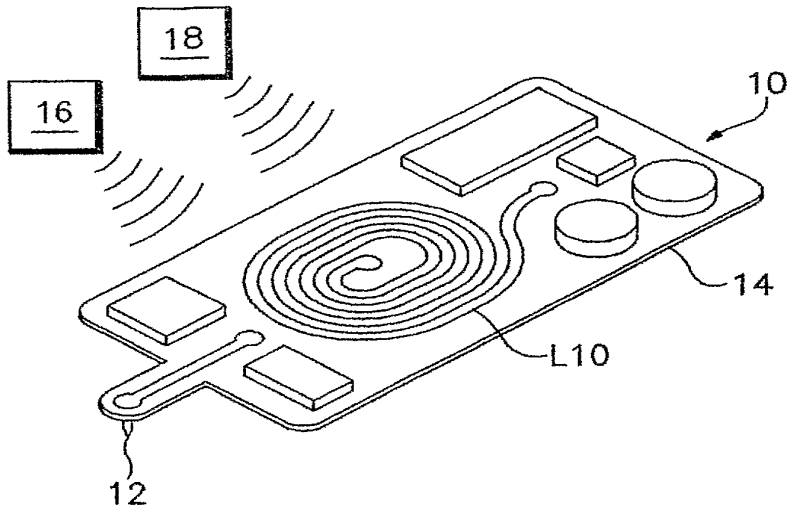
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(54) **Title:** INSERTABLE SENSOR ASSEMBLY HAVING A COUPLED INDUCTOR COMMUNICATIVE SYSTEM



(57) **Abstract:** A sensing system for determining the concentration of an analyte inside an animal body. The system includes an in vivo portion that is adapted to reside inside the animal body and that includes a sensing element that produces a sensing signal. In addition, a wearable ex vivo portion is physically attached to the in vivo portion. The ex vivo portion includes a first inductor that is adapted to receive a varying electro-magnetic signal and that has a pair of terminals. A variable load assembly presents a load across the pair of terminals and varies the load in response to the sensing signal. Also, an electronic monitoring unit is physically separate from the ex vivo portion and includes a second inductor, which is magnetically coupled to the first inductor and is adapted to transmit a varying electro-magnetic signal and to detect changes in load across the terminals of the first inductor.

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INSERTABLE SENSOR ASSEMBLY HAVING A COUPLED INDUCTOR COMMUNICATIVE SYSTEM

FIELD OF THE INVENTION

The invention is generally related to the field of percutaneous analyte sensors.

BACKGROUND ART

Implanted medical devices frequently include a wire coil that is used to receive an electromagnetic wave broadcast from outside the body. Often the transmitted signal is used for information content and to power the embedded device. Referring to FIGS. 1 and 2, which show a system under development that includes a few prior art features that will be discussed here, a system 10 that is currently being developed for the sensing of glucose relies on a very thin "wire" type sensing element 12 that is inserted into the patient's subcutaneous tissue for a few days to a few weeks, depending on the particularities of the implementation. The system 10 also includes an ex vivo portion 14 that is physically attached to the sensing element 12, but resides outside the body and may be adhered to the skin.

Another portion, referred to as the electronics monitoring unit 16 or "EMU," is in wireless communication with the ex vivo portion 14. The EMU 16 is typically quite a bit larger then the ex vivo portion 14 and may be worn by the patient by being suspended from his or her belt, or may be carried by the patient, for instance in a purse. The EMU 16 may be driven by standard AA batteries or by a rechargeable battery pack. It appears to be a commercial reality that smaller batteries have a higher cost per unit

of stored energy than do larger batteries. The EMU 16 would typically be located a little less than a foot away from the ex vivo portion.

A stationary EMU 18 may be made available for nighttime use. The stationary EMU 18 would be approximately the size of a clock radio and would be made to plug into a standard wall electrical outlet. Accordingly, the cost of electric power is inconsequential in the use of EMU 18, which may, consequently be placed as much as about 4 meters (13 feet) away from the ex vivo portion 14.

One problem encountered in the design of the ex vivo portion is the reduction of ex vivo portion size and the amelioration of any hard areas or objects that must be located on the ex vivo portion. In addition, the cost of the ex vivo portion should be as low as possible so that it will be practical to dispose of the ex vivo portion after a few days use. To achieve these goals it is desirable to reduce battery size on the ex vivo portion as much as possible.

Although electromagnetic coupling has been used for communications between an ex vivo device and an implantable device, this has typically been for actuators that communicate with an ex vivo transceiver only occasionally, or for instances in which the ex vivo portion can be retained directly on the other side of the skin from the in vivo portion. For example, U.S. Patent 6,015,386 describes a blood pressure measurement device having an implanted portion and an ex vivo portion that is strapped to the patient's wrist very near to the implanted portion. It appears that the movement of the device, caused by the pressure on the wall of a blood vessel, powers the implanted portion by causing changes in the inductance of

an implanted inductor. This inductor is coupled to an inductor in the ex vivo portion, which detects the changes in inductance.

DISCLOSURE OF THE INVENTION

In a first separate aspect, the present invention is a sensing system for determining the concentration of an analyte inside an animal body. The system includes an in vivo portion that is adapted to reside inside the animal body and that includes a sensing element that produces a sensing signal. In addition, a wearable ex vivo portion is physically attached to the in vivo portion. The ex vivo portion includes a first inductor that is adapted to receive a varying electro-magnetic signal and that has a pair of terminals. A variable load assembly presents a load across the pair of terminals and varies the load in response to the sensing signal. Also, an electronic monitoring unit is physically separate from the ex vivo portion and includes a second inductor, which is magnetically coupled to the first inductor and is adapted to transmit a varying electro-magnetic signal and to detect changes in load across the terminals of the first inductor.

In a second separate aspect, the present invention is an improvement to a biological sensing system that includes an in vivo portion, adapted to reside inside a patient, an ex vivo portion physically attached to the in vivo portion and having an antenna and an electronic monitoring unit that is physically separate from, but in wireless communication with, the ex vivo portion. The improvement is an electronic memory adapted to store memory contents in the ex vivo portion. Also, a transmitter in the electronic monitoring unit is adapted to transmit the

memory signal to the ex vivo portion, directing the ex vivo portion to transmit the memory contents to the electronic monitoring unit.

The foregoing and other objectives, features and advantages of the invention will be more readily understood upon consideration of the following detailed description of the preferred embodiment(s), taken in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a block diagram representation of an analyte sensing assembly, according to the prior art.

FIG. 2 is a side view of an analyte sensing patch that is a part of the assembly of FIG. 1.

FIG. 3 is a simplified schematic diagram of the electronics of an analyte sensing patch according to the present invention.

BEST MODE OF CARRYING OUT THE INVENTION

As described in the Background section, and as shown in FIGS. 1 and 2, in a preferred embodiment a glucose sensing and reporting assembly 10 includes an in vivo glucose sensing element 12 and an ex vivo portion 14, which transmits the data from sensing element 12 to an electronic monitoring unit 16. Together, elements 12 and 14 may be considered a glucose or analyte sensing patch.

In vivo portion 12 may be as described in U.S. Patent 5,165,407. This portion must have a voltage placed across it of 0.65 VDC and produces a sensor current that is generally proportional to the concentration of glucose in body tissue. A typical value for the sensor current is about 5-10 nanoAmps.

In FIG. 3, elements that could be the same as an element in FIGS. 1 or 2, are labeled with the same reference number as in FIGS. 1 or 2, plus 100. Referring to FIG. 3, ex vivo portion includes a 3 VDC battery 111 that drives a power supply U10. The 2.048 VDC output of power supply U10 is fed into a voltage divider 117 having a 0.65 VDC output that drives the noninverting input of an Op Amp U12. The output of Op Amp U12 provides feedback to the inverting input of Op Amp U12, by way of precision 10 MOhm resistor R10. Consequently, the inverting input of Op Amp U12 tracks the noninverting input, which is fixed at a 0.65 VDC reference, thus biasing the sensing element 112. Accordingly, the output of Op Amp U12 equals 0.65 VDC + 0.01*(sensing element current in nano Amps). If, for example, the sensing element current equals 5 nano Amps the output of U12 equals 0.70 VDC.

The op amp U12 output is fed into the input pin of microprocessor U14, which is preferably a Microchip model 16F676. Microprocessor U14 includes an internal analog-to-digital (A/D) converter 119, which converts the voltage at its input pin into a stream of 8 bit digital samples. A clock CL10 determines the rate at which microprocessor U14 operates. In one preferred embodiment, the clock CL10 is set at a rate of 32,768 Hz. The A/D converter 118, however, is operated only every 2 to 4 seconds when an internal counter of the microprocessor U14, which increments with every clock cycle, overflows. This activates an internal oscillator of the microprocessor U14, which then serves as a clock for the A/D, causing it to take one sample. A logic and switching unit 120 of microprocessor U14 averages or otherwise digital filters

the sample into an updated glucose measurement value, before microprocessor U14 returns to an inactive state.

Approximately once per minute, during the brief active period of microprocessor U14, a finished glucose measurement word is sent in serial form into the input pin of an asset identification ID chip U16, which stores the word in a memory subunit 122. A coil interface unit 124, that is part of chip U16, effectively transmits the word in serial form over coil L10, by altering the resistance placed between the terminals of coil L10.

ID chip U16 may be an ATMEL AT24RF08C. This chip includes a dual port 256 word memory and may either send or receive over the pins that are connected with the coil. Chip U16 is controlled by the microprocessor U14 to store data coming from microprocessor U14, so that this data will not be lost if the EMU 116 (or a stationary EMU 118) fails to receive the data. Also, commands from the EMU 116 are stored in chip U16 and are sent into microprocessor U14.

The use of an asset identification ID chip U16 as part of ex vivo portion 14 provides a number of advantages over other methods of providing data to the EMU 116. This type of chip is typically used to tag items in a store in order to prevent theft or to tag an item that is part of a collection of items for easy identification. This type of chip has even been used to tag pets, so that a pet can be easily identified if lost or stolen.

A first advantage of using an asset ID chip is that chip U16 does not require energy from any other part of ex vivo portion 14 to effectively communicate with EMU 116. Rather chip U16 captures enough energy from coil L10 to operate internally, in order to effect the changes in

resistance between the terminals of L10 that effectively transmit data to EMU 116.

Although chip U16 does require a small amount of energy to store data, the ability to store data greatly facilitates the EMU in saving energy, as a low EMU signal can generally be used for reading data from chip U16. The signal strength can be increased if it turns out that the EMU 116 did not provide enough energy to read the data from chip U16. Because the data is stored in chip U16, the data will still be available when the EMU 116 broadcasts with the requisite signal strength to read the data.

In the preferred embodiment, one glucose concentration measurement data word is created every minute. With this embodiment, using an ATMEL AT24RF08C for chip U16, 256 minutes (more than 4 hours) worth of data are stored. Accordingly, data could be stored and made available even in the event of an extended failure of EMU 116.

In one variant of this embodiment, microprocessor U14 is used to implement digital filtering of the data, so that the glucose concentration measurement word created every minute represents data collected over the entire minute interval. In another preferred embodiment, data words are formed more frequently than once per minute.

The Atmel AT24RF08C utilizes a 125 kHz frequency for communicating with the outside world. If this device were to be used for ID chip U16, then coil L10 would preferably be a ferrite-core inductor. If a different chip were to be used for asset ID chip U16, however, this could make possible the use of a higher frequency, making it more practical to implement coil L10 as an air core coil, as is shown in FIG. 1. In this embodiment the air core coil L10

is integrated into the flexible bandage structure that makes up the body of ex vivo portion 14 and is about two inches in diameter.

INDUSTRIAL APPLICABILITY

The invention generally finds industrial applicability in the production and providing of percutaneous analyte sensors.

The terms and expressions that have been employed in the foregoing specification are used as terms of description and not of limitation. There is no intention, in the use of such terms and expressions, of excluding equivalents of the features shown and described or portions thereof, it being recognized that the scope of the invention is defined and limited only by the claims which follow.

CLAIMS

1. A sensing system for determining the concentration of an analyte inside an animal body, said system including:

(a) an in vivo portion, adapted to reside inside said animal body and including a sensing element that produces a sensing signal;

(b) a wearable ex vivo portion physically attached to said in vivo portion, including:

(i) a first inductor adapted to receive a varying electro-magnetic signal and having a pair of terminals; and

(ii) a variable load assembly presenting a load across said pair of terminals and varying said load in response to said sensing signal; and

(c) an electronic monitoring unit that is physically separate from said ex vivo portion and includes a second inductor, which is magnetically coupled to said first inductor and adapted to transmit a varying electro-magnetic signal and to detect changes in load across said terminals of said first inductor.

2. The biological sensing system of claim 1, wherein said ex vivo portion also includes a battery.

3. The biological sensing system of claim 1, wherein said battery biases said sensing element.

4. The biological sensing system of claim 1, wherein said ex vivo portion also includes memory to store measurement values from said in vivo portion.

5. In a biological sensing system that includes an in vivo portion, adapted to reside inside a patient, an ex vivo portion physically attached to the in vivo portion and having an antenna, and an electronic monitoring unit that is physically separate from, but in wireless communication by way of electromagnetic signals with the ex vivo portion, an improvement comprising:

(a) electronic memory adapted to store memory contents in said ex vivo portion; and

(b) a transmitter in said electronic monitoring unit adapted to transmit a said electromagnetic signal to said ex vivo portion, directing said ex vivo portion to transmit at least a portion of said memory contents to said electronic monitoring unit.

6. The biological sensing system of claim 5 wherein said electronic monitoring unit includes a manual actuator adapted to permit a patient to enter a request for data and wherein said transmitter transmits a said electromagnetic signal requesting data to said ex vivo portion in response thereto.

7. The biological sensing system of claim 5 wherein said ex vivo portion is able to effectively transmit to said electronic monitoring unit by sequentially changing impedance across said antenna.

FIG.1

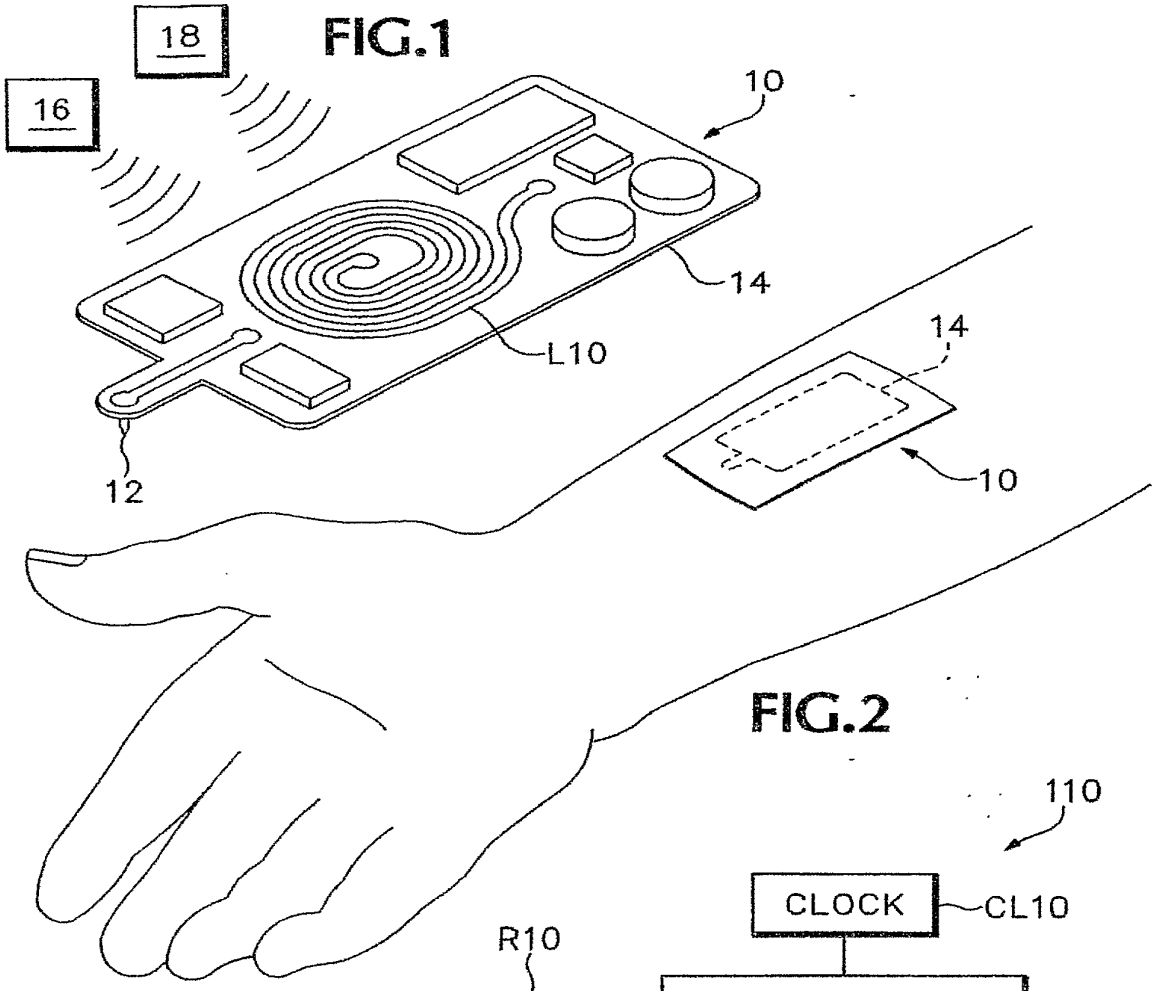


FIG.2

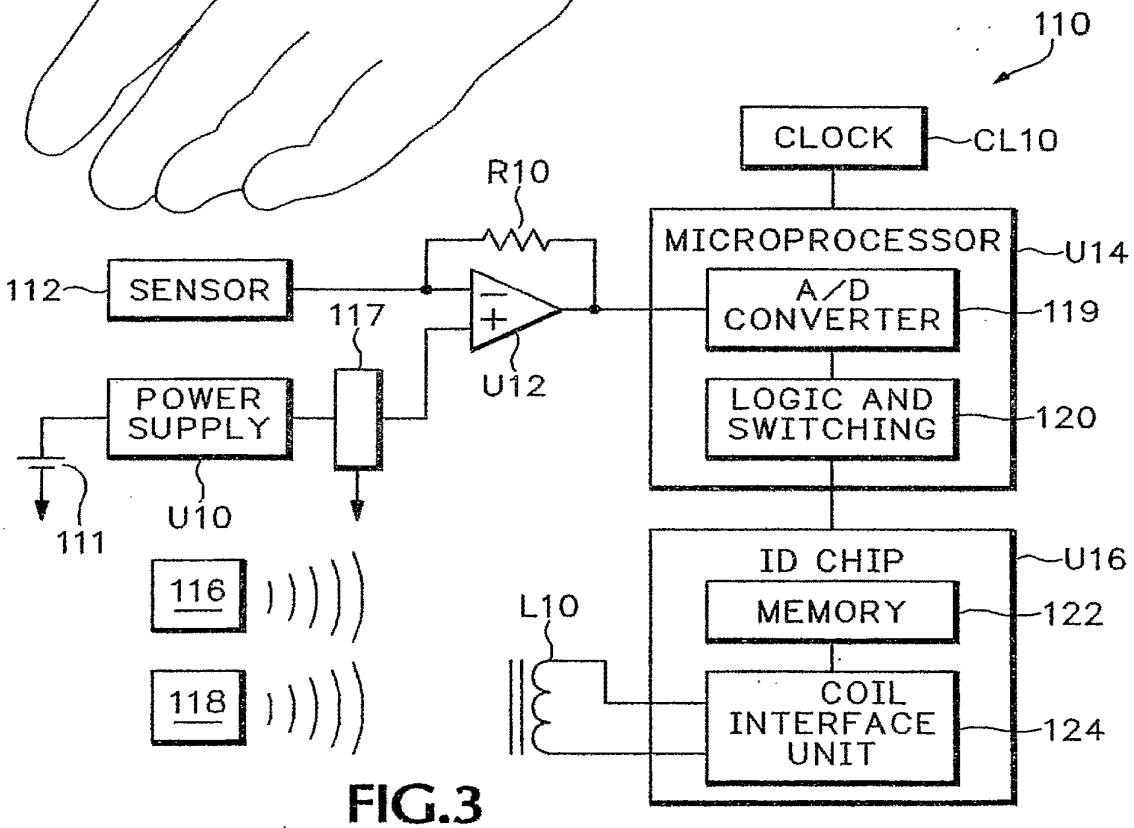


FIG.3

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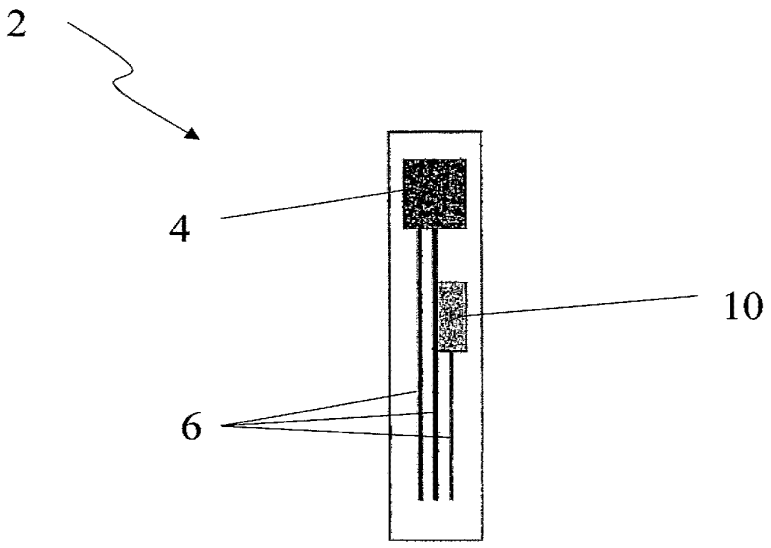
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(54) Title: WEARABLE SENSOR DEVICE AND SYSTEM



(57) Abstract: A system for determining the level of an analyte in a physiological fluid of a live individual is described. A wearable sensor periodically obtains data representative of the level of the analyte and has a passive RFID tag that stores the data. A receiver wirelessly interrogates the sensor with an RF interrogation signal. The RFID tag modulates or otherwise modifies the wireless interrogation signal using the data and the receiver receives back the modulated or otherwise modified interrogation signal and extracts the data from it. The receiver then determines, from the data, the level of the analyte in the fluid. The sensor may be a photometric or colorimetric sensor or an electrochemical sensor. The receiver may be, or be incorporated into, a hand-held device, a portable device, a PDA, a mobile telephone, or a laptop computer. The resulting system is more versatile and consumes less power than conventional systems.

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Wearable Sensor Device and System

Field of the Invention

[0001] The invention relates to an continuous sensor for use, in healthcare management, law-enforcement, dope-testing, sanitation or otherwise, for measuring the concentration of any analyte, such as glucose, lactate, urate, alcohol, therapeutic drugs, recreational drugs, performance-enhancing drugs, biomarkers indicative of diseased conditions, hormones, antibodies, metabolites of any of the aforesaid, combinations of any of the aforesaid, other similar indicators or any other analyte in a fluid, especially a physiological fluid such as blood, interstitial fluid (ISF) or urine. Much of the following discussion will concentrate upon the use of such a sensor for the purpose of blood glucose measurement and control, but the principles discussed are much more widely applicable; indeed, they are applicable to the detection of any analyte in any fluid.

Background to the Invention

[0002] Glucose monitoring is a fact of everyday life for diabetic individuals. The accuracy of such monitoring may have significant impact on the quality of life. Generally, a diabetic patient measures blood glucose levels several times a day to monitor and control blood sugar levels. Failure to control blood glucose levels within a recommended range can result in serious healthcare complications such as limb amputation and blindness. Furthermore, failure to accurately measure blood glucose levels may result in hypoglycaemia. Under such conditions the diabetic patient may initially enter a comatose state, and if untreated may die. Therefore, it is important that accurate and regular measurements of blood glucose levels are performed.

[0003] People suffering from diabetes are often at a higher risk of other diseases. Diabetes also contributes to kidney disease, which occurs when the kidneys do not filter properly and protein leaks into urine in excessive amounts, which eventually can cause kidney failure. Diabetes is a cause of damage to the retina at the back of the eye and also increases risk of cataracts and glaucoma. Nerve damage caused by diabetes may interfere with the

ability to sense pain and contributes to serious infections. A number of glucose meters are currently available which permit an individual to test the glucose level in a small sample of body fluid.

[0004] Many of the glucose meter designs currently available make use of a disposable test sensor, e.g. a strip, which in combination with the meter, electrochemically or photometrically measures the amount of glucose in the blood sample. To use these meters, the user first punctures a finger or other body part using a lancet to produce a small sample of blood or interstitial fluid. The sample is then transferred to a disposable test strip. The test strips are typically held in packaging containers or vials prior to use. Generally, test strips are quite small and the sample receiving area is even smaller. Usually, the disposable strip is inserted into a meter through a port in the meter housing prior to performing a test for an analyte in body fluids such as blood, ISF or urine etc.

[0005] Other meter designs are capable of providing more or less continuous measurements. One example is described in US patent application serial no. 10/882994, the entire contents of which are herein incorporated by reference. In this example, the system extracts interstitial fluid samples and monitors the level of glucose contained within it. The components of the system are a disposable cartridge, a local controller module, and a remote controller module. The disposable cartridge includes a sampling module that extracts the interstitial fluid sample from the skin and an analysis module that measures the glucose level. Examples of suitable sampling and analysis modules are described in international patent application WO 02/49507, the entire content of which is herein incorporated by reference. In particular, the system of US patent application serial no. 10/882994 may use that multi-use electrochemical or photometric analyte sensors discussed in WO 02/49507. A characteristic of the system described in US patent application serial no. 10/882994 is that the sampling and analysis modules are designed to be worn on the body for a relatively short period of time, say 12 hours, after which they are disposed of. Each measurement of glucose level is transmitted via an RF link from a local controller module that is attached to the sampling an analysis modules, to a remote

controller module. Because the local controller module is to be worn for 12 hours at a time, it must be relatively lightweight and relatively unsophisticated; most of the detailed analysis of the glucose measurements takes place only in the remote control module.

[0006] Another example of a meter design capable of providing more or less continuous measurements is described in US patent application serial no. 11/200768, the entire contents of which are herein incorporated by reference. A fluorescent light-emitting bead is implanted just beneath the skin. The bead includes a fluorescent reagent that emits fluorescent light as a result of absorbing incident light, the characteristics of the emitted fluorescent light being dependent on the concentration of glucose that is in contact with the bead. Fluorescent reactants that can be included in such a fluorescent light-emitting bead, and their behaviour when in communication with an analyte, are described in U.S. Patent Nos. 5,342,789, 6,040,194, and 6,232,130, the entire contents of which are herein incorporated by reference. The bead can also include an encapsulating material such as, for example, alginate. Any envelope that is substantially impermeable to the reagent, but is permeable to the analyte is suitable. An adhesive fluorescence measurement patch is adhered to the skin over the bead and communicates with a remote module via an RF link to transmit each glucose measurement. Again, the patch is relatively unsophisticated and most of the detailed analysis of the glucose measurements takes place only in the remote control module.

[0007] To enable the local module or skin patch as the case may be to take glucose measurements and to communicate the glucose measurement data each time to the remote module, the local module or skin patch must possess a source of power. Typically, this would be a battery. Transferring the data to the remote module typically consumes the greater part of the power it is able to supply, which means that the battery life is constrained for the most part by the need to power the RF communication. This is a particular problem because the local device or skin patch are for the most part out of sight and a low battery level may not immediately be apparent to the user. The result can be false measurements, or failure to supply measurement data to the remote module, either of

which can seriously compromise the welfare of the user, eventually leading in the worst cases to coma and death.

[0008] Similar problems arise with the remote module too. If the batteries in the remote module run low, exactly the same result may ensue.

Summary of the Invention

[0009] The present invention is designed to address the problems outlined above. Whilst those problems have been described particularly with reference to the management of diabetes, where accurate and timely measurement is absolutely essential, we nonetheless regard the problem as more general. Indeed, if one is testing any physiological fluid using a sensor that is to be exposed to the fluid, and a receiver with which it wirelessly communicates, and one wishes to avoid the inconvenience of frequent battery changes and the possibility of false readings, the present invention will be of considerable assistance.

[0010] We have considered the possibility of simply using larger batteries. But this is no good because the aim is to keep a wearable device as small and lightweight as possible. And the same applies to the remote device, which may itself be a handheld device, PDA or mobile phone. It is also very expensive in practice, and the business model for glucose monitoring systems that use disposable sensors is typically to give away the control electronics, including the local and remote modules, and to charge only for the disposable sensors.

[0011] Our solution is to propose a change in the way that the wireless link between the local module or patch and the remote module is used. In particular, we propose not to insist that every measurement of glucose or other analyte be transmitted to the remote module when it is taken. Instead, we suggest that the timing of the transmission of the data to the remote module be under the control of the remote module. The principal advantage of this suggestion is that the RF receiver circuits of the remote module need not be active at all times, just in case a signal is received from the local module or patch. Instead, those

circuits can be quiescent or powered down completely until the remote module determines, according to its schedule, that the transmission of data is required.

[0012] Therefore, one statement of the present invention is that it involves a system for determining the level of an analyte in a physiological fluid of a live individual, comprising:

a wearable sensor that is adapted to obtain periodically, data representative of the level of the analyte, and has a wireless device adapted to convey the data wirelessly when wirelessly interrogated; and

a receiver adapted to operate as follows:

to wirelessly interrogate the sensor; and

to receive the data conveyed by the wireless device.

[0013] Depending on the level of sophistication of the wearable sensor, it may itself determine the level of the analyte, for example by converting a current measurement into a glucose concentration measurement, in which case the data will directly represent the level of the analyte in the fluid. Alternatively, it may indirectly represent the level of the analyte in the fluid, with the receiver being adapted to determine, from the data, the level of the analyte in the fluid.

[0014] The present invention finds application in integrated systems for measuring and treating medical disorders or diseased conditions. Thus, the level of the analyte may be diagnostic of a medical disorder or diseased condition, such as diabetes. To complete the integrated system, when the medical disorder or diseased condition is remediable by the administration of a drug, the system may further comprise a drug dispensing unit for dispensing the drug. The drug dispensing unit is preferably adapted to dispense the drug in an amount that depends upon the level of the analyte in the fluid as conveyed by the sensor or determined by the receiver.

[0015] Analytes for which the system may test include glucose, HbA1C, lactate, cholesterol, alcohol, a ketone, urate, a therapeutic drug, a recreational drug, a performance-

enhancing drug, a biomarker indicative of a diseased condition, a hormone, an antibody, a metabolite of any of the aforesaid, a combination of any of the aforesaid, or another similar indicator. We describe the system principally in connection with the detection of glucose.

[0016] In an integrated system, where the analyte is glucose, the drug should be one that promotes cellular uptake of glucose, such as a drug comprising insulin or an insulin analog.

[0017] The dispensing unit may comprise an infusion pump or other mechanism, preferably a wearable pump or mechanism, adapted to dispense the drug directly into the body of the individual concerned.

[0018] As discussed, the receiver may be, or be incorporated within, a local device worn by the individual concerned or a device remote from the individual concerned.

[0019] Alternatively, there may be a local device and a device remote from the individual concerned with the local and remote devices in wireless communication with one another and adapted to transfer from the local device to the remote device either the data received from the sensor or the level of the analyte as determined by the receiver or both. Remote devices may be used as parental monitors for those suffering from childhood diabetes.

[0020] If the remote device is able to establish a communications link with a public switched telephone network or another circuit-switched communications network, or a mobile telephony network, the internet or another packet-switched communications network or the local device is able to establish a communications link with a mobile telephony network or another wireless communications network, either may be used to inform a physician or care-giver of a subject's state of health or notify the emergency services of the onset of an acute event.

[0021] In the former case, the communications link would typically be used to transmit the data received from the sensor or the level of the analyte as determined by the receiver, information concerning the variation of either over time, or other similar information.

[0022] In either case, it may be used to transmit an alarm condition such as an abnormal analyte level, an abnormal analyte level for a certain time of day, an abnormal analyte level as compared with dietary intake, abnormal or non-functional wireless transfer of information from the sensor or the local device, abnormal physiological fluid sampling frequency, abnormal establishment, or non-establishment, of wireless communication from the sensor or the local device, abnormal storage of information in the wireless device or other alarm conditions.

[0023] Having explained that causing the receiver to determine the schedule of wireless transmission from the wearable sensor reduces the power consumption of the overall system, we now wish to explain some further adaptations that either contribute to this aim or contribute to the aim of keeping the wearable sensor as small and lightweight as possible.

[0024] The first adaptation is for the wearable sensor, instead of using its own power supply to transmit data to the receiver, to use the power supply of the remote device. This can happen as follows. The receiver interrogates the wireless device by issuing a wireless interrogation signal, and the wireless device extracts energy from the wireless interrogation signal and uses the energy extracted to transmit data wirelessly to the receiver. Devices that operate in this way are known.

[0025] An alternative is for the wearable sensor not to transmit data in the conventional sense at all. The receiver will still interrogate the wireless device by issuing a wireless interrogation signal, but in this case the wireless device modulates or otherwise modifies the wireless interrogation signal using the data. The receiver receives back the modulated or otherwise modified interrogation signal and extracts the data from it. One way of

achieving this mode of operation is to use a wireless device that back-scatters the interrogation signal, such as an RFID tag.

[0026] A second adaptation takes the first of these ideas even further. The wearable sensor, instead of using its own power supply to obtain the data to be conveyed, for example by sampling the physiological fluid, again uses the power supply of the remote device. In this case, the receiver issues a wireless test signal and the wireless device extracts energy from the wireless test signal and uses the energy extracted to obtain the data to be conveyed.

[0027] So far, we have described the system, but the present invention also extends to the sensor. Thus, another statement of the present invention is that it involves a wearable sensor for use in determining the level of an analyte in a physiological fluid of a live individual, the sensor being adapted to obtain periodically data representative of the level of the analyte, and having a wireless device adapted to convey the data wirelessly when wirelessly interrogated.

[0028] Preferred sensors are of the type that, when exposed to the physiological fluid, develops a measurable characteristic that is a function of the level of the analyte in the fluid and of a calibration quantity of the sensor, in which case the wireless device should hold and convey information representing the calibration quantity of the sensor. The advantage of this is that, returning to the system, the receiver can also receive the information representing the calibration quantity of the sensor and to use it when determining the level of the analyte in the fluid.

[0029] The term "calibration quantity" will now be explained. Variations in the manufacturing process result in sensors having different physical, chemical or other inherent properties that affect the way they respond to an analyte. Thus, different sensors will respond slightly differently to the same concentration of analyte in a fluid. Because they respond differently, their response must then be adjusted by an amount that is determined by calibration. The calibration process allows one to determine one or more

adjustment coefficients that, when applied to the response of the sensor, will normalize it to a predefined standard. To help us to refer to the physical, chemical or other inherent characteristics of the sensor, we have coined the expression "calibration quantity". A calibration quantity is some property that the sensor possesses that affects its response. It may be a single property, such as sensitivity; it may be a combination of many, such as sensitivity, non-linearity, hysteresis, etc. It may be some structural property such as size that contributes to its response behaviour, either by affecting other calibration quantities like sensitivity, or by making an individual contribution. All of these things, alone or together, are calibration quantities, from which it can be seen that the term denotes a broad class. It is to be distinguished from the one or more adjustment coefficients that are derived from the calibration process and, when applied to the response of the strip, will normalize it to a predefined standard. These coefficients are shorthand representations of calibration quantities; they are information representing the calibration quantities, but they are not the calibration quantities themselves, which are real properties of the sensors. Thus, where we wish to refer to the adjustment coefficients or any other information representing them, and therefore representing the calibration quantities of the sensors, for example a code pointing to a location in a look-up table at which the relevant adjustment coefficients may be found, we use the expression "information representing the calibration quantity." The distinction is a simple one, but it is worth setting out here for the avoidance of doubt.

[0030] A particularly preferred form of sensor is the optometric sensor that described in US patent application serial no. 11/200768. Such a sensor comprises an intracorporeal part that is exposed to the physiological fluid by implantation in the individual concerned and, when so exposed, develops a measurable characteristic, being an indicator of the extent to which exposure of the sensor to the fluid affects its optical characteristics, that is a function of the level of the analyte in the fluid, and an extracorporeal part that acquires the measurable characteristic of the intracorporeal part by transdermal wireless communication. In the present invention, it is the extracorporeal part that includes the wireless device.

[0031] As described in US patent application serial no. 11/200768, the transdermal wireless communication is transdermal optical transmission, the intracorporeal part comprises a fluorescent reagent that reversibly binds to the analyte. The measurable characteristic may be: a fluorescence intensity; an emission or excitation spectrum, peak, gradient or ratio; any one or more parts of such a spectrum; an emission polarization; an excited state lifetime; a quenching of fluorescence; a change over time of any of the aforesaid; any combination of the aforesaid; or any other indicator of the extent to which exposure of the fluorescent reagent to the fluid affects its fluorescence characteristics.

[0032] Preferred embodiments use a reagent comprising or labelled with a donor molecule and an acceptor molecule, where the measurable characteristic is an indicator of the extent to which non-radiative fluorescence resonance energy transfer occurs between the donor and the acceptor upon reversible binding of the reagent to the analyte. The reagent may comprise a specific binding pair, one of which is, or is labelled with, the donor molecule and the other of which is, or is labelled with, the acceptor molecule. The sensor may comprise an envelope that contains and is substantially impermeable to the reagent, but is permeable to the analyte. The envelope may be a microdialysis vessel or a microcapsule or an alginate bead optionally covered with a polylysine covering.

[0033] Other optometric sensors to which the present invention may be applied are for extracorporeal use and include means for extracting the physiological fluid, a reagent, and means for exposing the reagent to the fluid. The reagent may include a catalyst and a dye or dye precursor and the catalyst catalyses, in the presence of the analyte, the denaturing of the dye or the conversion of the dye precursor into a dye. For glucose analysis, the catalyst may be a combination of glucose oxidase and horseradish peroxidase, with the reagent including a leuco-dye. Suitable Leuco-dyes are 2,2-azino-di-[3-ethylbenzthiazoline-sulfonate], tetramethylbenzidine-hydrochloride and 3-methyl-2-benzothiazoline-hydrazone in conjunction with 3-dimethylamino-benzoicacide.

[0034] In such photometric or colorimetric sensors, the measurable characteristic may be: an opacity; a transparency; a fluorescence intensity; a transmissivity, a reflectivity, an absorptivity or an emissivity; a transmission, reflection, absorption, emission or excitation spectrum, peak, gradient or ratio; any one of more parts of such a spectrum; a colour; an emission polarization; an excited state lifetime; a quenching of fluorescence; a change over time of any of the aforesaid; any combination of the aforesaid; or any other indicator of the extent to which exposure of the sensor to the fluid affects its optical characteristics.

[0035] Extracorporeal electrochemical sensors comprising electrodes, means for extracting the physiological fluid, a reagent, and means for exposing the reagent to the fluid, may be used with this invention too. In such cases, the measurable characteristic may be: an inter-electrode impedance; an inter-electrode current; a potential difference; an amount of charge; a change over time of any of the aforesaid; any combination of the aforesaid; or any other indicator of the amount of electricity passing from one electrode to another, or the extent to which exposure of the sensor to the fluid generates electrical energy or electrical charge or otherwise affects the electrical characteristics of the sensor.

[0036] Such sensors may include a substrate, an electrode layer containing the electrodes, and at least a first reagent layer. For glucose analysis, the reagent layer may comprise glucose oxidase.

[0037] As discussed, the receiver may be, or may be incorporated into, a hand-held device, a portable device, a PDA, a mobile telephone, or a laptop computer. So may the remote device.

[0038] A suitable wireless device is an RFID tag, for example ISO 14443 or ISO 15693, 13.56 MHz or 2.45 GHz..

Brief Description of the Drawings

[0039] A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and in the accompanying drawings.

[0040] Figure 1 shows a schematic plan view of a single use test strip for receiving a patient's blood, having an RFID tag integrated thereon. This figure is presented for purposes of illustration of some of the principles underlying the present invention.

[0041] Figure 2 shows a schematic plan view of a single use test strip for receiving a patient's blood and a blood glucose meter, according to a further exemplary embodiment of the invention having an RFID tag integrated on the single use test strip having conductive tracks feeding to an edge of the test strip. This figure is also presented for purposes of illustration of some of the principles underlying the present invention.

[0042] Figure 3 shows a schematic plan view of a single use test strip for receiving a patient's blood and a blood glucose meter, according to a further exemplary embodiment of the invention having an RFID tag integrated on the single use test strip. The RFID tag is written to by RF means during the manufacturing stage of the single use test strip Again, this figure is presented for purposes of illustration of some of the principles underlying the present invention.

[0043] Figure 4 shows a schematic plan view of a multi use test strip or module in the form of a disc for receiving a patient's blood, having an RFID integrated thereon.

[0044] Figure 5 shows a schematic plan view of a multi use test strip formed as an array. Each strip contained in the array has an RFID tag contained within it. Alternatively, or in addition a separate RFID tag can be used as the sole RFID tag. The RFID tag contains calibration code data specific to that multi use test strip 2.

[0045] Figure 6 shows a system diagram depicting a system for extracting and monitoring a bodily fluid sample within which, for example, the embodiments of figure 4 or figure 5 can be used.

[0046] Figure 7 shows a table of information which may be loaded from a RFID tag to the meter and from the meter to the RFID tag in accordance with example embodiments of the present invention.

[0047] Figure 8 is a simplified block diagram depicting a system for extracting a bodily fluid sample and monitoring an analyte.

[0048] Figure 9 is a simplified schematic diagram of an ISF sampling module being applied to a user's skin layer, with the dashed arrow indicating a mechanical interaction and the solid arrows indicating ISF flow or, when associated with element 28, the application of pressure.

[0049] Figure 10 is a simplified block diagram of an analysis module, local controller module and remote controller module.

[0050] Figure 11 is a simplified schematic illustration depicting interaction between a fluorescent light-emitting bead, light emitter and light detector .

[0051] Figure 12 is a simplified schematic illustration depicting interaction between a fluorescent light-emitting bead implanted in a user's body, a light emitter, and a light detector for detecting fluorescent light that is relevant to various embodiments of the present invention.

[0052] Figure 13A is a simplified cross-sectional view of an adhesive fluorescence measurement patch adhered to a user's body.

[0053] Figure 13B is a simplified schematic depicting the operative interaction of various electrical and optical components, including a light emitter and a light detector, suitable for use in the adhesive fluorescence measurement patch of figure 13A.

Detailed Description of the Drawings

[0054] RFID (Radio Frequency Identification) is a technique which is able to carry data in suitable transponders, generally known as tags, and to retrieve data, by machine-readable means, at a suitable time and place to satisfy particular application needs.

[0055] An example RFID system may have, in addition to at least one tag, a transceiver or means of reading or interrogating the tags and optionally means of communicating the data received from a tag to an information management system. Transceivers are also known as interrogators, readers, or polling devices. Typically the system may also have a facility for entering or programming data into the tags. RFID tags contain an antenna and an integrated circuit. Various configurations of RFID tags are currently available in the marketplace and one such supplier is Texas Instruments® and the RI-I11-112A tag.

[0056] Communication of data between tags and a transceiver is by wireless communication. Such wireless communication is via antenna structures forming an integral feature in both tags and transceivers. During operation, the transceivers transmit a low-power radio signal, through its antenna, which the tag receives via its own antenna to power an integrated circuit. Using the energy it gets from the signal when it enters the radio field, the tag briefly converses with the transceiver for verification and the exchange of data. Once the data is received by the reader it is sent to a controlling processor in a computer for example, for processing and management.

[0057] RFID systems have pre-defined distance ranges over which tags can be read, which depend on several factors such as size of the antenna in the tag, size of the antenna in the transceiver, and the output power of the transceiver. Typically, passive RFID tags operate

in the 100KHz to 2.5 GHz frequency range. Passive RFID tags are powered from the transceiver, whereas active RFID tags have a power source such as a battery, which powers the integrated circuit.

[0058] Data within a tag may provide identification data for an item in manufacture, goods in transit, a location, the identity of a vehicle, an animal or individual. By including additional data the tags can support applications through item specific information or instructions immediately available on reading the tag. For example, the colour of paint for a car body entering a paint spray area on the production line, or the diabetes testing requirements of an individual e.g. on polling of the tag on the first test strip of the day, a user can be informed by the meter that he requires a further three glucose measurements during the next 24 hours.

[0059] Transmitting data is subject to the influences of the media or channels through which the data has to pass such as the air interface. Noise, interference and distortion are sources of data corruption that arise in the communication channels that must be guarded against in seeking to achieve error free data recovery. To transfer data efficiently via the air interface that separates the two communicating components requires the data to be modulated with a carrier wave. Typical techniques for modulation are amplitude shift keying (ASK), frequency shift keying (FSK) or phase shift keying (PSK) techniques.

[0060] Figure 1 shows a test element strip or test strip 2 having a sample area 4, electrical tracks 6, and a Radio Frequency Identification (RFID) tag 10.

[0061] Figure 1 shows a schematic plan view of test strip 2 of an auto calibration system as will be described hereinafter. Typically test strip 2 may be sized or shaped to fit into a slot on a meter 40 (see figure 2). The strip consists of an area 4 within which a patient's blood or ISF interacts with bio-reactive elements e.g. enzymes. This reaction causes a change in current on the conductive tracks 6 which is measured. The conductive tracks 6 may be configured to switch the meter on during insertion as will be described hereinafter. The

meter 40 contains a means such as a transceiver including an RF source for polling or communicating with RFID tags. RFID tag 10 is fixed to the test strip 2 by means of pressure sensitive or heat seal or cold cure adhesive or alternatively printed on test strip 2 using e.g. carbon tracks during the manufacturing stage of the strip 2. For example, a coil in the RFID tag may be printed by screen printing a conductive track e.g. carbon, gold, silver in the form of a coil. The RFID tags can be written with calibration data, batch number, and expiry data or other data using RF encoding means after the strip has been manufactured.

[0062] The RFID tag can be placed in line on the tracks 6 so that during the activation and measurement of the fluid or during initial insertion the current also activates the RFID tag to cause it to transmit. Alternatively or in addition the RFID tag can be polled by exciting the tag via the transceiver both when the strip is in the meter and when the strip is not in the meter.

[0063] Referring to figure 1, the single use test strip 2 has an RFID tag 10 containing information pertaining to batch number, and/or specific calibration data, and, optionally, other information such as 'expiry date of strips' information. Examples of information which can be obtained in an RFID tag are shown in the table in figure 7. Optionally, before inserting the strip 2 into the meter, the user of the meter activates the meter to a pre-fully functional mode for example by pushing a button. When in this mode, the meter polls for the RFID tag 10 on the nearest test strip. Alternatively, the strip 2 is inserted and the meter switched on (by strip insertion to close a contact or otherwise). The strip 2 may also activate the meter on insertion into the strip port connector 8, 18 by using a conductive track 6 on the strip 2 which forms a bridge between two conductors inside the meter itself. Once the meter is switched on it polls wirelessly for the RFID tag 10 closest to its transceiver. Thus, the RFID tag 10 on the test strip transmits the encoded information such as calibration information and/or batch number and/or expiry date and/or other information as described herein to the meter. Alternatively the tag 10 can be read via RF whilst the strip is in meter, before, during or after blood is deposited on the sample area.

[0064] In an example system there is a meter and disposable test strip 2. The system containing a proximity interrogation system including a transceiver, a transponder (an RFID tag), and data processing circuitry. The transceiver includes a microprocessor, a transmitter, a receiver, and a shared transmit/receive antenna. The tag 10 is typically passive (having no on-board power source, such as a battery) and includes an antenna typically configured as a coil, and a programmable memory. As the tag 10 receives its operational energy from the reader, the two devices must be in close proximity. In operation, the transceiver generates sufficient power to excite the tag.

[0065] The polling for the RFID tag can either be continuous or activated by the user to enter a pre-fully functional status. When RF energy emanating from the reader's antenna impinges on the tag while it is in close proximity to the tag, a current is induced in the coil of the antenna. The tag does not need to be in line-of-sight of the meter and can typically operate in the range of a few centimetres or up to a few meters in circumstances as will be understood by persons skilled in the art. Alternatively, a transceiver having an antenna in a form of an array could be utilised which would increase the effectiveness of polling of the tag by increasing the angular range of communication. The induced current in the coil of the antenna is routed to the programmable memory of the tag, which then performs an initialization sequence. The transceiver transmits its energy transmitting interrogation signal to the tag and the memory in the tag begins to broadcast its identity and any other requested information over the tag antenna. Information transmitted to the transceiver is decoded as described below.

[0066] The transceiver in the meter, picks up the signal from the RFID 10 tag and the transmitted data is used in the processing of the test strip. Circuitry in the meter decodes and processes information received from the RFID tag 10. The strip 2 is inserted into a port 8 on a meter. A user lances a suitable site for example a finger or forearm or palm, and deposits blood or ISF on the sample area 4 on the strip 2. A measurement is made by the following method for example. A voltage is applied to test sensors within sample area 4 on

the strip 2 and a current measurement is made. Calibration data is received from the tag 10 specific to strip 2 and is used for calculating the blood glucose level. This level is communicated to the user on the meter display.

[0067] The meter records can optionally record when the first strip of that container is used. This can be used to calculate information for informing the user how long the vial has been opened, and if a use is recorded each time a strip is used, how many strips remain in a vial or cartridge. Thus, the circuitry in the meter can record the number of strips in a vial from strip information from the tag and then subtracts one from this number every time a strip is used from a specific batch of strips. This information combined with the batch number can be useful for a diabetic to either request additional strips from his physician or to calculate how fast a vial of strips is used over a period of time.

[0068] In case the RFID tag becomes damaged during the manufacturing process or during the transit to, e.g. the user, and cannot be read by the meter, or the battery level of the meter is too weak to poll for the RFID tag, the meter has circuitry for allowing a direct manual input of the calibration code. Indeed such direct manual entry can be provided as an option in any event. Typically, the calibration code would be printed on the side of the vial and the user could enter the calibration code before testing commenced. This would allow the user to continue using the strips, thus avoiding having potentially to discard a batch of strips because of a lack of calibration information due to a problem with the RFID tag.

[0069] Figure 2 shows a test strip 2 having a sample area 4, conductive tracks 6, an RFID tag 10, and a meter having a strip port connector 8, and a wireless transceiver 24.

[0070] Alternatively as seen in figure 2, the RFID tag 10 can be fixed to the test strips and to tracks 6 during manufacture. Figure 2 shows a test strip 2 having a sample area 4, conductive tracks from the sample area 6 to an edge of test strip 2, and an RFID tag 10. A schematic of a typical meter is also shown which has a strip port connector 8 which is

dimensioned to receive a strip 2. The meter also contains a wireless transceiver 24 which polls for information from the RFID tag 10. Conductive tracks emanate from the RFID tag to the edge of the test strip 2. Conductive tracks 6 to RFID tag provide the facility to write calibration code data, expiry of strip data, batch number to the strip 2 during manufacture i.e. to allow the manufacturer to determine the calibration code data of strip 2 after manufacture and write directly to the tag after manufacture of the strip 2.

[0071] The application of a hard wired RFID tag 10 as shown in figure 2 allows the calibration code data for each batch to be determined after the manufacturing process has been completed i.e. after the constituent parts of the basic strip are in place. The calibration code is then written into the memory of the RFID tag 10 using the electrical tracks 6 on the strip. Alternatively, or in addition in the same way as in figure 1, the RFID tags can be written with calibration data, batch number, and expiry data using RF encoding means after the strip has been manufactured. Alternatively, or in addition, the tag can be written to (with calibration data) and fixed or stuck onto strip 2 after the basic strip has been made.

[0072] During glucose testing, the diabetic inputs the test strip 2 into the meter. The diabetic lances himself and blood from his e.g. finger is drawn to the sample area of the strip. The meter is activated on insertion of the test strip 2 and current is applied to the reactive region of the strip. The meter either polls the RFID tag 10 for the calibration data, batch number, expiry date or alternatively the meter obtains calibration data, batch number, expiry date by using the tracks on the strip. This is a useful design feature of strips since if the meter has reduced power supply i.e. nearly life expired batteries or when a meter is being used in an RF noisy environment which may interfere with the polled RF signal transmission from and to the RFID tag, then the meter can still operate and obtain the calibration code for each batch of strips. Strips with an RFID tag hard wired or coupled through RF means, allows the user the option to check the validity of the calibration codes presented on the meter display or to cross check with calibration data presented on manufacturers' vials. Indeed, by producing both a hardwire connection to the RFID tag 10

and an RF connection to the RFID tag 10 from the meter, there is less scope for error in supplying the calibration code to the meter should one connection fail, or as a cross check.

[0073] The invention can be used with integrated lancing/test strip devices such as those described in US patent number 6,706,159. When the meter is activated with the strip 2 inserted into the meter, the meter polls the RFID tag 10 for information specific to that strip 2 such as calibration code data and/or any other information as shown in figure 7. The data is then passed to the meter processor. A voltage is applied to the strip 2 and the current versus time data is read by the meter which calculates the glucose value. This glucose value is calculated using the calibration data and an algorithm or a combination thereof and then presented in the form of visual, auditory display.

[0074] Figure 3 shows a test strip 2 having a sample area 4, conductive tracks 6 from the sample area 4 to a short edge of test strip 2, and an RFID tag 10. A schematic of a typical meter is also shown which has a strip port connector 8 dimensioned to receive a strip 2. The meter also contains a wireless transceiver 24 which polls for information from the RFID tag 10, when the meter is activated. Meter activation is either by insertion of a test strip 2 as hereinbefore described or by manual depression of a button. Information can be written to the RFID tag via RF only either prior to or after fixing of the tag to test strip 2.

[0075] Figure 4 shows a multi use test strip or module 12 in the form of a disc having three sample areas 14, conductive tracks 16, and an RFID tag 20. An RFID tag 20 is fixed to the test strip. The RFID tag can be activated to release information pertaining to calibration data and/or batch number and/or expiry of test strips 2 or other information as shown in figure 7 by providing a transceiver for example in a local controller or separate meter which transmits an appropriate RF field to activate the tag.

[0076] Figure 5 shows a series of test strips 27 formed as an array for example on a card or in a housing. An RFID tag 40 is attached to the test strip housing which contains information pertaining to calibration data and/or batch number and/or expiry of test strips

and/or any other information as shown in figure 12. Alternatively or in addition, the strips within the housing may contain two or more RFID tags for example individual RFID tags 30, one associated with each strip 2. Providing two or more tags introduces redundancy. This means that if one of the RFID tags becomes damaged, an alternative RFID tag can be used. Thus, there would be no need to discard that array of strips.

[0077] Figure 4 shows a system 49 in accordance with the present invention for extracting a bodily fluid sample (e.g., an ISF sample) and monitoring an analyte (for example, glucose) and includes a sampling device or cartridge (encompassed within the dashed box), a local controller module 44, and a remote controller module 43, a region of skin for sampling 47, a sampling module 46, and an analysis module 45.

[0078] A patient who controls his diabetes through continuous monitoring techniques would normally have a needle or similar attached to his skin. Blood or ISF is periodically or continuously pumped through the needle device to the continuous or multi use test strip 12 attached to the skin. In one embodiment, the continuous or multi use test strip 12 allows the diabetic to monitor his glucose levels without the daily repetitive lancing of his skin, which as previously discussed is a potentially limiting factor in testing due to several issues.

[0079] Before use of the continuous or multi use test strip module 12 the patient applies the module to his skin. The module is fixed in place either using adhesive or adhesive strip or a strap. A small power source such as button cell is affixed to the sampling module 46. This button cell generates the voltage required for the reaction to take place and to provide an electrical signal to the meter. The current developed at the sensor region 14, 24 in multi-use module 17, 27 is measured by the local controller 44. Once the local controller 44 has measured has measured the current, or the current versus time data, the local controller 44 polls a tag on the test module to obtain, typically at least calibration code information. Using the measured data and the calibration code data the local controller 44 calculates the glucose level. The local controller 44 would typically be attached to the diabetic on his

belt. The current or current versus time data is sent to the meter via RF when requested to do so by an RF interrogation signal from the meter. For example the power source can also power a small transmitter in the local controller module 44 as well as the test strip 17, 27. Alternatively, power for either or both of these activities can be extracted from the RF interrogation signal.

[0080] The user is informed of the glucose reading optionally initially through a vibration alert device and then through traditional notification means such as LCD display, sound alerts, voice alerts, or Braille instruction or a combination of these or simply through an audio alert and then a visual display.

[0081] Alternatively, the result of the measurement can be written into the RFID tag rather than being sent directly to the meter processor via wire or RF. This is now described in more detail. The multi use test strip is applied to the skin for continuous measurement techniques and has at least one writeable RFID tag 20, 30, 40 as shown in figure 4 and 5. Data is written into the memory of the RFID tag using a small battery contained either within the multi use module itself or within a separate attached local controller (see item 44 in figure 4). For example, during sampling of the analyte, the test module 17, 27 is supplied with a voltage by the power source which generates a measurement signal (e.g. current, current versus time etc). The measurement signal is then written to the RFID tag 20, 30, 40 ready to be read by a local controller module 44 (or remote controller module 43) using a transceiver. Remote controller module 43 can instead read data from local controller 44. The RFID tag 20, 30, 40 contains strip specific calibration data, expiry date, and batch information and/or any other information from figure 5, as well as the newly written measurement data. When the diabetic requires a glucose reading using this embodiment, the meter circuit (e.g. within remote controller module 43) would poll the RFID tag 20, 30, 40 and enter into a test reading mode. Calibration data and/or any other information from figure 7 would then be downloaded into the remote controller module, and the measurement information would also be downloaded into the meter. This would allow the user to check his blood glucose reading at any point in the day.

[0082] During use of a multi use strip 17 or an array of strips 27, one of the RFID tags 20, 30, 40 contained within the array or combinations thereof transmit the calibration data, expiry date of strips, batch number or other information when a transceiver polls for a tag and excites the tag to transmit such data. A monitoring device for example a remote controller (see 43 in figure 6) could be used as a parental monitor. The remote control or parental monitor comprises a transceiver, a modem for communication to the Public Switched Telephone Network (PSTN), a processor and circuitry to control and act upon predefined alarm conditions. When a sampling area 14, 24 on the multi use test strip or array of strips 17, 27 has been filled with a sample such as blood and a voltage applied to sampling electrodes (such as a working and counter/reference electrode) within sampling area 14, 24), an electrochemical reaction in the strip takes place. Either the current developed in the sample after a predetermined amount of time or the current versus time profile generated can be written into the memory of the RFID tag. Other types of measurement and reactions such as colorimetric or photometric and so on can be envisaged as being applicable to the present invention as would be understood by someone skilled in the art. During polling of the tag by a remote monitor e.g. a parental monitor, data held within the tag including for example calibration code data and measurement data and optionally other data as referred to in Figure 7 is transmitted back to the parental monitor. The glucose value is then calculated within the remote controlled using this data. The remote control (e.g. parental monitor contains an alarm (not shown) which can be configured to operate in a number of ways.

[0083] Of course, the remote control or parental module may establish a communications link with, instead of the public switched telephone network, any other circuit-switched communications network, or a mobile telephony network, the internet or another packet-switched communications network. Alternatively, the local controller may establish a communications link with a mobile telephony network or another wireless communications network for exactly the same purpose.

[0084] Pre-defined alarm thresholds within the parental monitor can be triggered. These alarm thresholds can include glucose levels at a certain time of day, or glucose levels compared to dietary intake. Similarly, alarm levels thresholds can show that an RF link has been lost (or never made) or that data has not been updated correctly and/or in a timely fashion. Furthermore, the alarm functionality can optionally be controlled by the patient. For example, the alarm could have a range of opt in or opt out functions. An example opt in function is the 'sleep monitor mode'. In this mode during sleep if the glucose level falls or rises above a set threshold, then the alarm could be activated to inform the patient, alternatively or in addition an automatic dial out facility could be provided. Thus, if a diabetic could not be roused to respond to the alarm, the remote control module could 'dial out' to inform a third party of the alarm condition. For example, the modem can be used either to dial out to a 'best friend' or with a recorded message stating the alarm condition, for example, that the diabetic of a named address is in a life threatening condition requiring urgent medical attention, or alternatively, to dial out to another designated number such as to a response centre or the emergency services again with the same or similar message. Indeed, the dial out number to the response centre such as the emergency services could be designated as the first dial out number to be dialled with the 'best friend' being informed thereafter.

[0085] A wireless alternative can be integrated within remote control monitor, the parental monitor. Such wireless alternative could be in the form of a mobile phone and as such, the connection to the response centre using either connection means would be seamless. This introduction of redundancy to the parental monitor is a useful feature and can give further reassurance to a patient that assistance would automatically be obtained in the event that the patient enters a hypoglycaemic or hyperglycaemic state.

[0086] The parental monitor can be either wearable or wall mounted or both, for example can be designed both for use as a removable wearable unit and for interaction with a docking station. It would be especially useful if the parental controller was wall mountable, since diabetics might want to continuously test their glucose levels whilst in bed, or a

physician might want to use such a system when he wishes to monitor a diabetic over a period of time, for example in hospital or during a period of low physical inactivity such as sleeping. The activation of the modem in the instance of a patient being under observation be it at hospital or at home or if say the patient could not meet his specialist physician face to face by being in a regional hospital which would not normally employ specialist physicians would be especially useful. In this respect, the parental monitor could then send glucose readings and/or dietary intake and/or other data to the remote physician using the modem in combination with the PSTN.

[0087] Figure 7 details in addition to the information listed above the types of information which might be uploaded from an RFID tag to the meter and the types of information which might be written back down from the meter to the RFID tag for later use by a patient or clinician, or for use during further testing in any of the embodiments of the present invention.

[0088] The above being a general description of glucose metering systems according to the invention, there now follows a more detailed description of two example systems. The first system is illustrated in figures 8-10 and described in more detail in US patent application serial no. 10/882994. The system 1010 includes a disposable cartridge 1012 (encompassed within the dashed box), a local controller module 1014, and a remote controller module 1016, as illustrated in figure 8.

[0089] In system 1010, disposable cartridge 1012 includes a sampling module 1018 for extracting the bodily fluid sample (namely, an ISF sample) from a body B, e.g., a user's skin layer, and an analysis module 1020 for measuring an analyte (i.e., glucose) in the bodily fluid. Sampling module 1018 and analysis module 1020 may be any suitable sampling and analysis modules known to those of skill in the art. Examples of suitable sampling and analysis modules are described in international patent application WO 02/49507. However, in system 1010, sampling module 1018 and analysis module 1020 are both configured to be disposable since they are components of disposable cartridge 1012.

[0090] As depicted in figure 9, the particular sampling module 1018 of system 1010 is, however, an ISF sampling module that includes a penetration member 1022 for penetrating a target site (TS) of body B and extracting an ISF sample, a launching mechanism 1024 and at least one pressure ring 1028. ISF sampling module 1018 is adapted to provide a continuous or semi-continuous flow of ISF to analysis module 1020 for the monitoring (e.g., concentration measurement) of an analyte (such as glucose) in the ISF sample.

[0091] During use of system 1010, penetration member 1022 is inserted into the target site (i.e., penetrates the target site) by operation of launching mechanism 1024. For the extraction of an ISF sample from a user's skin layer, penetration member 1022 may be inserted to a maximum insertion depth in the range of, for example, 1.5 mm to 3 mm. In addition, penetration member 1022 may be configured to optimize extraction of an ISF sample in a continuous or semi-continuous manner. In this regard, penetration member 1022 may include, for example, a 25 gauge, thin-wall stainless steel needle (not shown in figures 8 or 9) with a bent tip, wherein a fulcrum for the tip bend is disposed between the needle's tip and the needle's heel. Suitable needles are described in US patent no. 6,702,791 and US patent application no. 2003/0060784 (Serial No. 10/185,605) which are hereby fully incorporated by reference.

[0092] Launching mechanism 1024 may optionally include a hub (not shown in figures 8 or 9) surrounding penetration member 1022. Such a hub is configured to control the insertion depth of penetration member 1022 into the target site. Insertion depth control may be beneficial during the extraction of an ISF sample by preventing inadvertent lancing of blood capillaries, which are located relatively deep in a user's skin layer, and thereby eliminating a resultant fouling of an extracted ISF sample, clogging of the penetration member or clogging of an analysis module by blood. Controlling insertion depth may also serve to minimize pain and/or discomfort experienced by a user during use of system 10.

[0093] Although figure 9 depicts launching mechanism 1024 as being included in sampling module 1018, launching mechanism 1024 may optionally be included in disposable cartridge 1012 or in local controller module 1014 of system 1010. Furthermore, to simplify employment of system 1010 by a user, sampling module 1018 may be formed as an integral part of the analysis module 1020.

[0094] In order to facilitate the extraction of a bodily fluid (e.g., ISF) from the target site, penetration member 1022 may be arranged concentrically within at least one pressure ring 1028. Pressure ring(s) 1028 may be of any suitable shape, including but not limited to, annular. An example of such an arrangement is disclosed in U.S. Patent No. 5,879,367 which is hereby fully incorporated by reference.

[0095] During use of system 1010, pressure ring 1028 is applied in the vicinity of the target site TS, prior to penetration of the target site by penetration member 1022, in order to tension the user's skin layer. Such tension serves to stabilize the user's skin layer and to prevent tenting thereof during penetration by the penetrating member. Alternatively, stabilization of the user's skin layer prior to penetration by the penetrating member may be achieved by a penetration depth control element (not shown) included in sampling module 1018. Such a penetration depth control element rests or "floats" on the surface of the user's skin layer, and acts as a limiter for controlling penetration depth (also referred to as insertion depth). Examples of penetration depth control elements and their use are described in US patent application serial no. 10/690,083 and EP 1, 527, 736, which are hereby fully incorporated herein by reference.

[0096] Once penetration member 1022 has been launched and has penetrated the target site TS, a needle (not shown in figures 8 or 9) of penetration member 1022 will reside, for example, at an insertion depth in the range of about 1.5 mm to 3 mm below the surface of the user's skin layer. If desired, penetration member 1022 may be launched coincidentally with application of pressure ring(s) 1028 to the user's skin layer, thereby enabling a simplification of the launching mechanism. The pressure ring(s) 1028 applies/apply a force

on the user's skin layer (indicated by the downward pointing arrows of figure 9) that pressurizes ISF in the vicinity of the target site. A sub-dermal pressure gradient induced by the pressure ring(s) 1028 results/result in flow of ISF up the needle and through the sampling module to the analysis module (as indicated by the curved and upward pointing arrows of figure 9).

[0097] ISF flow through a penetration member's needle is subject to potential decay over time due to depletion of ISF near the target site and due to relaxation of the user's skin layer under the pressure ring(s) 1028. The systems and methods of the present invention address this by varying one or more aspects of the applied pressure.

[0098] In one variation, the amount of applied pressure may be varied over a given time. While contact between the pressure ring(s) and the skin might be constant, the amount of that pressure may be varied. For example, the amount of pressure may be progressively increased proportionately or otherwise to the volume or flow rate of the ISF being extracted. Alternatively, the increase in pressure may be staggered or applied in a step-wise fashion. Still yet, the pressure may be oscillated between various levels of greater and lesser pressure, where the reduction in pressure may include the discontinuance of pressure by completely removing the pressure ring(s) from contact with the skin. The oscillation frequency of the pressure ring(s) may be constant or varied depending on the application. For example, the application times of higher pressure ("on") and lower or no pressure ("off") may be the same (e.g., 3 minutes on followed by 3 minutes off, etc.) or different (e.g., 15 minutes on followed by 10 minutes off, etc.) or one may be constant and the other may vary (e.g., 15 minutes on followed by 20 minutes off followed by 15 minutes on followed by 10 minutes off, etc.).

[0099] In other variations, while the amount of applied pressure to the skin may be constant over a period of time, the location of that pressure relative to the needle penetration site may vary over time. For example, the initial pressure may commence at a certain radial distance (assuming a substantially annular configuration of the pressure ring)

from the penetration site where that radial distance is reduced or increased over time. The change in distance may be gradual or less so depending on the application or in response to ISF extraction flow or volume. This may be accomplished by the use of multiple pressure rings having varying diameters which are individually and successively applied to the target site.

[0100] The location of the initial pressure may be maintained, but the radial surface area over which the pressure is applied may be increased or decreased. In other words, the amount of surface area of the pressure ring in contact with the skin may be increased or increased. This may also be accomplished by the use of multiple pressure rings which are individually but cumulatively applied or successively removed from application to the skin.

[0101] Returning to figures 8-11, and as mentioned above, pressure ring(s) 1028 may be applied to the user's skin layer in an oscillating manner (e.g., with a predetermined pressure ring(s) cycling routine or with a pressure ring cycling routine that is controlled via and is responsive to ISF flow rate measurement and feedback) while the penetration member is residing in the user's skin layer in order to minimize ISF flow decay. In addition, during application of pressure in an oscillating manner, there may be time periods during which the pressure applied by the pressure ring(s) is varied or the local pressure gradient is removed and the net outflow of ISF from the user's skin layer is eliminated. In addition, pressure ring(s) 28 may be configured to apply an oscillating mechanical force (i.e., pressure) in the vicinity of the target site while the penetration member is residing in the user's skin layer. Such oscillation may be achieved through the use of a biasing element (not shown in figures 8 or 9), such as a spring or a retention block.

[0102] Any suitable glucose sensor known to those of skill in the art may be employed in analysis modules according to the present invention. Glucose sensor 1310 may contain, for example, a redox reagent system including an enzyme and a redox active compound(s) or mediator(s). A variety of different mediators are known in the art, such as ferricyanide,

phenazine ethosulphate, phenazine methosulfate, pheylenediamine, 1-methoxy-phenazine methosulfate, 2,6-dimethyl-1,4-benzoquinone, 2,5-dichloro-1,4-benzoquinone, ferrocene derivatives, osmium bipyridyl complexes, and ruthenium complexes. Suitable enzymes for the assay of glucose in whole blood include, but are not limited to, glucose oxidase and dehydrogenase (both NAD and PQQ based). Other substances that may be present in the redox reagent system include buffering agents (e.g., citraconate, citrate, malic, maleic, and phosphate buffers); divalent cations (e.g., calcium chloride, and magnesium chloride); surfactants (e.g., Triton, Macol, Tetronic, Silwet, Zonyl, and Pluronic); and stabilizing agents (e.g., albumin, sucrose, trehalose, mannitol and lactose).

[0103] In an embodiment in which the analysis module includes an electro-chemical based glucose sensor, the specific structure of the electrochemical sensor will depend on the nature of the analyte. In general, however, each device will include an electrode layer and at least one reagent layer deposited on a substrate. As used in the specification and claims hereof, the term "layer" refers to a coating applied to all or part of the surface of the substrate. A layer is considered to be "applied to" or "printed on" the surface of the substrate when it is applied directly to the substrate or the surface of a layer or layers previously applied to the substrate. Thus, deposition of two layers on the substrate may result in a three layer sandwich (substrate, layer 1, and layer 2) or in the deposition of two parallel tracks, as well as intermediate configurations with partial overlap.

[0104] The substrate used may be any dimensionally stable material. In general the substrate will be an electrical insulator, although this is not necessary if a layer of insulation is deposited between the substrate and the electrodes. The substrate should also be chemically compatible with the materials which will be used in the printing of any given sensor. This means that the substrate should not significantly react with or be degraded by these materials, although a reasonably stable print image does need to be formed. Specific examples of suitable materials include polycarbonate and polyester.

[0105] The electrodes may be formed of any conductive material which can be deposited in patterns. This would include carbon electrodes and electrodes formed from platinized carbon, gold, silver, and mixtures of silver and silver chloride. Insulation layers are deposited as appropriate to define the sample analysis volume and to avoid a short circuiting of the sensor. Insulating materials which can be printed are suitable, including for example polyester-based inks.

[0106] It will be well understood that this structure causes the generation of both charge and current in the presence of an analyte, allowing for the following to be measured: an inter-electrode impedance; an inter-electrode current; a potential difference; an amount of charge; a change over time of any of the aforesaid; any combination of the aforesaid; or any other indicator of the amount of electricity passing from one electrode to another, or the extent to which exposure of the sensor to the fluid generates electrical energy or electrical charge or otherwise affects the electrical characteristics of the sensor. Local controller module 14 may measure any of these things, preferably electrical current, via electrical contacts (not shown) and convert it to one that is representative of the ISF glucose concentration.

[0107] Other embodiments use photometric or colorimetric sensors comprising a substrate and at least a first reagent including a catalyst and a dye or dye precursor and the catalyst catalyses, in the presence of the analyte, the denaturing of the dye or the conversion of the dye precursor into a dye. For glucose sensors, the preferred combination is a combination of glucose oxidase and horseradish peroxidase as a catalyst and leuco-dye as a dye precursor. The leuco-dye may, for example, be 2,2-azino-di-[3-ethylbenzthiazoline-sulfonate], tetramethylbenzidine-hydrochloride or 3-methyl-2-benzothiazoline-hydrazone in conjunction with 3-dimethylamino-benzoicacide. The reagent may be laid down as a film or membrane over a opening in a substrate or over a portion of a substrate or placed into a chamber in a substrate as in WO02/49507.

[0108] It is well understood that this combination of enzyme and leuco-dye causes the colour or depth of colour of the reagent layer to change in the presence of glucose, allowing for the following to be measured: opacity; transparency; transmissivity reflectivity or absorptivity; a transmission, reflection or absorption spectrum, peak, gradient or ratio; any one of more parts of such a spectrum; colour; a change over time of any of the aforesaid; and any combination of the aforesaid.

[0109] If a fluorophore is used instead of a non-fluorescing leuco-dye, the amount of glucose can be determined by looking at the fluorescence properties of the reagent, such as: fluorescence intensity; emissivity; an emission or excitation spectrum, peak, gradient or ratio; any one of more parts of such a spectrum; an emission polarization; an excited state lifetime; a quenching of fluorescence; a change over time of any of the aforesaid; or any combination of the aforesaid.

[0110] Local controller module 1014 is depicted in simplified block form in figure 10. Local controller module 1014 includes a mechanical controller 1402, a first electronic controller 1404, a first data display 1406, a local controller algorithm 1408, a first data storage element 1410 and a first RF link 1412. Local controller module 1014 is configured such that it may be electrically and mechanically coupled to disposable cartridge 1012. The mechanical coupling provides for disposable cartridge 1012 to be removably attached to (e.g., inserted into) local controller module 1014. Local controller module 1014 and disposable cartridge 1012 are configured such that they may be attached to the skin of a user by, for example, by a strap, in a manner which secures the combination of the disposable cartridge 1012 and local controller module 1014 onto the user's skin.

[0111] During use of system 1010, first electronic controller 1404 controls the measurement cycle of the analysis module 1020, as described above. Communication between local controller module 1014 and disposable cartridge 1012 takes place via the electrical contacts on analysis module 1020 and the corresponding electrical contacts on local controller module 1014. Electrical signals representing the glucose concentration of

an ISF sample are then sent by the analysis module to the local controller module. First electronic controller 1404 interprets these signals by using the local controller algorithm 1408 and displays measurement data on a first data display 1406 (which is readable by the user). In addition, measurement data (e.g., ISF glucose concentration data) may be stored in first data storage element 1410. This element may be an RFID tag, in which case figure 10 should be understood as though data storage element 1410 and RF link 1412 were merged into a single functional block.

[0112] Prior to use, an unused disposable cartridge 1012 is inserted into local controller module 1014. This insertion provides for electrical communication between disposable cartridge 1012 and local controller module 1014. A mechanical controller 1402 in the local controller module 1014 securely holds the disposable cartridge 1012 in place during use of system 1010.

[0113] After attachment of a local controller module and disposable cartridge combination to the skin of the user, and upon receiving an activation signal from the user, a measurement cycle is initiated by first electronic controller 1404. Upon such initiation, penetration member 1022 is launched into the user's skin layer to start ISF sampling. The launching may be initiated either by first electronic controller 1404 or by mechanical interaction by the user.

[0114] First RF link 1412 of local controller module 1014 is configured to provide bi-directional communication between the local controller module and a remote controller module 1016, as depicted by the jagged arrows of figures 8 and 10. The local controller module incorporates a visual indicator (e.g., a multicolour LED) indicating the current status, e.g., a red light may be used to indicate a hypo or hyperglycaemic state and a green light may be used to indicate a euglycaemic state, etc., of the system.

[0115] Local controller module 1014 is configured to receive and store measurement data from, and to interactively communicate with, disposable cartridge 1012. For example, local

controller module 1014 may be configured to convert a measurement signal from analysis module 1020 into an ISF or blood glucose concentration value. Alternatively, the conversion might be done by the cartridge 1012. Information stored in local controller module 1014 is preferably stored in a passive RFID tag contained within the module; however, it may be otherwise stored so long as the local controller 1014 has some active or passive RF communications capability by means of which it can communicate with the remote module 1016 when interrogated by the remote module 1016. One form of passive communication is for the local controller 1014 to extract energy from an RF interrogation signal from the remote controller module 1016 to use in the transmission of the information. It may use the same technique to extract energy from an RF testing signal from the remote controller module 1016 to use in the operation of the launching mechanism and/or pressure rings. The testing and interrogation signals may be the same signal, in which case there may be no need to store the data in the RFID tag at all. Another form of passive communication is for the local controller 1014 to modulate or modify the interrogation signal, as with a passive RFID tag.

[0116] Another system according to the invention is illustrated in figures 11-13B. Figure 11 is a simplified schematic illustration depicting interaction between a fluorescent light-emitting bead 2010, light emitter 2012 and light detector 2014 that is relevant to various embodiments of the present invention. Fluorescent light-emitting bead 2010 includes at least one fluorescent reactant (e.g., a fluorescent dye) that emits fluorescent light FL as a result of absorbing incident light IL (that has been emitted by light emitter 2012), with characteristics of the emitted fluorescent light FL being dependent on the concentration of an analyte that is in communication with (e.g., in contact with) the fluorescent light-emitting bead. Fluorescent reactants that can be included in such a fluorescent light-emitting bead, and their behavior when in communication with an analyte, are described in U.S. Patent Nos. 5,342,789, 6,040,194, and 6,232,130, each of which is hereby fully incorporated by reference. Fluorescent light-emitting bead 2010 can also include an encapsulating material such as, for example, alginate. Preferred fluorescent reagents reversibly bind to the analyte.

[0117] When using a fluorescent reagent, the following characteristics can be measured, in this case by transdermal optometry: a fluorescence intensity; an emission or excitation spectrum, peak, gradient or ratio; any one or more parts of such a spectrum; an emission polarization; an excited state lifetime; a quenching of fluorescence; a change over time of any of the aforesaid; any combination of the aforesaid; or any other indicator of the extent to which exposure of the fluorescent reagent to the fluid affects its fluorescence characteristics.

[0118] Preferred embodiments use a reagent comprising or labelled with a donor molecule and an acceptor molecule, where the measurable characteristic is an indicator of the extent to which non-radiative fluorescence resonance energy transfer occurs between the donor and the acceptor upon reversible binding of the reagent to the analyte. The reagent may comprise a specific binding pair, one of which is, or is labelled with, the donor molecule and the other of which is, or is labelled with, the acceptor molecule. The sensor may comprise a envelope that contains and is substantially impermeable to the reagent, but is permeable to the analyte. The envelope may also a microdialysis vessel or a microcapsule. Further details of reagents can be found in US patent no. 6,040,194, which is hereby fully incorporated by reference.

[0119] Figure 12 is a simplified schematic illustration depicting interaction between a fluorescent light-emitting bead 2020 implanted in a user's body B, a light emitter 2022 and a light detector 2024 that is relevant to various embodiments of the present invention. The portion of user's body B depicted in figure 12 includes a Stratum Corneum portion SC, an Epidermis portion E and Dermis portion D.

[0120] As with fluorescent light-emitting bead 2010, fluorescent light-emitting bead 2020 includes at least one fluorescent reactant (e.g., a fluorescent dye) that emits fluorescent light FL as a result of absorbing incident light IL (that has been emitted by light emitter 2022), with characteristics of the emitted fluorescent light being dependent on the

concentration of an analyte that is in communication with the fluorescent light-emitting bead.

[0121] Figure 12 depicts fluorescent light-emitting bead 2020 implanted in a user's body B. In this circumstance, incident light IL and fluorescent light FL are of a wavelength(s) and intensity such that incident light IL is able to pass through the user's body B to reach fluorescent light-emitting bead 2020 and fluorescent light FL is able to pass through the user's body to reach light detector 2024. Fluorescent light-emitting bead 2020 includes at least one fluorescent reactant and is configured in such a way that a predetermined characteristic(s) of fluorescent light FL varies as a function of bodily fluid analyte concentration (e.g., glucose concentration) in the user' body B.

[0122] Figure 13A is a simplified cross-sectional view of an adhesive fluorescence measurement patch 2100 for use with a fluorescent light-emitting bead FB implanted within a user's body B, that includes a Stratum Corneum portion SC, an Epidermis portion E and Dermis portion D, according to an exemplary embodiment of the present invention. In figure 13A, adhesive fluorescence measurement patch 2100 is removably adhered to a user's body B and in communication with a remote module 2200 via radio-frequency signals RF. Adhesive fluorescence measurement patch 2100 includes an adhesive sheet 102 configured for removable adhesion to user's body B, a light emitter 2104 attached to adhesive sheet 2102, and a light detector 2106 also attached to adhesive sheet 2102. Although figure 13A depicts light emitter 2104 and light detector 2106 embedded in adhesive sheet 102, the attachment of light emitter 2104 and light detector 2106 to adhesive sheet 2102 can take any suitable form known to one skilled in the art.

[0123] Fluorescent light-emitting bead FB can be implanted, for example, in the range of approximately 1mm to 4mm below the surface of a user's skin. In addition, light emitter 2104 and light detector 2106 can be located, for example, in the range of 0mm to 10mm above the surface of the user's skin when adhesive fluorescence measurement patch 2100 is adhered to the user's body B (i.e., adhered to the user's skin).

[0124] For the sake of simplicity, figure 13A depicts adhesive fluorescence measurement patch 2100 as including only an adhesive sheet, light emitter and light detector. However, once apprised of the present disclosure, one skilled in the art will recognize that adhesive fluorescence measurement patches, kinematic adhesive fluorescence measurement patches and kinematic adhesive fluorescence measurement bands according to the present invention can include various other components, electrical and/or optical, that provide for suitable and beneficial operation. In this regard, figure 13B is a simplified schematic diagram depicting the operative interaction of various electrical and optical components, including a light emitter 2104 and a light detector 2106, suitable for use in the adhesive fluorescence measurement patch of figure 13A and other embodiments of the present invention. In figure 13B, elements or other items common with figure 13A are identically labeled.

[0125] As depicted in figure 13B, the electrical and optical components include a power module 2108, an RF transceiver module 2110, a micro-controller module 2112, a driver/amplifier module 2114, a buzzer module 2116 (for providing feedback to a user) and an optical filter module 2120. Light emitter 2104 can be, for example, an LED 525nm wavelength light emitter such as SMD LED part number LTST-C903TGKT available from Lite-On Corp. Light detector 2106 can be, for example, light detector part number S 8745-01 available from Hamamatsu. Optical filter module 2120 can include, for example, 600nm and 700nm band pass filters. Micro-controller module 2112 can be, for example, an MSP 430 series micro-controller available from Texas Instruments. Power module 2108 can be, for example, a rechargeable or non-rechargeable battery module or a circuit that extracts power from wireless signals from remote controller 2200. If desired, all the electrical and optical components depicted in figure 13B can be mounted on a printed circuit board (PCB) and the PCB attached to adhesive sheet 2102.

[0126] In addition, once apprised of the present disclosure, one skilled in the art will recognize that embodiments of the present invention can be readily modified for use with

suitable fluorescent light-emitting devices other than a fluorescent light-emitting bead. For example, such adhesive fluorescence measurement patches could be used with fluorescent injected oils or fluorescent tattoos as described in U.S. Patent No. 5,342,789, which is hereby fully incorporated by reference.

[0127] In figure 13A, fluorescent light-emitting bead FB is implanted in user's body B, and contains at least one fluorescent reactant that emits fluorescent light FL as a result of absorbing incident light IL. In addition, a characteristic(s) of fluorescent light FL varies as a function of analyte concentration in contact with fluorescent light-emitting bead FB. Therefore, adhesive fluorescence measurement patch 2100, in conjunction with fluorescent light-emitting bead FB and remote module 2200, can be used for measuring the concentration of an analyte (e.g., blood glucose) in the bodily fluid of a user's body.

[0128] Referring again to figure 13A, an imaginary optical axis X of adhesive fluorescence measurement patch 2100 is depicted by a broken line. Light emitter 2104 and light detector 2106 are attached to adhesive sheet 2102 in a predetermined relationship relative to imaginary optical axis X. In addition, imaginary optical axis X is positioned in a predetermined juxtaposition to the fluorescent light-emitting bead FB when the adhesive fluorescence measurement patch is removably adhered to a user's body (as in figure 13A). The predetermined juxtaposition of imaginary optical axis X and fluorescent light-emitting bead FB will typically be associated with a suitable alignment tolerance in the range of, for example, +/- 1mm to +/- 2mm.

[0129] The predetermined relationship of light emitter 2104 and light detector 2106 with imaginary optical axis X and the predetermined juxtaposition of imaginary optical axis X with the fluorescent light-emitting bead FB provide for (i) emitted incident light IL from light emitter 2104 to be incident on, and absorbed by, fluorescent light-emitting bead FB and (ii) fluorescent light FL emitted by fluorescent light-emitting bead FB to be detected by light detector 2106 (the emitted light IL and fluorescent light FL are, for the sake of simplicity, depicted as arrows in figure 13A (as well as in figures 11 and 12)). Therefore,

adhesive fluorescence measurement patch 100 can be readily adhered to user's body B in a position that provides for incident light IL to operatively reach fluorescent light-emitting bead FB, as well as for fluorescent light FL to operatively reach light detector 2106. Since light emitter 2104 and light detector 106 are securely attached to adhesive sheet 2102 in a proper predetermined relationship to imaginary optical axis X, an operable alignment of light emitter 2104 and light detector 2106 with an implanted fluorescent light-emitting bead FB is easily obtained and maintained during use.

[0130] It should be noted that although figure 13A depicts light emitter 2104 and light detector 2106 as being symmetrically disposed about imaginary optical axis X, such symmetry is not necessarily required. In addition, the predetermined relationship of light emitter 2104 and light detector 2106 with imaginary optical axis X, as well as the predetermined juxtaposition of imaginary optical axis X with the fluorescent light-emitting bead FB, can be such the amount of reflected light from the fluorescent light-emitting bead received by the light detector is relatively minimized while the amount of fluorescent light received by the light detector is relatively maximized.

[0131] Adhesive sheet 2102 can be any suitable adhesive sheet known to those of skill in the art including, for example, adhesive sheets that include commercially available pressure sensitive adhesives. Furthermore, adhesive sheets employed in embodiments of the present invention can include a top layer and at least one adhesive lower layer disposed on at least a portion of the top layer.

[0132] The top layer and adhesive lower layer(s) employed in the adhesive sheet can be any suitable combination of single-sided adhesive layers, double-sided adhesive layers, transfer adhesive layers and non-adhesive layers. The single-sided and double-sided adhesive layers can be pressure sensitive, in that they removably adhere to a surface of a user's body when pressure is applied. Typical pressure sensitive adhesive layers include those based on acrylics, natural rubber, synthetic rubber and silicone polymers. Suitable pressure sensitive adhesive layers are commercially available from, for example,

Adhesives Research, Inc., of Glen Rock, Pennsylvania under the commercial name ARcare®.

[0133] The top layer and adhesive lower layer(s) of an adhesive sheet can be clear or opaque, and are typically flexible. The top layer and adhesive lower layer(s) can be made, for example, from an extruded or cast polymer film, or can be made using woven or non-woven fabric and can be elastic, or inelastic. In addition, they can be made from any suitable material, including, for example polyester, polycarbonate, polystyrene, polypropylene, polyethylene, acrylonitrile butadiene styrene (ABS), polyurethane, silicone, and woven or non-woven fabrics. Suitable polymer films and fabrics can be purchased, for example, from Tekra Corporation of New Berlin, Wisconsin.

[0134] If desired, one or more release liners can be employed to cover all or a portion of adhesive sheets employed in embodiments of the present invention. Such release liners are typically made by, for example, siliconizing polyester, polyethylene, polypropylene or paper. Release liners can also be manufactured by treating the surface of a suitable material with a fluorocarbon-based compound. Prior to use of an adhesive fluorescence measurement patch, one or all of the release liners are pealed off of the adhesive sheet. Suitable release liners are commercially available from, for example, Rexam Release, of Bedford Park, Illinois.

[0135] The adhesive sheet employed in embodiments of the present invention can be any suitable thickness. However, a typical non-limiting thickness range is from 0.0005 inches to 0.040 inches (excluding the thickness of the light emitter and light detector that are attached to the adhesive sheet). A major surface of the adhesive fluorescence measurement patch (i.e., the surface facing a user's body when the adhesive fluorescence measurement patch is adhered) can have any suitable surface area with a typical surface area being, for example, in the range of from 0.40 square inches to 4 square inches. However, larger surface areas, for example, 40 square inches, can be employed if desired.

[0136] Any suitable light emitter 2104 and suitable light detector 2106 known to one skilled in the art can be employed in adhesive fluorescence measurement patches according to embodiments of the present invention. Suitable light emitters can be, for example, light emitting diodes (e.g., light emitting diodes commercially available from Lite-On Technology Corporation of Milpitas, California). Suitable light detectors can be, for example, photodiodes (e.g., photodiodes commercially available from Hamamatsu Corporation of Bridgewater, New Jersey).

[0137] In figure 13A, adhesive fluorescence measurement patch 2100 is depicted as in communication with remote module 2200 via radio frequency signals RF. However, once apprised of the present disclosure, one skilled in the art will recognize that other suitable means of providing wireless communication between an adhesive fluorescence measurement patch and a remote module can be employed. A passive RFID tag is employed to store and transmit information, using a non-radiative back-scattering communications mode, and the term "transceiver" as used with reference to this embodiment should be understood accordingly

[0138] Remote module 2200 can have any suitable capabilities, including the capability to control of light emitter 2104 and light detector 2106 and the capability to process communications received from adhesive fluorescence measurement patch 2100. For example, remote module 2200 can have the capability to continuously or intermittently correlate fluorescent light detected by light detector 2106 to analyte concentration and to then employ the correlation to control other devices, such as an insulin infusion pump supplying insulin to the patient's abdominal adipose tissue. The infusion pump thus supplies insulin in an amount that depends upon the level of the analyte in the fluid as determined by the remote module 200. Suitable remote controllers, as can be modified by one skilled in the art for use in embodiments of the present invention, are described in international paten application WO 03/071930, which is hereby fully incorporated by reference.

[0139] Fluorescent measurement patch 2100 is configured to receive and store measurement data from the light detector 2106. Fluorescent measurement patch 2100 may be configured to convert a measurement signal from light detector 2106 into an ISF or blood glucose concentration value. Alternatively, the conversion might be done by the remote module 2200. Information stored in fluorescent measurement patch 2100 is preferably stored in a passive RFID tag contained within the fluorescent measurement patch; however, it may be otherwise stored so long as the fluorescent measurement patch 2100 has some active or passive RF communications capability by means of which it can communicate with the remote module 2200 when interrogated by the remote module 2200. One form of passive communication is for the fluorescent measurement patch 2100 to extract energy from an RF interrogation signal from the remote controller module 2200 to use in the transmission of the information. It may use the same technique to extract energy from an RF testing signal from the remote controller module 200 to use in the operation of the light emitter 2104 and light detector 2106. The testing and interrogation signals may be the same signal, in which case there may be no need to store the data in the RFID tag at all. Another form of passive communication is for the fluorescent measurement patch 2100 to modulate or modify the interrogation signal, as with a passive RFID tag.

[0140] Fluorescent measurement patch 100 may of course be used with a parental or other care-giver monitoring module as discussed above.

[0141] Remote module 2200 may be, or maybe incorporated into, a hand-held device, a portable device, a PDA, a mobile telephone, or a laptop computer.

[0142] RFID tags in any embodiment of this invention may hold and convey information representing the calibration quantity of the sensors used. The module in which the analyte, e.g. glucose, measurement values are calculated will wirelessly receive that information and use it when determining the level of the analyte in the fluid.

Claims

1. A system for determining the level of an analyte in a physiological fluid , comprising:

a wearable sensor that is adapted to obtain data representative of the level of the analyte, and has a wireless device adapted to convey the data wirelessly when wirelessly interrogated; and

a receiver adapted to operate as follows:

to wirelessly interrogate the sensor; and

to receive the data conveyed by the wireless device.

2. A system according to claim 1 in which the data directly represents the level of the analyte in the fluid.

3. A system according to claim 1 in which:

the data indirectly represents the level of the analyte in the fluid; and

the receiver is adapted to determine, from the data, the level of the analyte in the fluid.

4. A system according to any preceding claim in which the physiological fluid is the individual's blood.

5. A system according to any one of claims 1-3 in which the physiological fluid is the individual's interstitial fluid.

6. A system according to any preceding claim in which the level of the analyte is diagnostic of a medical disorder or diseased condition.

7. A system according to claim 6 in which the medical disorder or diseased condition is remediable by the administration of a drug and the system further comprises a drug dispensing unit for dispensing the drug.

8. A system according to claim 7 in which the drug dispensing unit is adapted to dispense the drug in an amount that depends upon the level of the analyte in the fluid as conveyed by the sensor or determined by the receiver.

9. A system according to any preceding claim in which the analyte is glucose, HbA1C, lactate, cholesterol, alcohol, a ketone, urate, a therapeutic drug, a recreational drug, a performance-enhancing drug, a biomarker indicative of a diseased condition, a hormone, an antibody, a metabolite of any of the aforesaid, a combination of any of the aforesaid, or another similar indicator.

10. A system according to claim 9 in which the analyte is glucose.

11. A system according to claim 7 or claim 8 in which the analyte is glucose and the drug promotes cellular uptake of glucose.

12. A system according to claim 11 in which the drug comprises insulin or an insulin analog.

13. A system according to claim any one of claims 7, 8, 11 or 12 in which the dispensing unit comprises an infusion pump or other mechanism adapted to dispense the drug directly into the body of the individual concerned.

15. A system according to any preceding claim in which the receiver is, or is incorporated within, a local device worn by the individual concerned.

16. A system according to any one of claims 1-14 in which the receiver is, or is incorporated within, a device remote from the individual concerned.

17. A system according to claim 15 further comprising a device remote from the individual concerned, in which the local and remote devices are in wireless communication with one another and adapted to transfer from the local device to the remote device either the data received from the sensor or the level of the analyte as determined by the receiver or both.

18. A system according to any one of claims 15-17 in which:

the remote device is adapted to establish a communications link with a public switched telephone network or another circuit-switched communications network, or a mobile telephony network, the internet or another packet-switched communications network; or

the local device is adapted to establish a communications link with a mobile telephony network or another wireless communications network.

19. A system according to claim 18 in which the communications link is used to transmit the data received from the sensor or the level of the analyte as determined by the receiver, information concerning the variation of either over time, or other similar information.

20. A system according to claim 18 or claim 19 in which the communications link is used to transmit an alarm condition such as an abnormal analyte level, an abnormal analyte level for a certain time of day, an abnormal analyte level as compared with dietary intake, abnormal or non-functional wireless transfer of information from the sensor or the local device, abnormal physiological fluid sampling frequency, abnormal establishment, or non-establishment, of wireless communication from the sensor or the local device, abnormal storage of information in the wireless device or other alarm conditions.

21. A system according to any preceding claim in which:

the receiver is adapted to interrogate the wireless device by issuing a wireless interrogation signal; and

the wireless device is adapted to extract energy from the wireless interrogation signal and use the energy extracted to convey data wirelessly to the receiver.

22. A system according to any one of claims 1-20, in which:

the receiver is adapted to interrogate the wireless device by issuing a wireless interrogation signal;

the wireless device is adapted to modulate or otherwise modify the wireless interrogation signal using the data; and

the receiver is further adapted to receive back the modulated or otherwise modified interrogation signal and to extract the data from it.

23. A system according to claim 22 in which the interrogation signal is back-scattered by the wireless device.

24. A system according to any preceding claim in which:

the receiver is adapted to issue a wireless test signal; and

the wireless device is adapted to extract energy from the wireless test signal and use the energy extracted to obtain the data to be conveyed.

25. A wearable sensor for use in determining the level of an analyte in a physiological fluid, the sensor being adapted to obtain data representative of the level of the analyte, and having a wireless device adapted to convey the data wirelessly when wirelessly interrogated.

26. A sensor according to claim 23 in which:

the sensor, when exposed to the physiological fluid, develops a measurable characteristic that is a function of the level of the analyte in the fluid and of a calibration quantity of the sensor; and

the wireless device is adapted to hold and convey information representing the calibration quantity of the sensor.

27. A system according to claim 3 in which:

the sensor, when exposed to the physiological fluid, develops a measurable characteristic that is a function of the level of the analyte in the fluid and of a calibration quantity of the sensor;

the wireless device is adapted to hold and convey information representing the calibration quantity of the sensor; and

the receiver is adapted to receive the information representing the calibration quantity of the sensor and to use it when determining the level of the analyte in the fluid.

28. A sensor according to claim 25 or claim 26 that is a photometric or colorimetric sensor.

29. A sensor according to claim 28 in which the sensor comprises:

an intracorporeal part that is adapted to be exposed to the physiological fluid by implantation in the individual concerned and, when so exposed, develops a measurable characteristic, being an indicator of the extent to which exposure of the sensor to the fluid affects its optical characteristics, that is a function of the level of the analyte in the fluid; and

an extracorporeal part that is adapted to acquire the measurable characteristic of the intracorporeal part by transdermal wireless communication, and includes the wireless device adapted to convey wirelessly the data representative of the level of the analyte when wirelessly interrogated.

30. A sensor according to claim 29 in which the transdermal wireless communication is transdermal optical transmission.

31. A sensor according to claim 30 in which the intracorporeal part comprises a reagent that reversibly binds to the analyte.

32. A sensor according to claim 31 in which the reagent is fluorescent and the measurable characteristic is:

a fluorescence intensity;

an emission or excitation spectrum, peak, gradient or ratio;

any one or more parts of such a spectrum;

an emission polarization;

an excited state lifetime;

a quenching of fluorescence;

a change over time of any of the aforesaid;

any combination of the aforesaid; or

any other indicator of the extent to which exposure of the fluorescent reagent to the fluid affects its fluorescence characteristics.

33. A sensor according to claim 32, in which:

the reagent comprises or is labelled with a donor molecule and an acceptor molecule; and

the measurable characteristic is an indicator of the extent to which non-radiative fluorescence resonance energy transfer occurs between the donor and the acceptor upon reversible binding of the reagent to the analyte.

34. A sensor according to claim 33, in which the reagent comprises a specific binding pair, one of which is, or is labelled with, the donor molecule and the other of which is, or is labelled with, the acceptor molecule.

33. A sensor according to any one of claims 31-34 in which the sensor comprises a envelope that contains and is substantially impermeable to the reagent, but is permeable to the analyte.

34. A sensor according to claim 33 in which the envelope is a microdialysis vessel or a microcapsule or an alginate bead optionally covered with a polylysine covering.

35. A sensor according to claim 28 adapted for extracorporeal use and comprising means for extracting the physiological fluid, a reagent, and means for exposing the reagent to the fluid and the measurable characteristic is:

an opacity;

a transparency;

a fluorescence intensity;

a transmissivity, a reflectivity, an absorptivity or an emissivity;

a transmission, reflection, absorption, emission or excitation spectrum, peak, gradient or ratio;

any one of more parts of such a spectrum;

a colour;

an emission polarization;

an excited state lifetime;

a quenching of fluorescence;

a change over time of any of the aforesaid;

any combination of the aforesaid; or

any other indicator of the extent to which exposure of the sensor to the fluid affects its optical characteristics.

36. A sensor according to claim 28 or claim 35, in which the reagent includes a catalyst and a dye or dye precursor and the catalyst catalyses, in the presence of the analyte, the denaturing of the dye or the conversion of the dye precursor into a dye.

37. A sensor according to claim 35 or claim 36, in which the analyte is glucose, HbA1C, lactate, cholesterol, alcohol, a ketone, urate, a therapeutic drug, a recreational drug, a performance-enhancing drug, a biomarker indicative of a diseased condition, a hormone, an antibody, a metabolite of any of the aforesaid, a combination of any of the aforesaid, or another similar indicator.

38. A sensor according to claim 36, in which the analyte is glucose, the catalyst is a combination of glucose oxidase and horseradish peroxidase and the reagent includes a leuco-dye.

39. A method according to claim 38 in which the leuco-dye is 2,2-azino-di-[3-ethylbenzthiazoline-sulfonate], tetramethylbenzidine-hydrochloride or 3-methyl-2-benzothiazoline-hydrazone in conjunction with 3-dimethylamino-benzoicacide.

40. A sensor according to claim 25 or claim 26 that is an electrochemical sensor comprising electrodes, means for extracting the physiological fluid, a reagent, and means for exposing the reagent to the fluid and the measurable characteristic is:

an inter-electrode impedance;

an inter-electrode current;

a potential difference;

an amount of charge;

a change over time of any of the aforesaid;

any combination of the aforesaid; or

any other indicator of the amount of electricity passing from one electrode to another, or the extent to which exposure of the sensor to the fluid generates electrical energy or electrical charge or otherwise affects the electrical characteristics of the sensor.

41. A sensor according to claim 40, in which the electrochemical sensor comprises a substrate, an electrode layer containing the electrodes, and at least a first reagent layer.

42. A sensor according to claim 41 in which the analyte is glucose and the reagent layer comprises glucose oxidase.

43. A system according to any one of claims 1-24 and 27, in which the sensor is an accordance with any one of claims 25, 26 and 28-42.

44. A system according to any one of claims 1-24, 27 and 43, in which the receiver is, or is incorporated into, a hand-held device, a portable device, a PDA, a mobile telephone, or a laptop computer.

45. A system according to any one of claims 1-24, 27, 43 or 44, in which the wireless device is adapted to store the data pending later interrogation.

46. A sensor according to any one of claims 28-42, in which the wireless device is adapted to store the data pending later interrogation.

47. A system according to any one of claims 1-24, 27 and 43-45, in which the wireless device is an RFID tag.

48. A sensor according to any one of claims 28-42 and 46, in which the wireless device is an RFID tag.

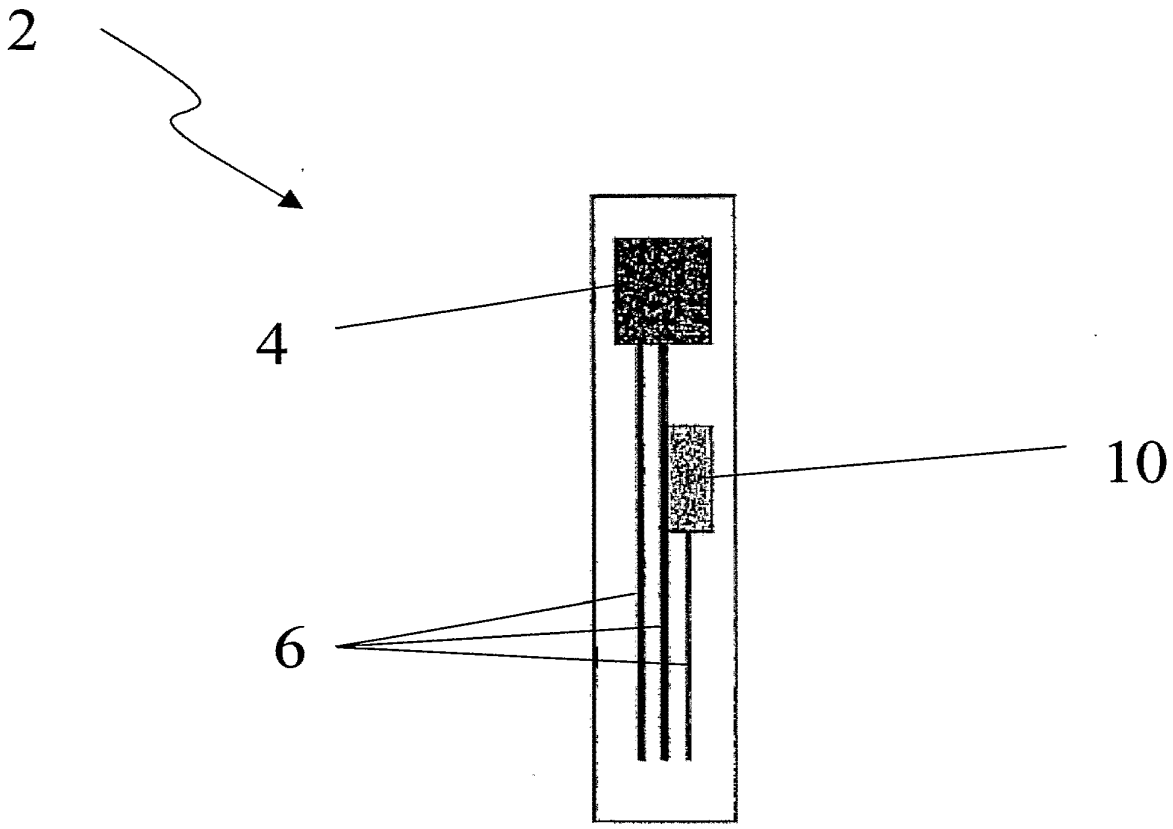


FIGURE 1

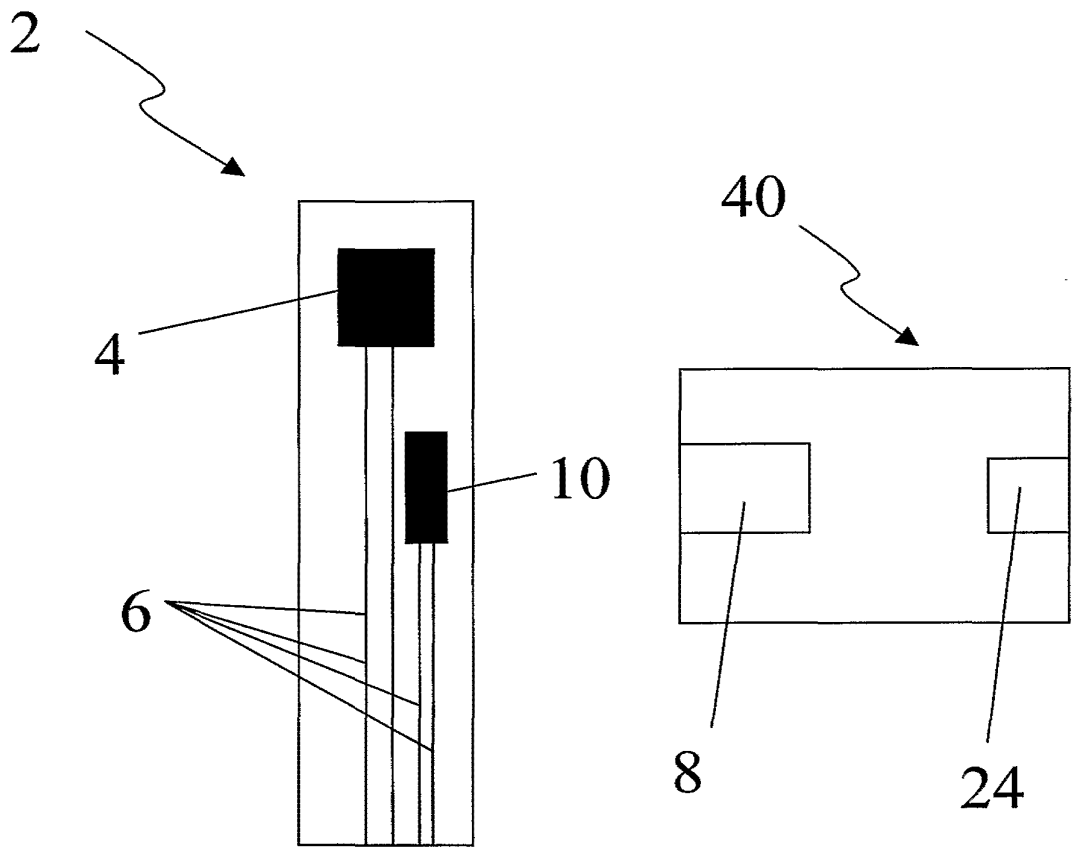


FIGURE 2

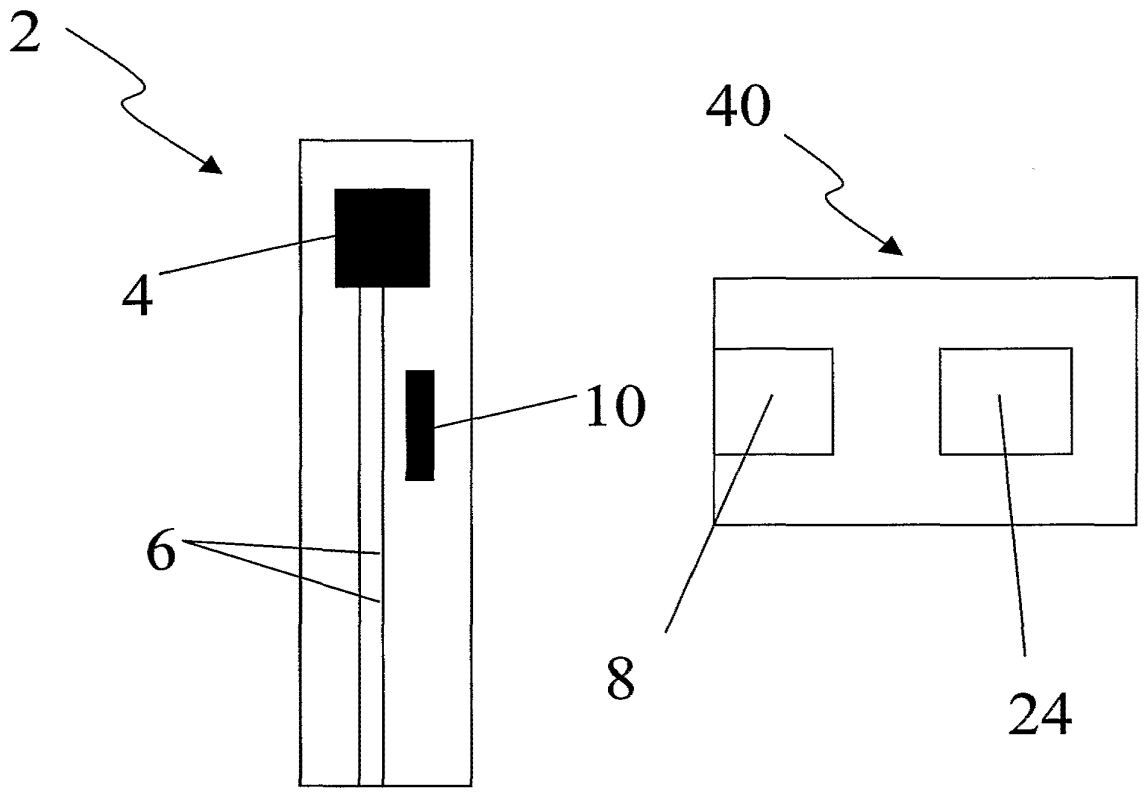


FIGURE 3

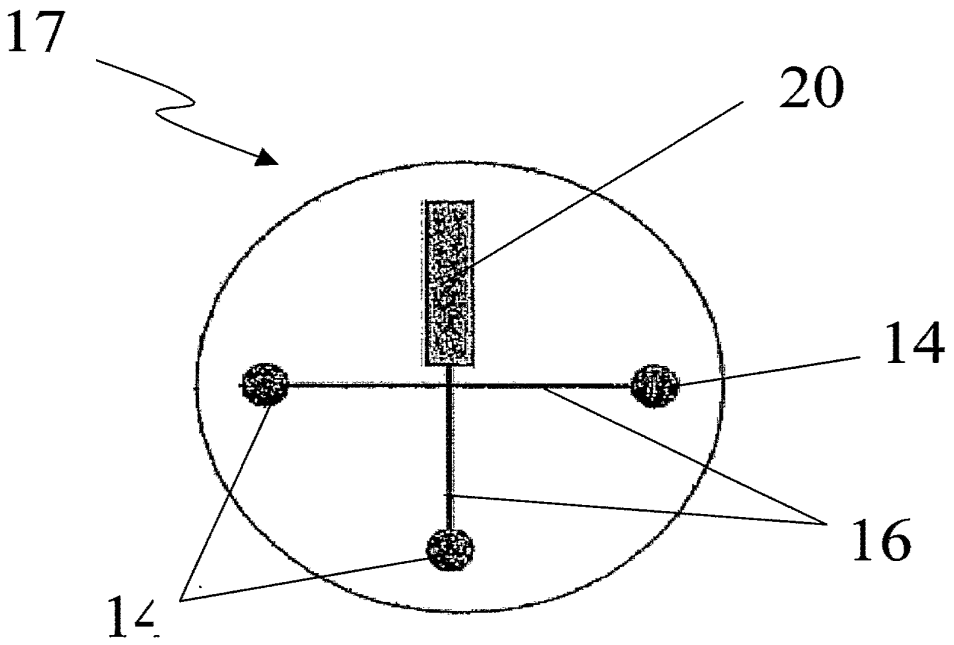


FIGURE 4

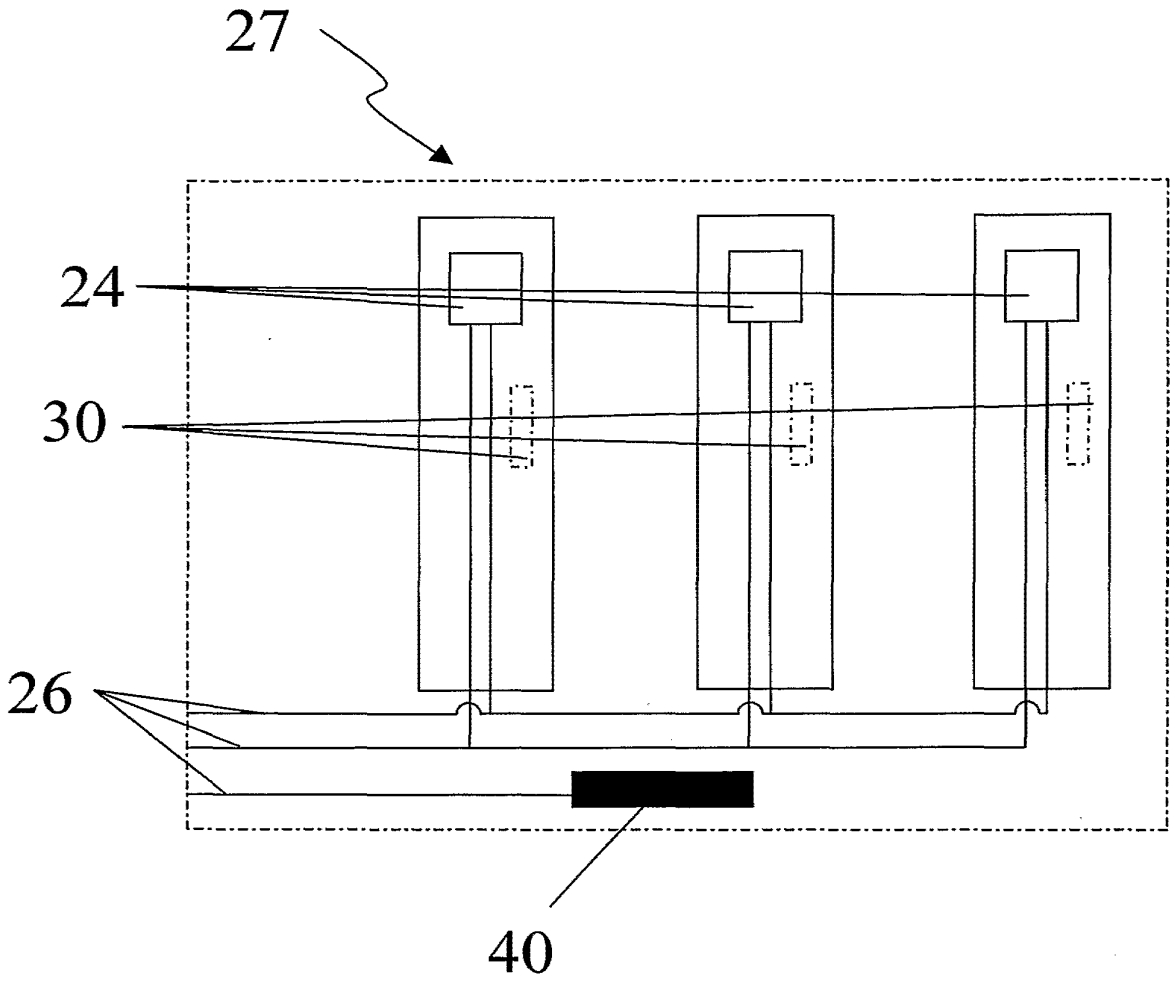


FIGURE 5

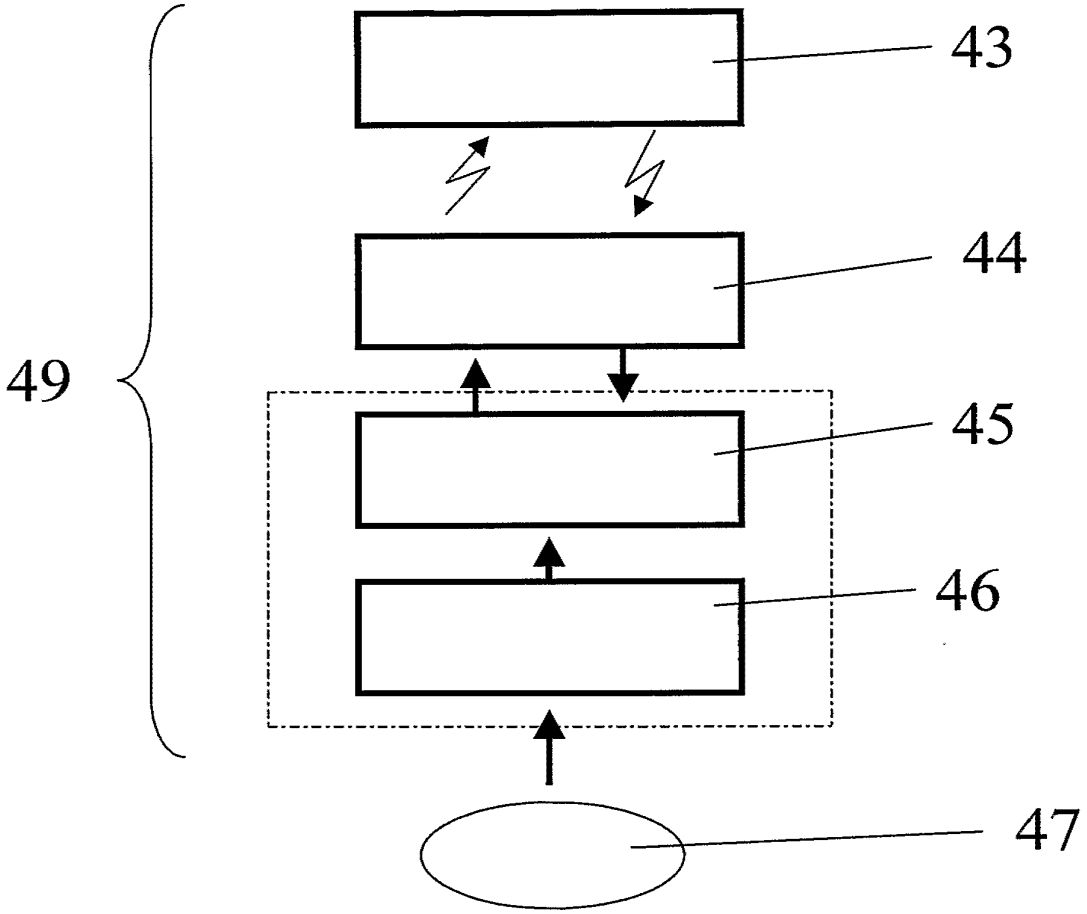


FIGURE 6

INFORMATION UP	*INFORMATION DOWN*
PERSONALISED DATA *HAEMATOCRIT* *CALIBRATION CODE INFORMATION* *STRIP LOT/BATCH NUMBER* *SHELF LIFE EXPIRY* *COUNTRY CODE* *COUNTRY FLAVOURING E.G.* *- LANGUAGE CHOICE* *- UNITS CHOICE (mg/dL, mm/L)* *- SOFTWARE UPGRADE/CORRECTIONS* *- PARAMETERS FOR TESTING ALGORITHM* *- SELF LEARNING PARAMETERS* *- CONTROL SOLUTION INFORMATION* *AND/OR PARAMETERS INFORMATION FOR USER INTERFACE FOR USER INTERFACE AND/OR INFORMATION ABOUT NEW PRODUCTS AND/OR INFORMATION ABOUT PERFORMANCE OF PRESENT PRODUCT* *- CONTAINER OPEN-LIFE EXPIRY (E.G.90 DAYS OR <90DAYS)*	*DATE FIRST STRIP REMOVED FROM VIAL* *UPDATE STRIP COUNT* *METER SERIAL NUMBER* *TEST RESULTS:-* *FROM THIS SENSOR BANK AND FOR PREVIOUS SENSOR BANKS* *TIME/SENSOR USE/DATA RESULT (RAW & FINAL)* *CALIBRATION CODE USED, BATCH/LOT OR STRIP NUMBER, FOOD (DATE, TYPE, AMOUNT); EXERCISE (DATE, TYPE, AMOUNT); HEALTH (TYPE OF CONDITION, PROGRESS ETC); STRES (DATE, AMOUNT); HYPO ALERTS (TYPE, AMOUNT); ETC* *SELF LEARNING PARAMETERS* *IDENTIFICATION INFORMATION* *FOOD AND EXERCISE INFORMATION* *NAME* *DETAILED PATIENT RECORD* *HBA1C* *BLOOD PRESSURE* *SYMPTOMS* *OTHER HEALTH FACTORS* *EXERCISE* *FOOD* *HISTORY* *CRC, CHECKSUM OR OTHER MEANS FOR CONFIRMING MEMORY CONTENTS*

FIGURE 7

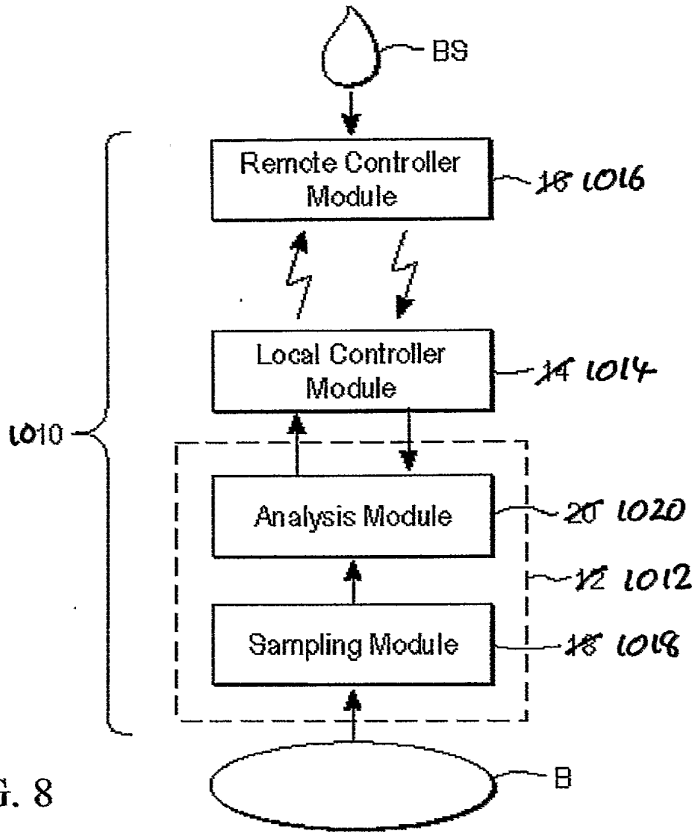

BS
Remote Controller Module
16 1016
Local Controller Module
14 1014
1010
Analysis Module
20 1020
12 1012
Sampling Module
18 1018
B

FIG. 8

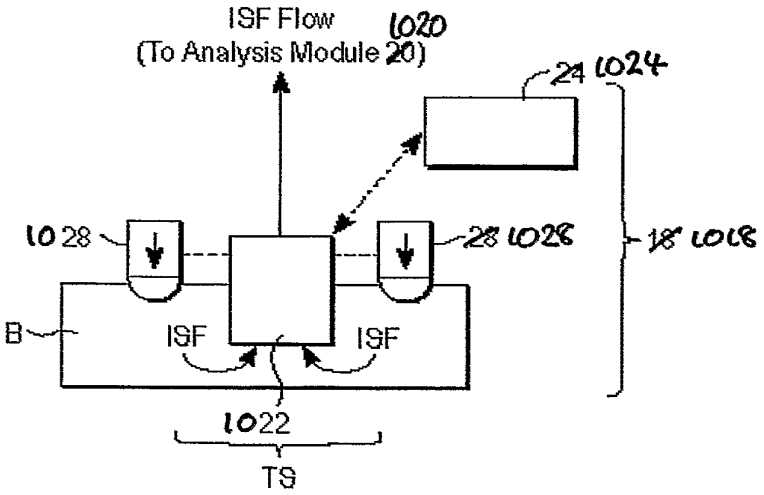

ISF Flow
(To Analysis Module 20)
1020
24 1024
1028
28 1028
18 1018
B
ISF
ISF
1022
TS

FIG. 9

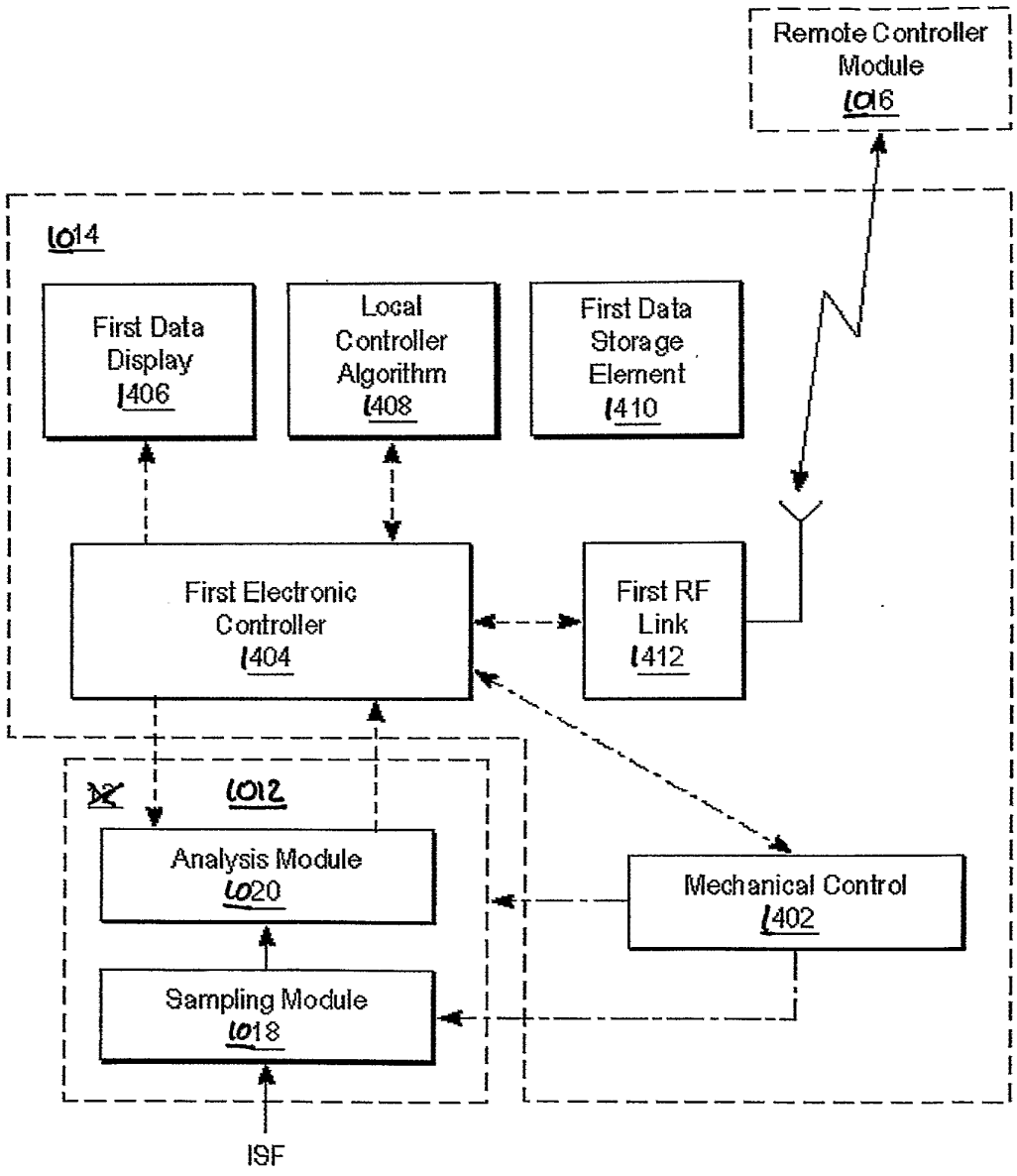

Remote Controller Module
1016
1014
First Data Display
1406
Local Controller Algorithm
1408
First Data Storage Element
1410
First Electronic Controller
1404
First RF Link
1412
1012
Analysis Module
1020
Mechanical Control
1402
Sampling Module
1018
ISF

FIG. 10

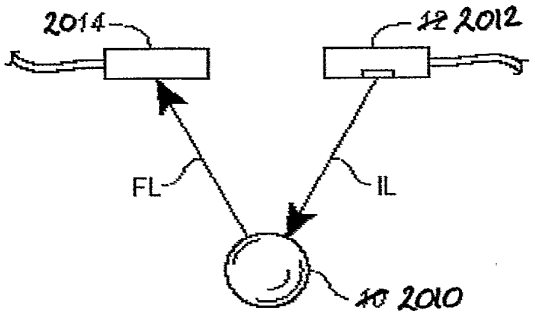


FIG. 11

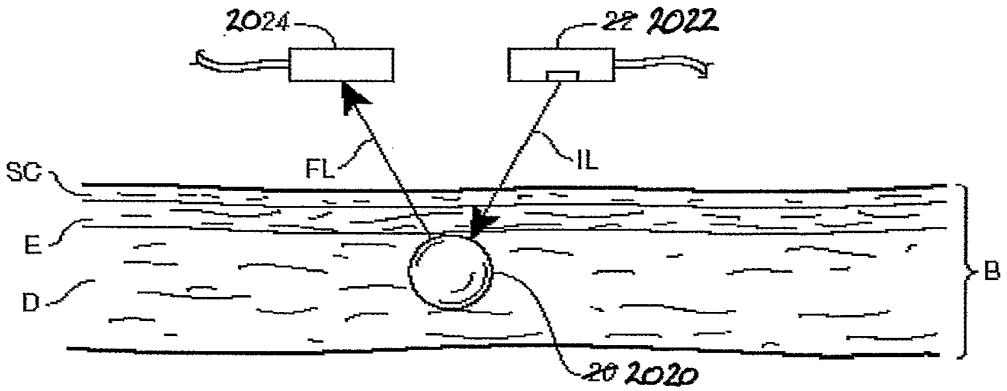


FIG. 12

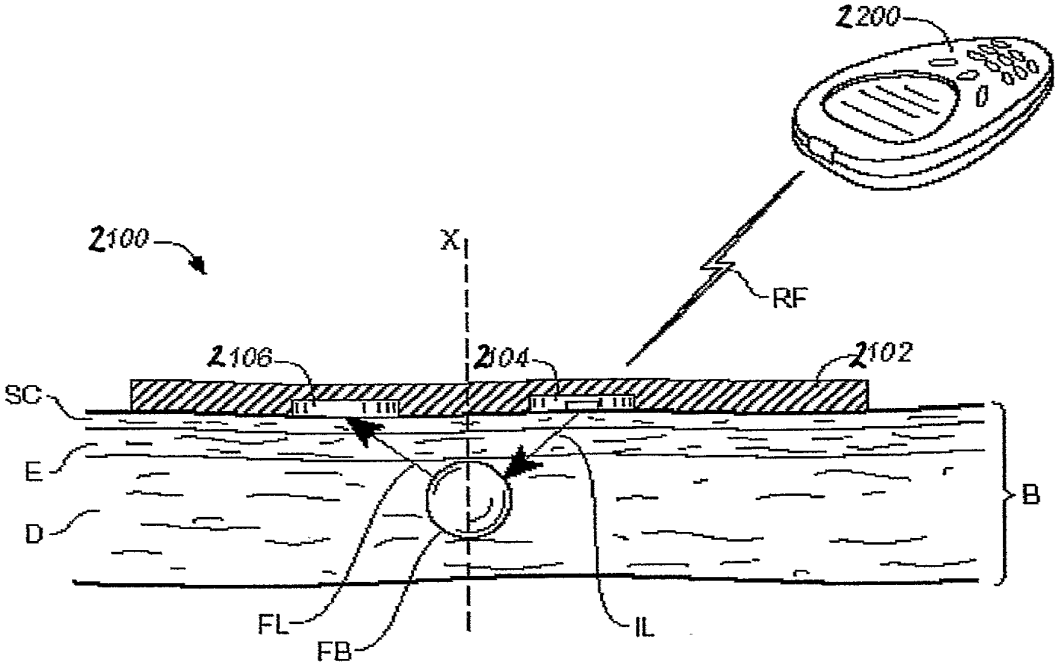


FIG. 13A

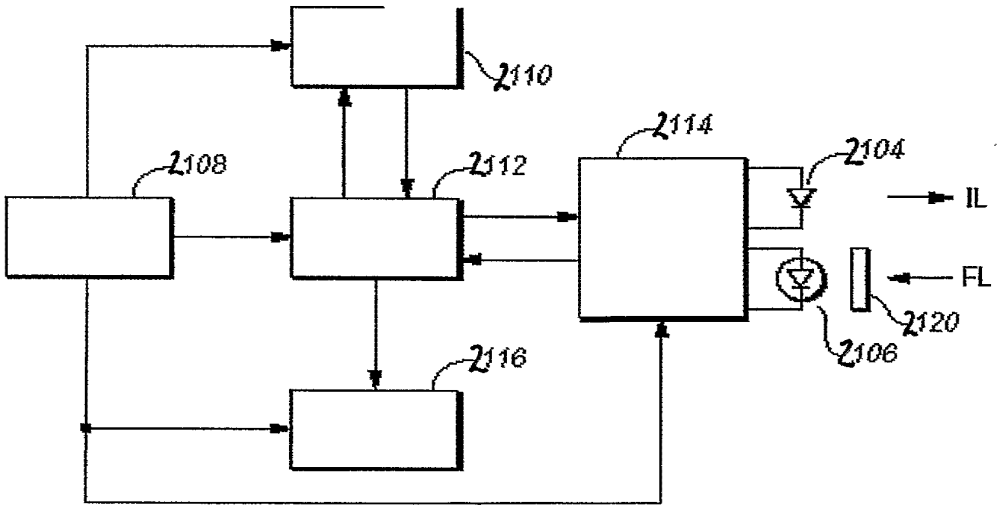


FIG. 13B

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2005/031271

A. CLASSIFICATION OF SUBJECT MATTER
G01N33/487 G01N33/58 A61B5/00 A61K49/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01N A61B A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS, INSPEC, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 102 37 602 A1 (I.E.M. INDUSTRIELLE ENTWICKLUNG MEDIZINTECHNIK UND VERTRIEBSGESELLSCHA) 18 March 2004 (2004-03-18) abstract	1-48
X	US 6 217 744 B1 (CROSBY PETER) 17 April 2001 (2001-04-17) the whole document	1-48
X	WO 03/048998 A (KIMBERLY-CLARK WORLDWIDE, INC) 12 June 2003 (2003-06-12) page 14, line 14 - line 31 page 26, line 27 - page 27, line 15 page 30, line 1 - page 39, line 2; figure 1	1-48

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
4 January 2006	13/01/2006

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Komenda, P

3

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2005/031271

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 2005/012900 A (ROCHE DIAGNOSTICS GMBH; F. HOFFMAN-LA ROCHE AG; BHULLAR, RAGHBIR, S; B) 10 February 2005 (2005-02-10) page 13, line 25 - line 29 page 22, line 1 - page 23, line 12; figures 1,2	1-48
P,X	WO 2005/074161 A (PEETERS, JOHN, P) 11 August 2005 (2005-08-11) paragraphs '0050!, '0056! - '0058!	1-48
Y	US 6 232 130 B1 (WOLF DAVID E) 15 May 2001 (2001-05-15) cited in the application the whole document	25-34
Y	US 6 285 899 B1 (GHAEM SANJAR ET AL) 4 September 2001 (2001-09-04) the whole document	25-34

3

Form PCT/ISA/210 (continuation of second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

[redacted]formation on patent family members

International Application No
PC[redacted]US2005/031271

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
DE 10237602	A1	18-03-2004	NONE		
US 6217744	B1	17-04-2001	NONE		
WO 03048998	A	12-06-2003	AU	2002348223 A1	17-06-2003
			US	2004078219 A1	22-04-2004
WO 2005012900	A	10-02-2005	WO	2004113910 A1	29-12-2004
WO 2005074161	A	11-08-2005	NONE		
US 6232130	B1	15-05-2001	NONE		
US 6285899	B1	04-09-2001	NONE		

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum
Internationales Büro

PCT

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20. April 2006 (20.04.2006)

(10) Internationale Veröffentlichungsnummer
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(25) Einreichungssprache: Deutsch

(26) Veröffentlichungssprache: Deutsch

(30) Angaben zur Priorität:
10 2004 048 864.9 7. Oktober 2004 (07.10.2004) DE

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(75) Erfinder/Anmelder *(nur für US)*: **ROESICKE, Bernd** [DE/DE]; Unter den Birken 6, 68305 Mannheim (DE). **SEIDENSTRICKER, Manfred** [DE/DE]; Mosbacher Strasse 16, 68259 Mannheim (DE).

(74) Gemeinsamer Vertreter: **ROCHE DIAGNOSTICS GMBH**; Früh, Johanna, Patentabteilung, 68298 Mannheim (DE).

(81) Bestimmungsstaaten *(soweit nicht anders angegeben, für jede verfügbare nationale Schutzrechtsart)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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Erklärungen gemäß Regel 4.17:

— *hinsichtlich der Berechtigung des Anmelders, die Priorität einer früheren Anmeldung zu beanspruchen (Regel 4.17 Ziffer iii)*

— *Erfindererklärung (Regel 4.17 Ziffer iv)*

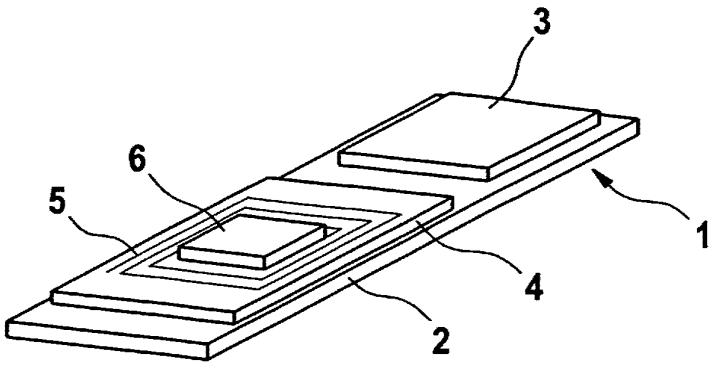
Veröffentlicht:

— *mit internationalem Recherchenbericht*

Zur Erklärung der Zweibuchstaben-Codes und der anderen Abkürzungen wird auf die Erklärungen ("Guidance Notes on Codes and Abbreviations") am Anfang jeder regulären Ausgabe der PCT-Gazette verwiesen.

(54) Title: ANALYTICAL TEST ELEMENT WITH WIRELESS DATA TRANSMISSION

(54) Bezeichnung: ANALYTISCHES TESTELEMENT MIT DRAHTLOSER DATENÜBERTRAGUNG



(57) Abstract: The invention relates to a system for determining the concentration of an analyte in a body fluid, which comprises an analytical test element and an implement which is separate from said test element. At least a part of the electrical components of the system are polymer electronic components. The analytical test element carries an area comprising an analytical chemical for detection of the analyte and a transponder for the wireless transmission of batch-specific data and/or measured values. The implement is provided with a reading module for the wireless transmission of data and power to the test element and an evaluation unit for evaluating the data or measured values received by the transponder.

(57) Zusammenfassung: Die Erfindung betrifft ein System zur Bestimmung der Konzentration eines Analyten aus einer Körperflüssigkeit, das ein analytisches Testelement und davon getrennt ein Instrument beinhaltet, wobei zumindest ein Teil der elektrischen Komponenten des Systems auf der Basis von Polymerelektronik ausgebildet ist. Auf dem analytischen Testelement befindet sich ein Bereich mit Nachweischemie zum Nachweis des Analyten sowie ein Transponder zur drahtlosen Übertragung von chargenspezifischen Daten und/oder Messwerten. Das Instrument weist ein Lesemodul zur drahtlosen Übertragung von Daten und Energie zum Testelement sowie eine Auswerteeinheit zur Auswertung der vom Transponder empfangenen Daten oder Messwerte auf.

WO 2006/040083 A1

Analytisches Testelement mit drahtloser Datenübertragung

Beschreibung

Die vorliegende Erfindung betrifft ein System zur Bestimmung der Konzentration eines Analyten aus einer Körperflüssigkeit. Weiterhin betrifft die Erfindung ein Verfahren zur Herstellung eines solchen Systems.

Die Untersuchung von Körperflüssigkeiten ermöglicht in der klinischen Diagnostik das frühzeitige und zuverlässige Erkennen von pathologischen Zuständen sowie die gezielte und fundierte Kontrolle von Körperzuständen. Für einzelne Analysen, die gezielt auf einen Parameter gerichtet sind, werden heutzutage oftmals wenige Mikroliter bis hin zu weniger als einem Mikroliter Blut benötigt. Zur Blutgewinnung wird üblicherweise durch die Haut z. B. in die Fingerbeere oder das Ohrläppchen der zu untersuchenden Person mit Hilfe einer sterilen, scharfen Lanzette gestoßen. Diese Methode eignet sich insbesondere, wenn die Analyse der Blutprobe unmittelbar nach der Blutgewinnung durchgeführt werden kann.

Für die chemische und biochemische Analyse von Körperflüssigkeiten haben sich in den dafür spezialisierten Labors, aber insbesondere auch für den Einsatz außerhalb fester Labors trägergebundene Schnelltests etabliert. Basierend auf einer eigens entwickelten Trockenchemie sind solche trägergebundenen Schnelltests, trotz der oftmals komplexen Reaktionen unter Beteiligung empfindlicher Reagenzien, einfach und unkompliziert, selbst von Laien, durchzuführen. Prominentestes Beispiel für trägergebundene Schnelltests sind Teststreifen für die Bestimmung des Blutglukosegehalts bei Diabetikern.

Bei heute verwendeten diagnostischen Testen für den Nachweis eines Analyten (z. B. Blutglukose) in einer Körperflüssigkeit (z. B. Blut) sind die Funktion des Stechens zum Erzeugen einer Hautöffnung und die Nachweisfunktion üblicherweise auf mehrere Bauteile aufgeteilt, z. B. eine Stechhilfe zum Stechen und Erzeugen eines Bluttropfens, und ein analytisches Testelements, z. B. ein Teststreifen, für die Aufnahme des Bluttropfens, die Weiterleitung des Blutes von der Aufnahmestelle zum Nachweisbereich, und den Nachweis eines Analyten, z. B. der Blutglukose.

Vor allem im Bereich des so genannten "Home-Monitoring", also dort, wo medizinische Laien selbst einfache Analysen des Bluts durchführen, und dort insbesondere für die regelmäßige, mehrmals täglich durchzuführende Blutgewinnung durch Diabetiker für die Kontrolle der Blut-

BESTÄTIGUNGSKOPIE

glukosekonzentration, werden Lanzetten und dazu passende Geräte angeboten, die eine möglichst schmerzarme und verlässliche Blutgewinnung ermöglichen. Als Beispiele für Lanzetten und Stechhilfen seien die kommerziell erhältlichen Geräte (Stechhilfen) und Lanzetten Glucolet® der Bayer AG und Softclix® der Roche Diagnostics GmbH genannt. Solche Lanzetten und Geräte sind z. B. Gegenstand von WO 98/48695, EP 0,565,970, US 4,442,836 oder US 5,554,166.

Die eigenhändige Blutzuckerbestimmung ist heute eine weltweit verbreitete Methode in der Diabetes-Kontrolle. Blutzuckergeräte im Stand der Technik wie z. B. Accu-Chek Sensor® (von Roche Diagnostics) bestehen aus einem Messgerät, in das ein Testelement (Teststreifen) eingeführt wird. Der Teststreifen wird beispielsweise mit einem Blutstropfen in Kontakt gebracht, der zuvor mittels einer Stechhilfe aus der Fingerbeere gewonnen wurde. Das Blut wird auf dem Teststreifen in den Bereich transportiert, in dem sich die Nachweischemie befindet. Dort reagiert der gesuchte Analyt mit der Nachweischemie und generiert dabei ein messbares Signal, z. B. einen elektrischen Stromimpuls oder eine Farbänderung. Das Messsignal wird vom Messgerät ausgewertet und auf dem Display des Blutzuckergerätes wird dem Benutzer der aktuelle Blutzuckerwert angezeigt.

Stand der Technik

Für eine konsequente Überwachung des Blutzuckergehaltes ist es erforderlich, die Glukosemessung regelmäßig, beispielsweise mehrmals täglich, durchzuführen. Für jede Messung wird ein neuer Teststreifen benötigt, der in Vorratsdosen zu beispielsweise 50 Stück bereitgestellt wird. Hierbei ist zu beachten, dass die Teststreifen je nach Charge eine unterschiedliche Qualität und unterschiedliche Eigenschaften aufweisen können, die das Messergebnis beeinflussen. Es ist daher erforderlich, das Glukosemessgerät vor dem Einlegen des Messstreifens zu kalibrieren. Der Grund für diese Schwankungen liegt in unvermeidbaren Toleranzen während der Herstellung der Teststreifen sowie in der empfindlichen Nachweischemie. Um dies zu kompensieren, werden von jeder Produktionscharge umfangreiche Stichproben vermessen und daraus chargenspezifische Kalibrationsdaten ermittelt. Diese Daten werden zusammen mit den Teststreifen zum Kunden ausgeliefert, sind für diesen aber nicht sichtbar. Der Datensatz besteht aus einer Chargennummer und Werten die eine Korrekturfunktion beschreiben.

Es ist bekannt, dass der Vorratsbehälter eine aufgedruckte Nummerncodierung enthält, die über eine entsprechende Eingabeeinheit am Glukosemessgerät eingegeben werden muss, um das Glukosemessgerät auf die in dieser Vorratsdose befindlichen Teststreifen einzustellen. Weiterhin

ist bekannt, dass eine Filmfolie jeder Teststreifenpackung beiliegt. Die transparente Filmfolie enthält einen Barcode, der binär codiert die Koeffizienten eines Polynoms n-ter Ordnung enthält. Bei den Glukosemessgeräten Accu-Chek Compact© und Accu-Chek Comfort© von der Roche Diagnostics GmbH beispielsweise wird den Teststreifen ein elektronisches Speichermedium, ein sog. ROM Key, beigelegt, auf dem ein kompletter Satz der Koeffizienten eines Polynoms gespeichert ist (siehe US 5,053,199). Dieser ROM Key wird in das Messgerät eingesteckt, die Daten werden vom Messgerät aus dem Speicherchip gelesen und zur Korrekturrechnung verwendet. US 6,689,320 beschreibt ebenfalls einen elektronischen Datenträger, der allerdings in einem sog. Code Carrier in das Messgerät eingelegt wird; die Daten werden hierbei mit einem Transponder übertragen.

Allen vorgenannten Kalibriermethoden ist gemeinsam, dass der Anwender eine Vielzahl von Schritten durchführen muss, um das Glukosemessgerät auf die Teststreifen-Charge zu kalibrieren. Es besteht die Gefahr, dass bei der manuellen Eingabe Fehler auftreten, oder dass das Einlesen des Speicherchips oder das Einlegen der Filmfolie mit dem Chargen-Code vergessen wird. Insbesondere, wenn der Anwender mehrere Dosen mit Teststreifen verwendet, besteht die Gefahr, dass eine Kalibrierung des Glukosemessgeräts auf die aktuell verwendete Teststreifencharge unterbleibt. Zur Vermeidung dieses Risikos wird heutzutage meist zusätzlich zu dem externen Datenspeicher, der die Kalibrationsdaten enthält, auf die Teststreifen selbst eine Chargenidentifikation in Form eines Barcodes oder Magnetstreifens aufgebracht. Darüber hinaus muss besonders darauf geachtet werden, dass trotz der getrennten Logistik von Teststreifen und Datenträger sicher gestellt ist, dass die richtigen Korrekturwerte den Teststreifen beigelegt werden.

Eine Methode, die erwähnte Verwechslungsgefahr zu vermeiden, besteht darin, die gesamten Kalibrationsdaten direkt mit dem Teststreifen zu verbinden. Der Teststreifen für das Reflochek© von der Roche Diagnostics GmbH beispielsweise hat einen Barcode aufgedruckt, und auf den Reflotron©-Streifen (Roche Diagnostics GmbH) ist ein Magnetstreifen aufgeklebt.

Im Zuge der Entwicklung hin zu immer kleineren Teststreifen und gleichzeitig immer mehr Kalibrationsdaten stößt jedoch die Datenkapazität entsprechend verkleinerter Barcode- oder Magnetstreifen an ihre Grenzen.

DE 102 37 602 beschreibt daher ein System zur Blutglukosemessung, bei der auf dem Teststreifen selbst ein Datenträger mit ausreichender Kapazität vorhanden ist, um alle erforderlichen Daten

darauf zu speichern. Die Kalibriereinheit in diesem Blutglukosemess-System besteht aus einer Empfangseinheit, die mit einer Sendeeinheit auf dem Testträger zusammenwirkt, um drahtlos ein Signal zu übermitteln, das die Qualität und/oder die Eigenschaften des Teststreifens wiedergibt. Durch diese drahtlose und berührungslose Übermittlung der Kalibrationsdaten wird erreicht, dass der Anwender keine zusätzlichen Schritte zur Kalibrierung auf den aktuell verwendeten Teststreifen durchführen muss. Es ist lediglich erforderlich, dass der Testträger in die Nähe des Messgeräts gehalten wird, was z. B. beim Einschieben in das Messgerät der Fall ist. Die Empfangseinheit und die Sendeeinheit bilden hierbei ein sog. Transpondersystem.

R. Puers beschreibt ein Transpondersystem, das in orthopädischen Implantaten eingesetzt wird (Linking sensor systems with telemetry: impact on the system design; Sensors and Actuators (1996) 169-174).

Als ein Beispiel für eine Übertragung analoger Daten beschreibt J. Black et al. einen implementierbaren amperometrischen Glukosesensor mit integrierter Telemetrieeinheit (Integrated sensor-telemetry system for in vivo glucose monitoring; Sensors and Actuators (1996) 147-153).

In WO 031 00942 ist ein Herzschrittmacher beschrieben, der seine Energie über einen Transponder von einer extrakorporalen Batterieeinheit erhält. Im Gegenzug sendet der Herzschrittmacher seinen Ladezustand nach außen.

US 6,217,744 betrifft ein Disposable zur Blutglukosemessung, das seine Messdaten über einen Transponder zum Informationsgerät überträgt, wobei die Blutprobe selbst als Elektrolyt für die Batterie in dem Disposable dient.

Ein Transpondersystem umfasst ein Lesesystem, das hier der Empfangseinheit im Instrument entspricht, und den eigentlichen Transponder, in diesem Fall die Sendeeinheit auf dem Teststreifen. Vom Lesesystem wird die für die Messung notwendige Energie in den Teststreifen eingebracht, d. h. der Teststreifen besitzt keine eigene Stromversorgung. Die Sendeeinheit auf dem Teststreifen sendet im Gegenzug die gespeicherten Kalibrationsdaten sowie die Messsignale der aktuellen Messung an das Messgerät. Die Transponder werden üblicherweise mit Mikroprozessoren in Siliziumtechnologie realisiert. Auch wenn die Produktionskosten für Siliziumchips in den letzten Jahren aufgrund von Miniaturisierung, Integration und Optimierung der Herstellprozesse deutlich gesunken sind, sind sie dennoch immer noch so hoch,

dass sie eine Messung unverhältnismäßig verteuern würden, wenn jeder einzelne Teststreifen, der nach einer einzigen Messung verworfen wird, mit einem solchen Siliziumchip ausgestattet wäre.

Beschreibung der Erfindung

Die Erfindung beschreibt ein System, das sicherstellt, dass bei jeder Messung vertauschungssicher die korrekten Kalibrationsdaten verwendet werden. Darüber hinaus wird die Qualität der Messwerte verbessert, indem die Messwertgenauigkeit durch einen verbesserten Messaufbaus erhöht wird.

Die vertauschungssicheren Kalibrationsdaten werden dadurch gewährleistet, dass auf jedem Teststreifen die Chargenkennung und die Kalibrationsdaten gespeichert sind. Um die erforderliche Datenmenge zu speichern und auf das Messgerät zu übertragen, wird die eingangs erwähnte Transpondertechnologie verwendet. Insbesondere werden hierbei die elektrischen Komponenten auf dem analytischen Testelement zumindest teilweise auf der Basis von Polymerelektronik ausgebildet.

Die Qualität der Messwerte wird erfindungsgemäß dadurch erhöht, indem das elektrochemische Messsystem nach außen galvanisch isoliert wird. Für diese galvanische Trennung wird die eingangs erwähnte Transpondertechnologie verwendet. Insbesondere werden die elektrischen Komponenten auf dem analytischen Testelement zumindest teilweise auf der Basis von Polymerelektronik ausgebildet.

Es wurde gefunden, dass die erfindungsgemäße Anwendung der Transpondertechnologie auf Systeme zur Bestimmung eines Analyten aus einer Körperflüssigkeit unter Nutzung der Polymerelektronik besonders vorteilhaft ist.

Die Polymerelektronik basiert auf der Tatsache, dass bestimmte Polymere (z. B. Pentacen, Polythiophen) halbleitende Eigenschaften besitzen und somit elektronische Schaltkreise realisiert werden können. So kann beispielsweise ein binärer Datenspeicher direkt in das Substrat eines Teststreifens eingebracht werden (Vom organischen Transistor zum Plastik-Chip, Physik Journal 2 (2003) Nr. 2, S. 31-36). Hierbei werden durch punktuelles Anlegen elektrischer Felder je nach Polarität, räumlich diskrete Zonen entweder niederer oder hoher Leitfähigkeit durch das leitfähige Polymersubstrat hindurch, erzeugt. Nach Entfernen der Spannung bleibt der Zustand erhalten. Durch Umpolen der elektrischen Spannung kann der Zustand wieder rückgängig

gemacht werden. Es sind somit Schreib/Lesevorgänge und Speicherung von Informationen wie Chargennummern und Korrekturkurven direkt auf dem Testsubstrat möglich. Die punktuellen Felder werden beispielsweise durch das Anlagen von Spannung an Spalten- und Zeilenleitungen mittels einer Decoderschaltung, vorzugsweise aus halbleitenden Polymeren, gebildet (Polymer Memory, Technology Review September 2002, S. 31). Darüber hinaus können auch weitere Bauteile die zur Realisierung elektrischer Transponderfunktionen notwendig sind (Transistoren, Dioden, Widerstände, Kondensatoren, Spulen, Leitungen, Kontakte) mit leitfähigen Polymeren unmittelbar auf dem Teststreifen realisiert werden (Fast polymer integrated circuits, American Institute of Physics 2002, S. 1735-1737).

Für diese neue Technologie werden Begriffe wie Integrated Plastic Circuits (IPC), organische Elektronik, Polytronik, Electronic Plastic, organische Halbleiter oder Conductive Polymers oft synonym verwendet. Diese Polymere lassen sich beispielsweise durch einfache Drucktechniken, wie Offset-, Tampon-, Siebdruck oder auch Technologien ähnlich dem Laser- oder Tintenstrahldruck, aufbringen, z. B. unter Verwendung von Polymeren in Lösung (sog. elektronischer Tinte). Diese Technik ist insbesondere bei Anwendung auf flache Trägerfolien vorteilhaft, wie sie üblicherweise bei analytischen Testelementen der Fall ist. Da zudem Druck- und Laminiertechniken bereits für die Herstellung analytischer Testelemente routinemäßig eingesetzt werden, lässt sich die Polymerelektronik ohne großen Aufwand in den vorhandenen Produktionsablauf integrieren. Beispielsweise ist in DE 102 53 154 beschrieben, wie die Elektronik für ein komplettes Blutglukose Messsystem im Kreditkartenformat, bestehend aus Messeinheit und Biosensor, in einem einzigen drucktechnischen Prozess in Polymerelektronik aufgebracht wird.

Üblicherweise werden Teststreifen in so genannten Endlos-Prozessen (Rolle-zu-Rolle Prozessen) produziert. Die Rollen werden anschließend zu Teststreifen vereinzelt und in Verpackungseinheiten (Dosen, Magazine) abgefüllt. Gleichzeitig werden von jeder Produktionscharge Stichproben gezogen und validiert. Die ermittelten Abweichungen von den Sollwerten werden über einen Algorithmus in einen Datensatz gewandelt und auf einem Datenträger gespeichert. Die verpackten Teststreifen werden mit den Datenträgern zusammengeführt und konfektioniert ausgeliefert.

Der erfindungsgemäße Einsatz der Transpondertechnologie in Kombination mit der Polymerelektronik ermöglicht das Aufbringen eines Transponders auf das analytische Testelement in einem einfachen und leicht in eine Rolle-zu-Rolle Produktion integrierbaren

Prozessschritt. Darüber hinaus ist ein Transponder aus Polymerelektronik extrem kostengünstig herstellbar, was insbesondere bei Einzelmessstreifen, die nach einmaligem Gebrauch verworfen werden, von großer Bedeutung ist. Die Erfindung ermöglicht es, die analytischen Testelemente während des Rolle-zu-Rolle Prozesses mit einer Chargenidentifikation zu versehen, und den vereinzelten und verpackten Testelementen berührungslos die Kalibrationsdaten aufzuspielen. D. h. das Speichern der Kalibrationsdaten auf einen gesonderten Datenträger und das Sicherstellen des korrekten Konfektionierens der Teststreifen mit dem entsprechenden Datenträger entfallen. Über das Transpondersystem können sowohl Daten auf das analytische Testelement aufgespielt als auch auf dem Testelement gespeicherte bzw. während der Messung generierte Daten abgefragt werden.

So können beispielsweise im Produktionsprozess zunächst die Chargennummern der in einer Verpackungseinheit abgefüllten Testelemente von einer speziellen Leseeinheit abgefragt werden. In der Leseeinheit sind die Kalibrationsdaten zu den dazugehörigen Chargennummern gespeichert. Die Leseeinheit wählt die passenden Kalibrationsdaten aus und überträgt diese auf die Testelemente. Zur Kontrolle ob die Kalibrationsdaten korrekt übertragen wurden, können abschließend die gespeicherten Daten abgefragt werden. Hierbei kann beispielsweise die Anzahl der Antwort-Signale zur Kontrolle dienen, ob die korrekte Teststreifenanzahl verpackt wurde und ob alle Teststreifen den korrekten Datensatz gespeichert haben. Zusätzlich ist es denkbar, die analytischen Testelemente neben der Chargen- auch noch mit einer eindeutigen Identifikationsnummer zu versehen, um so gezielt jeden einzelnen Teststreifen beschreiben und abfragen zu können. Auf diese Weise stellt das erfindungsgemäße Verfahren sicher, dass bei jeder Messung die korrekten Kalibrationsdaten verwendet werden und eine Vertauschung, sowohl während der Konfektionierung in der Produktion als auch in der Anwendung beim Kunden, ausgeschlossen wird.

Bei den chargenspezifischen Kalibrationsdaten kann es sich beispielsweise um eine komplette Kalibrationskurve handeln, oder es werden bestimmte Stützstellen festgelegt, an die ein festgelegter und beispielsweise im Instrument hinterlegter Kurvenverlauf angepasst wird. Darüber hinaus kann die Kalibrationskurve als eine Polynomfunktion dargestellt werden, wobei beispielsweise entweder die gesamte Funktion oder, bevorzugterweise, die Variablen des Polynoms als chargenspezifische Kalibrationsdaten dienen, während die Polynomfunktion im Instrument abgelegt ist. Der Kurvenverlauf bzw. die Polynomfunktion können auch statt direkt im Instrument auf einem ROM Key abgespeichert sein, der dem Instrument beiliegt und vom Kunden in das Instrument eingesteckt wird. Falls zu einem späteren Zeitpunkt der Kurvenverlauf

angepasst werden muss, beispielsweise bei Einführung einer neuen Teststreifengeneration mit leicht verändertem Messverhalten, kann durch einen einfachen Austausch des ROM Key das Instrument daran angepasst werden.

In einer bevorzugten Ausführungsform sind die chargenspezifischen Kalibrationsdaten auf dem analytischen Testelement bzw. auf dessen Verpackung gespeichert und der Kurvenverlauf der Kalibrationskurve ist, beispielsweise in Form einer Polynomfunktion, im Instrument gespeichert. Eine alternative Möglichkeit besteht darin, dass auf einem ROM Key mehrere Kalibrationskurven, beispielsweise unter verschiedenen Kennnummern, gespeichert sind und auf den Teststreifen ist die Kennnummer der zu dieser Charge passenden Kalibrationskurve gespeichert.

Ein weiteres Merkmal der erfindungsgemäßen Kombination von Transpondertechnologie und Polymerelektronik besteht in der Möglichkeit einer Verbesserung der Messtechnik auf dem analytischen Testelement. Das Messen elektrochemischer Größen beruht im Wesentlichen auf elektrolytischen Prozessen oder Elektronenbeweglichkeiten in flüssigen Phasen. Werden in einem gemeinsamen Flüssigkeitskreis mehrere elektrochemische Sensorsysteme verwendet, werden diese zwangsläufig durch gemeinsame elektrische Schaltkreise wie Spannungsversorgung und Masseleitungen, oder parasitäre Leitungsmechanismen elektrolytisch oder elektrisch undefiniert verbunden. In der Regel handelt es sich bei elektrochemischen Messungen um Gleichstrom- oder niederfrequente Prozesse, d. h. es sind im Wesentlichen galvanische, also stromleitende, Mechanismen. die zu Fehlerströmen führen, die einerseits die Messwerte, und andererseits die chemische Reaktion selbst verfälschen können. Um diese Problematik zu umgehen, bedient man sich heutzutage oft aufwendiger Trennverstärker. Hierbei werden die elektrochemischen Messsysteme soweit getrennt, dass nur die Verbindung über den unvermeidlichen flüssigen, elektrochemischen Pfad selbst besteht. Durch diese "Einfachverbindung" ist kein überlagerter Stromkreis vorhanden, über den parasitärer elektrischer Strom fließen kann. Heutzutage übliche transformatorische Trennverstärker sind meist teuer, da kleine Gleichgrößen (Strom, Spannung) aufwendig in Wechselgrößen überführt werden müssen. Für ein solches analytisches Testelement müsste eine zum restlichen System galvanisch getrennte zusätzliche Stromquelle bereitgestellt werden. Dies sind meist Batterien oder transformatorisch getrennte Netzteile, die eine relativ große Baugröße aufweisen. Alternativ zu elektrischen Trennverstärkersystemen gibt es auch optische Trennsysteme. Hierbei werden nach dem opto-elektrischen Prinzip die als elektrische Gleichgrößen gewonnenen Messwerte mit Lichtschranken übertragen. Bei optischen

Trennsystemen kann jedoch die Versorgungsenergie nur in Grenzen und mit relativ schlechtem Wirkungsgrad übertragen werden.

Es wurde gefunden, dass anstelle von Trennverstärker insbesondere auch Transponder geeignet sind, um elektrische Systeme galvanisch zu trennen. Die erfindungsgemäße Kombination von Transpondertechnologie und Polymerelektronik ermöglicht die Bereitstellung eines kostengünstig in großer Stückzahl herstellbaren analytischen Testelements, bei dem durch galvanische Entkopplung parasitäre Kriechströme vermieden werden. Insbesondere die geforderte Übertragung kleiner Messwerte bei hohen Potentialunterschieden ist mit Transpondern ohne Potentialverschleppungen möglich. Hierbei wird die Energie in Form einer Wechselspannung transformatorisch nach dem Induktionsprinzip von dem im Instrument befindlichen Lesemodul drahtlos und berührungslos zum auf dem analytischen Testelement befindlichen Sendemodul übertragen. Besonders die flachen, auf Folien aufgebrachten Aufbaustrukturen der Polymerelektronik ermöglichen eine gute, lineare magnetische Übertragung der Signale über die Transformatorspulen. Die Energie setzt die Messung auf dem analytischen Testelement in Gang. Das elektrische Messsignal wird zunächst als Gleichgröße (Strom oder Spannung) gewonnen, anschließend in eine Wechselgröße gewandelt und dann induktiv zum Instrument übertragen, beispielsweise durch magnetische Feldkopplung im Nahfeld, indem das Signal auf eine Trägerfrequenz aufmoduliert wird. Das erfindungsgemäße System ermöglicht daher eine kontaktlose, bidirektionale Datenübertragung.

Mit Polymerelektronik aufgebrachte Übertragungsspulen können extrem nah neben- bzw. übereinander liegen, etwa in einem Abstand von 0,1 mm. Dies ermöglicht den Einsatz kleiner Spulenabmessungen, was insbesondere im Zuge der Miniaturisierung der analytischen Testelemente von Vorteil ist. Mit der Technologie der Polymerelektronik können nicht nur planare Strukturen, sondern durch den Einsatz mehrere Layer dreidimensionale Strukturen wie die eines Feldeffekttransistors aufgebracht werden (Organic field-effect transistors – the breakthrough at last, Chemphyschem 2001, 2, 163-165).

Die Erfindung betrifft ein System zur Bestimmung der Konzentration eines Analyten in einer Körperflüssigkeit, das ein analytisches Testelement und davon getrennt ein Instrument beinhaltet, wobei zumindest ein Teil der elektrischen Komponenten des analytischen Testelements auf der Basis von Polymerelektronik ausgebildet ist. Auf dem analytischen Testelement befindet sich ein Bereich mit Nachweischemie zum Nachweis des Analyten und das Instrument weist eine Auswerteeinheit zur Auswertung von Daten auf.

Eine bevorzugte Ausführungsform der Erfindung betrifft ein oben beschriebenes System, wobei sich auf dem analytischen Testelement ein Sendemodul zur drahtlosen Übertragung von Daten befindet und das Instrument ein Lesemodul zur drahtlosen Übertragung von Daten aufweist. Sendemodul und Lesemodul arbeiten nach der eingangs beschriebenen Transpondertechnologie.

Das erfindungsgemäße System umfasst die Komponenten, die zur Bestimmung der Konzentration eines Analyten in einer Körperflüssigkeit notwendig sind. Minimal beinhaltet das System ein analytisches Testelement mit Nachweischemie und ein Instrument mit Auswerteeinheit. Insbesondere kann das System darüber hinaus beispielsweise eine Stechhilfe und eine Anzeigeeinheit umfassen, wobei diese beiden Komponenten sowohl in Testelement bzw. Instrument integriert als auch eigenständige Einheiten sein können.

Mit Analyt ist ein Bestandteil der Körperflüssigkeit gemeint, der im Nachweisbereich mit der Nachweischemie reagiert, so dass – ab einer gewissen Menge des Analyten – die Reaktion in einer Messanordnung gemessen werden kann. Eine bevorzugte Ausführungsform besteht darin, Blut als Probenflüssigkeit zu verwenden und Blutglukose als Analyt im Nachweisbereich nachzuweisen und daraus die Konzentration der Blutglukose zu ermitteln.

Neben Blut sind auch interstitielle Flüssigkeit und andere körpereigene Flüssigkeiten als Körperflüssigkeiten möglich. Ebenfalls ist es möglich, nicht nur einen Analyten, z. B. Blutglukose, sondern auch mehrere Analyten, z. B. HbA1C, nachzuweisen, und dies sowohl aus einer Körperflüssigkeit, z. B. Blut, als auch aus einem Gemisch mehrerer Körperflüssigkeiten, z. B. Blut plus interstitielle Flüssigkeit, durchzuführen.

Unter einem analytischen Testelement ist jede Form von trägergebundenen Schnelltests für die Diagnostik zu verstehen, insbesondere Schnelltests in Streifenform, sog. Teststreifen, hierbei insbesondere zur Bestimmung des Blutglukosegehalts bei Diabetikern.

Das Instrument bezeichnet den Teil des Systems, der die Messsignale, die im analytischen Testelement erzeugt werden, empfängt und in der Auswerteeinheit auswertet. Das Instrument kann außerdem eine Halterung enthalten, in der ein analytisches Testelement oder eine Verpackung für ein oder mehrere Testelemente, z. B. ein Container oder ein Magazin, positioniert wird. Darüber hinaus kann auch eine Anzeigeeinheit, z. B. ein LCD Display, in das

Instrument integriert sein. Üblicherweise stellt das Instrument ein batteriebetriebenes Handgerät dar.

Heutzutage werden häufig die elektrischen Leitungen und Kontakte auf dem analytischen Testelement in Gold oder ähnlich inerten Metallen ausgeführt und z. B. durch Laserablation strukturiert abgetragen. Erfindungsgemäß können die Leiterbahnen und Kontakte anstelle von Metall auch in Polymerelektronik ausgeführt werden. So kann beispielsweise ein heute auf dem Markt verfügbarer Teststreifen mit Goldkontakten und einem Datenträger (z. B. einem Magnetstreifen bzw. Barcode) zur Streifenidentifikation durch ein analytisches Testelement ersetzt werden, bei dem die elektrischen Leitungen und Kontakte durch Polymerelektronik-Leiterbahnen und -Kontakte ausgebildet sind. Bevorzugter Weise ist die Streifenidentifikation in einem Polymerelektronikspeicher abgelegt. In besonders bevorzugter Weise befindet sich auf dem analytischen Testelement auch ein Polymerelektronik-Transponder zum Beschreiben und Auslesen des Speichers. Selbstverständlich ist es auch möglich, nur die Goldkontakte oder nur den Datenträger durch Polymerelektronik zu ersetzen.

Erfindungsgemäß kann die Polymerelektronik sowohl auf dem Testelement als auch im Instrument verwendet werden. In einer bevorzugten Ausführungsform sind ein Teil oder auch alle elektrischen Komponenten auf dem analytischen Testelement auf der Basis von Polymerelektronik ausgebildet und im Instrument ist die Elektronik in konventioneller Technologie realisiert.

Das Sendemodul auf dem analytischen Testelement dient als Transponder, auf dem während der Produktion Daten gespeichert werden, wie zum Beispiel Identifikationsdaten (Chargennummer, Streifentyp, ggf. Seriennummer), Verfallsdatum sowie chargenspezifische Kalibrationsdaten. Es ist auch möglich, nach der Produktion zusätzlich Daten zu speichern, beispielsweise aktuelle Kundenhinweise, Logistikdaten, Informationen des Einzelhandels, z. B. der Apotheke, oder anderes. Sobald der Teststreifen in das Instrument eingelegt ist, werden dem Instrument beispielsweise die Identifikationsdaten zur Kontrolle übermittelt, beispielsweise ob der für das Instrument passende Teststreifen eingelegt und ob das Verfallsdatum abgelaufen ist. Gegebenenfalls können auch Hinweise oder Informationen für den Kunden, die vorab auf dem analytischen Testelement abgespeichert wurden, angezeigt werden. Anschließend können die Messsignale, die während der Messung der Konzentration des gesuchten Analyten erzeugt werden, vom Teststreifen zum Instrument übertragen werden.

Das Lesemodul wandelt die vom Sendemodul empfangenen Signale um und leitet sie weiter an die Auswerteeinheit, in der sie ausgewertet werden. Das Ergebnis, beispielsweise die Konzentration der Blutglukose, wird in der Anzeigeeinheit, z. B. einem LCD Display, dem Anwender angezeigt. Üblicherweise ist die Anzeigeeinheit in das Instrument integriert, es ist jedoch auch möglich, dass die Anzeige in einer eigenständigen Einheit realisiert ist. Beispielsweise kann das Testelement als Implantat oder Teilimplantat ausgebildet sein, das Instrument mit dem Lesemodul wird entsprechend über dem Testelement direkt auf der Haut oder über der Kleidung getragen, und die Anzeigeeinheit kann eine Art Armbanduhr sein, die am Handgelenk befestigt wird. Die Übertragung der Daten von Auswerteeinheit zur Anzeigeeinheit ist ebenfalls mit einem Transpondersystem realisiert. Darüber hinaus können auf diese Art natürlich auch noch weitere Module, insbesondere eine Insulinpumpe oder ein elektronisches Diabetik-Tagebuch, angesteuert werden.

Beispielsweise nutzt das erfindungsgemäße Transpondersystem zur drahtlosen Übertragung von einem implantatierten Testelement zu einem extra-korporalem Lesemodul Frequenzen im Bereich von 125 kHz mit einer Reichweite im Körper von cirka 10 bis 20 cm, wie sie z. B. bei Implantaten zur Tieridentifikation verwendet werden. Für die Übertragung von einem Lesemodul zu einer eigenständigen Anzeigeeinheit oder anderen externen Systemkomponenten, z B. einer Insulinpumpe oder einem Datenmanagementsystem wie einem elektronischen Tagebuch, werden beispielsweise Frequenzen im Bereich von 13,56 MHz benutzt, mit denen in Luft ungefähr bis zu 1m Distanz überbrückt werden kann. Sollen darüber hinaus Daten über weitere Strecken übertragen werden, z. B. zu weiterführenden externen Geräten, beispielsweise einem PC zur Datenverwaltung, so können mit Frequenzen im Bereich von 800 bis 2.000 MHz (UHF Bereich) Entfernungen bis zu ungefähr 4 m überbrückt werden.

Die Messwerte, die während der Messung der Konzentration der gesuchten Analyten erzeugt werden, werden drahtlos und berührungslos vom Messmodul zum Sendmodul übertragen. Unter drahtlos und berührungslos soll hier nur die Signalübertragung und gegebenenfalls die Energieübertragung als solche verstanden werden. Selbstverständlich sind die elektrischen Komponenten auf dem analytischen Testelement bzw. im Messgerät mit elektrischen Schaltungen "verdrahtet" und natürlich ist es möglich, dass das analytische Testelement das Instrument berührt, insbesondere wenn das Testelement in das Instrument eingeschoben wird. Die drahtlose und berührungslose Datenübertragung bietet mehrere Vorteile gegenüber kontaktgebundener Übertragung: so ist, abhängig von der Dimensionierung der Transponderspulen, die Lagetoleranz des analytischen Testelements relativ zum Messgerät

deutlich größer. Zudem ist der Übertragungswiderstand von elektrischen Kontakten bei hochohmigen niederstromigen Signalen, wie sie für die vorliegende Anwendung typisch sind, sehr kritisch. Es wird zwar versucht, die Kontakte möglichst zuverlässig zu gestalten, z. B. indem inerte Materialien wie Gold verwendet werden und indem die Gegenkontakte spitz ausgeformt sind und sich auf den flachen Kontaktflächen eingraben, um eventuell vorhandene Ablagerungen zu beseitigen. Dennoch kommt es vor, dass beispielsweise während der Handhabung des Testelements durch Handschweiß eine isolierende Schicht oder ein Kurzschluss bzw. Leckstrom zwischen den eng nebeneinander liegenden Kontakten entsteht, durch Kratzer ein Kontakt unterbrochen wird oder ein Leckstrom zu einem benachbarten Kontakt auftritt.

Diese Kontaktproblematik wird durch das erfindungsgemäße Transpondersystem gelöst. In einer Ausführungsform werden beispielsweise zumindest die sensiblen Messdaten drahtlos übertragen, beispielsweise wenn die Energie zum Betreiben der Messung auf dem Testelement weiterhin über elektrische Kontakte zur Verfügung gestellt wird oder wenn das Testelement eine eigene Energiequelle aufweist. In einer weiteren, bevorzugten Ausführungsform werden sowohl die Messdaten als auch die zur Messung notwendige Energie mit dem Transpondersystem kontaktlos übertragen. In einer dritten Ausführungsform sind die Kontakte in Polymerelektronik ausgebildet. Polymere sind auch gegenüber aggressivem Schweiß unempfindlich. Durch Erzeugen einer Spannungsspitze an den Kontaktflächen ist es zudem möglich, die Kontakte zwischen Testelement und Messgerät punktuell zu verschweißen und dadurch reproduzierbar einen sehr geringen Übergangswiderstand zu generieren.

Eine weitere bevorzugte Ausführungsform der Erfindung betrifft ein System zur Bestimmung der Konzentration eines Analyten aus einer Körperflüssigkeit das ein analytisches Testelement beinhaltet, das einen Bereich mit Nachweischemie zum Nachweis des Analyten aus einer Körperflüssigkeit sowie einen Speicher zur Speicherung elektronischer Daten aufweist. Außerdem beinhaltet das System ein Instrument, das eine Auswerteeinheit zur Auswertung der Daten und eine Anzeigeeinheit aufweist. Das System ist dadurch gekennzeichnet, dass die elektrischen Komponenten des Systems zumindest teilweise auf der Basis von Polymerelektronik ausgebildet sind.

Die elektronischen Daten, die auf dem analytischen Testelement gespeichert werden, können eine Teststreifen-Identifikation, chargenspezifische Kalibrationsdaten und die bei der Konzentrationsmessung erzeugten Messwerte umfassen. Die Identifikation, z. B. Chargennummer, Streifentyp sowie eventuell zusätzlich das Verfallsdatum, werden bevorzugt

bereits während der Herstellung des Teststreifens auf dem Testelement gespeichert und anschließend nicht mehr geändert. Daher könnte dies auch durch eine feste Verdrahtung realisiert werden. Ansonsten werden hierfür auch ein- oder mehrfach beschreibbare Software-Speicher, z. B. EPROM oder EEPROM, verwendet. Erfindungsgemäß ist hierzu insbesondere ein wieder beschreibbarer Polymerelektronik-Speicher bevorzugt.

Um die Kalibrationsdaten auf den bereits verpackten analytischen Testelementen zu speichern, ist ein über ein Transpondersystem beschreibbarer Speicher notwendig. Darüber hinaus kann es sinnvoll sein, die während der Konzentrationsmessung erhaltenen Messsignale auf dem analytischen Testelement zu speichern, bevor die Daten zum Messgerät übertragen werden. Auf diese Weise können die Messwerte bei Bedarf mehrfach gesendet werden, z. B. wenn bei der Übertragung zum Messgerät ein Fehler auftritt.

Darüber hinaus ist es auch möglich, dass das Sendemodul vom Lesemodul übermittelte Energie empfängt, z. B. sobald das analytische Testelement in das Instrument eingeschoben wird, insbesondere falls das analytische Testelement keine eigene Energieversorgung besitzt. Bei einem passiven Transpondersystem besitzt der Transponder keine eigene Energieversorgung und ist daher nur aktiv, solange er in Verbindung mit der Leseeinheit steht. In der Regel arbeiten die Transponder über magnetische Feldkopplung im Nahfeld, d.h. der Transponder muss nahe genug an die Leseeinheit gebracht werden. Beim Beschreiben des Transponders werden die Daten in elektrisch beschreibbare Speicher, z. B. einem EPROM oder einem EEPROM, abgelegt und sind nach Wegnahme der Energie dauerhaft gespeichert.

In einer bevorzugten Ausführungsform der Erfindung weist das analytische Testelement keine eigene Energiequelle auf. In diesem Fall wird die zur Messung und eventuell auch zur Speicherung notwendige elektrische Energie drahtlos über das Transpondersystem vom Instrument zum Testelement übertragen. Diese Ausführungsform ist insbesondere bei Implantaten vorteilhaft, da dann die Verweildauer des Implantats nicht durch die Lebensdauer der Stromquelle, z. B. einer Batterie, limitiert wird. Insbesondere bei analytischen Testelementen, die als Disposable für die In-vitro Einmalmessung verwendet werden (so genannte Einmal-Teststreifen), kann es aus Kostengründen vorteilhaft sein, wenn das Testelement keine eigene Energieversorgung benötigt.

Zusätzlich ist es möglich, einen temporären Energiespeicher in das Testelement zu integrieren, beispielsweise eine Kapazität oder ein Akkumulator. Hierdurch kann beispielsweise die

Kontaktzeit flexibler gehandhabt werden, so kann z. B. ein kontinuierlich messendes System mit einem solchen Energiepuffer über längere Zeit weiter messen, unabhängig davon, ob sich das Instrument permanent in der Nähe des Testelements befindet.

In einer weiteren erfindungsgemäßen Ausführungsform weist das analytische Testelement eine eigene Energieversorgung auf. Ein solcher so genannter aktiver Transponder kann insbesondere dann sinnvoll sein, wenn das Testelement mehrere Messungen durchführen kann. So könnte beispielsweise ein solches, z. B. (teil-)-implantiertes, Testelement über 24 Stunden die erforderlichen bzw. eingestellten Messungen durchführen und der Anwender braucht nur einmal am Tag die Messdaten vom Testelement zum Instrument zu übertragen. Besitzt das Testelement eine wiederaufladbare Energieversorgung (Akkumulator, Kapazität), so kann während der Datenübertragung im Bedarfsfall der Energiespeicher aufgeladen werden.

In einer weiteren Ausführungsform beinhaltet das analytische Testelement des erfindungsgemäßen Systems mehrere Elektroden, insbesondere mehr als zwei Elektroden, die in Kontakt mit der Nachweischemie stehen. Die Elektroden sind zu einem bzw. mehreren elektronischen Schaltkreisen verschaltet, wobei die elektronischen Schaltkreise galvanisch getrennt sind. D. h. die Schaltkreise weisen keine gemeinsame Energiequelle oder gemeinsame Masse auf und sind soweit nach außen galvanisch isoliert, dass nur die Verbindung über den unvermeidlichen flüssigen Pfad der Nachweischemie selbst besteht. Da der elektrische Kontakt nur an einer Stelle besteht, kann sich kein parasitärer Kriechstrompfad aufbauen, der den Messwert verfälschen könnte. Um die galvanische Trennung zu realisieren, müsste beispielsweise jeder Schaltkreis eine eigene Stromversorgung aufweisen, was sehr kostspielig wäre. Erfindungsgemäß wird die galvanische Entkopplung durch das Transpondersystem gelöst. Alle Schaltkreise auf dem analytischen Testelement besitzen einen Transponder und sind gegeneinander galvanisch getrennt. Ein gemeinsames Lesemodul oder auch für jeden Transponder ein eigenes Lesemodul überträgt die Energie auf die Schaltkreise. Hierbei kann sich das Lesemodul im Instrument oder aber auch auf dem analytischen Testelement befinden. Im letztgenannten Fall kann die Übertragung der Energie vom Lesemodul, das sich auf dem Teststreifen befindet, zum Instrument entweder über elektrische Kontakte oder über ein weiteres Transpondersystem, bestehend aus einem gemeinsamen Transponder oder wieder aus mehreren Transpondern, vonstatten gehen.

Einfache elektrochemische Systeme bestehen meist aus zwei bis drei Elektroden. Häufig kommen sog. Potentiostaten mit 3 Elektroden (Arbeits-, Gegen- und Referenzelektrode) zur Anwendung.

Insbesondere ist hierbei ein parasitärer Widerstand von der Gegenelektrode zum Ausgang des Potentiostaten kritisch, da dieser direkt in die Signalverstärkung einfließt. Es ist daher von Vorteil, wenn der gesamte Potentiostat, bis auf die Elektroden, hermetisch mit einer Isolierschicht versiegelt ist. In dieser Ausführungsform verarbeitet und speichert der Transponder beispielsweise keine digitalen Informationen, sondern verarbeitet den analogen Signalstrom und überträgt diesen zum Lesemodul. Die für den Messprozess notwendigen Funktionen sind dabei im Transponder integriert, wie z. B. die permanente Versorgung der Arbeitselektrode mit einem Potenzial (typischerweise einige 100 mV, vorzugsweise -350 mV). Dabei ist das Transpondersystem so ausgelegt, dass die benötigte Energie in geeigneten Refresh-Intervallen vom Instrument zur Verfügung gestellt und zwischen gespeichert wird.

Insbesondere bei einem Potentiostat, der als Implantat oder Teilimplantat ausgeführt ist, z. B. zur kontinuierlichen Messung eines Analyten, ist es von besonderer Bedeutung, dass sich durch die erfindungsgemäße Verwendung der Transpondertechnologie das elektrische System hermetisch kapseln lässt und dennoch Information und Energie übertragen werden kann.

Eine bevorzugte erfindungsgemäße Ausführungsform betrifft implantierte analytische Testelemente. Der Einsatz der Transpondertechnologie ermöglicht es, ein Testelement in den Körper zu implantieren und ohne transkutane Verbindungen durch die Haut von außen zu betreiben. Durchführungen durch die Haut vermindern den Tragekomfort, z. B. beim Duschen, und bergen inhärent das Risiko einer Infektion. So kann beispielsweise ein analytisches Testelement zur kontinuierlichen Messung der Blutglukose in das Unterhautfettgewebe in der Bauchgegend eingesetzt werden und außen auf der Haut wird das Instrument gehalten, entweder nur temporär, um eine Messung durchzuführen, oder permanent, z. B. von einem Gürtel oder einem Pflaster, insbesondere bei kontinuierlichen Messungen des Analyten im Minutenbereich. In beiden Fällen kann zumindest kurzzeitig das Instrument entfernt werden, z. B. zum Duschen. Auch bei teilimplantierten analytischen Testelementen, die beispielsweise an ihrem einen Ende in ein Pflaster integriert sind, während das andere, meist lanzettenförmige Ende in die Bauchdecke gestochen wird, kann das relativ große und schwere Instrument für die Messungen in der Nähe des Testelements platziert und wenn nötig einfach entfernt werden. Da das Teilimplantat keine offenen elektrischen Kontakte hat, ist auch hier die Empfindlichkeit gegen Umwelteinflüsse deutlich geringer. Darüber hinaus kann das Instrument, insbesondere wenn es auch die Anzeigeeinheit beinhaltet, auch über der Kleidung getragen werden. Das Instrument kann unabhängig davon, ob es mit oder ohne Anzeigeeinheit ausgestattet ist, die empfangenen Daten in größerem Umfang, beispielsweise mehrere Hundert Messwerte, speichern.

Eine bevorzugte Methode, mit dem erfindungsgemäßen Transpondersystem Daten zu übertragen, besteht darin, die Signale, typischerweise Gleichstrom- oder Gleichspannungssignale, in eine Frequenz zu wandeln und einer Trägerfrequenz, die beispielsweise der Energieübertragung dient, aufzumodulieren.

Eine Variante der Erfindung beschreibt die Verwendung unterschiedlicher Trägerfrequenzen. Dies kann zur Unterscheidung der Transpondersysteme genutzt werden. Insbesondere wenn mehrere Transponder gleichzeitig angesprochen werden, beispielsweise bei mehreren parallelen Transpondern auf einem analytischen Testelement oder beim Beschreiben mehrerer Teststreifen, die sich in einer Verpackung befinden, kann es vorteilhaft sein, jeden Transponder einzeln anzusprechen. Durch die Verwendung schmalbandiger Filter kann beispielsweise jede Trägerfrequenz einzeln behandelt und Übersprechen vermieden werden.

Ein weiteres Merkmal der Erfindung besteht darin, dass die mit dem Transpondersystem übertragenen Signale nicht nur digitale Daten, z. B. die Kalibrationsdaten, sondern darüber hinaus auch analoge Signale, insbesondere die bei der Messung der Analytkonzentration erhaltenen Messwerte, enthalten können. Die heute üblichen Transpondersysteme werden zumeist nur zur Übertragung digitaler Daten verwendet. DE 103 22 167 beschreibt beispielsweise den Einsatz von Transpondern für die logistische Rückverfolgung von wieder verwendbaren Lastträgern; US 6,579,498 offenbart eine Transponder-gestützte Übertragung von digitalen Daten bei einem implantierten Blutglukosesensor. In der eingangs erwähnten Publikation von J. Black ist beispielsweise die Machbarkeit einer drahtlosen Übertragung von analogen Daten zur Glukosemessung gezeigt.

Üblicherweise liegen die Kalibrations- und Identifikationsdaten des analytischen Testelements als digitale Daten und die bei der Konzentrationsmessung eines Analyten erhaltenen Messsignale in Form von analogen Daten vor. Bei der erfindungsgemäßen Anwendung der Transpondertechnologie werden die digitalen Daten beispielsweise gemäß der oben erwähnten Amplitudenmodulation übertragen. Die analogen Daten werden entweder vor dem Senden digitalisiert oder als Analogsignale, z. B. ebenfalls mit Amplitudenmodulation, übermittelt.

Die Kalibrations- und Identifikationsdaten, die auf dem analytischen Testelement gespeichert sind, sind entweder in einem elektronischen Speicher, z. B. aus Polymerelektronik, abgelegt oder sie sind in einem Magnetstreifen bzw. Barcode, der sich auf dem Teststreifen befindet, codiert.

Die Messsignale werden entweder auf einem elektronischen Datenspeicher gespeichert, bevor sie an das Instrument, z. B. per Transpondersystem, weitergegeben werden, oder sie werden direkt ohne Zwischenspeicherung an das Instrument weitergegeben. Der elektronische Speicher auf dem analytischen Testelement ist bevorzugterweise ein nicht-flüchtiger Speicher, insbesondere der Speicher bzw. Speicherbereich, in dem die Kalibrations- und Identifikationsdaten gespeichert sind.

In einer bevorzugten Variante der Erfindung beinhaltet das analytische Testelement einen Speicher zur Speicherung elektronischer Daten, wobei dieser Speicher auch beschreibbar ist, wenn sich das analytische Testelement in einer Verpackung befindet. Beispielsweise werden die Teststreifen in einen Container (Einzeltest-Magazin oder Band-Magazin) verpackt und anschließend werden die Kalibrationsdaten von einem außen befindlichen Lesemodul durch die Verpackung zu dem auf dem Testelement befindlichen Transponder gesendet und dort gespeichert. Die Verpackung ist hierbei so gestaltet, dass eine drahtlose Übertragung der Daten möglich ist, insbesondere besteht das Verpackungsmaterial vorzugsweise aus Kunststoff oder Pappe, was für die eingesetzte Übertragungsstrahlung nahezu vollständig durchlässig ist.

In einer weiteren erfindungsgemäßen Ausführungsform weist das analytische Testelement keine elektrischen Kontakte zum Instrument auf, über die Daten oder elektrische Energie zwischen dem Testelement und dem Instrument übertragen werden, beispielsweise weil sämtliche Daten und gegebenenfalls die Energie über ein Transpondersystem übermittelt werden.

Beispielsweise besteht die elektrische Schaltung auf dem analytischen Testelement, beispielsweise die Transponderantenne oder die Leiterbahnen und Kontakte, zumindest teilweise aus Polymerelektronik, der Transponder selbst ist jedoch als Siliziumchip ausgebildet. Die höheren Herstellkosten des Siliziumchips können bei komplexen analytischen Testelementen, die beispielsweise mehrere Messungen durchführen können, akzeptabel sein. Insbesondere kann diese Ausführungsform günstig sein, wenn sich der Transponder nicht direkt auf dem analytischen Testelement, sondern auf einer Verpackung für ein oder mehrere Testelemente befindet. In dieser alternativen Ausführungsform beinhaltet das System zusätzlich eine derartige Verpackung, die insbesondere ein Container oder ein Magazin für mehrere Testelemente, z. B. eine Trommel, sein kann. Zusätzlich ist es möglich, auf der Verpackung einen sog. Testzähler zu implementieren, der in dem Speicher auf dem Container die Anzahl der mit diesem Container durchgeführten bzw. noch durchführbaren Tests ablegt. Auf diese Wiese kann jederzeit vom Instrument abgefragt werden, wie viele unbenutzte Testelemente sich noch in der Verpackung

befinden. Ist diese Information nur im Instrument angelegt, könnte es zu Fehlfunktionen kommen, beispielsweise wenn ein angebrochener Container aus dem Instrument herausgenommen und durch einen anderen angebrochenen oder neuen ersetzt wird. Selbstverständlich kann auch auf dem Testelement selbst ein Indikator gespeichert werden, der anzeigt, ob das Testelement bereits benutzt wurde oder nicht.

Eine weitere bevorzugte Ausführungsform der Erfindung betrifft ein System, das ein analytisches Testelement, das einen Bereich mit Nachweischemie zum Nachweis des Analyten aufweist, wobei die elektrischen Komponenten auf dem Testelement zumindest teilweise auf der Basis von Polymerelektronik ausgebildet sind, sowie eine Verpackung, in der ein oder mehrere analytische Testelemente verpackt sind, wobei die Verpackung einen Speicher zur Speicherung elektronischer Daten und ein Sendemodul zur drahtlosen Übertragung von Daten aufweist. Darüber hinaus beinhaltet das System ein Instrument, das eine Auswerteeinheit zur Auswertung der Daten sowie ein Lesemodul zur drahtlosen Übertragung von Daten aufweist.

Beispielsweise werden die Teststreifen in einen Container (Trommel, Magazin) verpackt. Die Kalibrations- und Identifikationsdaten sind hierbei auf dem Container gespeichert und nicht auf den Testelementen. Der Container, z. B. eine Trommel mit analytischen Testelementen ähnlich der, wie sie beim Accu-Chek Compact© verwendet wird, wird in das Instrument eingesetzt und der Transponder auf dem Container sendet die Daten an das Lesemodul im Instrument. Der Vorteil dieser Variante liegt darin, dass beispielsweise für mehrere Teststreifen nur ein Sendemodul notwendig ist, insbesondere wenn die Verarbeitung der Messsignale ohne Transponder arbeitet (z. B. bei foto-optischen Testelementen).

Gemäß einer weiteren erfindungsgemäßen Ausführungsform, insbesondere für Einmalteststreifen, weist das analytische Testelement keine eigene Energieversorgung auf. Auf dem Testelement sind z. B. Chargennummer, Streifentyp, Verfallsdatum und Kalibrationsdaten gespeichert. Das Testelement wird vom Anwender oder automatisch vom Instrument aus der Verpackung entnommen und beispielsweise in eine Halterung im Instrument gebracht. Die Positionierung des Testelements in der Halterung gewährleistet eine korrekte Position von Sende- und Lesemodul. Insbesondere gewährleistet die Halterung das Einbringen des analytischen Testelements in den Sende- und Empfangsbereich des Lesemoduls. Der Sende- und Empfangsbereich beschreibt den Bereich, innerhalb dessen elektronische Daten drahtlos zwischen Lesemodul und Sendemodul ausgetauscht werden können. Die Ausdehnung dieses Bereichs wird insbesondere durch die Abmessungen der Transponderspulen, der Energie und

Frequenz der übertragenen elektromagnetischen Wellen sowie eventueller Abschirmungen, z. B. durch Metallteile, definiert. Beispielsweise kann die Halterung so gestaltet sein, dass die Transpondermodule sehr nahe, typischerweise auf einen Abstand von 0,1 bis 3 mm, zusammen kommen. Aufgrund der geringen Distanz, die überbrückt werden muss, können die Transponderspulen sehr klein sein und es wird nur wenig Energie zur drahtlosen Übertragung benötigt, beispielsweise im Bereich von 0,1 bis 10 mJ. Ein geringer Energiebedarf ist insbesondere bei batteriebetriebenen Instrumenten von Vorteil. Außerdem kann der Sende- und Empfangsbereich räumlich stark eingegrenzt werden, um sicher zu stellen, dass nur das eingebrachte Testelement angesprochen wird und nicht zusätzlich in der Nähe befindliche weitere Testelemente. Alternativ kann der Sende- und Empfangsbereich auch so gestaltet sein, dass das analytische Testelement zur drahtlosen Datenübertragung, mit oder ohne eine Halterung, beispielsweise dicht neben oder auf dem Instrument positioniert werden kann. Darüber hinaus kann sich die Halterung zum Einbringen des analytischen Testelements in den Sende- und Empfangsbereich in einer Verpackung für mehrere Testelemente befinden und die Verpackung wird entsprechend zum Instrument positioniert, beispielsweise durch eine Halterung für die Verpackung am Instrument bzw. durch eine Halterung für das Instrument an der Verpackung.

In einer weiteren bevorzugten Ausführungsform befindet sich das Sendemodul nicht auf dem Testelement, sondern auf einer Verpackung, die ein oder mehrere Testelemente beinhaltet, und eine Halterung positioniert die Verpackung im Instrument so, dass Sende- und Lesemodul sehr nahe zusammen kommen, so dass sich das Sendemodul der Verpackung im Sende- und Empfangsbereich des Lesemoduls befindet.

Eine weitere bevorzugte Ausführungsform der Erfindung betrifft ein analytisches Testelement, das einen Bereich mit Nachweischemie zum Nachweis eines Analyten aufweist, wobei sich auf dem analytischen Testelement ein Sendemodul und ein Lesemodul befinden und zwischen diesen beiden Modulen drahtlos Daten innerhalb des Teststreifens übertragen werden. Darüber hinaus kann neben den Daten auch elektrische Energie übertragen werden. Die elektrischen Komponenten auf einem solchen analytischen Testelement sind bevorzugterweise zumindest teilweise auf der Basis von Polymerelektronik ausgebildet. Ein derartiges analytisches Testelement kann darüber hinaus auch zum Instrument Daten bzw. Daten und Energie drahtlos übertragen, z. B. mittels eines zweiten Transpondersystems mit einem Sendemodul auf einem Teststreifen und einem Lesemodul im Instrument. Selbstverständlich kann es sich bei den Daten, die mit einem Transpondersystem innerhalb des Teststreifens übertragen werden, sowohl um digitale als

auch um analoge Daten handeln. Beispielsweise kann ein solches Teststreifen-internes Transpondersystem dazu genutzt werden, die elektrischen Stromkreise auf einem elektro-chemischen Teststreifen galvanisch zu entkoppeln, wobei die Energie vom Instrument zum Nachweisbereich übertragen wird, und die Messsignale, z. B. als analoge Spannungs- oder Stromwerte, werden im Gegenzug vom Nachweisbereich zum Instrument gesendet.

Bei dem erfindungsgemäßen System kann sowohl ein elektro-chemisches als auch ein foto-optisches Messverfahren zur analytischen Bestimmung verwendet werden, insbesondere wenn sich beispielsweise bei einem foto-optischen Teststreifen die Messeinheit auf dem Teststreifen befindet und somit wie bei einem elektro-chemischen Teststreifen die elektrischen Messsignale auf dem Teststreifen zu generieren und auf das Instrument zu übertragen sind.

Beispielsweise kann ein Lichtstrahl vom Instrument auf den Nachweisbereich gelenkt werden und ein auf dem Teststreifen befindliches Fotoelement, z. B. eine Solarzelle aus Polymerelektronik, empfängt das optische Messsignal und wandelt es in ein elektrisches Signal um. Dieses Signal kann dann mit dem Transpondersystem berührungslos zum Instrument übertragen werden.

Zur sensorischen Erfassung des Analyten, insbesondere von Blutglukose, werden die im Stand der Technik bekannten Verfahren eingesetzt. Hierbei werden foto-optische bzw. elektrochemische Verfahren bevorzugt. Foto-optische Messverfahren sind beispielsweise Reflexionsphotometrie, Absorptionsmessung oder Fluoreszenzmessung, elektro-chemische Verfahren sind zum Beispiel Potentiometrie, Amperometrie, Voltametrie, Coulometrie.

Ein weiterer Gegenstand der Erfindung ist ein Verfahren zur Herstellung eines analytischen Testelements, das einen Bereich mit Nachweischemie zum Nachweis eines Analyten in einer Körperflüssigkeit, einen Speicher zur Speicherung elektronischer Daten und ein Sendemodul zur drahtlosen Übertragung von Daten aufweist, wobei die Herstellung die Schritte Speichern einer Chargenidentifikation auf dem analytischen Testelement; Verpacken des analytischen Testelements; und Speichern von Kalibrationsdaten auf dem verpackten analytischen Testelement beinhaltet.

Ein weiterer Gegenstand der Erfindung ist ein Verfahren zur Herstellung eines analytischen Testelements, das einen Bereich mit Nachweischemie zum Nachweis eines Analyten in einer Körperflüssigkeit aufweist, wobei die Herstellung die Schritte Speichern einer

Chargenidentifikation auf einer Verpackung, die einen Speicher zur Speicherung elektronischer Daten und ein Sendemodul zur drahtlosen Übertragung von Daten aufweist; Verpacken des analytischen Testelements in der Verpackung; und Speichern von Kalibrationsdaten auf der Verpackung beinhaltet.

Ein weiterer Gegenstand der Erfindung ist ein Verfahren zur Bestimmung der Konzentration eines Analyten in einer Körperflüssigkeit, das die Schritte Einlegen eines analytischen Testelements, das einen Bereich mit Nachweischemie zum Nachweis eines Analyten in einer Körperflüssigkeit, einen Speicher zur Speicherung elektronischer Daten und ein Sendemodul zur drahtlosen Übertragung der Daten aufweist, in ein Instrument, das eine Auswerteeinheit zur Auswertung der Daten und ein Lesemodul zur drahtlosen Übertragung der Daten aufweist; Auftragen der Körperflüssigkeit auf das analytische Testelement; drahtlose Übertragung der Daten vom analytischen Testelement zum Instrument; und Auswerten der Daten in der Auswerteeinheit des Instruments beinhaltet.

Ein weiterer Gegenstand der Erfindung ist ein Verfahren zur Bestimmung der Konzentration eines Analyten in einer Körperflüssigkeit, das die Schritte Einlegen einer Verpackung, in der ein oder mehrere analytische Testelemente mit Nachweischemie zum Nachweis eines Analyten in einer Körperflüssigkeit verpackt sind, und die Verpackung einen Speicher zur Speicherung elektronischer Daten sowie ein Sendemodul zur drahtlosen Übertragung der Daten aufweist; Bereitstellen eines analytischen Testelements aus der Verpackung; Auftragen der Körperflüssigkeit auf das analytische Testelement; drahtlose Übertragung der Daten von der Verpackung zu einem Instrument , das eine Auswerteeinheit zur Auswertung von Daten und ein Lesemodul zur drahtlosen Übertragung der Daten aufweist; und Auswerten der Daten in der Auswerteeinheit des Instruments beinhaltet.

Beispielsweise sind auf dem Teststreifen die chargenspezifischen Kalibrationsdaten gespeichert. Der Teststreifen wird vom Benutzer in die entsprechende Halterung im Instrument eingelegt, beispielsweise von Hand oder der Teststreifenvoratsbehälter besitzt eine Entnahmevorrichtung, die den Teststreifen aus den Voratsbehälter in das Instrument transportiert. Bevorzugterweise schaltet sich das Instrument automatisch ein, sobald der Teststreifen eingelegt wird und ist nach einem kurzen Selbsttest messbereit. Anschließend gibt der Benutzer die zu messende Probe mit Körperflüssigkeit auf. Die Probe reagiert mit der Nachweischemie auf dem Teststreifen und generiert dabei ein Messsignal. Bei foto-optischen Systemen kann dies beispielsweise ein Farbumschlag sein, bei elektro-chemischen Systemen wird beispielsweise ein Stromsignal erzeugt.

Der Farbumschlag wird von der Messoptik in ein elektrisches Signal umgewandelt. Die Optik ist üblicherweise in das Instrument integriert, sie kann sich jedoch auch auf dem Teststreifen befinden, insbesondere wenn die Optik zumindest teilweise in Polymerelektronik realisiert ist. Mit Hilfe des Transpondersystems werden die Kalibrationsdaten vom Teststreifen zum Instrument drahtlos übertragen bzw., falls die Optik auf dem Teststreifen ist, wird zusätzlich zunächst die Energie zum Betreiben der Optik vom Instrument zum Testsreifen übertragen und nach der Messung die Messsignale vom Teststreifen zum Instrument. Unter Einbeziehen der chargenspezifischen Kalibrationsdaten werden die Messsignale in der Auswerteeinheit im Instrument ausgewertet. Bevorzugtermaßen weist das Instrument eine Anzeigeeinheit, z. B. ein LCD Display, auf, die dem Benutzer den Messwert anzeigt.

In einer alternativen Ausführungsform befinden sich ein oder bevorzugt mehrere Teststreifen in einer Verpackung, z. B. einem Container. Auf der Verpackung sind die chargenspezifischen Kalibrationsdaten gespeichert und der Transponder befindet sich ebenfalls in der Verpackung. Die Verpackung wird vom Benutzer in das Instrument eingelegt. zur Benutzung wird das Instrument eingeschaltet, wobei es bevorzugterweise automatisch einen Teststreifen in eine Position transportiert, in der der Benutzer die Probe auftragen kann. Anschließend erfolgt Probenauftrag und foto-optischer bzw. elektro-chemischer Messung wie oben beschrieben. Bevorzugtermaßen handelt es sich um foto-optische Teststreifen und die Messoptik befindet sich im Instrument. Die Kalibrationsdaten werden vor oder nach der Messung vom Transponder auf der Verpackung drahtlos zum Instrument übertragen, während die optischen Messsignale von der Optik im Instrument empfangen und unter Einbeziehen der Kalibrationsdaten in der Auswerteeinheit ausgewertet und bevorzugterweise in einer Anzeigeeinheit angezeigt werden. Bei einem elektro-chemischen Teststreifen werden ebenfalls die Kalibrationsdaten vom Transponder auf der Verpackung drahtlos zum Instrument übertragen und beispielsweise werden die elektrischen Messsignale über elektrische Kontakte vom Teststreifen zum Instrument übertragen, über die auch die benötigte Energie zur Erzeugung des Messsignals eingespeist wird.

Beschreibung der Figuren

Die Erfindung wird durch die nachfolgenden Figuren näher erläutert: Die Figuren 1 bis 23 zeigen schematisch Prinzipskizzen für konkrete Ausführungsformen der Erfindung.

Figur 1 zeigt ein analytisches Testelement mit einem Transpondersystem.

Figur 2 zeigt ein erfindungsgemäßes analytisches Testelement eingelegt in ein Instrument.

Figur 3 zeigt die Verwendung eines leitfähigen Polymersubstrats als Datenspeicher.
Figur 4 zeigt die Übermittlung von Daten auf mehrere analytische Testelemente mit dem erfindungsgemäßen Transpondersystem.
Figur 5 zeigt eine Skizze eines Systems mit mehreren galvanisch getrennten Schaltkreisen.
Figur 6 zeigt ein schematisches Blockschaltbild eines Systems mit mehreren galvanisch getrennten Schaltkreisen.
Figur 7 zeigt ein Mehrelektrodensystem mit Transponder.
Figur 8 zeigt ein teilimplantiertes analytisches Testelement.
Figur 9 zeigt ein implantiertes analytisches Testelement.
Figur 10 zeigt eine Prinzipschaltung eines Potentiostat-Transponders.
Figur 11 zeigt einen elektro-chemischen Teststreifen mit Transponder aus Polymerelektronik.
Figur 12 zeigt eine Schnittdarstellung des Teststreifens aus Figur 11 eingelegt in ein Instrument.
Figur 13 zeigt einen foto-optischen Teststreifen mit Transponder aus Polymerelektronik.
Figur 14 zeigt eine Schnittdarstellung des Teststreifens aus Figur 13 eingelegt in ein Instrument.
Figur 15 zeigt ein Testelement mit mehreren Potentiostat-Sensor Systemen.
Figur 16 zeigt das Testelement aus Figur 15 eingesetzt in ein Instrument.
Figuren 17 und 18 zeigen ein teilimplantierbares analytisches Testelement.
Figuren 19-21 zeigen Beispiele für Datenübertragung auf verpackte Teststreifen.
Figuren 22 und 23 zeigen einen Schreib-Lese-Speicher aus Polymerelektronik.

In Figur 1 ist ein analytisches Testelement 1 gezeigt, bestehend aus einem Substrat 2, auf dem sich ein Nachweisbereich 3 zum Nachweis eines Analyten aus einer Körperflüssigkeit sowie ein Sendemodul, das das Transpondersubstrat 4 beinhaltet, in bzw. auf dem sich die Transponderantenne 5 und die Transponderelektronik 6 befinden, die als Polymerelektronik hergestellt sind.

Figur 2 zeigt eine Prinzipskizze eines analytischen Testelementes 1, das in ein Instrument 7 eingelegt ist. Die Identifikations- und Kalibrationsdaten des Teststreifens sind in der Transponderelektronik 6 gespeichert und werden über die Transponderantenne 5 zum Lesemodul 8, das sich ebenfalls im Instrument 7 befindet, übertragen. Die drahtlose Datenübertragung wird mit dem Pfeil 9 angedeutet. Die im Nachweisbereich 3 ermittelten Messsignale werden über die elektrischen Kontakte 15 zum Instrument 7 weitergeleitet. Der hier dargestellte Teststreifen kann für eine elektro-chemische und für eine foto-optische Messung geeignet sein. Bei einem foto-optischen Testelement entfallen entweder die Kontakte 15 und die Auswerteoptik ist im Instrument 7, oder die Auswerteoptik ist zumindest teilweise auf dem

Teststreifen integriert, so dass die optischen Messsignale auf dem Testelement in elektrische Größen umgewandelt und die elektrischen Signale über die Kontakte 15 an das Instrument weitergegeben werden.

Die Verwendung eines leitfähigen Polymersubstrats 14 als binärer Speicher für elektronische Daten ist in Figur 3 schematisch dargestellt. Die Steuerelektronik 10 steuert die Elektrodenmatrix 11 so an, dass punktuell zunächst hochohmige Zonen 12 zu niederohmigen Zonen 13 werden.

Figur 4 zeigt die drahtlose Übermittlung von Daten 9 zwischen einem Lesemodul 8 und mehreren analytischen Testelementen 1. Die Sendemodule auf dem Testelement sind hier durch das Transpondersubstrat 4 und die Transponderelektronik 6 dargestellt. Diese Anwendung kann zum Beispiel in der Produktion verwendet werden. Hierbei sind die Teststreifen 1 in einer Verpackung, z. B. einem Container der das elektromagnetische Feld nicht behindert, verpackt und ein spezielles Lesemodul 8 in der Produktion fragt zunächst die Teststreifen-Identifikation von den Testelementen ab, um die Chargennummern abzufragen, überträgt dann die chargenspezifischen Kalibrationsdaten und kontrolliert abschließend durch erneute Abfrage, ob die Datenübertragung korrekt war. In einer zweiten Verwendung des hier dargestellten Aufbaus befinden sich die Testelemente 1 in einem Container im Instrument oder dicht neben dem Instrument und das Lesemodul 8, das sich im Instrument befindet, liest die Daten vom Testelement aus. Hierbei handelt es sich beispielsweise um Streifentyp, Verfallsdatum und Kalibrationsdaten. Darüber hinaus ist es auch möglich, dass benutzte Testelemente nach der Messung wieder in den Container zurückgelegt werden. Die Benutzung wird beispielsweise auf dem Testelement gespeichert, z. B. zusammen mit den Messwerten, und an das Lesemodul gemeldet, oder direkt an das Lesemodul gesendet und dort, beispielsweise zusammen mit den Messwerten, gespeichert, oder ein Testelement, zu dem ein Messwert auf dem Testelement bzw. im Instrument gespeichert ist, wird automatisch als benutzt angesehen.

Figur 5 zeigt anhand einer Prinzipskizze ein System mit galvanisch getrennten Schaltkreisen. Auf dem Transpondersubstrat 4 befinden sich mehrere gegeneinander isolierte elektrische Schaltkreise bestehend aus Transponderantenne 5, Transponderelektronik 6, sowie in den elektro-chemischen Nachweisbereich 3 hineinragende Messelektroden 16. Die Messsignale werden von ebenso vielen parallel angeordneten Antennen 17 im Lesemodul 8 empfangen.

Figur 6 zeigt ein vereinfachtes Blockschaltbild des in Figur 5 dargestellten Beispiels, wobei auch noch von weiteren Modulen 30, z. B. ein elektrochemisch arbeitender Durchflusssensor, Signale gesendet und/oder empfangen werden können.

Figur 7 zeigt ein komplexes Mehrelektrodensystem als Potentiostat-Transponder für die elektrochemische Messung beispielsweise von Blutglukose und Blutgerinnung mit elektrischen Zuleitungen 18, die von der Transponderelektronik und –antenne 6 bzw. 5 zu den Messelektroden 16 im Nachweisbereich 3 reichen. Eine Deckschicht 19 gewährleistet eine hermetische Trennung des Transpondersystems.

Figur 8 zeigt ein teilimplantierbares lanzettenartiges Testelement 1 mit Potentiostat-Transponder, das bevorzugt für eine kontinuierliche Glukosemessung eingesetzt wird. Hierbei wird regelmäßig die Glukosekonzentration bestimmt, die Daten im Transponder abgespeichert, und immer wenn das Lesemodul 8 in der Nähe ist, werden die Signale an das Instrument übertragen. So kann der Anwender das Instrument problemlos kurzzeitig, z. B. zum Umziehen oder Duschen, abnehmen. Das Testelement 1 besteht aus einem an einem Ende spitzen und relativ steifen Substrat 2, an dessen Spitze sich die Messelektroden 16 befinden. Elektrische Leiterbahnen 18 führen von den Elektroden 16 zum anderen, außerhalb des Körpers befindlichen, Sendemodul bestehend aus Transponderelektronik und –antenne, 6 bzw. 5. Das ganze Testelement 1 ist mit einer Deckschicht 19 wasserdicht verkapselt, lediglich die Messelektroden 16 haben, gezwungenermaßen, nach außen offene Kontakte. Über dem Testelement 1 kann sich beispielsweise ein Pflaster 22 befinden, bzw. das Lesemodul 8 kann bequem über einer Kleidung 22 getragen werden.

Figur 9 zeigt ein Potentiostat-Testelement 1 ähnlich dem in Figur 8 gezeigten Beispiel als (voll-) implantierte Version. Die gesamte Elektronik, bis auf die Messelektroden 16, ist hermetisch in einer Glas- oder Polymerkapsel 23 verkapselt. Um höhere Eindringtiefen in die Gewebeschichten zu erreichen verwendet man bevorzugt Niederfrequenztransponder im Bereich von 125 kHz. Um dafür geeignete, kleine Antennenspulen zu erreichen, werden diese mit Stabferritkernen 24 ausgestattet.

Figur 10 beschreibt eine Prinzipschaltung eines Potentiostat-Transponders. Die Transponderelektronik beinhaltet u. a. einen Lastmodulator 25, einen Energiespeicher 26, z. B. in Form einer Kapazität, und einen Spannungs-/Frequenzwandler 27. Das Ruhepotential 28 liegt permanent an der Arbeitselektrode 29 an. 30 und 31 bezeichnen Referenz- bzw. Gegenelektrode. Das Lesemodul weist unter anderem Bandpassfilter 32, Energiesender und Schreibeinheit 33, Leseeinheit 34, Speicher 35 sowie Steuerungseinheit 36 auf.

Figur 11 zeigt ein analytisches Testelement 1 mit einem Transponder aus Polymerelektronik, das nach einem elektro-chemischen Messverfahren arbeitet. Auf dem Substrat 2 befindet sich eine Abstandsfolie 51, die zwischen Substrat 2 und Deckfolie 52 eine Blutkapillare 50 bildet, in die die Messelektroden 16 für die elektro-chemische Messung hineinragen. In bzw. auf die Transponderfolie 4 sind die Transponderantenne 5, die Transponderelektronik 6 und

Transponderspeicher 54 in Polymerelektronik realisiert. Der Transponder dient hierbei zur Übertragung von Teststreifen-Identifikations- und Kalibrationsdaten. Die Messsignale werden über die Sensorkontakte 15 übertragen.

Durch das Einlegen des Teststreifens 1 aus Figur 11 in ein Instrument wird das Sendemodul 37 und insbesondere Transponderantenne 5 nah zum Lesemodul 55 und insbesondere zur Lesemodul-Antenne 17 positioniert (siehe Figur 12). Das Lesemodul 55 befindet sich hier mit auf der Elektronikleiterplatine 56 des Instruments 7, ebenso wie die Instrumentkontakte 70, die die Sensorkontakte 15 auf dem Teststreifen 1 kontaktieren.

Bei dem Testelement 1 in Figur 13 befindet sich der Nachweisbereich 3, der über die Blutkapillare 50 befüllt wird, unter dem Transpondermodul aus Polymerelektronik, bestehend aus Transpondersubstrat 4, -antenne 5, -elektronik 6 und –speicher 54. Die Blutkapillare 50 wird durch die Abstandsfolie 51 zwischen Substrat 2 und Deckfolie 52 gebildet.

Ist das Testelement 1 aus Figur 13 in ein Instrument 7 eingesetzt, liegen Transponderantenne 5 und Lesemodul-Antenne 17 sehr nah übereinander und gewähren so eine leichte Datenübertragung über kurze Distanz (siehe Figur 14). Das Transpondermodul 37 befindet sich auf der Oberseite des Teststreifens, der fotometrische Nachweisbereich 3 wird von der Unterseite von der Beleuchtung 58 beleuchtet und dem optischen Leser 59 ausgelesen. Eine oben- und eine untenliegende Leiterplatte 56 sind mit dem Lesemodul 55 bzw. den Optikmodulen 58 und 59 bestückt.

Das Testelement 1 in Figur 15 weist einen Nachweisbereich 3 in Form eines Flüssigkeitskanals auf, durch den die Probe vom Einlass 60 zum Auslass 61, z. B. für kontinuierliche Blutglukosemessung, fließt. Drei Messelektroden 16 eines Potentiostats ragen in den Flüssigkeitskanal hinein. Auf dem Transpondersubstrat 4 befinden sich eine Polymerelektronik-Transponderantenne 5 und die Transponderelektronik 6, die aus Polymerelektronik oder (zumindest teilweise) mit Siliziumchips aufgebaut ist. Parallel zu dem ersten Potentiostat-Sensor-System befindet sich noch ein baugleiches paralleles System, wobei beide Systeme galvanisch voneinander getrennt sind.

Eingelegt in ein Instrument 7, korrespondieren die parallelen Transponderantennen 5 auf dem Testelement 1 mit den entsprechenden Lesemodul-Antennen 17, die die Daten an die Lesemodul-Elektronik 55 weiterleiten, für eine drahtlose Datenübertragung 9 (siehe Figur 16).

Ein weiteres Beispiel eines kontinuierlich messenden analytischen Testelements 1 ist in Figur 17 und 18 dargestellt. Das Substrat 2 weist ein nadelförmiges Ende auf, das durch die Haut 20 in das Gewebe 21 gestochen wird, so dass die Messelektroden 16 direkt im Gewebe 21 messen können. Auf dem flächigen extrakorporalen Teil des Substrats 2 befinden sich die Potentiostatelektronik und das Transpondermodul 37 als Polymerelektronik oder Siliziumchip. Eine Deckschicht 19 kapselt die Elektronik bis auf die Messelektroden ein. Ein Pflaster 62 fixiert das Testelement 1 auf der Haut.

Figur 19 bis 21 zeigen Beispiele für eine Datenprogrammierung in Produktion und Logistik. In Figur 19 und 20 schreibt ein Lesemodul 8 während der Produktion die chargenspezifischen Kalibrationsdaten auf Teststreifen 1, die bereits fertig verpackt in einer Trommel 63 bzw. einem Magazin 64 vorliegen. In Figur 21 sind mehrere Teststreifendosen 63 in einem Karton 65 zu einem Gebinde zusammengefasst und werden dann von einem Lesemodul 8 in der Produktion oder in der Logistikkette beschrieben. Es ist auch möglich, Daten (z. B. Chargen- oder Seriennummern der Teststreifen) bei der Herstellung des Polymerelektronik-Transponders fest zu verdrahten. Die Daten müssen dann nicht extra aufgespielt werden, sind aber auch nachträglich nicht mehr zu ändern.

Figur 22 und 23 zeigen einen Schreib-Lese-Speicher aus Polymerelektronik, wie er beispielsweise für einen Transponderspeicher 54 verwendet wird. Das Polymersubstrat 4, z. B. aus PDOT (Polyethylenedioxythiophene), besitzt an der Oberseite Zeilenleitungen 66 und an der Unterseite Spaltenleitungen 67. Durch Anlegen einer Spannung an eine bestimmte Zeilen- 66 und einer bestimmten Spaltenleitung 67 ändert das Polymer 4 am Kreuzungspunkt seine elektrische Leitfähigkeit von hochohmig 12 zu niedrigohmig 13. Durch Umpolen der Spannung ist der Effekt umkehrbar, bei Wegnahme der Spannung bleibt der letzte Widerstandswert erhalten. Auf diese Weise erhält man einen binären Datenspeicher. Für die Speicherung der Kalibrationsdaten eines Blutglukoseteststreifens sind beispielsweise 10 Zeilen und 10 Spalten ausreichend. Durch messen der Widerstände zwischen definierten Spalten- und Zeilenleitungen werden die Daten wieder ausgelesen.

Patentansprüche

1. Ein System zur Bestimmung der Konzentration eines Analyten in einer Körperflüssigkeit beinhaltend
- ein analytisches Testelement, das einen Bereich mit Nachweischemie zum Nachweis des Analyten in einer Körperflüssigkeit aufweist, und davon getrennt
- ein Instrument, das eine Auswerteeinheit zur Auswertung von Daten aufweist,
dadurch gekennzeichnet, dass zumindest ein Teil der elektrischen Komponenten des analytischen Testelements auf der Basis von Polymerelektronik ausgebildet ist.

2. Ein System gemäß Anspruch 1, wobei
- das analytische Testelement ein Sendemodul zur drahtlosen Übertragung von Daten aufweist, und
- das Instrument ein Lesemodul zur drahtlosen Übertragung von Daten aufweist.

3. Ein System gemäß einem der Ansprüche 1 oder 2, wobei
- das analytische Testelement einen Speicher zur Speicherung von Daten aufweist.

4. Ein System gemäß einem der Ansprüche 1 bis 3 , wobei das analytische Testelement ein Sendemodul zur drahtlosen Übertragung von Daten und Energie sowie das Instrument ein Lesemodul zur drahtlosen Übertragung von Daten und Energie beinhalten.

5. Ein System gemäß einem der Ansprüche 1 bis 4, wobei die elektronische Schaltung auf dem analytischen Testelement mehrere Elektroden, die in Kontakt mit der Nachweischemie stehen, und mehrere galvanisch getrennte elektronische Schaltkreise beinhaltet, und zur drahtlosen Übertragung von Daten bzw. Daten und Energie das analytische Testelement mehrere parallele Sendemodule und das Instrument mehrere parallele Lesemodule aufweisen.

6. Ein System gemäß einem der Ansprüche 1 bis 5, wobei die Daten, die drahtlos zwischen dem Sendemodul auf dem analytischen Testelement und dem Lesemodul auf dem Instrument übertragen werden, zumindest teilweise analoge Daten beinhalten.

7. Ein System gemäß einem der Ansprüche 1 bis 6, wobei das analytische Testelement einen Speicher zur Speicherung von Daten beinhaltet und der Speicher auch beschreibbar ist, wenn sich das analytische Testelement in einer Verpackung befindet.

8. Ein System gemäß einem der Ansprüche 1 bis 7, wobei sich auf dem analytischen Testelement ein Sendemodul und ein Lesemodul befinden und zwischen diesen beiden Modulen drahtlos Daten bzw. Daten und Energie innerhalb des analytischen Testelementes übertragen werden.

9. Ein System gemäß einem der Ansprüche 1 bis 8, wobei das Instrument eine Halterung zur Positionierung des analytischen Testelements beinhaltet.

10. Ein System zur Bestimmung der Konzentration eines Analyten in einer Körperflüssigkeit beinhaltend
- ein oder mehrere analytische Testelemente, die einen Bereich mit Nachweischemie zum Nachweis des Analyten in einer Körperflüssigkeit aufweisen, davon getrennt
- ein Instrument, das eine Auswerteeinheit zur Auswertung von Daten sowie ein Lesemodul zur drahtlosen Übertragung von Daten aufweist, und
- eine Verpackung, in der die ein oder mehreren analytischen Testelemente verpackt sind, und die Verpackung einen Speicher zur Speicherung von Daten sowie ein Sendemodul zur drahtlosen Übertragung von Daten aufweist,

dadurch gekennzeichnet, dass zumindest ein Teil der elektrischen Komponenten der Verpackung auf der Basis von Polymerelektronik ausgebildet ist.

11. Ein System gemäß Anspruch 10, wobei das Instrument eine Halterung zur Positionierung der Verpackung beinhaltet.

12. Ein analytisches Testelement zur Bestimmung der Konzentration eines Analyten in einer Körperflüssigkeit, das einen Bereich mit Nachweischemie zum Nachweis des Analyten in einer Körperflüssigkeit aufweist, dadurch gekennzeichnet, dass zumindest ein Teil der elektrischen Komponenten des analytischen Testelements auf der Basis von Polymerelektronik ausgebildet ist.

13. Ein analytisches Testelement gemäß Anspruch 12 dadurch gekennzeichnet, dass das analytische Testelement ein Sendemodul zur drahtlosen Übertragung von Daten aufweist.

14. Eine Verpackung, in der ein oder mehrere analytische Testelemente verpackt sind, dadurch gekennzeichnet, dass die Verpackung einen Speicher zur Speicherung von Daten sowie ein Sendemodul zur drahtlosen Übertragung von Daten aufweist.

15. Ein Verfahren zur Herstellung eines analytischen Testelements, das einen Bereich mit Nachweischemie zum Nachweis eines Analyten in einer Körperflüssigkeit, einen Speicher zur Speicherung von Daten und ein Sendemodul zur drahtlosen Übertragung von Daten aufweist, wobei die Herstellung die Schritte beinhaltet:
- Verpacken des analytischen Testelements, sowie
- Speichern von Kalibrationsdaten auf dem verpackten analytischen Testelement.

16. Ein Verfahren zur Herstellung eines analytischen Testelements gemäß Anspruch 15 dadurch gekennzeichnet, dass das Verfahren vor den Schritten
- Verpacken des analytischen Testelements, sowie
- Speichern von Kalibrationsdaten auf dem verpackten analytischen Testelement
den Schritt
- Speichern einer Chargenidentifikation auf dem analytischen Testelement
beinhaltet.

17. Ein Verfahren zur Herstellung eines analytischen Testelements, das einen Bereich mit Nachweischemie zum Nachweis eines Analyten in einer Körperflüssigkeit aufweist, wobei die Herstellung die Schritte beinhaltet:
- Verpacken des analytischen Testelements in der Verpackung, sowie
- Speichern von Kalibrationsdaten auf der Verpackung.

18. Ein Verfahren zur Herstellung eines analytischen Testelements gemäß Anspruch 17 dadurch gekennzeichnet, dass das Verfahren vor den Schritten
- Verpacken des analytischen Testelements in der Verpackung, sowie
- Speichern von Kalibrationsdaten auf der Verpackung
den Schritt
- Speichern einer Chargenidentifikation auf einer Verpackung, die einen Speicher zur Speicherung von Daten und ein Sendemodul zur drahtlosen Übertragung von Daten aufweist,
beinhaltet.

19. Ein Verfahren zur Bestimmung der Konzentration eines Analyten in einer Körperflüssigkeit, das die Schritte beinhaltet:
- Einbringen eines Sendemoduls eines analytischen Testelements in einen Sende- und Empfangsbereich eines Lesemoduls eines Instruments, wobei
  das analytische Testelement einen Bereich mit Nachweischemie zum Nachweis eines Analyten in einer Körperflüssigkeit, einen Speicher zur Speicherung von Daten und das Sendemodul zur drahtlosen Übertragung der Daten aufweist, und das Instrument eine Auswerteeinheit zur Auswertung der Daten und das Lesemodul zur drahtlosen Übertragung der Daten aufweist,
- Auftragen der Körperflüssigkeit auf das analytische Testelement,
- drahtlose Übertragung der Daten vom analytischen Testelement zum Instrument, sowie
- Auswerten der Daten in der Auswerteeinheit des Instruments.

20. Ein Verfahren gemäß Anspruch 19 dadurch gekennzeichnet, dass das analytische Testelement in das Instrument eingelegt oder eingeschoben wird und dadurch das Sendemodul des analytischen Testelements in den Sende- und Empfangsbereich des Lesemoduls des Instruments eingebracht wird.

21. Ein Verfahren zur Bestimmung der Konzentration eines Analyten in einer Körperflüssigkeit, das die Schritte beinhaltet:
- Einbringen eines Sendemoduls einer Verpackung, in der ein oder mehrere analytische Testelemente mit Nachweischemie zum Nachweis eines Analyten in einer Körperflüssigkeit verpackt sind, in einen Sende- und Empfangsbereich eines Lesemoduls eines Instruments, wobei
  die Verpackung einen Speicher zur Speicherung von Daten sowie das Sendemodul zur drahtlosen Übertragung der Daten aufweist, und
  das Instrument eine Auswerteeinheit zur Auswertung der Daten und das Lesemodul zur drahtlosen Übertragung der Daten aufweist,
- Bereitstellen eines analytischen Testelements aus der Verpackung,
- Auftragen der Körperflüssigkeit auf das analytische Testelement,
- drahtlose Übertragung der Daten von der Verpackung zum Instrument, sowie
- Auswerten der Daten in der Auswerteeinheit des Instruments.

22. Ein Verfahren gemäß Anspruch 21 dadurch gekennzeichnet, dass die Verpackung in das Instrument eingelegt oder eingeschoben wird und dadurch das Sendemodul der

Verpackung in den Sende- und Empfangsbereich des Lesemoduls des Instruments eingebracht wird.

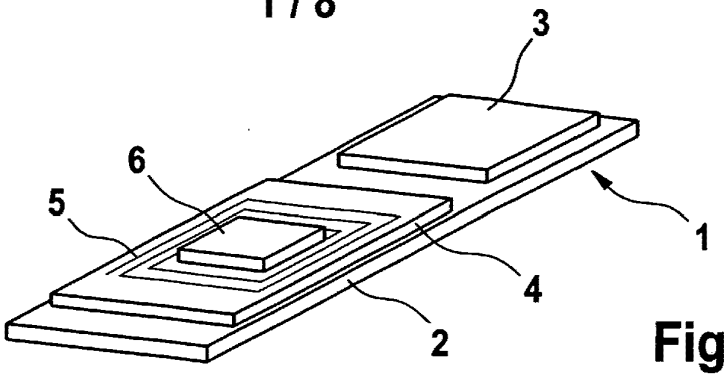


Fig. 1

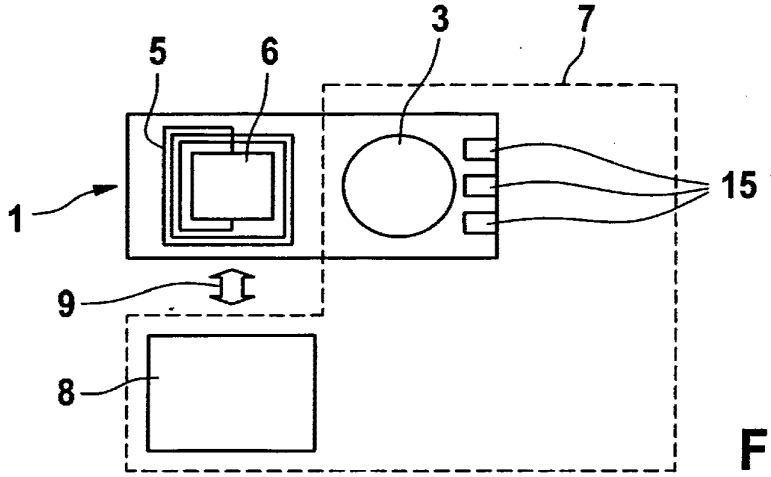


Fig. 2

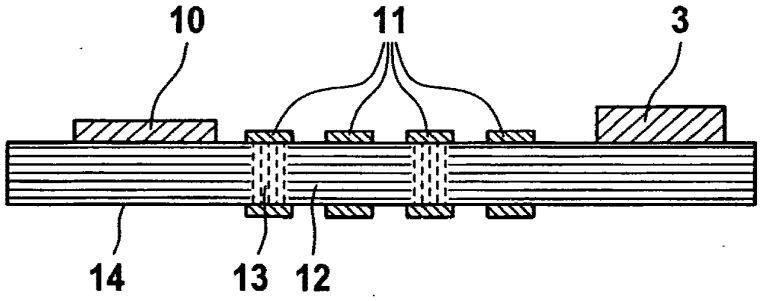


Fig. 3

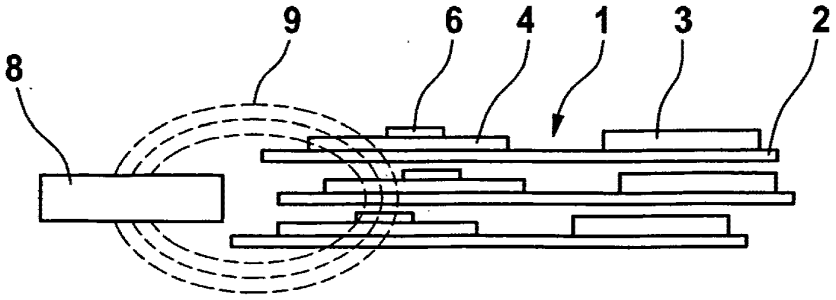


Fig. 4

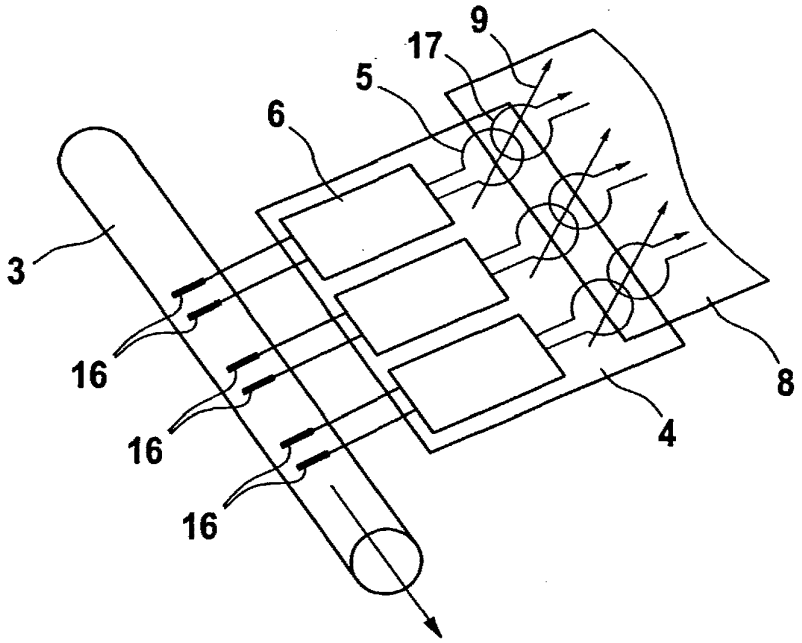


Fig. 5

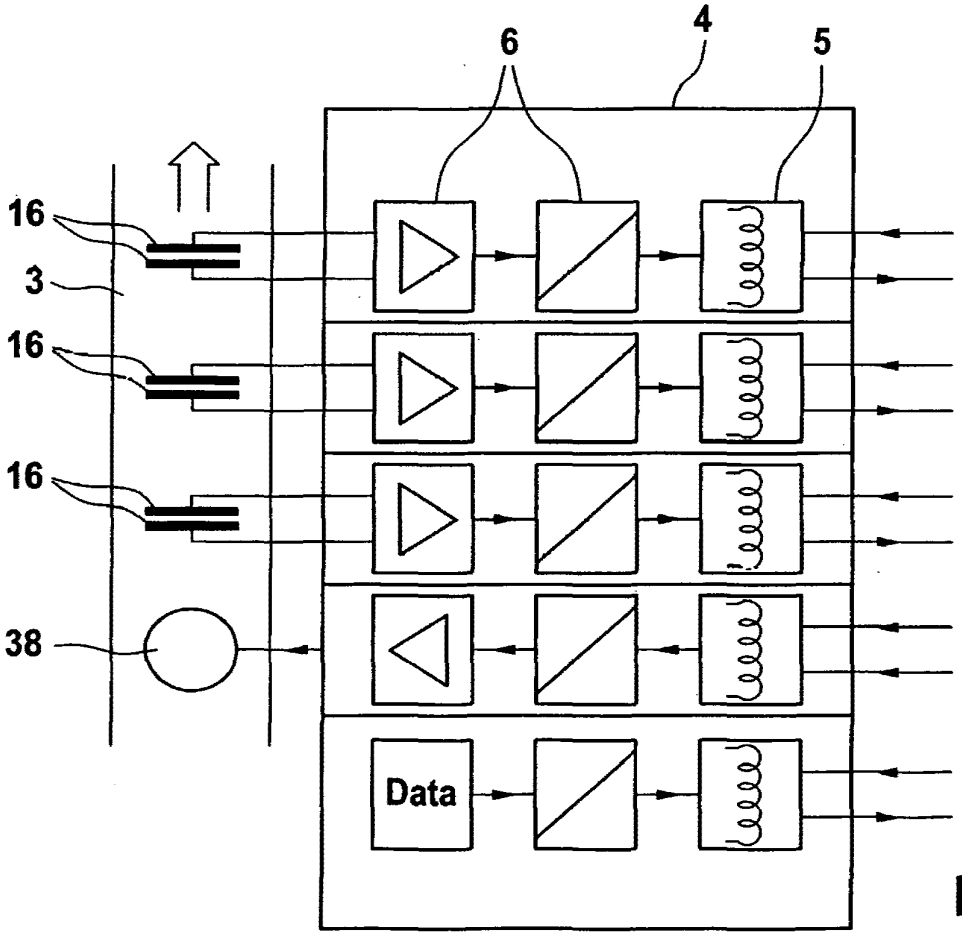


Fig. 6

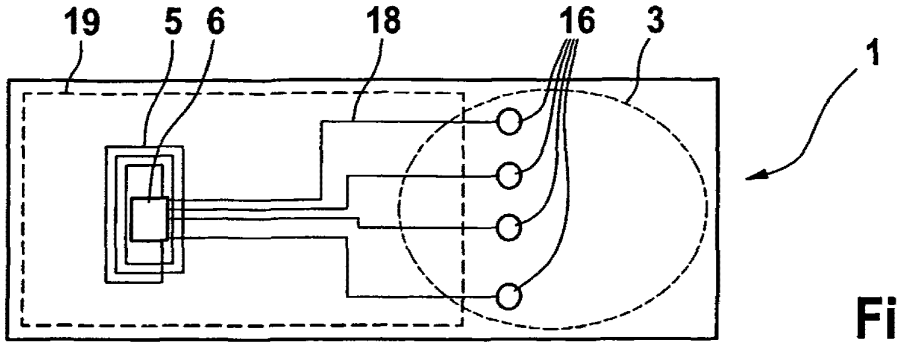


Fig. 7

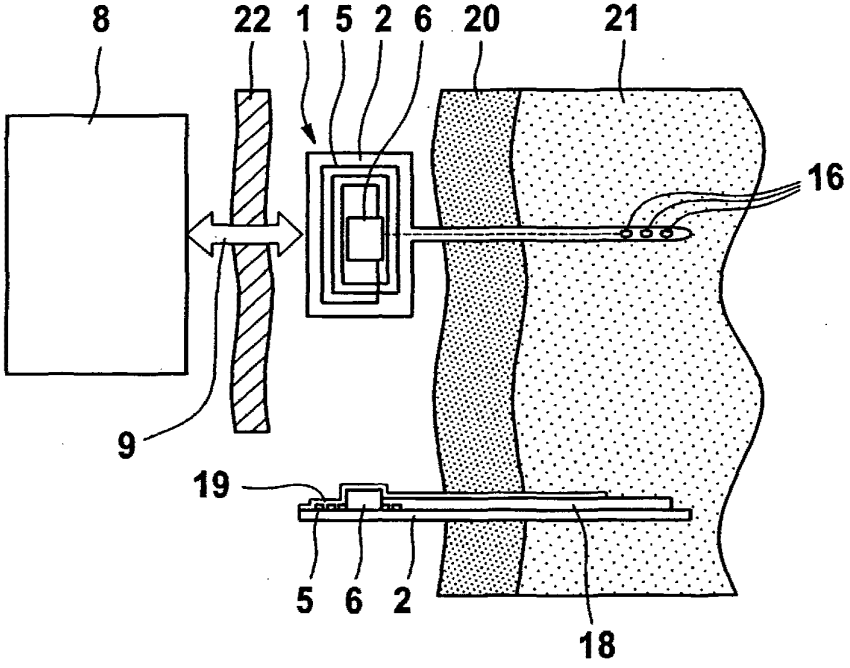


Fig. 8

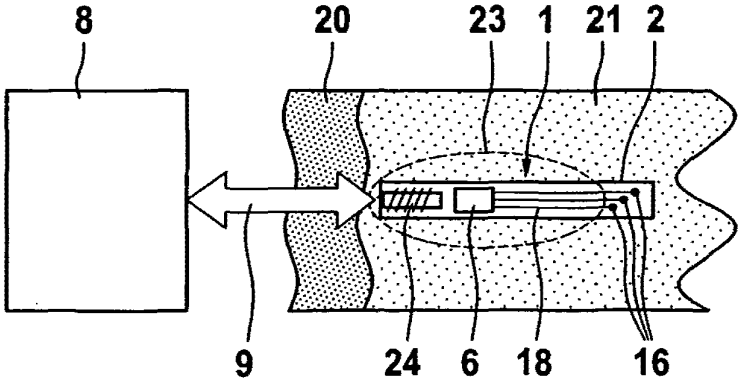


Fig. 9

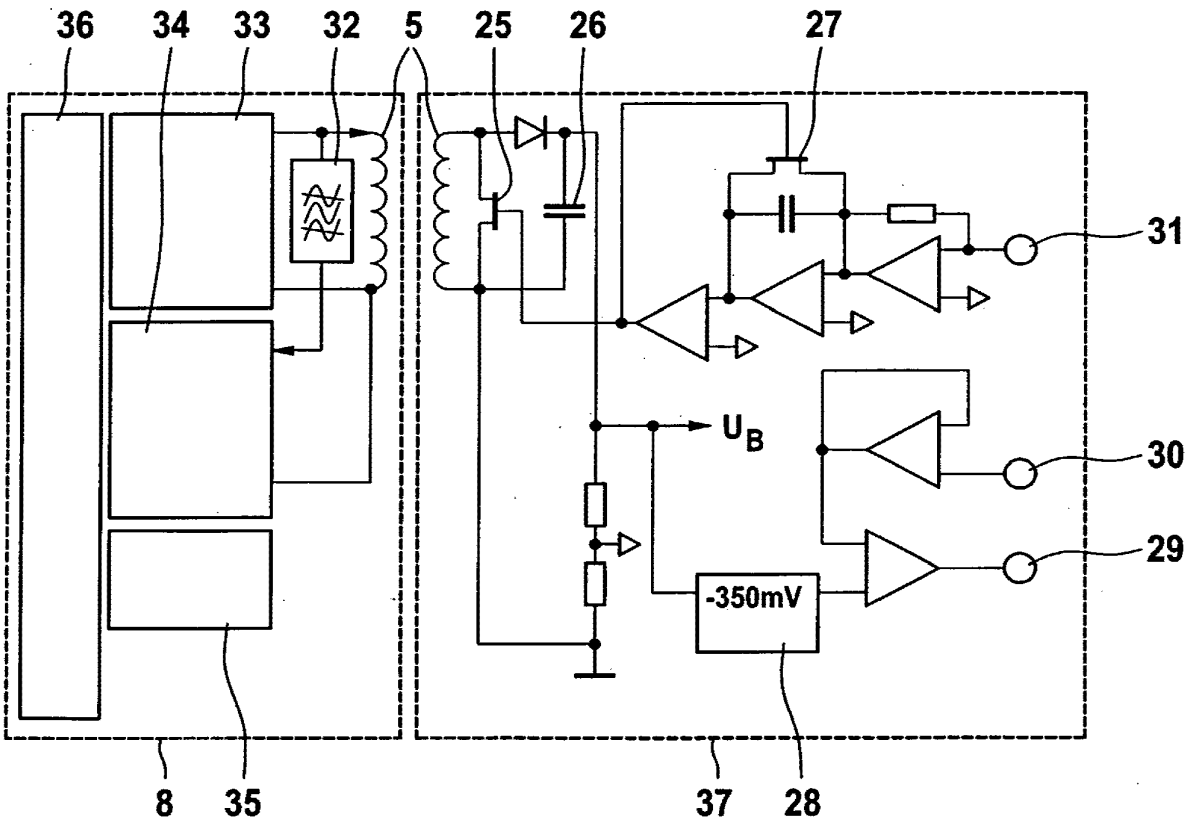


Fig. 10

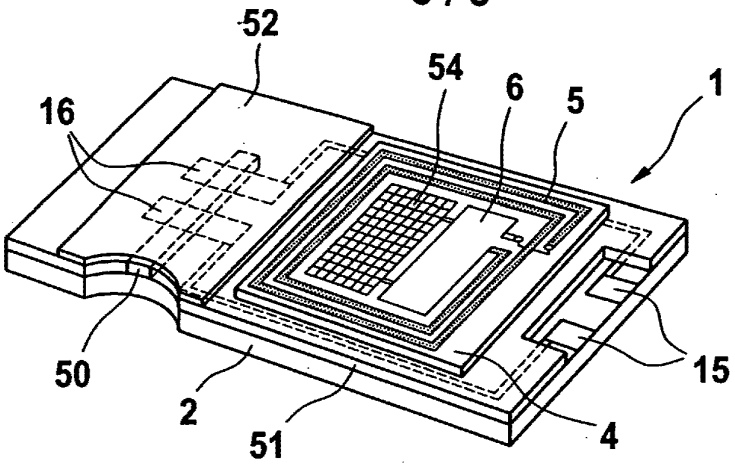


Fig. 11

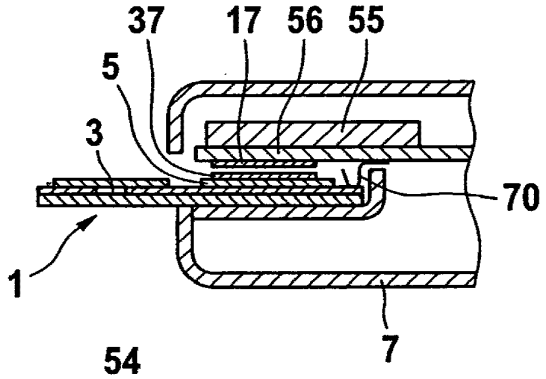


Fig. 12

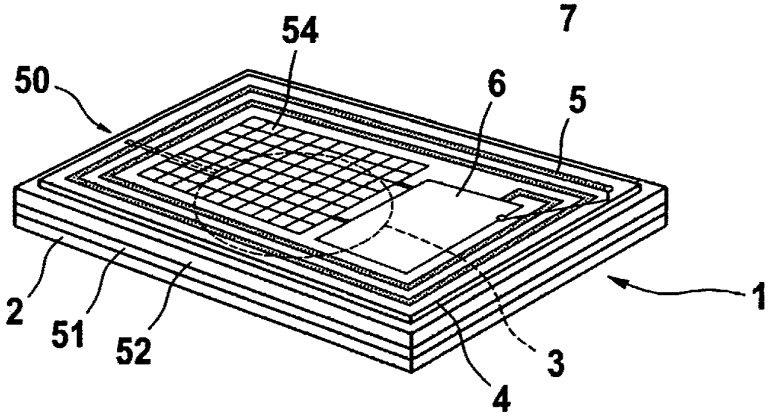


Fig. 13

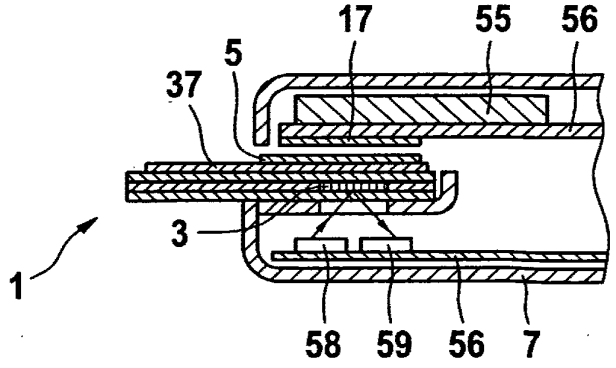


Fig. 14

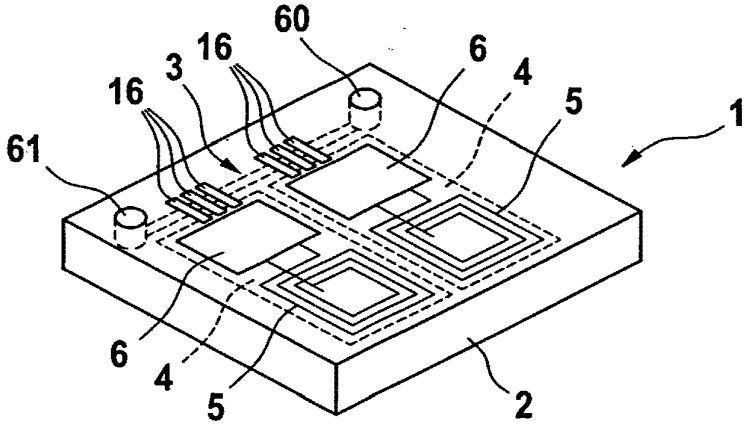


Fig. 15

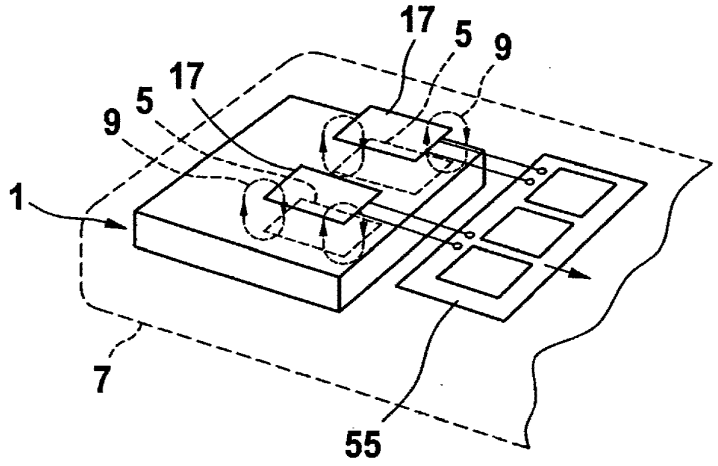


Fig. 16

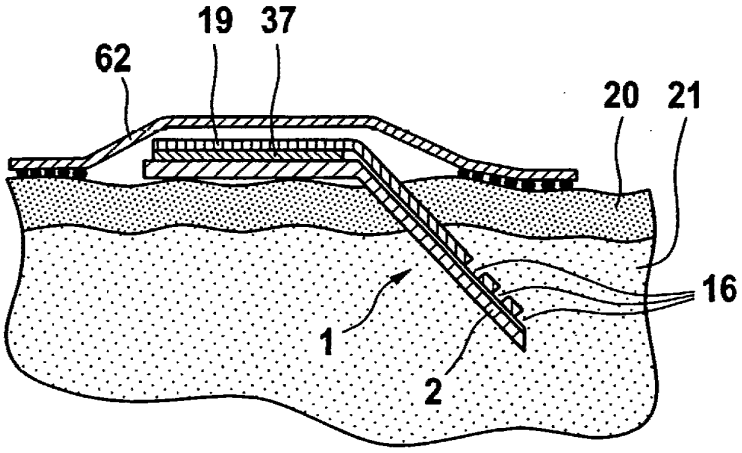


Fig. 17

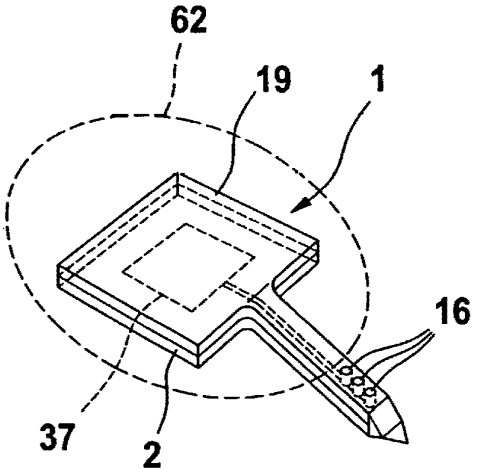


Fig. 18

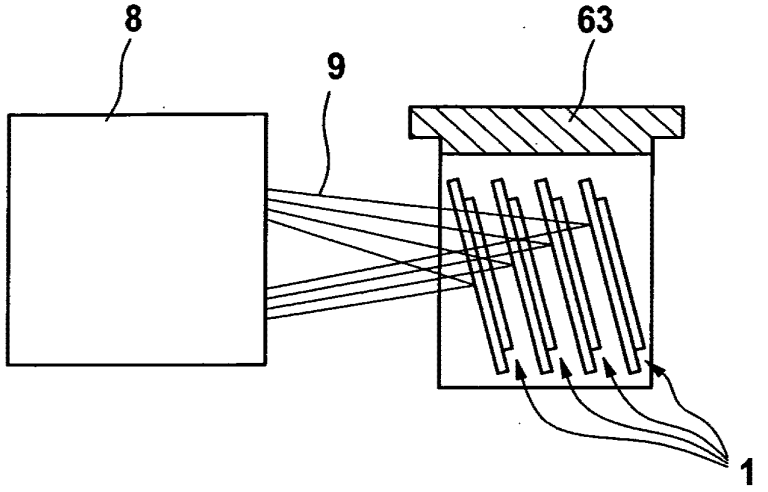


Fig. 19

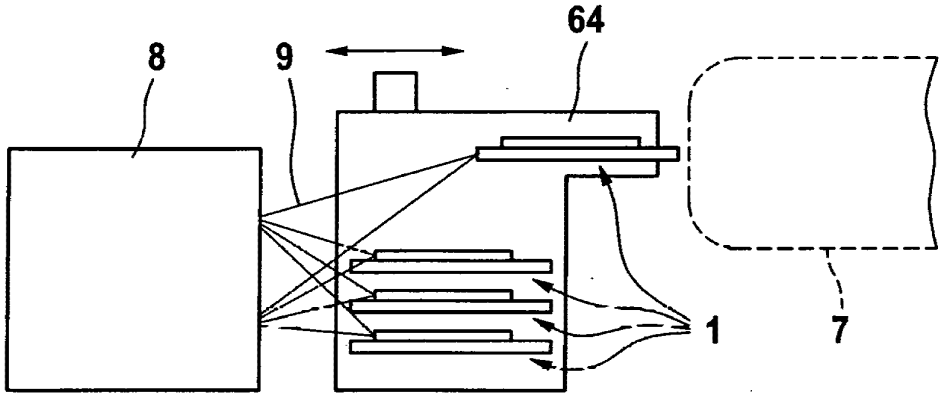


Fig. 20

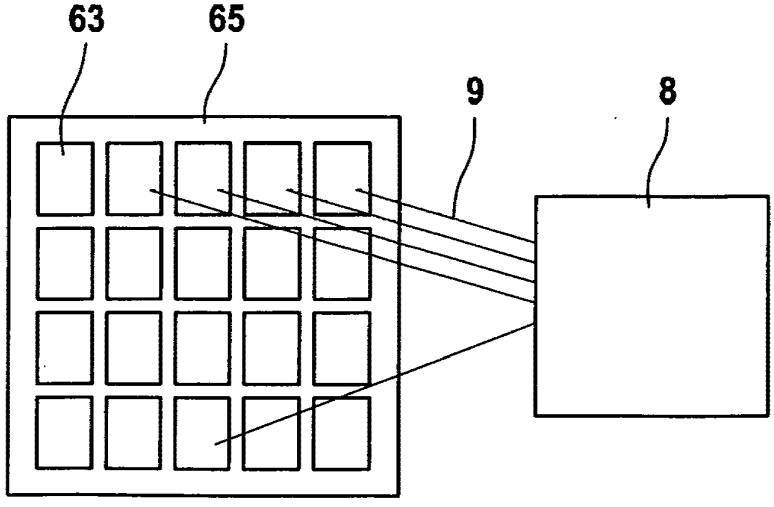


Fig. 21

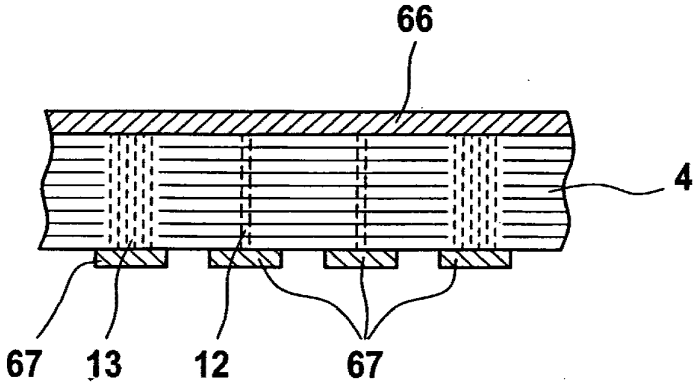


Fig. 22

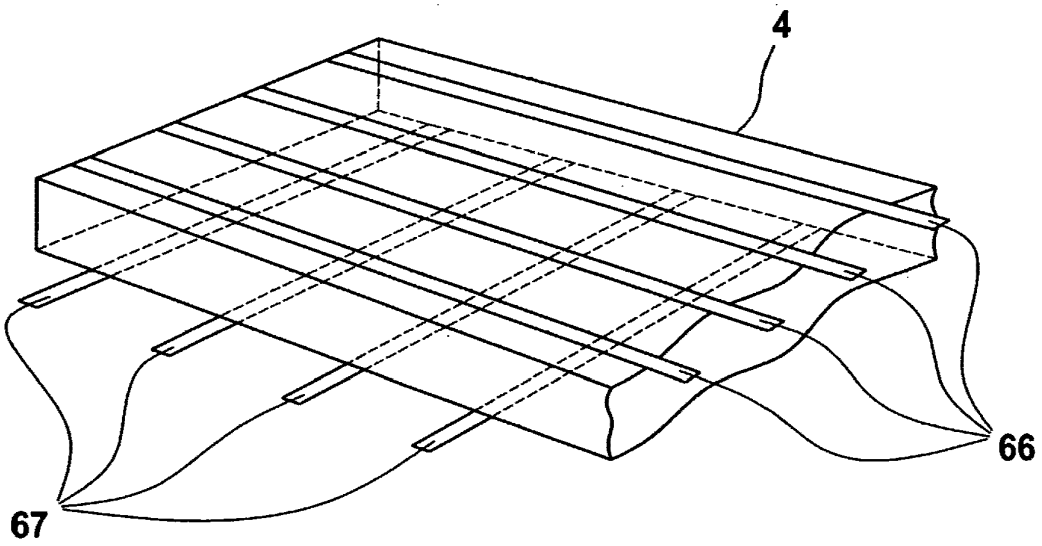


Fig. 23

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/010806

A. CLASSIFICATION OF SUBJECT MATTER
G01N33/487 A61B5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01N A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, INSPEC, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 217 744 B1 (CROSBY PETER) 17 April 2001 (2001-04-17) cited in the application the whole document	2-9
Y	DE 102 37 602 A1 (I.E.M. INDUSTRIELLE ENTWICKLUNG MEDIZINTECHNIK UND VERTRIEBSGESELLSCHA) 18 March 2004 (2004-03-18) cited in the application the whole document	2-9
Y	DE 102 53 154 A1 (SIEMENS AG; ROCHE DIAGNOSTICS GMBH) 27 May 2004 (2004-05-27) cited in the application the whole document	2-9

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[X] Further documents are listed in the continuation of box C.

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Date of the actual completion of the international search	Date of mailing of the international search report
22 December 2005	10/01/2006

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Komenda, P

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/010806

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	"Polytronic: Chips von der Rolle" FRAUNHOFER MAGAZIN, FRAUNHOFER GESELLSCHAFT, MUENCHEN, DE, no. 4, 2001, pages 8-13, XP002257822 ISSN: 1434-7113 the whole document	2-9
A	US 5 580 794 A (ALLEN ET AL) 3 December 1996 (1996-12-03) column 9, line 12 - line 28; figures 1,2	2-9
P,A	WO 2005/024375 A (POLYIC GMBH & CO. KG; CLEMENS, WOLFGANG; GERLT, AXEL; HAHN, ALEXANDER;) 17 March 2005 (2005-03-17) page 4, line 6 - line 26	2

1

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INTERNATIONAL SEARCH REPORT

mation on patent family members

International Application No
PCT/EP2005/010806

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6217744 B1	17-04-2001	NONE	
DE 10237602 A1	18-03-2004	NONE	
DE 10253154 A1	27-05-2004	AU 2003294625 A1	03-06-2004
		CA 2516490 A1	27-05-2004
		WO 2004044571 A1	27-05-2004
		DE 10394075 D2	06-10-2005
		EP 1563288 A1	17-08-2005
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		CA 2170402 A1	02-03-1995
		EP 0722563 A1	24-07-1996
		JP 9503581 T	08-04-1997
		WO 9506240 A1	02-03-1995
WO 2005024375 A	17-03-2005	DE 10341093 A1	14-04-2005

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2005/010806

A. KLASSIFIZIERUNG DES ANMELDUNGSGEGENSTANDES
G01N33/487 A61B5/00

Nach der Internationalen Patentklassifikation (IPK) oder nach der nationalen Klassifikation und der IPK

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Recherchierter Mindestprüfstoff (Klassifikationssystem und Klassifikationssymbole)
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C. ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie°	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	US 6 217 744 B1 (CROSBY PETER) 17. April 2001 (2001-04-17) in der Anmeldung erwähnt das ganze Dokument -----	2-9
Y	DE 102 37 602 A1 (I.E.M. INDUSTRIELLE ENTWICKLUNG MEDIZINTECHNIK UND VERTRIEBSGESELLSCHA) 18. März 2004 (2004-03-18) in der Anmeldung erwähnt das ganze Dokument -----	2-9
Y	DE 102 53 154 A1 (SIEMENS AG; ROCHE DIAGNOSTICS GMBH) 27. Mai 2004 (2004-05-27) in der Anmeldung erwähnt das ganze Dokument -----	2-9
	-/--	

[X] Weitere Veröffentlichungen sind der Fortsetzung von Feld C zu entnehmen

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Datum des Abschlusses der internationalen Recherche	Absendedatum des internationalen Recherchenberichts
22. Dezember 2005	10/01/2006

Name und Postanschrift der Internationalen Recherchenbehörde	Bevollmächtigter Bediensteter
Europäisches Patentamt, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Komenda, P

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INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2005/010806

C.(Fortsetzung) ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie°	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
A	"Polytronic: Chips von der Rolle" FRAUNHOFER MAGAZIN, FRAUNHOFER GESELLSCHAFT, MUENCHEN, DE, Nr. 4, 2001, Seiten 8-13, XP002257822 ISSN: 1434-7113 das ganze Dokument	2-9
A	US 5 580 794 A (ALLEN ET AL) 3. Dezember 1996 (1996-12-03) Spalte 9, Zeile 12 - Zeile 28; Abbildungen 1,2	2-9
P,A	WO 2005/024375 A (POLYIC GMBH & CO. KG; CLEMENS, WOLFGANG; GERLT, AXEL; HAHN, ALEXANDER;) 17. März 2005 (2005-03-17) Seite 4, Zeile 6 - Zeile 26	2

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INTERNATIONALER RECHERCHENBERICHT

Angaben zu Veröffentlicht[illegible] lie zur selben Patentfamilie gehören

Internationales Aktenzeichen
PCT/EP2005/010806

Im Recherchenbericht angeführtes Patentdokument		Datum der Veröffentlichung	Mitglied(er) der Patentfamilie		Datum der Veröffentlichung
US 6217744	B1	17-04-2001	KEINE		
DE 10237602	A1	18-03-2004	KEINE		
DE 10253154	A1	27-05-2004	AU	2003294625 A1	03-06-2004
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			WO	2004044571 A1	27-05-2004
			DE	10394075 D2	06-10-2005
			EP	1563288 A1	17-08-2005
US 5580794	A	03-12-1996	AU	7563294 A	21-03-1995
			CA	2170402 A1	02-03-1995
			EP	0722563 A1	24-07-1996
			JP	9503581 T	08-04-1997
			WO	9506240 A1	02-03-1995
WO 2005024375	A	17-03-2005	DE	10341093 A1	14-04-2005

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60/650,912	8 February 2005 (08.02.2005)	US
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11/350,398	7 February 2006 (07.02.2006)	US

(71) Applicant *(for all designated States except US)*: **THERASENSE, INC.** [US/US]; 1420 South Loop Road, Alameda, California 94502 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **GOODNOW, Timothy, T.** [US/US]; 8280 Regency Drive, Pleasanton, California 94588 (US). **HE, Lei (Lawrence)** [—/US]; 1419 Camino Peral, Moraga, California 94556 (US).

(74) Agent: **SMITH, Andrew, V.**; DLA Piper Rudnick Gray Cary US LLP, 153 Townsend Street, Suite 800, San Francisco, California 94107 (US).

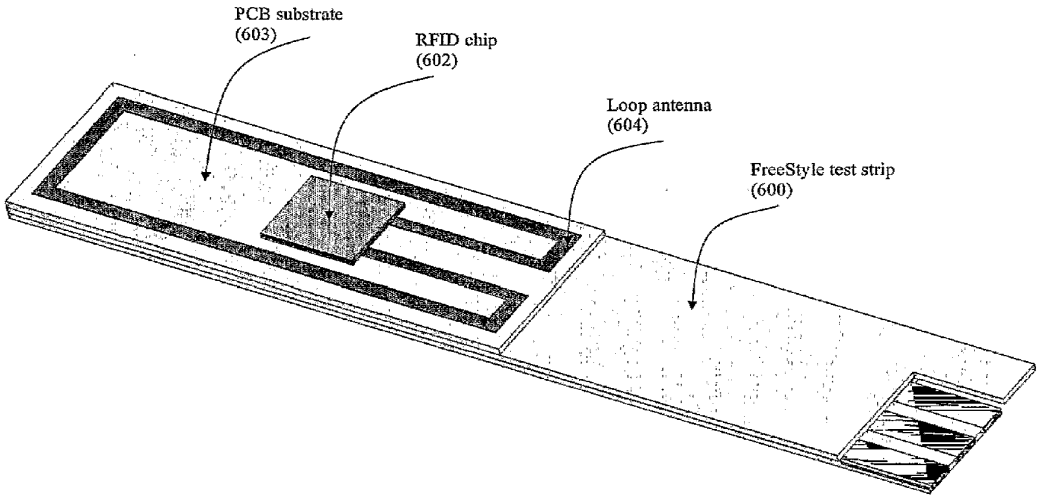
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: RF TAG ON TEST STRIPS, TEST STRIP VIALS AND BOXES



(57) Abstract: A glucose monitoring system, includes a glucose sensor strip or package of strips. The strip includes a substrate and a glucose monitoring circuit that has electrodes and a bodily fluid application portion of selected chemical composition. An antenna is integrated with the glucose sensor strip. A RFID sensor chip is coupled with the glucose sensor strip and the antenna. The chip has a memory containing digitally-encoded data representing calibration and/or expiration date information for the strip.

WO 2006/086423 A2

RF TAG ON TEST STRIPS, TEST STRIP VIALS AND BOXES

PRIORITY

This application claims the benefit of priority to United States provisional patent applications numbers 60/650,912, filed February 8, 2005 and 60/701,654, filed July 21, 2005, and to United States patent application filed February 7, 2006, entitled RF TAG ON TEST STRIPS, TEST STRIP VIALS AND BOXES,. By inventors Timothy T. Goodnow and Lei (Lawrence) He, which are incorporated by reference.

BACKGROUND

Diabetes care involves periodically checking the blood glucose level of a bodily fluid such as blood. Based on the measured bodily fluid level, a diabetic may take one or more steps such as injecting insulin or consuming carbohydrates to bring the level back to a desired level.

GLUCOSE METERS

Figure 1 illustrates a conventional blood glucose meter 100 (see United States Design patent no. D393,313, which is hereby incorporated by reference). The meter 100 includes a test strip slot 102, a display 104 and one or more operational buttons 106. Although not shown in Figure 1, the meter 100 also includes component circuitry for receiving signals that depend on the glucose level of a fluid applied to a strip that is inserted into the slot 102, and component circuitry for determining the glucose level based on the received signals. Figure 2 illustrates a blood glucose meter 200 with display 104 and operational buttons 106, and also having a glucose test strip 202 inserted into a slot 102 for testing a body fluid sample applied to the strip 202.

GLUCOSE SENSORS

Small volume (e.g., less than 0.5 microliter), in vitro, electrochemical sensors are used with Freestyle® and Freestyle Flash™ glucose meters (see http://abbottdiabetescare.com, which is hereby incorporated by reference). These test strip sensors generally include a working electrode on a first substrate, a counter (or counter/reference) electrode on a second

substrate, and a sample chamber. The sample chamber is configured so that when a sample (e.g., of blood) is provided in the chamber, the sample is in electrolytic contact with both the working electrode, the counter electrode and any reference electrodes or indicator electrodes that may be present. This allows electrical current to flow between the electrodes to effect the electrolysis (electrooxidation or electroreduction) of the analyte. A spacer is generally positioned between first substrate and second substrate to provide a spacing between electrodes and to provide the sample chamber in which the sample to be evaluated is housed.

Figures 3A-3C illustrates one of these test strips (see US patent no. 6,942,518, which is assigned to the same assignee as the present application, and is hereby incorporated by reference). This configuration is used for side-filling, and end-filling is an alternative. Figure 3A illustrates a first substrate 340 with a working electrode 342. FIG. 3B illustrates a spacer 344 defining a channel 346. FIG. 3C (inverted with respect to FIGS. 3A and 3B) illustrates a second substrate 348 with three counter (or counter/reference) electrodes 350, 352, 354. This multiple counter electrode arrangement can provide a fill indicator function, as described below. The length of the channel 346 is typically defined by the two parallel cuts along the sides 356, 358 of the sensors.

Glucose test strip sensors can be manufactured adjacent to one another, as illustrated in Figures 4A-4B. Such positioning during manufacture produces less waste material. This often results in better efficiency as compared to other techniques, such as individually placing components within the individual channels of test strip sensors.

GENERAL METHOD FOR MANUFACTURING GLUCOSE SENSORS

Figures 4A-4B illustrate the processing of a sheet 1000 of test strips. Referring now to Figures 4A and 4B, one example of a method for making thin film sensors is generally described, and can be used to make a variety of sensor arrangements. When the three layers of the test strips of Figures 3A-3C, e.g., are assembled, a sensor is formed.

In Figures 4A and 4B, a substrate 400, such as a plastic substrate, is moving in the direction indicated by the arrow. The substrate 400 can be an individual sheet or a continuous roll on a web. Multiple sensors can be formed on a substrate 400 as sections 422 that have working electrodes thereon and sections 424 that have counter electrodes and indicator electrodes thereon. These working, counter and indicator electrodes are electrically connected to corresponding traces and contact pads. Typically, working electrode sections 422 are produced on one half of substrate 400 and counter electrode sections 424 are produced on the

other half of substrate 400. In some embodiments, the substrate 400 can be scored and folded to bring the sections 422, 424 together to form the sensor. In some embodiments, as illustrated in FIG. 4A, the individual working electrode sections 422 can be formed next to or adjacent each other on the substrate 400, to reduce waste material. Similarly, individual counter electrode sections 424 can be formed next to or adjacent each other. In other embodiments, the individual working electrode sections 422 (and, similarly, the counter electrode sections 424) can be spaced apart, as illustrated in FIG. 4B.

RADIO FREQUENCY IDENTIFICATION (RFID)

RFID provides an advantageous technology for remotely storing and retrieving data using devices called RFID tags. A RFID tag is a small object, such as an adhesive sticker, that can be attached to or incorporated into a product. There are passive and active RFID tags. Passive RFID tags are small devices that are generally used at shorter range and for simpler tracking and monitoring applications than active tags. Passive tags generally act over ranges up to 3-5 meters, and a few hundred are typically readable simultaneously within three meters of a reader. Because they are powered by radio waves from RFID tag reader, passive tags do not use a battery. Therefore these devices are generally inexpensive and smaller than active tags, and can last long. Active RFID tags have a power source, such as a battery, and generally have longer range and larger memories than passive tags. For example, active tags generally act over ranges up to 100 meters, and thousands of tags are typically readable simultaneously within 100 meters of a reader. For more details on passive and active RFID tags, see http://RFID-Handbook.com, which is hereby incorporated by reference.

RFID SYSTEM

An RFID system generally includes a RFID tag and RFID reader. A RFID tag includes an antenna and digital memory chip. A RFID reader, also called an interrogator, includes an antenna and a transceiver, and emits and receives RF signals. RFID readers can read tags and can typically write data into the tags. For example, Figure 5 schematically illustrates component circuitry of a passive RFID tag. A transceiver/receiver 502 of a RFID reader 505 is directionally coupled 504 to an antenna 506 of the reader 505. An RFID transponder 510 includes an antenna 512 (e.g., a dipole antenna) and memory 514.

It is desired to incorporate RFID tag technology into glucose test strips, test strip vials and/or boxes of strips. It is also desired to incorporate RFID reader into glucose meters.

SUMMARY OF THE INVENTION

A glucose monitoring system includes a glucose sensor strip or package of strips. The strip includes a substrate and a glucose monitoring circuit that has electrodes and a bodily fluid application portion of selected chemical composition. An antenna is integrated with the glucose sensor strip. A RFID sensor chip is coupled with the glucose sensor strip and the antenna. The chip has a memory containing digitally-encoded data representing calibration and/or expiration date information for the strip.

The antenna may be a loop antenna that has a conducting loop extending around substantially a perimeter of the substrate and has two ends coupled with the chip. A RFID reader may read, power and/or program the chip. The RFID reader may be integrated with a glucose meter that has a port for inserting the strip and measuring a glucose level. Alternatively, a glucose meter may include a RFID reader as a component. The calibration and/or expiration date data may be automatically read when the strip is inserted into the port of the glucose meter. The chip may include a battery or other power source, or may be a passive chip. The memory may also contain data representing a lot number of the strip, manufacture date for the strip, a type of strip, and/or a calibration code. The RFID sensor chip may operate at 13.56 MHz. The calibration data may include chemical composition information for the strip for accurately computing a glucose level based on the chemical composition.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 illustrates a conventional blood glucose meter.

Figure 2 illustrates a blood glucose meter having a strip inserted into a slot for testing a body fluid sample applied to the strip.

Figures 3A-3C illustrate a conventional test strip.

Figures 4A-4B illustrate the processing of a sheet of test strips.

Figure 5 illustrates a conventional passive RFID tag.

Figure 6 illustrates a glucose test strip including a RFID chip and antenna in accordance with a preferred embodiment.

Figure 7 is an exploded view of a glucose test strip in accordance with a preferred embodiment.

Figure 8 illustrates a RFID chip mounted on a glucose test strip in accordance with a preferred embodiment.

Figure 9 illustrates a communication system including a glucose test strip and a RFID reader in accordance with a preferred embodiment.

Figure 10 illustrates a RFID chip mounted on a package for holding glucose test strips in accordance with a preferred embodiment.

Figure 11 illustrates a glucose meter communicating with a RFID tag that is mounted on a package or box of glucose test strips in accordance with a preferred embodiment.

Figure 12 illustrates a glucose meter communicating with a RFID tag that is mounted on a glucose test strip in accordance with a preferred embodiment.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

A RFID sensor is advantageously coupled with a blood glucose test strip or with a group of strips in accordance with a preferred embodiment. The RFID sensor preferably includes calibration and/or expiration date information for the strips. The calibration information preferably includes information relating to the chemical composition of the strip, so that a blood glucose reading can be accurately computed from a reading obtained using the strip with the particular chemical composition.

In one embodiment, an individual strip includes a RFID sensor. Figure 6 illustrates a glucose test strip 600, e.g., a Freestyle® test strip manufactured by Abbott Diabetes Care of Alameda, California, that includes a RFID chip 602, which is mounted on a PCB substrate 603 or other suitable substrate, and an antenna 604, in accordance with a preferred embodiment. The antenna 604 may be a loop antenna, or a dipole antenna, or another antenna configuration.

Figure 7 is an exploded view of a Freestyle® or other glucose test strip 600 including a sample application end 601, with sample chamber and electrodes, a RFID chip 602 in accordance with a preferred embodiment. The RFID chip 602 is mounted on a PCB substrate 603 that is attached to, integral with or part of the strip 600. There is a top-side loop antenna 708 and a bottom side loop antenna 710. Figure 8 illustrates a RFID chip 602 mounted on a glucose test strip 600 in accordance with another embodiment.

Preferably a RFID reader programs the RFID sensor with the calibration data and/or powers the RFID sensor. The RFID reader may be integrated with a blood glucose meter, or the meter may include an RFID reader as a component. Figure 9 illustrates a communication system including a RFID reader 902 and a tag 904 in accordance with a preferred embodiment. The reader 902 includes a reader antenna 903. The tag 904 may be coupled with a glucose test strip or with a package or box of strips. The tag 904 includes a substrate 906, tag antenna 908 and RFID chip 910. The reader 902 sends a radio wave that impinges upon the tag 904. A backscattering radio wave is propagated back from the tag 904 as a result.

Figure 10 illustrates a RFID chip mounted on a package for holding glucose test strips in accordance with a preferred embodiment. The package illustrated is a lid of a vial container of several tens of test strips. Preferably, each of the test strips in the vial was manufactured on a same sheet of strips, such that the chemical compositions of the strips are very similar and that the strips have a common expiration date.

METERS EQUIPPED WITH A RFID TAG READER (or vice-versa)

In accordance with another advantageous embodiment, a RFID tag reader or interrogator may be adapted for providing glucose testing. As such, a test strip receptacle and glucose measurement circuitry and/or programming may be provided in a glucose meter module that plugs into a RFID reader device or is integrated therein or otherwise communicates data and/or power by cable or multi-pin connection, or wirelessly (at least for the data communication) with the RFID reader. The glucose meter module can use the power and processing capabilities of the reader, thus streamlining the meter module compared with a stand-alone meter. Even data storage for both the reader and meter may be combined into one location or otherwise synchronized.

In another embodiment, a glucose meter may be adapted for providing RFID reading and/or writing. A RFID reader may be provided that plugs into a glucose meter or is integrated therein or otherwise communicates data and/or power by cable, or multi-pin connection, or wirelessly (at least for the data communication) with the glucose meter. The RFID reader can use the power and processing capabilities of the meter, thus streamlining the RFID reader module compared with a stand-alone reader. Even data storage for both the reader and meter may be combined into one location or otherwise synchronized.

Human errors are advantageously prevented by automatically retrieving a calibration code of one or more test strips stored in a RFID tag. Expiration date information for the test strip can also be detected from the tag. Different types of test strips can also be detected, which is advantageous particularly for different strips that appear alike and/or that may be used with a same piece of diabetes care equipment. Several other possible types of data may be stored in and read from a RFID tag, which may used alone and/or may be combined with other diabetes care data to enhance the reliability of a diabetes treatment regimen, including the recording, retrieval and/or use of relevant data (see, e.g., US patent applications no. 10/112,671 and 11/146,897, which are assigned to the same assignee and are hereby incorporated by reference). Embodiments disclosed in the 10/112, 671 application, and in US patents nos. 5,899,855, 5,735,285, 5,961,451, 6,159,147 and 5,601,435, which are hereby incorporated by reference, describe alternative arrangements for combining functionalities of devices that may be modified for use with an advantage glucose meter and RFID reader combination in accordance with a preferred embodiment.

Figure 11 illustrates a glucose meter 1100 sending radio waves 1101 for communicating with a RFID tag (not specifically shown) that is mounted on a package such as a vial 1104 or a box 1106 of glucose test strips in accordance with preferred embodiments. In a first embodiment, a RFID sensor is coupled with a package or vial container 1104 of glucose test strips. The container 1104 may have a lid 1108 with the RFID sensor attached on its inside surface, or embedded therein, or mounted on the outside with a protective layer affixed over it, or alternatively on the bottom of the container 1104 or otherwise. In another embodiment, the strips are contained within a box 1102 having a RFID tag mounted preferably on the inside of the box to protect the tag, or alternatively on the outside having a protective layer over it.

Containers 1102 or 1104 preferably include only strips from a same sheet of strips having same or similar chemical compositions and expiration dates. One strip may be tested from the sheet, while the remaining strips are placed into the container. The rest of the strips that are placed in the container and not tested will reliably have the same or very similar chemical composition as the tested strip. The RFID sensor may be read only, or may also be write programmable. The data contained within the memory of the RFID sensor preferably includes calibration data regarding the chemical compositions of the strips in the container 1102, 1104 which are each estimated to have the same chemical composition as the test strip, and expiration date data for the strips, which should be the same for all of the strips that were manufactured on the same sheet at the same time. In accordance with another embodiment,

Figure 12 illustrates a glucose meter 1200 communicating with a RFID tag using radio waves 1201 that is mounted on a glucose test strip 1202 in accordance with a preferred embodiment.

RFID FREQUENCY BAND ALLOCATION

Multiple frequency bands are available for RFID communication in accordance with preferred embodiments. For example, there is a low frequency band around 125 kHz – 134 kHz. There is a worldwide standard high frequency band around 13.56 MHz. There are also UHF frequency bands around 868 MHz for European Union countries, and around 902 MHz – 928 MHz for the United States. There is also a microwave frequency band around 2.45 GHz.

It is preferred to use the worldwide standard around 13.56 MHz as the frequency band of operation in accordance with a preferred embodiment. This is the most popular frequency band, and a silicon-based RFID chip operating at this frequency band may be provided at low cost. This frequency band has a high efficiency RF energy transition, and complies with a world-wide RF standard.

TEST STRIP CODING AND METER CALIBRATING

Test strip coding and meter calibrating are the processes by which a blood glucose meter is matched with the reactivity of the test strips. A glucose meter will calculate a glucose level of a fluid applied to a strip based on a predetermined chemical composition of the strip. If the predetermined composition varies from the actual composition, then glucose test results provided by the meter will also vary from actual glucose levels.

Even test strips intended to be manufactured with a same chemical composition can vary based on uncertainties in the manufacturing process. Although this variance may be only very small when great care is taken in the manufacturing process, these very small variances can alter glucose measurement results that are output by a glucose meter from actual values unless the meter is properly calibrated. As illustrated at Figures 4A-4B and described briefly above, multiple test strips are advantageously manufactured together on a same sheet. Test strips that are manufactured on a same sheet have reduced variances in chemical composition compared with test strip manufactured separately. Therefore, one strip from a sheet is advantageously tested in accordance with a preferred embodiment to determine its precise composition. Then, blood glucose meters are calibrated according to

that composition when utilizing other strips from that same sheet for testing. As a consequence, glucose testing results are more reliably precise and accurate.

To ensure this precision and accuracy of glucose test results using blood glucose meters in accordance with a preferred embodiment, the strips may be coded, e.g., by the strip manufacturer before they are shipped out. In addition, the glucose meter is calibrated. Calibration of the meter can be performed by inserting a code strip into the meter and executing a calibration routine. The Precision™ meter of Abbott Diabetes Care® preferably uses this technique. Another method of calibration can be performed by entering a code number into the meter. This technique is preferred for use with the Freestyle® meter also of Abbott Diabetes Care®. Advantageously, the encoded calibration data can be stored in the RFID chip described above that is affixed to a strip, or a vial, box or other container of strips. Enhanced efficiency and reliability is achieved whether an RFID chip is mounted to each strip or to a vial, box or other container of strips. However, when the RFID chip from which the encoded calibration data is read is affixed to the vial, box or other container of strips, and preferably all of the strips within that vial, box or other container were manufactured from the same sheet of strips, as described above, then even greater efficiency, i.e., programming and use of a reduced number of RFID chips, is achieved. Advantageously, one RFID chip may be used for initially programming and for later obtaining calibration data for multiple strips. Moreover, expiration date data may be stored and obtained in RFID chips with the same efficiencies and advantages.

It is preferred to provide passive RFID tags on test strips, vials, boxes and/or other containers of strips. The preferred passive RFID tags can store approximately two kilobytes of data or more. The memory of the passive tag can be read and written repeatedly. In the memory, the following are preferably stored: test strip calibration codes, lot number, manufacture date, expiration date, other calibration information, or type of strip, or combinations thereof.

By using RFID tags, a test strip manufacturing process is advantageously upgraded. IN this embodiment, test strips are manufactured and preferably packed directly into final packages in vials or boxes or other containers, instead of waiting, e.g., for two weeks, for labeling of calibration codes. The calibration codes are preferably written into the RFID tags after the codes are determined. A lot group size of the test strips can be broken into a smaller geometry to achieve a more precise uniformity of chemical reactivity code. Further data can be stored into RFID tags, as desired.

The calibration, expiration date and/or other diabetes care information may be provided in a RFID chip or module associated with glucose sensors other than test strips and test strip containers. For example, continuous glucose sensors that may be implanted or partially in vivo or otherwise can include RFID features described otherwise herein. In addition, diabetes care devices other than glucose sensors such as insulin pumps can use the RFID communication of data such as pump calibration data, insulin infusion data, computed or received dose data or glucose data available at the pump. As to the latter feature, glucose data may be communicated to a pump by a glucose meter, and then read by a RFID reader.

The present invention is not limited to the embodiments described above herein, which may be amended or modified without departing from the scope of the present invention as set forth in the appended claims, and structural and functional equivalents thereof.

In methods that may be performed according to preferred embodiments herein and that may have been described above and/or claimed below, the operations have been described in selected typographical sequences. However, the sequences have been selected and so ordered for typographical convenience and are not intended to imply any particular order for performing the operations.

In addition, all references cited above herein, in addition to the background and summary of the invention sections, are hereby incorporated by reference into the detailed description of the preferred embodiments as disclosing alternative embodiments and components.

What is claimed is:

1. A glucose monitoring system, comprising:

(a) a glucose sensor, including:

(i) a substrate; and

(ii) a glucose monitoring circuit having multiple electrodes and a bodily fluid application portion of selected chemical composition;

(b) an antenna integrated with the glucose sensor; and

(c) a RFID sensor chip coupled with the glucose sensor and the antenna, wherein the chip comprises a memory containing digitally-encoded data representing expiration date information for the sensor.

2. The system of claim 1, wherein the antenna comprises a loop antenna.

3. The system of claim 2, wherein the loop antenna comprises a conducting loop extending around substantially a perimeter of the substrate and having two ends coupled with the chip.

4. The system of claim 1, further comprising a RFID reader for reading the chip.

5. The system of claim 4, wherein the RFID reader is further for powering the chip.

6. The system of claim 4, wherein the RFID reader is further for programming the chip.

7. The system of claim 1, further comprising a RFID reader integrated with a glucose meter that has a port for inserting a glucose sensor strip and measuring a glucose level, wherein the a RFID reader is for reading, programming or powering the chip, or combinations thereof.

8. The system of claim 7, wherein the expiration date data is automatically read when the strip is inserted into the port of the glucose meter.

9. The system of claim 1, further comprising a glucose meter including a RFID reader component for reading, programming or powering the chip, or combinations thereof.

10. The system of claim 9, wherein the glucose meter comprises a port for inserting a glucose sensor strip and measuring a glucose level, and wherein the expiration date data is automatically read when the strip is inserted into the port of the glucose meter.

11. The system of claim 1, wherein the chip comprising a battery or other power source.

12. The system of claim 1, wherein the memory further contains data representing a lot number of a glucose sensor strip, manufacture date for the strip, a type of strip or other sensor, or a calibration code or other calibration data, or combinations thereof.

13. The system of claim 1, wherein the RFID sensor chip operates at 13.56 MHz.

14. The system of claim 1, wherein the glucose sensor comprises a strip.

15. The system of claim 1, wherein the glucose sensor comprises a continuous glucose sensor.

16. A glucose monitoring system, comprising:

(a) a glucose sensor, including:

(i) a substrate; and

(ii) a glucose monitoring circuit having multiple electrodes and a bodily fluid application portion of selected chemical composition;

(b) an antenna integrated with the glucose sensor; and

(c) a RFID sensor chip coupled with the glucose sensor and the antenna, wherein the chip comprises a memory containing digitally-encoded data representing calibration information for the sensor.

17. The system of claim 16, wherein the antenna comprises a loop antenna.

18. The system of claim 17, wherein the loop antenna comprises a conducting loop extending around substantially a perimeter of the substrate and having two ends coupled with the chip.

19. The system of claim 16, further comprising a RFID reader for reading the chip.

20. The system of claim 19, wherein the RFID reader is further for powering the chip.

21. The system of claim 19, wherein the RFID reader is further for programming the chip.

22. The system of claim 16, further comprising a RFID reader integrated with a glucose meter that has a port for inserting a glucose sensor strip and measuring a glucose level, wherein the a RFID reader is for reading, programming or powering the chip, or combinations thereof.

23. The system of claim 22, wherein the calibration data is automatically read when the strip is inserted into the port of the glucose meter.

24. The system of claim 16, further comprising a glucose meter including a RFID reader component for reading, programming or powering the chip, or combinations thereof.

25. The system of claim 24, wherein the glucose meter comprises a port for inserting a glucose sensor strip and measuring a glucose level, and wherein the calibration data is automatically read when the strip is inserted into the port of the glucose meter.

26. The system of claim 16, wherein the chip comprising a battery or other power source.

27. The system of claim 16, wherein the memory further contains data representing a lot number of a glucose sensor strip, manufacture date for the strip, a type of strip or other sensor, a calibration code or expiration date data, or combinations thereof.

28. The system of claim 16, wherein the RFID sensor chip operates at 13.56 MHz.

29. The system of claim 16, wherein the calibration data includes chemical composition information for a glucose sensor strip for accurately computing a glucose level based on said chemical composition.

30. The system of claim 16, wherein the glucose sensor comprises a strip.

31. The system of claim 16, wherein the glucose sensor comprises a continuous glucose sensor.

32. A glucose monitoring system, comprising:

(a) a package of glucose sensor strips, the strips each including:

(i) a substrate; and

(ii) a glucose monitoring circuit having multiple electrodes and a bodily fluid application portion of selected chemical composition;

(b) an antenna integrated with the package; and

(c) a RFID sensor chip coupled with the package and the antenna, wherein the chip comprises a memory containing digitally-encoded data representing expiration date information for the strip.

33. The system of claim 32, wherein the antenna comprises a loop antenna.

34. The system of claim 33, wherein the loop antenna comprises a conducting loop extending around substantially a perimeter of the substrate and having two ends coupled with the chip.

35. The system of claim 32, further comprising a RFID reader for reading the chip.

36. The system of claim 35, wherein the RFID reader is further for powering the chip.

37. The system of claim 35, wherein the RFID reader is further for programming the chip.

38. The system of claim 32, further comprising a RFID reader integrated with a glucose meter that has a port for inserting one of the strips and measuring a glucose level, wherein the a RFID reader is for reading, programming or powering the chip, or combinations thereof.

39. The system of claim 38, wherein the expiration date data is automatically read when one of the strips is inserted into the port of the glucose meter.

40. The system of claim 32, further comprising a glucose meter including a RFID reader component for reading, programming or powering the chip, or combinations thereof.

41. The system of claim 40, wherein the glucose meter comprising a port for inserting the strip and measuring a glucose level, and wherein the expiration date data is automatically read when one of the strips is inserted into the port of the glucose meter.

42. The system of claim 32, wherein the chip comprising a battery or other power source.

43. The system of claim 32, wherein the memory further contains data representing a lot number of the strips, manufacture date for the strips, a type of the strips, or a calibration code or other calibration data, or combinations thereof.

44. The system of claim 32, wherein the RFID sensor chip operates at 13.56 MHz.

45. A glucose monitoring system, comprising:

(a) a package of glucose sensor strips, the strips each including:

(i) a substrate; and

(ii) a glucose monitoring circuit having multiple electrodes and a bodily fluid application portion of selected chemical composition;

(b) an antenna integrated with the package; and

(c) a RFID sensor chip coupled with the package and the antenna, wherein the chip comprises a memory containing digitally-encoded data representing calibration information for the strip.

46. The system of claim 45, wherein the antenna comprises a loop antenna.

47. The system of claim 46, wherein the loop antenna comprises a conducting loop extending around substantially a perimeter of the substrate and having two ends coupled with the chip.

48. The system of claim 45, further comprising a RFID reader for reading the chip.

49. The system of claim 48, wherein the RFID reader is further for powering the chip.

50. The system of claim 48, wherein the RFID reader is further for programming the chip.

51. The system of claim 45, further comprising a RFID reader integrated with a glucose meter that has a port for inserting one of the strips and measuring a glucose level, wherein the a RFID reader is for reading, programming or powering the chip, or combinations thereof.

52. The system of claim 51, wherein the calibration data is automatically read when one of the strips is inserted into the port of the glucose meter.

53. The system of claim 45, further comprising a glucose meter including a RFID reader component for reading, programming or powering the chip, or combinations thereof.

54. The system of claim 53, wherein the glucose meter comprising a port for inserting one of the strips and measuring a glucose level, and wherein the calibration data is automatically read when one of the strips is inserted into the port of the glucose meter.

55. The system of claim 45, wherein the chip comprises a battery or other power source.

56. The system of claim 45, wherein the memory further contains data representing a lot number of the strips, manufacture date for the strips, a type of the strips, a calibration code or expiration date data, or combinations thereof.

57. The system of claim 45, wherein the RFID sensor chip operates at 13.56 MHz.

58. The system of claim 45, wherein the calibration data includes chemical composition information for the strips for accurately computing a glucose level based on said chemical composition.

FIGURE 1

FIGURE 2

FIGURE 3A

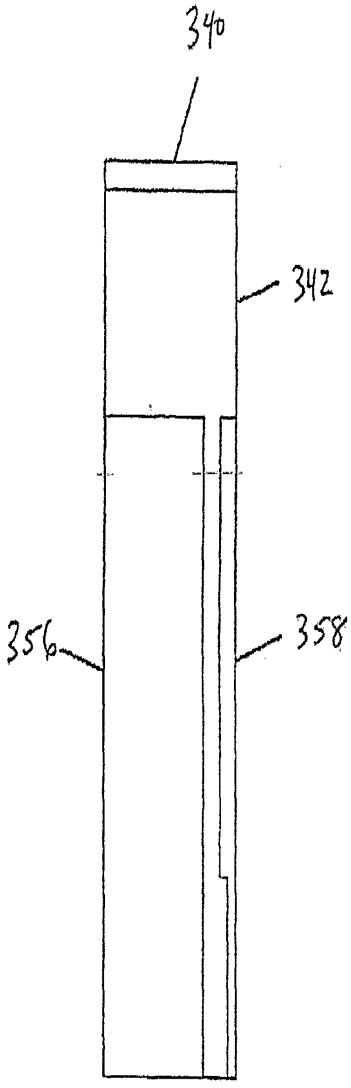


FIGURE 3B

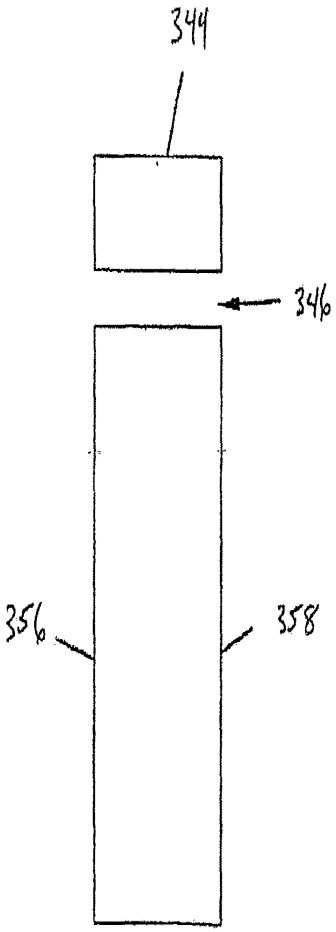


FIGURE 3C

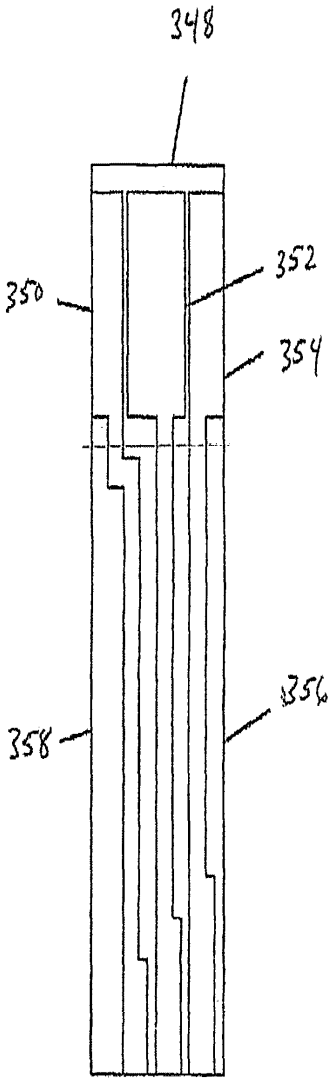


FIGURE 4A

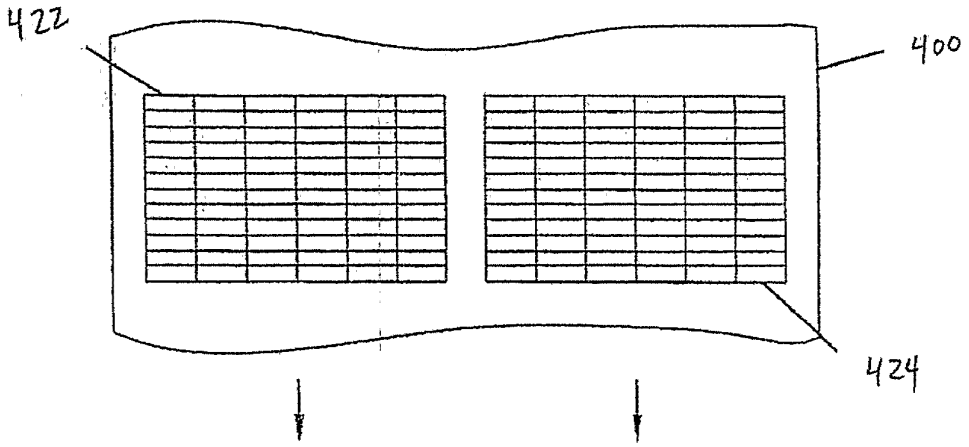
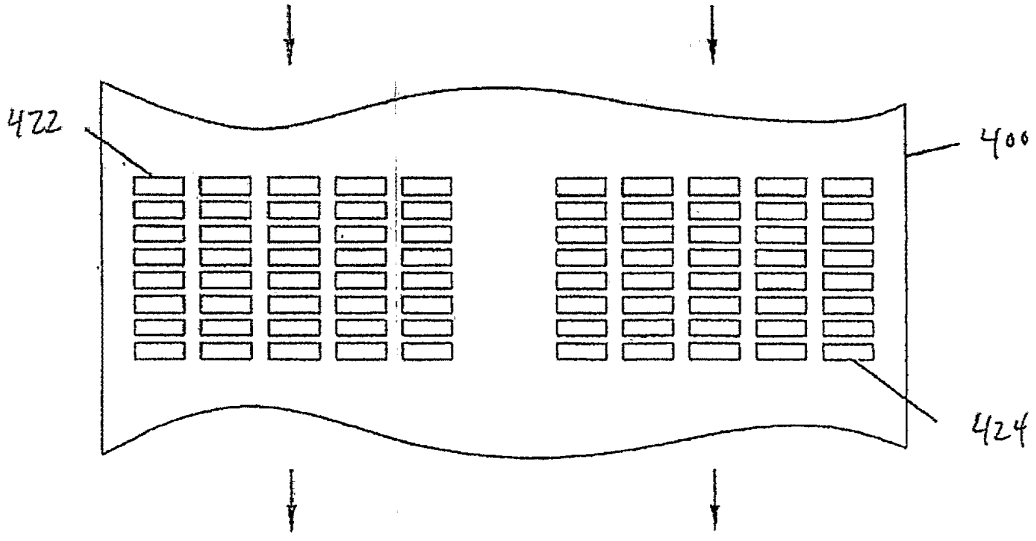


FIGURE 4B



505
510
Directional
coupler
P1
P1'
TX
Tranceiver-
receiver
RX
Reader
504
P2'
P2
Dipole-antennae
(512)
D1
D2
D3
Memory
514
RL
Transponder
502
506

FIGURE 5

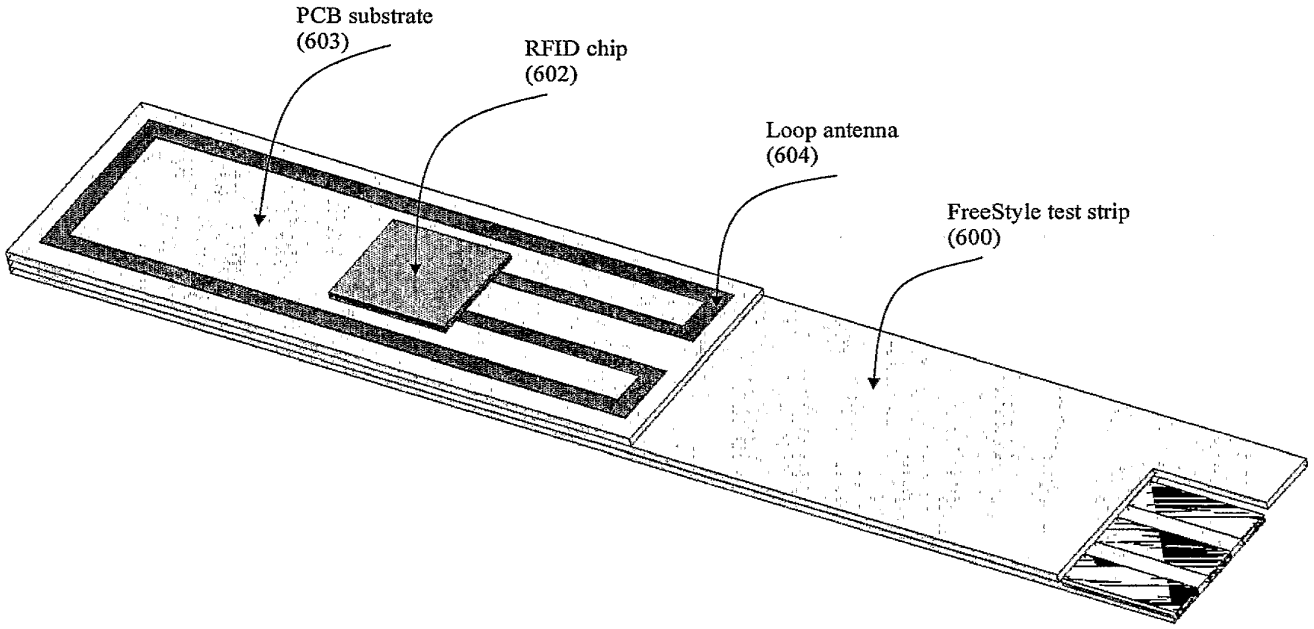

PCB substrate
(603)
RFID chip
(602)
Loop antenna
(604)
FreeStyle test strip
(600)

FIGURE 6

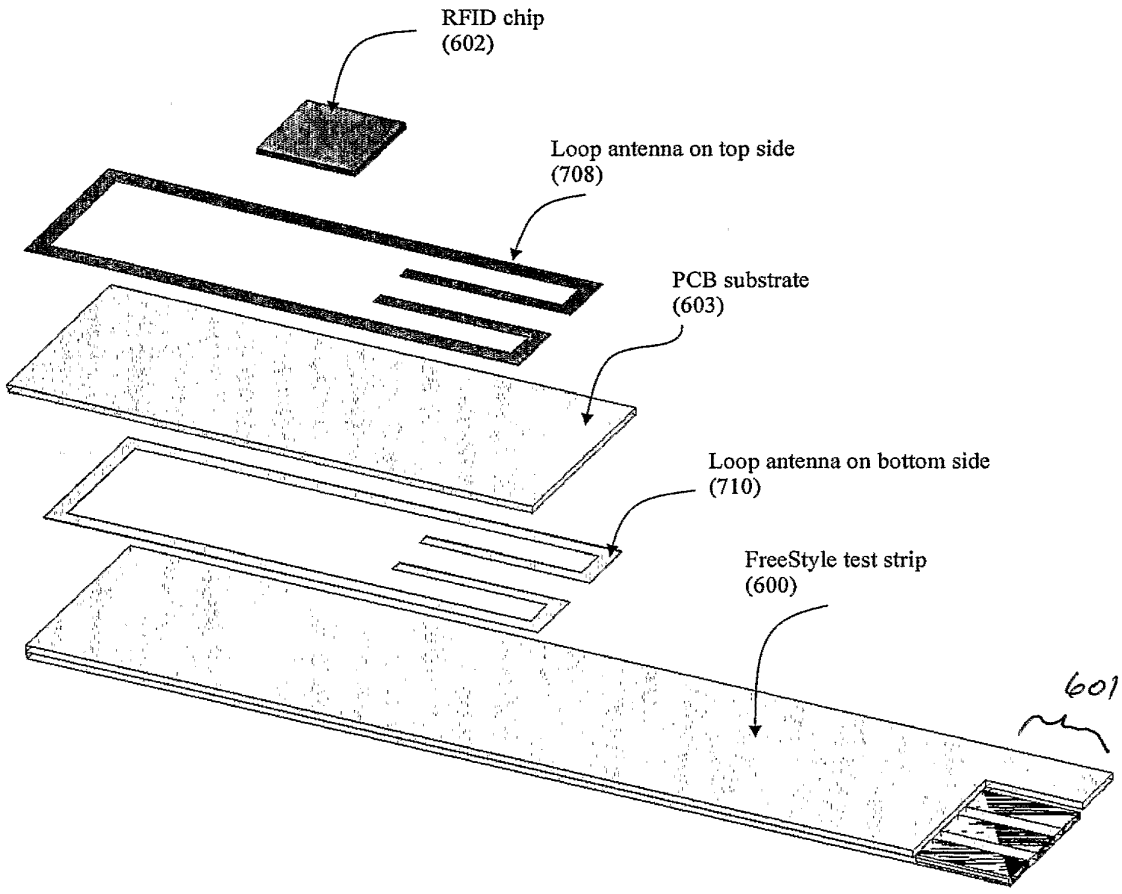

RFID chip
(602)
Loop antenna on top side
(708)
PCB substrate
(603)
Loop antenna on bottom side
(710)
FreeStyle test strip
(600)
601

FIGURE 7

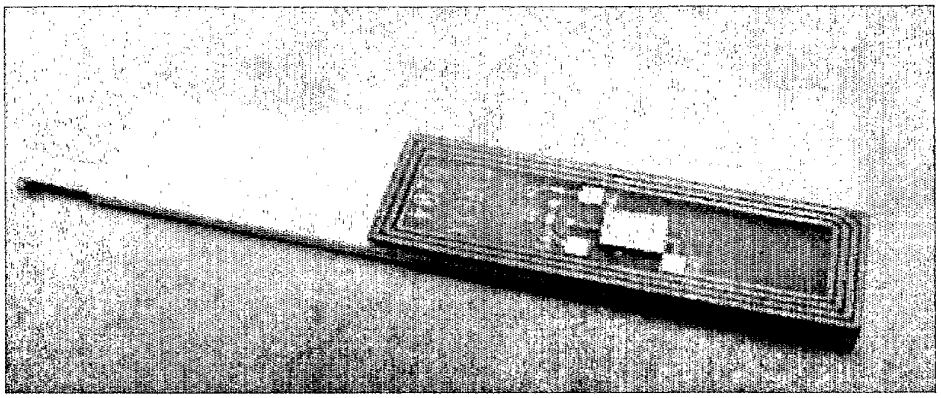


Figure 8

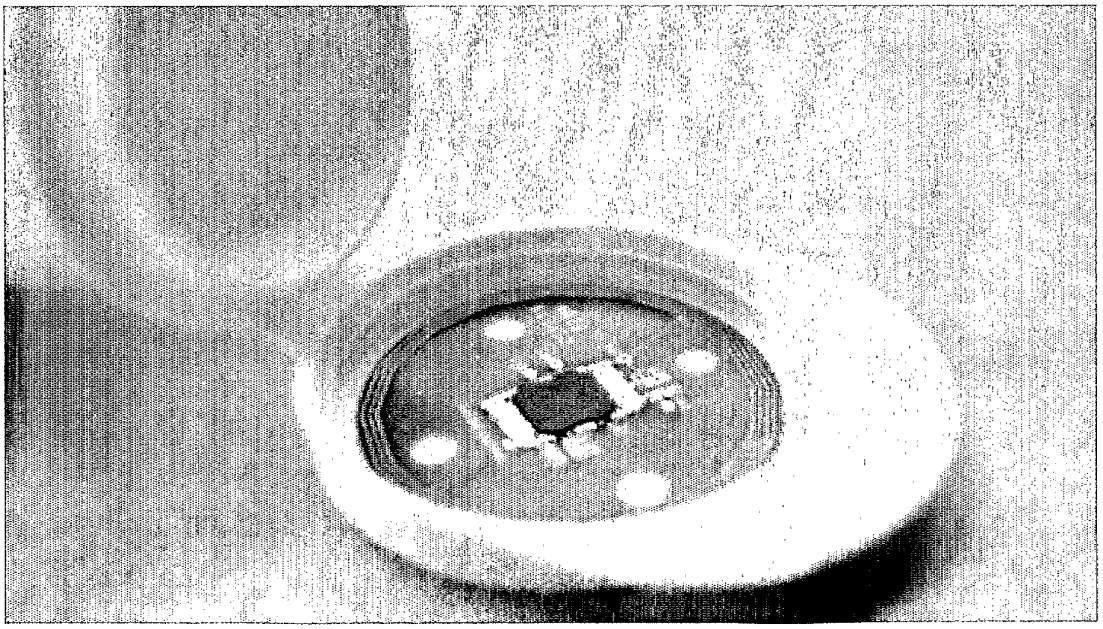


Figure 10

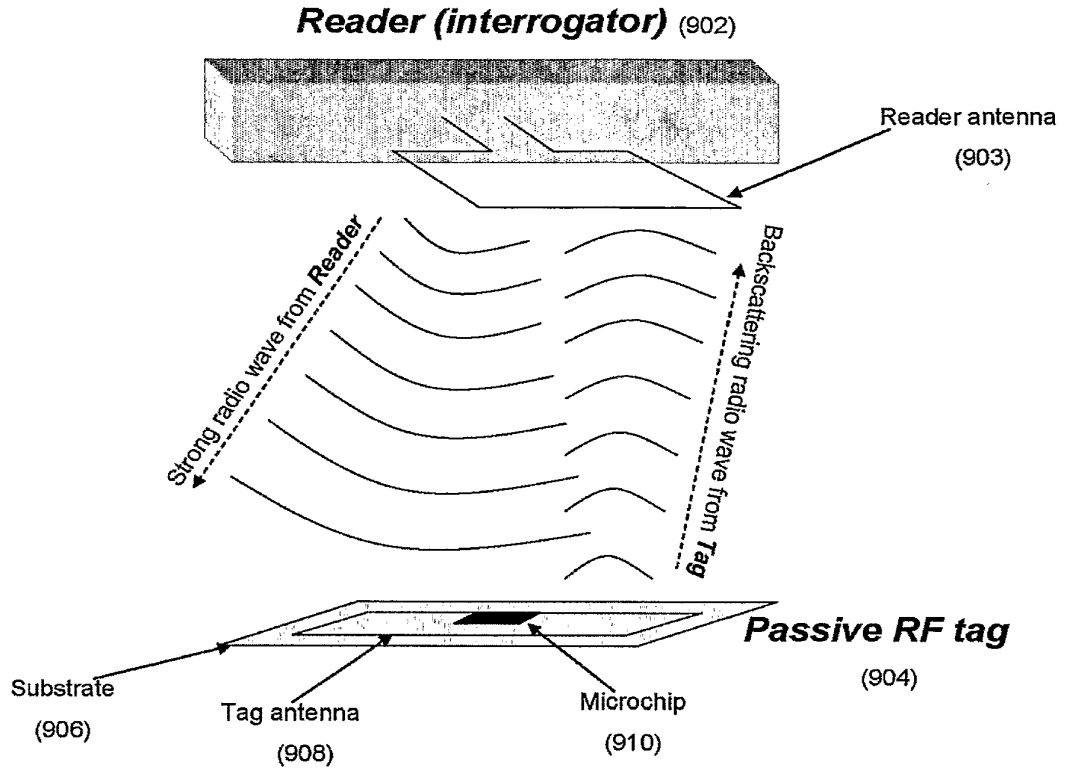

Reader (interrogator) (902)
Reader antenna
(903)
Strong radio wave from Reader
Backscattering radio wave from Tag
Passive RF tag
(904)
Substrate
(906)
Tag antenna
(908)
Microchip
(910)

Figure 9

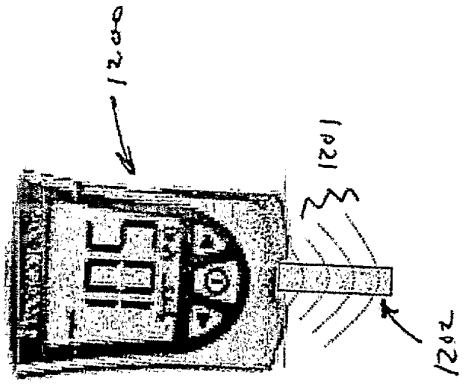


FIGURE 12

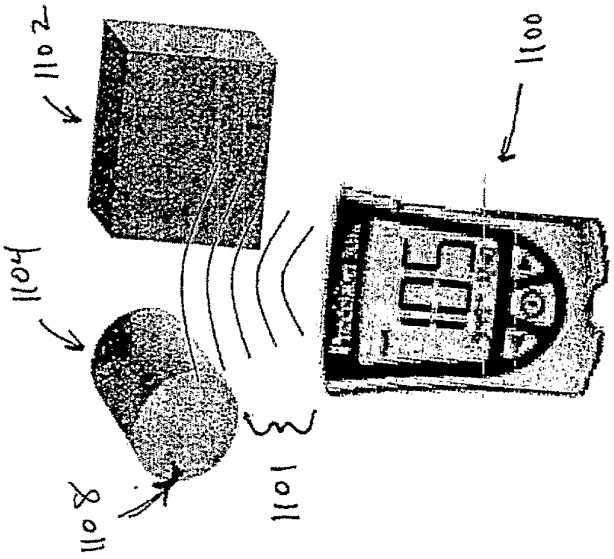


FIGURE 11

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(54) Title: A THREE-DIMENSIONAL ADHESIVE DEVICE HAVING A MICROELECTRONIC SYSTEM EMBEDDED THEREIN

(57) Abstract: Accordingly, the present invention relates to a three-dimensional adhesive device to be attached to the body surface of a mammal comprising a microelectronic sensing system 5 characterized by (a) a three-dimensional adhesive body made of a pressure sensitive adhesive having an upper surface and a bottom surface; (b) a microelectronic system embedded in the body of the pressure sensitive adhesive; 10 (c) one or more cover layer(s) attached to the upper surface; and (d) optionally a release liner releasable attached to the bottom surface of the adhesive device. Suitably the microelectronic system is a microelectronic sensing system capable of 15 sensing physical input such as pressure, vibration, sound, electrical activity (e.g. from muscle activity), tension, blood-flow, moisture, temperature, enzyme activity, bacteria, pH, blood sugar, conductivity, resistance, capacitance, inductance or other chemical, biochemical, biological, mechanical or electrical properties. 1

A three-dimensional adhesive device having a microelectronic system embedded therein

Field of invention

The invention relates to micro electronic systems predominantly for monitoring physiological or neurological conditions. More particular the invention relates to invasive and non-invasive microelectronic systems embedded in a three-dimensional adhesive device, which may be attached to the surface, suitably the skin, of a mammal. The microelectronic systems suitably utilises wireless communication and are useful for measuring ECG (Electro CardioGraphy), EMG (Electro MyoGraphy), EEG (Electro EncephaloGraphy), blood glucose, pulse, blood pressure, pH, and oxygen.

Background

The attachment of sensing systems to the skin by means of pressure sensitive adhesives is well established. Thus, AMBU A/S, DK has a number of products for measuring ECG, which is attached to the skin by foam adhesives, micro-porous adhesives or hydrogel adhesives. These sensors are in general connected with wires to a monitoring device.

In WO 03/065926 A2 Ozgus et al disclose a wearable biomonitor with a flexible and thin integrated circuit. The patent application addresses a way to achieve high comfort of wear by using a thin layer adhesive or pads of adhesive for fixation to the skin. However, the adhesives used are occluding. The application further describes a sensor module for wireless data collection having a thin sheet of silicon comprising the circuit and a flexible power source being build into the sensor module as layers.

In US 5,054,488 Mus et al disclose an opto-electronic sensor for producing electrical signals representative of a physiological condition. The sensors may be attached to the body by a double-sided pressure sensitive adhesive on a polyester lining.

In US 5,458,124 Stanko et al disclose electro-cardiographic-electrodes being attached to the body by double-sided pressure sensitive adhesive.

In US 6,372,951 Ter-Ovanesyan et al disclose a sensor operatively connected to a disposable article, fitted to the wearer by an adhesive patch. A wide variety of body adhering compositions may be used.

In US 6,385,473 Haines et al disclose a laminated sensor device attached to mammalian subject with two strips of hydrocolloid adhesive. The laminated structure consists also of hydrogel in contact with hydrocolloid adhesive. The lifetime of the device is specified to 24 hrs.

In WO 99/59465 Feierbach et al disclose an apparatus for monitoring the physiological condition of a patient. The apparatus includes a patch having a distal side for being fixed to the patient. Also the apparatus may include an electronics housing that may be coupled with said patch. In one embodiment the surface of the apparatus may be pre-formed to the contours of a body part. The patch carrying the electronic housing may be soft and provide a natural feel and may be produced from latex, silicon or another rubberised fabric. The upper surface of the patch with the electronic housing may have a smooth convex shape as illustrated in figure 2B and figure 8 of the patent. The patch is coupled to the skin of the the patient by an adhesive. Such adhesive may be a hydrocolloid skin protective adhesive manufactured by 3M. Hence the patent application teaches the use of a hydrocolloid adhesive liner for fixation of a sensor having a smooth and soft backing optionally in a pre-formed shape to fit a contour of the body.

In US application 2003/0009097 A1 Sheraton et al disclose a sensor having a hydrogel electric conducting central skin contacting part and a hydrocolloid adhesive part surrounding this central part for adhesion of the sensor and on said combined disc a conductive terminal connected to a wire. This construct is further protected by laminate film layers adhered to the terminal and the outer rim of adhesive. The patent application teaches the use of hydrocolloid adhesives for fixation of sensors to the skin and emphasizes the aspect of making very thin and flexible electrodes. The patent application is peculiar in the sense that it combines the use of hydrocolloid adhesives and hydrogels. For any practical purpose the disclosed constructs will be useless as the moisture from the hydrogel will migrate into the hydrocolloid adhesive and disrupt this over time.

Recent developments in devices for monitoring physiological conditions are wire-less types. Apart from being able to monitor a physiological condition invasively or non-

invasively and potentially compare to a reference, they are be able to process data and transmit them to a portable device. In fact the attachable device may also function as an alarm itself, e.g. by use of e.g. light emission, audio alarm or another warning signal.

When monitoring physiological or neurological conditions of the human body it is important that the attached microelectronic system is as comfortable to wear as possible, especially when the person carrying the device is not bedridden and shows normal physical activity or even excess physical activity like in sport or in sports medicine. The user should preferably not feel the attached microelectronic system and the monitoring should preferably be kept in private. However, in this respect the known microelectronic systems suffer from several major drawbacks as described below.

Attachment to the skin by means of occlusive pressure sensitive adhesives often leads to skin irritation due to the occlusion of moisture and due to irritants, such as monomers from the pressure sensitive adhesive polymer system, e.g. from for instance acrylic adhesives. Irritation may be the in form of itching and erythema and may especially develop when the adhesive device is attached for a prolonged period of time. Occlusion may also increase the risk of creating allergy to the adhesive composition. One often used way to solve the negative effects of occlusion is to use micro porous tapes, but such tapes are essentially two-dimensional and thin and does not protect the microelectronic system from shear forces due to friction against clothes and the like.

In the above references, the devices are attached to the skin by thin planar adhesive layers carrying the microelectronic system as a bulky part leading to discomfort of the patient or person carrying the device due to stiffness or friction against clothing and increasing the risk of involuntarily detachment from the skin. When such a device is to be used for a prolonged period of time, it is important to reduce any type of discomfort due to skin irritation or inconvenience of carrying a bulky device. Furthermore it is crucial for the signal detection that the adhesive device is kept fixed to the skin until it is deliberately removed.

Proper adhesion of the device requires a fairly thick layer of the planar adhesive. However, a fairly thick layer may show a tendency of adhering at the edge to clothing or linen and by doing so a tendency to roll and detach is created.

Many sensors are connected to the monitoring systems with wires. The disadvantage of such a system is that the patient does not have freedom to move since the wires are attached to the sensors on the body and connected to a monitoring system. Whenever the patient wants to move he must be careful not to dislodge any of the wires attached to the sensors, and he must further pick up the monitoring system and carry it along.

None of the above mentioned references describes a body sensor device consisting of an optionally hydrocolloid containing thermoplastic pressure sensitive adhesive and/or chemically curing pressure sensitive adhesive, moulded or cast into a three-dimensional adhesive body having a micro electronic system embedded therein as according to the present invention.

The known sensors overcoming some of the above-mentioned disadvantages are not as simple and inexpensive to manufacture with respect to the adhesive part of the device as the adhesive devices of the invention.

The adhesive devices of the invention having a microelectronic system embedded therein may be produced relatively easily and besides a cover layer and optionally a release layer, without the need of any other layers in the device and is therefore commercially attractive.

With an embedment of the micro electronic components an improved protection against mechanical damage and penetration of moisture from the surrounding environment is also achieved.

Furthermore, today many types of electronics are temporarily attached to different surfaces. Especially within medical care different types of medical devices such as probes and sensors are attached to different areas of the skin in order to, for example, detect different biomedical signals or retrieve samples from a patient. Often these medical devices are only attached for a limited period of time until a disease is diagnosed or a patient's health has improved. However, some chronic diseases may require periodical monitoring, for example while the patient is sleeping, or in some cases constant monitoring is desired day and night. The medical device, which is attached to the skin of the patient, may be adapted to detect many types of signals, it could for example be a sensor for detecting one or more signals such as electromyographic (EMG) signals, electrocardiographic (ECG) signals and electroencephalography (EEG) signals.

Such medical devices may be broken up into at least three general elements, a microelectronic element for measuring a desired value, such as for example a biosignal; an adhesive for attaching the microelectronic element to a surface; and a power source for powering at least a part of the microelectronic circuit.

The different elements have different lifespan, however, since the elements are typically assembled in one inseparable unit they are all disposed after use. When looking at the elements individually it may however be understood that they have different lifespan. Thus, the adhesive element typically has a one-time use only. The power source may in some cases be reused a few times depending on the application and the size of the battery. However, the microelectronic element may be reused a large number of times thereby making it an expensive element to dispose after one use only.

Thus in order to improve the cost effectiveness of the medical device there exists a need to be able to reuse the element(s), which are still operable after use.

US 2002/0180605 discloses a method of monitoring a physiological characteristic. The method disclosed can include subsequent steps of removing adhesive pads from a sensor module and heating the senor module in an autoclave for sterilization after data has been transferred from the sensor module to the receiver module.

Summary of the Invention

Accordingly, the present invention relates to a three-dimensional adhesive device comprising an microelectronic sensing system characterized by

(a) a three-dimensional adhesive body made of a pressure sensitive adhesive having an upper surface and a bottom surface;
(b) a microelectronic system embedded in the body of the pressure sensitive adhesive;
(c) one or more cover layer(s) attached to the upper surface; and
(d) optionally a release liner releasable attached to the bottom surface of the adhesive device.

Suitably, the microelectronic system is a microelectronic sensing system. The microelectronic sensing system is suitably capable of sensing physical input such as pressure, vibration, sound, electrical activity (e.g. from muscle activity), tension, blood-flow, moisture, temperature, enzyme activity, bacteria, pH, blood sugar, conductivity, resistance, capacitance, inductance or other chemical, biochemical, biological, mechanical or electrical input.

Brief description of the Drawings

Figure 1 shows a die section of the shape of a typical representative of the adhesive device according to the invention. CT is the maximal thickness of the device and PT is the thickness in the periphery of the device.

Figure 2 illustrates a microelectronic system embedded/integrated in a three-dimensional (3D) adhesive. The zoom-box indicates the part of the adhesive device illustrated in figure 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12.

Figure 3 illustrates a microelectronic system (hatched box) that is completely integrated within the adhesive body.

Figure 4 illustrates that parts of the microelectronic system may be positioned in different locations integrated within the adhesive device with proper mechanical or electrical interconnection between the parts.

Figure 5 illustrates a microelectronic system, which is applied into a recess in the adhesive body. The recess is distal to skin fixation area. The microelectronic system may optionally be exchangeable, or reusable.

Figure 6 illustrates the microelectronic system in which the upper part may be exchangeable or reusable and the lower part be permanently integrated in the adhesive body.

Figure 7 illustrates that parts of the microelectronic system may be situated in different locations within the adhesive device with proper mechanical or electrical interconnection between the parts.

Figure 8 illustrates a microelectronic system, which is embedded/applied into a recess on the adhesive side of the adhesive body.

Figure 9 illustrates a device with a microelectronic system in which the lower part may be exchangeable or reusable and the upper part be permanently integrated in the adhesive body.

Figure 10 illustrates a system with some microelectronic components integrated within the adhesive body during production (small hatched box) and some microelectronic components applied later thereby establishing the necessary mechanical/electrical connections.

Figure 11 illustrates a microelectronic system embedded in the adhesive which system is applicable and accessable both from the distal side and the skin fixation side of the adhesive body.

Figure 12 illustrates a system where the microelectronic system is assembled from two parts one of which, or each of which may be exchangeable or reusable.

In all the above constructs of the invention the upper surface remains smooth irrespective the presence of components of the microelectronic system at the upper surface. This may be achieved by proper construction of the microelectronic components, encapsulation etc.

The constructions shown in figures 8, 9, 10, 11 and 12 are particularly suitable for microelectronic systems including an element, e.g. an electrode which should have skin contact.

Figures 13 -18 illustrates an embodiment of the invention where an antenna, a Central Processing Unit, a battery and electrodes are embedded in an adhesive device. Figure 13 illustrates the two-dimensional shape of the device indicating a cross-section by A-A. In Figure 15 the third dimension is shown as the cross-section A-A. The circle B from the rim of the device is further magnified in figure 16 and the circle C of the centre is like wise magnified in figure 17. Figure 14 illustrates the position of the antenna placed in the outer part of the adhesive device and being connected to the central part of the microelectronic

system. Figure 16 shows more in detail the building of the antenna lying embedded in the adhesive. Figure 17 shows the position of the central part of the microelectronic system with a battery, a CPU and an electrode protruding the adhesive. The battery and the CPU are enveloped in a transparent silicone rubber. Finally figure 18 illustrates the adhesive device in a three-dimensional mode.

Fig. 19 shows one embodiment of a sensor assembly according to the invention seen in a exploded perspective view.

Fig. 20 shows the embodiment of a sensor assembly in a sectional view along line XX – XX in Fig. 19.

Fig.21 shows the embodiment of a sensor assembly seen from the bottom.

Fig. 22a and 22b shows another embodiment of a device according to the invention wherein Fig. 22b shows a portion of Fig. 22a in an enlarged view.

Fig. 23 shows yet another embodiment of a device according to the invention seen in a perspective view.

Fig. 24 shows the embodiment of a device according to the invention in a sectional view along line XXIV – XXIV in Fig. 23.

Detailed description of the Invention

The present invention relates to adhesive devices having a microelectronic system embedded in an adhesive body made from a pressure sensitive adhesive.

In the following the term "three-dimensional" used when defining an element e.g. an adhesive body or device, refers to an element having a considerable varying contour when seen in cross section. Thus, for example a three-dimensional adhesive body will have a maximum thickness and a minimal thickness. According to the invention the maximum thickness will be at least twice the thickness of the minimal thickness. In a preferred

embodiment the outer rim or the peripheral edge of the adhesive device has a thickness which is less than half of the thickest part of the sensor, normally the central part.

In contrast to the term "three-dimensional" the term "two-dimensional" used when defining an element refers to an element, which has a generally planar surface. Thus, the maximum thickness of a two-dimensional adhesive body is below two times the minimal thickness of the adhesive body.

As used herein in relation to the micro electronic system or components thereof, the term "embedded", means that the pressure sensitive adhesive of the adhesive body is surrounding all or some of components of the micro electronic system, either partly or fully. Thus, the term embedded covers the situation where all sides of the system or component(s) is covered by the adhesive of the adhesive body and also the cases where not all sides of the embedded item is covered with the adhesive of the adhesive body, e.g. when the item is placed in a recess or cavity in the adhesive body and is accessible from the outside.

As "embedded" is the general term used for the description of the way the micro electronic system is positioned in the adhesive body the term "integrated" means that the micro electronic system or specific components thereof are covered by adhesive on all sides and the term "applied" is used when the micro electronic system only is partly covered.

Integrated and covered on all sides also covers the situation where the integrated component is connected, e.g. electrically or otherwise to another component embedded in the adhesive body.

As used herein, a microelectronic "sensing" system means a microelectronic system comprising a transducer having an element capable of detecting a physiological or neurological condition.

As used herein through hole means a hole through the adhesive body having opening(s) at the upper surface of the adhesive body and opening(s) at the bottom surface of the adhesive body. Preferably the through hole has one opening at the upper surface and one at the bottom surface of the adhesive body. The through hole may have any suitable shape.

By the "thickness" of the adhesive device is meant the length of the shortest line which may be drawn between a specific point on the upper surface to a point on the bottom surface, or the shortest line which may be drawn between a specific point on the bottom surface to a point on the upper surface.

For the purpose of the present invention the expression "skin" is used to designate the outer surface of mammals.

As mentioned above, it has surprisingly been found that a wire-less microelectronic systems in which the micro electronic parts are embedded in a three-dimensionally shaped pressure sensitive adhesive body solve the problems of the known sensor devices.

Due to the properties of the three-dimensional pressure sensitive adhesives, an optimal protection of the micro electronic system is created. The adhesive provide sealing towards the skin surface and the adhesive device is protected from exterior liquids due to the polymeric cover layer(s) on top of the adhesive device. Furthermore the adhesive protects the embedded micro electronic parts from mechanical damage.

The adhesive bodies according to the invention are made from pressure sensitive adhesives that are shaped three-dimensionally, having a varying thickness from the centre to the peripheral edge of the adhesive body and having the micro electronic sensing system embedded within the adhesive body, suitably where the adhesive body is thickest.

A device with such a shape and suitably with bevelled edges provides a smooth interface with the skin. The adhesive device will give a gentle feel and will not tend to give friction to clothes and linen. A special advantage will be that the adhesive device will less easily involuntarily fall off due to bulkiness and adhesiveness at the edge. This is very important to the very function of the device.

Moreover, the construction of the adhesive device is simple and convenient as the adhesive body have a triple function as the means for fixation of the device to the skin, the means for protection of the microelectronic system and the means for shaping the device into a convenient shape. The construction require less components and process

steps in the assembly of the three-dimensional device and is therefore less expensive and easier to manufacture.

According to one embodiment of the invention, the three-dimensional adhesive body has an essentially planar bottom surface adapted to adhere to the body surface of a mammal and an smooth upper surface. The adhesive device is suitably thickest at the central part of the body and thinnest at the periphery of the body.

Preferably, the upper surface has a smooth convex surface, but it may in principle take any form.

The outer rim or the peripheral edge of the adhesive device must be shaped to a thickness less than half of the thickest part of the sensor, normally the central part.

Thus, in a further embodiment of the invention, the thickness of the adhesive device at the periphery is less than 50 % of the thickness of the adhesive device where it is thickest, suitably the thickness at the periphery is less than 25 % of the thickness of the adhesive device where it is thickest, preferred the thickness at the periphery is less than 10 % of the thickness of the adhesive device where it is thickest, and most preferred the thickness at the periphery is less than 5 % of the thickness of the adhesive device where it is thickest.

The thickness at the periphery of the adhesive device is typically under 0.4 mm. In one embodiment the thickness may be between 0.01 and 0.4 mm. Suitably, the thickness at the periphery of the adhesive device is above 0.05 mm, preferably between 0.05-0.4 mm.

Typically the adhesive device is between 0.5 and 15 mm, more suitably between 1 – 5 mm where it is thickest, typically but not necessarily, at the centre of the adhesive body.

Suitably, the angle between the bottom surface of the adhesive device and a line drawn from any point of the circumference of the bottom surface and the point at the upper surface where the adhesive body is thickest is below 60 degrees, preferably below 45 degrees and most preferably below 30 degrees.

The outer rim of the adhesive body may suitably be shaped circular or oval, with or without flaps and lobes, or it may be shaped rectangular or triangular to obtain as convenient and safe a device as possible.

Normally the outer rim of the adhesive body will consist of the adhesive of the adhesive body. However, there may be embodiments where the microelectronic system or component(s) thereof, is placed in/or at the outer rim, whereby the outer rim does not solely consists of the adhesive of the adhesive body.

The pressure sensitive adhesive making up the three-dimensional adhesive body is suitably a mouldable thermoplastic or chemically curing pressure sensitive adhesive having a flexibility enabling the adhesive device to conform to the curvature of body parts while retaining its adhesive properties even under movements.

Suitable, pressure sensitive adhesives making up the adhesive body is an adhesive based on polymers selected from block-copolymers such as styrene-block-copolymers, and hydrogenated styrene-block-copolymers, amorphous poly-alpha-olefins (APAO), polyacrylics, polyvinylethers, polyurethanes, polyelhylenevinylacetate, silicone or from the group of hydrogel pressure sensitive adhesives.

Pressure sensitive adhesives based on these polymers are known and the skilled person knows how to prepare adhesives based on these polymers.

The block-copolymers, such as styrene-block-copolymers, and hydrogenated styrene-block-copolymers, may suitable be selected from Styrene/ethylene-Butylene/Styrene (SEBS), Styrene/Isoprene/Styrene (SIS), and Styrene/Ethylene-Propylene/Styrene (SEPS).

The adhesive may also be based on PDMS (polydimethylsiloxane), and may suitably be a PDMS gel.

Hydrogel adhesives may also be based on or comprise amfifilic polymers, polyvinylpyrrolidone, polyvinyl alcohol, polyethyleneoxide, gelatins, natural gums and cellulose derivatives or any combinations thereof.

The pressure sensitive adhesive may be formulated according to the principles and based on the polymers listed and disclosed in the handbook of Donatas Satas: Handbook of pressure sensitive adhesive technology, Third edition.

In one particular embodiment of the invention, the pressure sensitive adhesive making up the adhesive body comprises hydrocolloids. The pressure sensitive adhesive comprising the hydrocolloids may be any of the above-mentioned types of pressure sensitive adhesive or any other pressure sensitive adhesive known in the art.

Thus, U.S. Patent No. 3,339,549 discloses a blend of a rubbery elastomer such as polyisobutylene and one or more water-soluble or water swellable hydrocolloids such as a powdery mixture of pectin, gelatine and carboxymethylcellulose. The adhesive mass has a water-insoluble film applied to one surface. A composition of this type is available commercially from E.R. Squibb & Sons Inc. under the trademark "Stomahesive" and is used as a skin barrier around stomas to prevent skin breakdown by the corrosive fluids discharged by the stoma.

In adhesive compositions of this type, the polyisobutylene is responsible for provision of the adhesive properties and the dispersed hydrocolloid powders absorb fluid and render the adhesive agent capable of also adhering to moist skin (wet tack). These compositions are also gaining increasing acceptance as wound dressings for dermal ulcers, burns and other exuding wounds.

In a number of embodiments, styrene copolymers have been incorporated which are disclosed in a number of patent references.

Thus, US Patent No. 4,231,369 Sorensen et al. disclose an ostomy skin barrier consisting of a styrene copolymer having dispersed therein a water-soluble hydrocolloid gum and a tackifier.

In US Patent No. 4,367,732 Poulsen et al. disclose an ostomy skin barrier consisting of a water soluble hydrocolloid dispersed in a continuous phase consisting of a styrene copolymer, a hydrocarbon tackifier, and a plasticizer, an antioxidant, and an oily extender.

US Patent No. 4,551,490 (Doyle et al.) discloses medical grade pressure sensitive adhesive compositions comprising a homogeneous mixture of 5-30% of one or more polyisobutylenes, 3-20% of one or more styrene radial or block type copolymers having a content of diblock copolymer below 20%, mineral oil, one or more water soluble hydrocolloid gums, and a tackifier. One or more water swellable cohesive strengthening agents, an antioxidant, and various other optional ingredients also may be included within the adhesive composition.

US patent No. 5,492,943 discloses a pressure sensitive adhesive composition including a blend of two viscoelastic adhesive elastomers, specifically, high molecular weight polyisobutylene and a styrene block copolymer, which along with a plasticizer (preferably petrolatum) and a suitable tackifier and antioxidant, form a continuous phase in which hydrocolloids such as sodium carboxymethylcellulose and pectin are dispersed.

In US patent 4,867,748 Samuelsen disclose geometries of sealing pads from hydrocolloid adhesives combined with backing films and the processing of such.

The adhesive compositions disclosed in US patent No. 5,492,943 are stated to be used for wafers for adhering ostomy appliances to the skin and differ from known compositions by comprising styrene block-copolymers having a higher content of diblock copolymer, completely avoiding the use of low molecular weight polyisobutylene and furthermore by preferably not including gelatine.

Pressure sensitive adhesives containing hydrocolloids is a particularly suitable group of adhesives being characterized by having a particulate phase of hydrocolloids dispersed in the adhesive phase. An adhesive containing hydrocolloids may absorb moisture from the skin avoid occlusion of the skin, while maintaining its adhesive properties to skin. Moreover, and adhesive body containing hydrocolloids may have any thickness and still having the non-occlusive properties. A hydrocolloid adhesive may be processed as a hot melt and is easily moulded into specific shapes.

This means that the hot melt property combined with the easy moulding enables graduation of the thickness of the adhesive body from the edge of the adhesive device comprising the microelectronic system to the central parts giving a smooth non-abrupt projecting profile.

Recipes for making pressure sensitive adhesives useful for an adhesive body according to the invention are described in more detail below.

Thus, a typical pressure sensitive adhesive composition comprises a substantially homogeneous mixture of 10-60 weight percent of one or more rubbery elastomeric components, 5-60% of one or more absorbent particles, 0-50% tackifier resin, 0-10% of a plasticiser and 0-60 % of a non-polar oily extender, based on the total weight of the composition.

The rubbery elastomeric base could be selected from the group consisting of physically cross-linked elastomers (suitably block copolymers containing polystyrene blocks), a chemically cross-linked natural or synthetic rubbery elastomer, or a rubbery homopolymer.

A physically cross-linked elastomer selected from block-copolymers of styrene, and one or more butadienes may be a styrene-butadiene-styrene block copolymer, a styrene-isoprene copolymer and is preferably a mixture of styrene-isoprene-styrene and styrene-isoprene block copolymers.

A chemically cross-linked rubbery elastomer may be e.g. butyl rubber or natural rubber.

A rubbery homopolymer may be a polymer of a lower alkene such as low density polyethylene or propylene, preferably atactic polypropylene (APP) or polyisobutylene.

A tackifying resin optionally used in accordance with the invention is preferably a hydrogenated tackifier resin and is more preferred selected from a group comprising polymers and copolymers of cyclopentadiene, dicyclopentadiene, alpha-pinene or beta-pinene.

When the physically cross-linked elastomer is a styrene-butadiene-styrene block copolymer or a styrene-isoprene-styrene block copolymer, the adhesive suitably comprise 0-10% of a plasticiser e.g. (citrofol BII, DOA).

The swelling hydrocolloid particles preferably consist of one or more water-soluble or water swelling hydrocolloid polymers or gums.

Suitable hydrocolloids include synthetic polymers that may be either linear or cross-linked, such as hydrocolloids prepared from lactams or polyvinyl pyrrolidone. Other monomers useful to prepare a synthetic hydrocolloid include acrylates, methacrylates and watersoluble amides.

Other hydrocolloidal polymers, either naturally occurring or synthetically prepared, are useful according to the present invention. These materials include polyvinyl alcohol, polyoxyalkylenes, and naturally occurring or synthetically modified hydrocolloids such as polysaccharides, gums, and modified celluloses.

Representative polysaccharides include starch, glycogen, hemicelluloses, pentosans, celluloses, pectin, chitosan, and chitin. Representative gums include Arabic, Locust Bean, Guar, Agar, Carrageenan, Xanthan, Karaya, Alginates, Tragacanth, Ghatti, and Furcelleran gums. Representative modified celluloses include methyl cellulose, hydroxypropyl methyl cellulose, carboxymethyl, cellulose, and hydroxypropyl cellulose.

Preferred hydrocolloids include polysaccharides, such as starch, glycogen, hemicelluloses, pentosans, gelatin, celluloses, modified celluloses, pectin, chitosan, and chitin. Modified celluloses include methyl cellulose, hydroxypropyl methyl cellulose, carboxymethylcellulose, and hydroxypropyl cellulose. A most preferred hydrocolloid is a water soluble or swelling hydrocolloid chosen from the group consisting of polyvinyl alcohols, powdered pectin, gelatin, methyl cellulose, hydroxypropyl methyl cellulose, carboxymethyl cellulose, hydroxypropyl cellulose and mixtures thereof. In one preferred embodiment, the hydrocolloid is carboxymethyl cellulose (CMC).

Suitable swelling colloids are small spherical particles based on cross-linked polyacrylic acid polymers. Examples of such materials may be found in U.S. Patent No. 4,867,748, EP 0 122 344, and US patent application No. 2004065232.

Sometimes the skin for attachment of the adhesive device may be moist or even wet. In these circumstances, the normal adhesives may not give a sufficient strong and permanent attachment of the adhesive device. Specialised adhesives useful in these circumstances are hydrogel adhesives. Such adhesives are based on hydrophilic polymers and extenders enabling an even uptake of moisture over the complete skin-contacting surface of the adhesive. A wide range of compositions of such hydrophilic

adhesives exists. Hydrophilic polyacrylates with high content of acid groups optionally being partly neutralised, is a major representative in this group of adhesives. These adhesives may be inherent adhesive or may be formulated with tackyfiers and extenders to the desired adhesive properties in dry conditions. When getting moist, the adhesiveness will increase vastly depending on the formulation as the uptake of water will transform the adhesive to a more plastic state. Alternative adhesives are based on polymers like polyvinyl pyrrolidone, polyvinyl alcohol, polyethylene oxide and the like. Amphiphilic polymers or polymers which may be chemically cross-linked by radical polymerisation may be added to improve the cohesion of the adhesive and extenders like polyethylene glycol, polypropylene glycol and glycerol are typically preferred.

Adhesive compositions based on polydimethylsiloxane (PDMS) have been known since the 1970's. Recently a new subclass of PDMS based pressure sensitive adhesives has developed namely soft silicone adhesives. Soft silicone adhesives (SSA' s) are two-part, solventless adhesives based on a cross-linked, silicone elastomeric structure. The cross-linking is a result of an addition reaction between a polydimethylsiloxane with vinyl groups and hydrogen functional siloxanes. The cure reaction is catalysed by a platinum complex and can occur at room temperature or can be accelerated at elevated temperature (80 degree C to 145 degree C) without the formation of by-products. Such adhesives are characterised by being soft and by conforming to the surface structure of the skin, whereby quickly wetting of the skin is achieved. Because the viscous component is minimal, the material does not flow and only small dissipation of the energy occurs when deformation pressure is applied. The result is an immediate debonding, which happens at low-peel or shears force, which for some instances may be advantageous.

Apart from being excellent skin adhesives PDMS based pressure sensitive adhesives may have the further properties of being reusable, since they can be cleaned with tap water and be reapplied to the skin.

The pressure sensitive adhesive used for making the adhesive body of the invention could also be a PDMS gel often described as a tacky gel. Examples of such commercially available systems are Dow Corning 7-9800 A&B, from Dow Corning HealthCare US or SilGel 612 from Wacker-Chemie GmbH, Burghausen, Germany, and MED-6340 from NuSil Technology, Carpinteria, USA.

The above mentioned pressure sensitive adhesive can either be used in a non-foamed version or in a foamed version. When gas bubbles are introduced into pressure sensitive adhesives during the manufacturing process a lightweight, cellular structure is produced. Such a pressure sensitive adhesive is more flexible than the non-foamed versions. (see US patent No. 6,326,524 and US patent application No. 2004065232).

In general the adhesive body of the present invention has the desirable elastic, adhesive, moisture transmitting and/or absorptive properties as well as a high conformability and flexibility. The flexibility provides a composition that has the ability to conform to the curvature of body parts while retaining its adhesive properties even under movements. The high initial tack at room temperature provides for easy application of the adhesive device.

The adhesive device of the invention has on the upper surface one or more cover layers of any nature, preferably only one cover layer, to protect against adhesion to linen, clothes and other environment.

As a cover material, it is preferred to use a film in the form of a thermoplastic polymer film or a woven or non-woven layer. The cover layer is preferably made of an elastic material. The cover layer is suitably capable of transmitting moisture and may e.g. be made from polymers such as polyolefin types e.g. polyethylene, polypropylene or polybutylene, polyamide such as nylon, polyurethane, polyvinyl acetate, polyvinyl chloride, fluorinated polyvinyl compound, polyvinylidene chloride, polyvinyl alcohol, ethylene vinyl acetate, cellulose acetate or other thermoplastic polysaccharides, polyether block amides like PEBAX , block copolymers like styrene-isoprene-styrene block copolymers or ethylene acrylate block copolymers, polyesters such as polyethylene terephthalate (PET) or derivates thereof and any laminates from such polymers. The cover layer may suitably be a thin foam layer like made from polyurethane, polyethylene or polyvinyl acetate.

The cover layer or film protects the integrated /embedded microelectronic components as well as the adhesive body against the environment.
In one particular embodiment of the invention, an antenna can be printed directly on the cover layer by means of conductive ink or printed metal.

Prior to application to the skin a protective release liner covers the skin contacting side of the pressure sensitive adhesive body, in order to ensure that the properties of the adhesive are preserved and that the adhesive surface is not laid open until just before the use. The release liner is suitably a siliconised or fluorinated release liner, such as a siliconised or fluorinated craft paper, polyethylene, polypropylene or polyethylene terephthalate film. Suitably, the release liner is a siliconised polyethylene film, such as medium density polyethylene from the company Huhtamaki.

The microelectronic system comprises a number of components, which may be assembled into one, optionally encapsulated unit, which is incorporated into the adhesive device of the invention. The components of the microelectronic sensing system may also be an assembly of the individual, optionally encapsulated, components located at different positions in the adhesive device. This embodiment of the invention covers the situation where the adhesive devices have all the individual components of the microelectronic device located in different positions, as well as the situation where one or more of the components is located at a position different from the position of the rest of the components which are located at the same position.

When the components of the microelectronic device are located at different positions in the adhesive device, the adhesive device also has the necessary mechanical or electrical connections between the components integrated into the adhesive body.

Thus, according to one embodiment of the invention, the entire microelectronic system is integrated into the adhesive body and is completely covered by the adhesive body on all sides.

According to another embodiment of the invention, the entire microelectronic system is contained in a recess provided in the upper surface of the adhesive body facing the cover layer.

According to another embodiment of the invention, the entire microelectronic system is contained in a recess provided in the adhesive bottom surface of the adhesive body. In another embodiment of the invention, the microelectronic system is contained in a through hole in the adhesive body and is accessible from both the upper surface facing the cover layer and from the adhesive bottom surface.

In an alternative embodiment of the invention, one or more components of the microelectronic system is integrated into the adhesive body and is covered by the adhesive body on all sides and the other component(s) of the microelectronic system is located elsewhere in the adhesive body, the components of the microelectronic sensing system having the necessary mechanical and electrical connection to each other.

According to the above mentioned embodiment of the invention, one or more components of the microelectronic system may be integrated into the adhesive body and covered by the adhesive body on all sides and the rest of the microelectronic system is contained in one or more a recesses (suitably one recess) provided in the upper surface of the adhesive body facing the cover layer.

Alternatively, one or more components of the microelectronic system is integrated into the adhesive body and is covered by the adhesive body on all sides and the rest of the microelectronic system is contained in one or more recesses (suitably one recess) provided in the adhesive bottom surface of the adhesive body.

In another alternative embodiment one or more components of the microelectronic system is integrated into the adhesive body and is covered by the adhesive body and the rest of the microelectronic system is contained in one or more through holes (suitably one through hole) in the adhesive body and is accessible from both the upper surface facing the cover layer and the adhesive bottom surface.

In still another embodiment one or more components of the microelectronic system is integrated into the adhesive body and is covered by the adhesive body, while other components of the microelectronic system is contained in one or more through holes (suitably one through hole) in the adhesive body and is accessible from both the upper surface facing the cover layer and the adhesive bottom surface, and the rest of the microelectronic system is contained in one or more recesses (suitably one recess) in the upper and/or bottom surface of the adhesive body.

In still an alternative embodiment one or more components of the microelectronic system is contained in one or more through holes (suitably one through hole) in the adhesive body and is accessible from both the upper surface facing the cover layer and the adhesive

bottom surface and the rest of the microelectronic system is contained in one or more recesses (suitably one recess) in the upper and/or bottom surface of the adhesive body.

In another suitable embodiment one or more components of the microelectronic system is contained in one or more recesses (suitably in one recess) in the upper surface of the adhesive body and the rest of the microelectronic system is contained in one or more recesses (suitably one recess) in the bottom surface of the adhesive body.

Where the microelectronic system or components thereof is placed in the upper surface of the adhesive body, they are suitably formed with an upper surface following the contours, or shaped to fit the upper surface of the adhesive body. This may be achieved by proper encapsulation of the components.

As mentioned above, the individual components, groups of individual components or all the components of the microelectronic system may be encapsulated before they are embedded into the adhesive body. Encapsulation is chosen when additional protection of the components from the environment and/or the reverse is desired, e.g. when already present in the adhesive body or during the production process leading to integration into the adhesive body. The encapsulated components of the microelectronic system are connected to each other via the necessary electrical and/or mechanical connections.

In some cases it is required that the micro electronic system or components thereof are protected from humidity and/or perspiration in the adhesive since this will initiate corrosion, or needs shielding from exterior influence for other reasons. In such cases the micro electronic system or components thereof is encapsulated.

A number of encapsulation techniques are known and includes coating, hot-melt encapsulation, ceramic encapsulation and glass encapsulations. Other methods for encapsulation of electric components are known in the art.

The microelectronic system or components thereof is suitably encapsulated in a polymer film, a polymer foil, or a polymer coating or the microelectronic system or components thereof is moulded into a polymer material, or is encapsulated in a glass or ceramic material.

Encapsulation by coating typically involves coating the component(s) with materials such as epoxy, PDMS (silicone), acrylate, polyurethane or UV curing resins.

Encapsulation in silicone, such as PDMS, is particularly preferred when the microelectronic components is to be placed in a through hole or a recess in the adhesive body and where it is desirable to enable easy removal or replacement of the encapsulated microelectronic component(s), as the silicone surface is easily released from the adhesive of the adhesive body. Other materials, which are easily releasable from the adhesive, may also be used for the encapsulation.

Hot-melt encapsulation typically involves incorporation of the microelectronic system or components thereof in a thermoplastic material by injection moulding. The thermoplastic material used may be selected from Styrene-block copolymers, polyurethane, ABS (acrylonitrile-butadiene-styrene copolymer), SAN (styrene-acrylonitrile copolymer), polyvinylchloride, PDMS, POM (polyoxymethylene), polystyrene, polyester, polyacrylate, polyolefines; e.g. polyethylene or polypropylene.

The components of the microelectronic system require interconnection. Each system may consist of one or more discrete components, which need to be assembled mechanically and electrically. The mechanical or electrical connection may be established by PCB (printed circuit board), snap locks, thin flexible PCB, glue etc.

In one embodiment as described above, all parts of the micro electronic sensing system is integrated in the adhesive body during production, meaning that the adhesive device with the microelectronic system has a disposable nature.

The adhesive device according to the invention may also be constructed in such a way that components of the microelectronic system may be exchanged during the lifetime of the adhesive device or may reused in a new adhesive device.

Certain components of the micro electronic system are integrated into the adhesive body during production whereas the remaining components is applied to the adhesive device of the invention afterwards, just prior to attachment on the skin, or after attachment to the skin. The components applied to the adhesive body after production of the adhesive body is typically exchangeable, or reusable.

The component, which may be exchanged, is for example the energy source, e.g. the battery.

In a particular embodiment of the invention the entire micro electronic system is exchangeable or reusable and may be applied to the adhesive device just prior to attachment or after it has been applied to the skin.

Suitably, the exchangeable component(s) or the reusable component(s) is encapsulated as described above and forms a package, which fit a recess or hole in the adhesive body.

In the case of exchangeable or reusable components they must have some sort of secure attachment to the adhesive body during use. Such attachment may be provided by an adhesive, for instance by the pressure sensitive adhesive of the adhesive body already present in the indentation, the cavity of the hole in the adhesive body.

In this case it may be preferred that the encapsulation material is a material which does not adhere too strongly to the adhesive of the adhesive body, see above.

Alternatively, the package of the encapsulated, exchangeable or reusable components is attached to the adhesive body via mechanical couplings to the adhesive body. The above-mentioned encapsulated package containing the replaceable or reusable component(s) could thus be fitted into the adhesive body by a snap lock mechanism.

The encapsulation function as a housing for the microelectronic system or components thereof and is suitably formed of from injection-moulded polymer material, but could in principle be of any material and any construction.

The package of encapsulated microelectronic component may have any suitable shape, suitably three-dimensional shape, fitting a recess or through hole in the adhesive body. On one embodiment the encapsulated electronics will have the shape of a rod shaped capsule with rounded ends.

As mentioned above, the present invention uses invasive as well as non-invasive techniques for acquiring physiological data. In the case of non-invasive measurement one

or more metal electrodes may be used for the skin contact. However, any conductive material may be used for the skin contact, such as conducting polymers, conducting hydrogels and electrolytes. In case of invasive measurements regular needles or micro needles may be used. Such invasive techniques are already well known today e.g. for measuring oxygen or blood glucose.

By combining well-described components, all sorts microelectronic sensing systems may be designed and incorporated into the adhesive device of the invention. Examples of systems suited for embedment in adhesive device are systems suitable for measurement of biosensor signals, EKG, EMG, EEG, blood glucose, pulse, blood pressure, pH and oxygen.

The micro electronic system incorporated into the adhesive device of the invention typically requires the following components: Communication components, CPU (central processing unit), power source, storage components, transducer components, interconnections and optionally actuator components.

The CPU (Central Processing Unit) controls and communicates with the components of the microelectronic system. The CPU handles the execution of application software, data decisions making (like data signal processing), A/D conversion, DSP (digital signal processing), routing, timing, power management, sleep function, interruption.

The CPU is the component of the microelectronic system controlling other components and making the appropriate data analysis. In general, the more speed and data analysis required, the more power is needed. Therefore a sleep function is often used in order to save power. At certain times or if certain events happen (triggered by a very low power monitoring subsystem) the CPU wakes up, makes the necessary calculations, communicates with relevant components and return to sleep mode. Depending on need very rudimentary CPU to a full-fledged microcontroller can be used according to the invention.

The communication components control all communication to and from the microelectronic system. Suitably, the microelectronic system is a system enabling wireless communication with a receiver unit placed at a distance from the adhesive device. However, the present invention is not limited to wireless communication, such as RF-

wireless communication. Other communication means could be audible or optical communication means. The component includes the necessary electronics for achieving this wireless communication but also the antenna along with the necessary hardware and software.

The antenna may be of different shape and form depending on frequency, power and signal form. Some antennas are useful for communicating information a few cm, others range several meters. Examples of antennas are; a coil around a small ferrite core (e.g. less than 4 mm in diameter, a flat coil with turns (diameter typically 10 mm or more), single and double wire radio antennas such as monopole or bipole antennas, and an antenna integrated in the adhesive.

An antenna only having few turns and a large diameter e.g. 50 mm may be laminated and integrated into the adhesive body or printed or directly on the cover layer of the adhesive device. The antenna is typically made of a metal such as copper or aluminium but could also be of conductive ink.

The power source consists of power regulating electronics, recharge electronics and an energy source, typically an internal or exchangeable battery. However other means of getting power to the microelectronic system may be suggested, such as kinetic energy conversion, fuel cells, isotope radiation, solar cells or via a radio frequency (RF) link. Further the antenna may be used for loading energy to the microelectronic system.

Preferably the power source is a battery, and may be for one time use or it may be rechargeable.

The storage component is for storage of the embedded system software and/or storage of data acquired during operation of the device. The storage component may be a part of the CPU, a component of its own or an exchangeable storage device such as FLASH RAM that can be removed and exchanged.

The transducer component is a component designed to convert energy from one form to another. The transducer is typically, but not necessarily, the sensor or sensing part of the microelectronic sensing system. A transducer may thus be able to convert for example a

physical input and the transducer will usually but not necessarily convert this energy into electrical form to be interpreted by the CPU etc.

Examples of the physical input a transducer may convert is acceleration, chemical/gas, flow, humidity, inertia, capacitance, conductance, conductivity, current, impedance, inductance, pH, resistance, resistivity, voltage, photo detection, light, magnetisme, pressure, angular, linear position, velocity, temperature, sound and mechanical force.

A tangible representative of the transducer is the detecting component. The detecting component is typically selected from electrodes (polar, bipolar), pressure sensors, needles with electrodes, accelerometers, photo detectors, microphones, ion specific field effect transistors (ISFET), a NTC (negative temperature coefficient) resistors, band gap detectors, ion membranes, enzyme reactors or condensers.

In one embodiment of the invention the transducer includes a detector for non-invasive detection, such as an electrode.

In another embodiment of the invention, the transducer includes an invasive detector, such as a needle containing an electrode.

An actuator is the reverse of a transducer. It converts energy from one form to another in much the same way as a transducer but in the reverse order. Usually it converts electric signals to physical signals. A tangible representative of an actuator is e.g. electrodes (for instance for neural- or neuro-stimulation), pumps, injection needles, light emission diodes (LED) or another light source, loudspeakers, current generators or chemical synthesizers. A possible use of actuator is at certain events decided by the CPU to activate an alarm in the microelectronic system, such as loudspeaker or LED, or to indicate low battery.

Thus, the actuator may be used as a component in the system reacting to the input obtained from the transducer component such as an alarm (visible and audible), injection pump, valve etc. It can either be a one time use, a multiple use or continuous use actuator.

Many sensing systems are only informative systems transmitting information about the physical condition of a mammal and in this case an actuator is not needed.

The microelectronic system will be modular build in the sense that in a device for a given application only some of the components may be needed. Some applications will utilize fewer components and some applications may use all components. These components can be fitted into same physical ASIC (application specific integrated circuit), electrical system or subsystem, such as but not limited to, PCBs (printed circuit boards), flexible PCBs, thick film, thin film, or ceramic technologies or the system or its components may be separately encapsulated

RFID (Radio Frequency IDentification) tags are commercially available in various sizes, ranges and functionality. When the RFID reader applies the appropriate field (e.g. an inductive field) the basic RFID tag return a bit sequence. The sequence is programmed prior to use. RFID range varies from 1 cm to app. 2 meter for passive tags (no power source included) to over 100 meters for active tags (power source included). More sophisticated RFID tags available have storage components where data can be read or stored.

The RFID tag may be incorporated into the adhesive body either as a standalone part or in combination with other microelectronic components. Complex microelectronic systems can easily be made to include various forms of RFID tags without adding significantly to the complexity or price of the system. In a complex system the tag can be used as a simple track and trace component for identification of the product, such as shelf life, life time, however it can also be utilized for identification for other systems in sensor networks.

For a stand-alone solution the RFID tag consist basically of a RF chip and a coil. Suitable forms of the RFID tag is a RFID tag encapsulated in a glass housing, a RFID tag encapsulated in plastic/epoxy (typically pill shaped), a flat RFID tag with coil and a RF chip laminated between 2 polyimide layers, or a flat RFID tag with large coil antenna with few turns printed on or in the adhesive body and with the RF chip interconnected to the antenna without any further protection/encapsulation.

These systems can be completely integrated within the adhesive bodyduring production of the adhesive body.

The above-mentioned flat RFID tag may be sandwiched between 2 layers of pressure sensitive adhesive during production. As the RF chip is very small (1 mm x 1 mm) and the coil is flexible, no rigid encapsulation is needed. The glass encapsulated RFID tag has very good chemical resistance and small size to ensure no discomfort. The RFID tag encapsulated in plastic or epoxy may be of more complex design and can be added both during and after production of the adhesive body of the invention.

The encapsulated RFID tag is a component, which may be reused, in one or more adhesive bodies. The encapsulated RFID tag is transferred from one adhesive body to another and thereby reused time after time, and is ideal for storing person specific data.

Normally embedded microelectronic systems incorporate some kind of sensor in its system, however this is not necessary for all applications.

The adhesive device of the invention may also be part of a network of adhesive sensor devices placed on different locations on the body. These individual adhesive devices may vary in complexity ranging from a small basic sensor system to more complex system, depending on location and sensing property. Some adhesive devises of the network have reduced functionality called RFD (reduced function devices) whereas other devices are FFD (Full Function Devices).

The FFD devices may function at any topology and be the coordinator of the Network, or it may be a coordinator that can talk to any other device. A RFD device is limited to star topology, it cannot become a network coordinator, it talks only to a network coordinator and has very simple implementation.

FFDs may be a dedicated network coordinator acting as communication Hub, gateway or router within the Body Area Network (BAN) and handling communication with external unit(s). A communication Hub or gateway may have large storage capacity and store data from the sensor network, and when in proximity with external unit or when otherwise appropriate wireless transmit these data.

These hubs are easily integrated within the adhesive body as no skin contact or actuator is needed, and may be placed strategically on the body. As hubs will generally be larger and more centrally placed on the body, it is of great advantage that the microelectronic

hub may be completely integrated within an adhesive body as this reduces discomfort and visibility.

In case of person monitoring, the microelectronic system could incorporate GPS technology. The system is either data logging the positional data for later analysis or could transmit (e.g. via the mobile net) position. Such a system within an adhesive could be place in an inaccessible location on the body.

A GPS device incorporated in an adhesive body of the invention need not be a single device in itself, but could be an add-on to an adhesive devices comprising other microelectronic systems, so the system can transmit GPS at certain event such as alarms.

Thus, the adhesive device may also contain a micro electronic system where no physical contact between the detector and the skin of the mammal is necessary. Systems that do not necessarily use transducers with a detecting element are Network Hubs, network coordinators, gateways and GPS (Global Positioning System).

Accordingly, microelectronic systems useful for use in the adhesive device of the invention could be:

A glass encapsulated RFID tag comprising communication components and a CPU. The glass encapsulated components may suitably be embedded in the adhesive device as shown in figure 1.

An epoxy or plastic encapsulated RFID tag comprising communication components and a CPU. The epoxy /plastic encapsulated components could for example be embedded in the adhesive body as shown in figure 1 or 2.

A coil antenna and a RFID tag comprising communication components and a CPU laminated between two polyamide layers. The system may be embedded in the adhesive body as illustrated in figure 1A.

A coil with few turns and a non-encapsulated passive read/write RFID tag comprising storage and communication components and a CPU. The system may be embedded in the adhesive body as illustrated in figure 1A.

A passive read/write RFID tag comprising storage and communication component(s) and a CPU encapsulated in an epoxy or plastic pill. The system may be embedded in the adhesive body as illustrated in figure 2.

An active read/write RFID tag encapsulated in a epoxy/plastic pill comprising storage and communication components, a CPU and a battery. The system may be embedded in the adhesive body as illustrated in figure 1.

RFID tags of the above-mentioned type are commercially available.

The microelectronic system may also be a gateway comprising storage and communication components, a CPU and a battery encapsulated in plastic and working as a dedicated network coordinator for transmission of data to a central unit (CU). Such a microelectronic system may for example be embedded in the adhesive body as illustrated in figure 1.

The microelectronic system may also be a system comprising storage and communication components, a CPU, battery, GPS, components for wireless synchronisation of real time clock for data logging of GPS data, optionally encapsulated in plastic, or a system comprising storage and communication components, a CPU, battery, GPS, components for wireless synchronisation of real time clock for data logging of GPS data, mobile net for data logging and transmission of data and position to mobile phones, optionally encapsulated in plastic. These systems may also be embedded in an adhesive body as illustrated in figure 1.

The adhesive device according to the invention may also be used for applications where body implants are applied electrical power and electrical data communications via wireless means across the skin barrier (trans-cutanously). In these cases it is important to fix the adhesive device at an exact spot on the skin surface for long periods of time with minimal annoyance or inconvenience for the person carrying the device.

A typical example of wireless trans-cutaneous power transfer and electronic data communication is in implanted nerve stimulators for people who suffer from disable control of their muscles in the lower part of their leg (the drop foot syndrome). The drop foot

stimulator is implanted inside the leg and has direct contact the nerves controlling the relevant muscles. The implant is typically powered wirelessly by means of an electromagnetic coupling between a coil or an antenna inside the leg and a coil or antenna placed nearby on the outside of the body on the skin surface.

The coil or antenna is connected to the electronics providing the needed power and control signals. The timing for the simulation signal is normally controlled by a pressure sensitive switch at the heel of the person or in his shoe. Often the transmission of the signals from the switch to the simulator placed on the skin of the leg is wireless.

These drop foot simulators will be substantially improved by using the adhesive device described in the invention. It enables reliable power and data transfer because of the very stable fixation of the external part of the simulator on the skin surface for long periods of time with minimal inconvenience. Further it can also enable better long-term fixation of the switch placed on the foot.

Thus, in one embodiment, the microelectronic system is useful for nerve stimulation and comprises storage and communication components, a CPU, power source and transducer for transmitting data and power to implant for nerve stimulation. The system may suitably be embedded in the adhesive body as illustrated in figure 3.

In another embodiment, the embedded microelectronic system is useful for surface electromyography (sEMG) or invasive electromyography. In both cases the transducer is a relatively simple 2-3 electrode device. The signal measured is a direct voltage generated by a muscle or a muscle group. In order to understand this signal it must be analysed either by the microelectronic system or stored for future analysis.

The data collected are transmitted to a Central Unit (CU) either when relevant, when certain events occurs or at certain time intervals. The CU is suitably a portable hardware device with wireless reception/sending capability, such as but not limited to a PDA (personal digital assistant), a mobile phone or other dedicated hardware.

The transducer is suitably designed to overcome or neglect the difference from time to time of the surface resistance of the skin. Dry skin has resistance of e.g. 500 kOhms and sweaty skin could be as low as 500 Ohms. This problem may be over come by utilizing a

high impedance amplifier, where impedance is above 500 MOhms. The transducer may be designed to activate other system components on the first skin contact thereby ensuring longer lifetime.

The central processing unit (CPU) handles the amplification (e.g. x30-x1000) of the transducer signal, typically by differential instrumentation amplifier with rejection of common modes (unwanted signals/noise that is common for both electrodes), filtered either analogically or digitally. The CPU handles conversion of analogous signal to digital signal. Signal analysis such as rms (root mean square), FFT (Fast Fourier Transformation) and digital filters combined with software are employed to achieve a data decision on certain events.

Furthermore the CPU could employ timers or sleep mode, so measurement is only during certain events or only a fraction of each second or other time period, thereby saving power.

The microelectronic system also comprises storage components for storage of Software and EMG data storage in those cases where, only some or no data are transmitted wireless during data acquisition. These data may be transmitted at a later time.

The power source is thought to be either a single use battery as the CPU ensures long lifetime due to power down in inactive periods, or a rechargeable battery. The rechargeable battery is recharged either through a RF link or by placing the microelectronic system in a recharge cradle when the system is not in use. Several weeks of lifetime after activation are possible with one battery or charge up.

Data is transmitted to Central Unit with a protocol or method that can ensure no corruption of data. Furthermore after activation battery life condition and/or a data burst are transmitted in order validate operational status of the system. On request the system will transmit storage data.

The microelectronic system for electromyography may optionally include an actuator, which at certain events decided by the CPU activates an alarm in the microelectronic system, such as loudspeaker or LED. The event activating the actuator could also be

low battery.

According to this embodiment of the invention the various components are interconnected mechanically and electrically and may be encapsulated into a module. However, various components may also be integrated separately into the adhesive body. These components could be but is not limited to, the battery, the antenna and the actuator.

The various components could also be mounted on PCB (printed circuit board) or flexible PCB and coated with a protective layer and directly be embedded in the adhesive.

Thus, in a specific embodiment of the invention, the microelectronic system is a system useful for electromyography and comprises a transducer (2-3 electrodes and an Instrumentation Amplifier), a CPU (µ Controller e.g. ATMEGA 128L), a power source (e.g. battery), communication (e.g. to CU) and storage components and an actuator (LED). This system may be embedded in the adhesive body as illustrated in figure 3 and 3A.

During sport or fitness exercise different or several of the same microelectronic systems may be used in combination. Furthermore several transducers could be used in the same adhesive device.

A fitness sensor network may thus consist of:

Adhesive devices with a muscle activity (sEMG) sensor, one for both sides of the body (arms, legs etc). The electromyography system could be designed in such a way to determine the fatigue of the muscles and indicate when muscle growth is optimal or when exercise has no benefit. Frequency analysis of the sEMG signal may be used to achieve the desired output of the measurements. Typically the adhesive devices are placed on muscle groups that are actively exercised.

Two or three adhesive devices of the invention comprising a Heart Rate (ECG) sensor system of for monitoring heart beat and heart pulse shape.

Adhesive devices comprising microelectronic systems for determining levels of fatigue poisons in muscles.

A sensor Hub/gateway centrally located on the body for storing and routing signals to either a central unit or directly communicating with fitness hardware.

The microelectronic system may be reusable from one fitness session to another with change or charge up of battery.

Thus, the adhesive device according to the invention may suitably be used for measuring physiological conditions that relate to diseases, health care surveillance, rehabilitation, sports medicine or general surveillance. Typically applications will be for patients at risk for instance when suffering from weak heart, epilepsy, fever and fever spasms, diabetes, apoplexy, arteriosclerosis and muscular dystrophy. Applications may be associated with general monitoring for optimising medication, for registering of the disease or for alarming. Other applications will be for rehabilitation in respect to monitoring of physical work, muscle strength, lung capacity, or in the sports medicine for determination of work and repetition, acceleration, heart rate, muscular stress and strength, orientation etc. Yet other applications will be for surveillance of objects or mammals in motion. Mentally disable patients or individuals like elderly people suffering from dementia will be typical for such applications.

The adhesive device according to the invention will preferably be wireless as this will be meaningful in respect to obtaining as smooth a shape and surface of the device as possible and still achieving the protection of the microelectronic system. In certain occasions it may, however, be important to be able to interconnect the devices by wires. This may especially be an option when the microelectronic system is divided in two parts each being present in an adhesive device as defined in the invention.

The microelectronic sensing system or the components thereof may be incorporated into the adhesive body either during production of the adhesive body, or after production of the adhesive body, e.g. just prior to application of the adhesive device to the skin, or after application of the adhesive device to the skin.

As described above, parts of the adhesive device such as parts of or the entire microelectronic system may be exchangeable or reusable.

Thus, in one aspect of the invention the present invention discloses a device comprising at least an adhesive element and a power source element, said device adapted to attach an electronic circuit, such as the microelectronic system, to a surface and to power said electronic circuit, wherein at least one of the device elements is releasable attachable to the electronic circuit; the power source element is electrical connectable to the electronic circuit; and the adhesive has at least a first area for adhering to the surface.

Such a device as described may attach and power the electronic circuit to a surface, such as e.g. the skin of a mammal, for a specific purpose. When the specific purpose is fulfilled the device and the electronic circuit is removed from the surface and the device is separated from the circuit and disposed. Thus, the elements forming the device, which are relative cheap compared to the electronic circuit, is disposed while the electronic circuit may be reused together with a new device according to the invention for attaching the electronic circuit to a surface and powering the circuit. Advantageously this allows reducing costs considerably while also protecting the environment as more components are reused than done until now.

By the terms 'releasable attachable' and 'releasable connectable' it should be understood that the device and the electronic circuit may be temporarily attached in such a way that the risk of unintentionally separating them is minimal. However the device and the electronic circuit should be attached in such a way that they may be separated if desired.

Furthermore, by the term 'electrical connectable' it should be understood that the power source element and the electrical circuit is arranged in such a way that an electrical current may be transmitted between them. This may for example be done by use of standard electrical contacts, typically made of copper alternatively gold or silver plated, or the electrical connection may be provided in a wireless manner where the power source induces a current in the electrical circuit.

Typically the electronic circuit is a microelectronic system formed of a number of microelectronic digital components and /or analog components connected with appropriate wiring. The components are typically arranged on a print circuit board whereon the proper traces and tracks are etched, electroplated, or otherwise provided on the board. Digital components may for example be microprocessors, storage elements such as RAM-blocks

and analog components may for example be resistors and capacitors provided on the print board.

In one embodiment the power source element is attached to the adhesive element and the adhesive element has a second area for adhering to the electronic circuit.

By attaching the power source element and the adhesive element to each other only one physical part is provided, avoiding that the user has to keep track of both the power source element and the adhesive element and spend time on applying both. Thus a small and discrete device, which is convenient for the user, is provided. Furthermore the electronic circuit may be adhered to the adhesive element for improved handling, as only one unit will have to be manipulated when applying the electronic circuit to the surface.

Advantageously a first peel force between the second area and the electronic circuit is smaller than a second peel force between the power source element and the adhesive element. This allow for easy separation of the microelectronic circuit from the device after use.

To further ensure that the power source element and the adhesive element do not separate from each other the power source element may at least partly be contained in the adhesive element.

By 'contained' it should be understood that the power source may be fully or partly embedded in the adhesive. When fully embedded only electrical contacts are exposed through the adhesive or thin flexible electrical wires are embedded in the adhesive extending from the power source to an outer surface of the adhesive where it may be brought into contact with the electronic circuit. Furthermore, within the meaning of the term contained the power source may also be partly embedded in the adhesive thereby exposing a larger section through the adhesive. This allows for a large contact surface between the electronic circuit and the power source while at the same time being safely attached to the adhesive.

To protect the different parts of the electronic circuit it will typically be encapsulated, for example by coating it in silicone or hot-melt polymers. The encapsulation may for example be formed as a housing containing at least a part of the electronic circuit. In one

embodiment the housing may be formed of a proximal housing part and a distal housing part. The device is adapted to be releasable connectable to said housing.

A number of encapsulation techniques are known and includes coating, two component polymer, hot-melt polymer encapsulation, ceramic encapsulation and glass encapsulations. Other methods for encapsulation of electric components are known in the art.

The microelectronic system or components thereof is suitably encapsulated in a polymer film, a polymer foil, or a polymer coating or the microelectronic system or components thereof is moulded into a polymer material, or is encapsulated in a glass or ceramic material.

Encapsulation in silicone, such as PDMS, is particularly preferred when the microelectronic components are to be placed in a through hole or a recess in the adhesive body and where it is desirable to enable easy removal or replacement of the encapsulated microelectronic component(s), as the silicone surface is easily released from the adhesive of the adhesive body. Other materials, which are easily releasable from the adhesive, may also be used for the encapsulation.

In order for the adhesive element to be easily released from the housing after use the housing may advantageously be made from a material, or coated with, which allows the housing to easily release. Such a material may for example be a silicone, which often is used for release liners in different adhesive applications.

In yet another embodiment the at least one power source element is adapted to be received in a recess formed in the distal housing part. At least one electrical contact is provided in the distal housing providing electrical connection between the power source element and the electrical circuit.

By providing a recess as described above the power source element is protected from being displaced and thereby losing electrical contact with the circuit. The recess also creates a flush assembly when the power source is placed therein giving it a smooth surface which will not get caught as easy as from a surface where the power source would protrude.

Many types of electronic circuits having many different applications and which is powered and attached to a surface may be used with the device according to the invention. The device may after use be disposed but the electronic circuit may be reused. In one embodiment the device is thus adapted to be releasable connected to electronic circuit, which is a sensor circuit, said sensor circuit is to be attached to the body surface of a mammal, typically the skin.

By the term ' sensor' or 'sensoring' it should be understood that a parameter of the ambient environment of the electronic circuits is detected by the sensor circuit. Such parameters may among many for example be temperature, humidity, electrical signal, electrical fields, light, noise, biosignals and magnetic fields.

Thus, the invention also relates to a sensor assembly adapted to be attached to the body surface of a mammal, comprising; a sensor circuit, comprising a number of electrical components; at least one power source element for powering at least one of the electrical components; at least one adhesive element for attaching the sensor assembly to the body surface of a mammal; and that at least one of the power source element and the adhesive element is releasable connected to the sensor circuit.

Thus, the sensor assembly provides the advantages as disclosed above when different elements are disposable, such as the device comprising the power source and the adhesive element, and others are reused, such as the electronic circuit.

In one embodiment of the sensor assembly the sensor circuit is at least partly contained in a housing where the housing is formed of a proximal housing part and a distal housing part. Advantageously a sensor assembly may be provided where a first peel force between the adhesive and the housing is smaller than a second peel force between the adhesive and the battery. This allows for easy separation of the sensor circuit from the adhesive and power source elements.

Typically the sensor assembly will comprise at least one transducer attached to a proximal surface of a proximal part. Together with a distal part the proximal part makes up a housing, as described earlier, for protecting at least a part of the sensor circuit. This transducer will transform different physiological signals into electrical signals. Such

transducers may for example potentiometric, caliometric, conducmetric, chemomechanical or optical.

To prevent that the power source accidentally moves out of electrical contact with the sensor circuit a recess may be formed in the distal housing part, the recess is adapted to receive the at least one power source and that at least one electrical contact is provided in the distal housing providing electrical connection between the at least one power source and the electrical components. The recess thus protects the power source from outside movement, for example when the adhesive moves due to movement of the surface whereto the sensor assembly is attached. Additionally, by protecting the power source from outside movement the electrical connection between the power source and the microelectronic circuit is also protected from disconnection.

In another aspect the present invention relates to the use of a device comprising an adhesive element and a power source element, and where the device is used for attaching an electronic circuit to a surface and to power said electronic circuit, wherein said electronic circuit is releasable connectable to the adhesive element and the power source element.

Many sensors are connected to the monitoring systems with wires. The disadvantage of such a system is that the patient does not have freedom to move since the wires are attached to the sensors on the body and connected to a monitoring system. Whenever the patient wants to move he must be careful not to dislodge any of the wires attached to the sensors, and he must further pick up the monitoring system and carry it along.

Furthermore, an isolated power source, such as a battery, where no external wiring is necessary is preferred. Such isolated power source elements preferably used with the present invention are well known in the art.

In general, batteries may be divided into primary batteries, which are single use and secondary batteries, which are rechargeable.

Primary batteries are produced in various types based on different combinations of anode, cathode and electrolyte materials. Common chemistries for primary batteries include zinc-carbon, zinc chloride, alkaline manganese dioxide, silver oxide, zinc / air and lithium in

these combinations: lithium / sulfur dioxide (Li-SO2), lithium / thionyl chloride (Li-SoCL2), lithium / manganese dioxide (Li-MnO2), lithium / carbon monofluoride (Li-(CF)n), lithium / copper oxide (Li-CuO), and lithium / iodine (Li-I2).

Secondary batteries are rechargeable and are typically based on Nickel Cadmium (NiCd), Nickel Metal Hydride (NiMH) or Lithium–ion technologi. Secondary batteries usually have more active chemistries that need special handling and disposal.

Many battery sizes and cell casing exist, including standard cylindrical cells, multi-cell batteries, coin cells, pouch cells and thin film batteries.

Standard cylindrical cells and multi-cell batteries are known from common household appliances, e.g. flash lights and remote controls. This group includes the well known sizes AA, D, C, and 9V rectangular.

Coin or button cells are typically small, round and a few millimetres high. This group is often found in watches, hearing aids and memory backup. Since they are based on solid-state cathodes, these systems are considered very safe.

Duracell, Panasonic, Sony and Energizer are some of the major manufacturers of standard and coin cell batteries.

Alternatively, using pouch casings along with Lithium Polymer cells with solid electrolytes can provide another type of batteries. This provides a low cost bendable construction. The batteries are characterized by a high energy density in addition to being re-chargeable. The solid electrolyte permits safer, leak-proof cells. The foil construction allows very thin and lightweight cell designs.

Bullith Batteries manufactures flexible batteries based on this technology.

Yet another type of batteries are thin film batteries, which are based on the printing of solid state lithium polymer chemistry on a variety of substrates. They can be printed directly onto plastics, thin metal foils or paper resulting in ultra thin and flexible power sources. The batteries can be made in any shape or size, but are generally limited in energy

storage and current capacity. The batteries are very safe as they contain no caustic chemicals, cannot overheat, explode or cause electrical shock.

The Israeli company Powerpaper are selling products based on thin film technologies. Other companies producing this type of batteries are Oak Ridge Micro Energy Inc. and Infinite Power Solutions.

In one embodiment the adhesive element is formed as a three-dimensional adhesive body as described earlier, i.e. the adhesive element has a considerable thickness, typically several times thicker than the backing layer whereon it is applied.

The pressure sensitive adhesive making up the three-dimensional adhesive body is suitably a mouldable thermoplastic or chemically curing pressure sensitive adhesive having a flexibility enabling the adhesive device to conform to the curvature of body parts while retaining its adhesive properties even under movements.

The backing layer may furthermore function as a cover layer, where said backing/cover layer is provided to function as base wherein the adhesive is applied and to protect the adhesive from the outer environment, e.g. against adhesion to linen, clothes or moisture.

Furthermore, an electromechanical display system may be applied to the cover layer. Such display system may allow the user to test the charge of battery, either before adding the powered adhesive to a microelectronic system and during use.

Simple battery indicators known in the art may thus be used. For example a foil consisting of two contact electrode and a conductive thermochromic ink, typically liquid crystals or leucodyes, may be used.

When for example using a common coin battery, one electrode is in contact with the anode of the battery and the other electrode in contact with cathode of the battery. By pressing the contact device on top of battery the battery test circuitry is closed and the thermochromic ink will light up indicating battery status.

The cover layer or film protects the integrated /embedded microelectronic components as well as the adhesive body against the environment.

The adhesive device of the invention may be constructed in a number of ways, as it will be described in more detail below. Common for all constructions are that the three-dimensional geometries provide good protection for the microelectronics and at the same time give the device as smooth a surface as possible. Especially the shaping of the edges of the device need paid attention, otherwise linen will easily stick to them and cause rolling. Therefore the outer rim of the adhesive device with the embedded micro electronic system must be shaped to thickness less than half of the thickest part of the device, normally the central part comprising the microelectronic electronic system.

Detailed description of the drawings

Figure 1 shows a die section of the shape of a typical representative of the adhesive device according to the invention. CT relates to the maximal thickness of the device and PT to the thickness in the periphery of the device. The device does not necessarily need to be shaped symmetrically.

Figure 2 has a box showing the part of the adhesive device, which is illustrated in figures 3-12. As illustrated in figure 2 the electronic parts 101 are embedded in an adhesive body 102 with a cover layer 103 and a release liner 104.

In one embodiment of the invention, all the electrical components are assembled in one unit, which is embedded in the adhesive body and is covered on all sides with the pressure sensitive adhesive, essentially making it a disposable pad. As illustrated in figure 3 an assembly of electronic parts 101 are embedded in an adhesive body 102 with a cover layer 103 and a release liner 104.

Figure 4 illustrates that the components of the microelectronic sensing system may be positioned at different locations within the adhesive body, provided there is the required mechanical or electrical connection between the components. All components are completely embedded in the adhesive body and are covered on all sides by the pressure sensitive adhesive of the adhesive body.

The integration of all microelectronic components within the adhesive body is useful for cheap throw away one time one use devices. Because of the short usage time of the

adhesive device the electronics need little or none extra protection, such as encapsulation. The adhesive body itself acts as protection of the microelectronic components.

Even though all the components of the microelectronic system are covered on all sides with the adhesive body, several sensing applications (humidity, optical or chemical/gas) are still possible.

Systems, which may be covered on sides, may also be a RFID TAG, a Network Hub, a network coordinator, a gateway, or other systems capable of collecting, communicating and/or transmitting data. These systems would often need some kind of activation to start the system, such as a pressure contact or magnetic contact to overcome the need for large shelf life compared to the active period.

Figure 5 illustrates an embodiment of the invention where the microelectronic system is embedded/applied into a recess in the adhesive body. The recess is positioned in the upper surface of the adhesive body. The microelectronic system may be embedded/attached during fabrication of the adhesive body, just before or after the adhesive device has been attached to the skin. According to this embodiment of the invention, the microelectronic system may be reused.

Figure 6 shows a microelectronic system analogous to the system of figure 5, however, in figure 6 the system consists of two parts. One part, the upper, is exchangeable of reusable and the lower is embedded in the recess of the adhesive from start. The upper part may for instance be the power supply.

Figure 7 illustrates an embodiment where some components of the microelectronic system is embedded within the adhesive device during production and some components are applied in a recess in the upper surface of the adhesive body, i.e. are exchangeable or reusable. According to the invention one or more component(s) may be embedded within the adhesive body and one or more component(s) may be present in a recess at the surface of the adhesive body. The necessary mechanical or electrical connection between the components are also embedded in the adhesive body. Although the figure only illustrates one, there may be two or more recesses in the upper surface of the adhesive body and there may be two or more components integrated into the adhesive body.

The exchangeable parts in the recess may be locked in the recess by the adhesive properties of the pressure sensitive adhesive in the recess. In an alternative the microelectronic components in the recess is encapsulated in a coupling or plug designed to fit into a lock, such as a snap lock, present in the recess.

Figure 8 illustrates an embodiment of the invention where the microelectronic system is embedded/applied into a recess in the adhesive bottom surface of the adhesive body. The microelectronic system is embedded/attached during fabrication of the adhesive device or just before attaching the adhesive device to the skin. This system is typically used where it is required that some of the components of the system are in contact with skin either non-invasively or invasively.

Figure 9 illustrates en embodiment where some components of the microelectronic system is integrated within the adhesive device during production and some components are applied in a recess in the lower surface of the adhesive body, i.e. are exchangeable. According to the invention one or more component(s) may be integrated into the adhesive body and one or more component(s) may be present in a recess at the surface of the adhesive body. The necessary mechanical or electrical connection between the components are also integrated into the adhesive body. Although the figure only illustrates one, there may be two or more recesses in the bottom surface of the adhesive body and there may be two or more components integrated into the adhesive body at different locations.

Figure 10 illustrates an embodiment where some components of the microelectronic sensing system is integrated into the adhesive device during production and some components are applied in a recess in the bottom surface of the adhesive body, i.e. are exchangeable or reusable. According to the invention one or more component(s) may be integrated separately into the adhesive body and one or more component(s) may be present in a recess at the surface of the adhesive body. Although the figure only illustrates one, there may be two or more recesses in the bottom surface of the adhesive body.

This construction is suitable where the transducers or actuators utilize skin contact or skin penetration (e.g. electrodes and needles), whereas the rest of the microelectronic system may be embedded in the adhesive body (batteries, antenna, electrode, A/D converter, amplifier). This configuration also has several production advantages.

Thus, figures 8, 9 and 10 illustrates a construction where the exchangeable part e.g. the battery, is attached to the adhesive part facing the patient. Prior to mounting the adhesive sensor device on dermis of the mammal the protective release liner is removed, the exchangeable battery is coupled to the rest of the microelectronic system enabling the electronic system to function. Thereafter the adhesive part of the device and the whole construction is mounted on the dermis of the patient.

After use the exchangeable part e.g. the battery, is replaced and the adhesive device may be used in the context of a new monitoring of the patient.

In order to be able to remove the battery following detachment of the adhesive device, the inner part of the recess in the adhesive device could be coated with a PDMS curable coating or other non-adhesive coating; this operation will facilitate the exchange of the battery.

The battery as well as other exchangeable components, such as the chip, may be present in a recess in the bottom surface of the adhesive body. According to this embodiment, it may be an advantageous to have the exchangeable microelectronic parts contained in a capsule, e.g. embedded in an injection-moulded capsule.

Just prior to mounting the capsule containing the microelectronic components the release liner is removed and the exchangeable capsule is attached to the adhesive body in the recess of the adhesive construction. The microelectronic components may be coated with curable PDMS or other non-adhesive coating in order to facilitate detachment of the exchangeable capsule.

When the microelectronic components have a longer life than the adhesive body, the cheap components, such as the transducer, the antenna or the power source, may be integrated into the adhesive body and the components that may be reused are placed in a recess before use.

Another application is where customised preparation or programming of the system is done prior to application.

The features and applications described in connection with figure 3 apply equally well to the embodiment illustrated in figure 5 and vice versa.

Figure 11 illustrates the integration of a microelectronic system within a through hole in the adhesive body providing access to the microelectronic system from both the upper surface and the bottom surface of the adhesive body. The application of the microelectronic system is possible both during production/fabrication of the adhesive or just prior to application to the skin, and/or after application to the skin.

Figure 12 illustrates a system where two components or assemblies of components of the microelectronic system are connected in some way. One of the components may be integrated during production, whereas the other is applied afterwards.

Alternatively, the components or assemblies of components are applied afterwards. This is useful where different lifetime make is feasible to exchange electronic components at different times, such as battery or transducer. Mechanical and/or electrically interconnection schemes such as snap locks or plugs are advantageous in this configuration.

The system illustrated in figure 4 is useful where skin contact and simultaneous access to electronic components from the upper surface is needed. One or both subsystems can be reused.

The features and applications described in connection with figure 5 and 8 applies equally well to the embodiment illustrated in figure 11 and vice versa.

Figures 13 - 18 illustrates an embodiment of the invention where an antenna, a central processing unit, a battery and electrodes are embedded in an adhesive device.

Figure 13 illustrates the two-dimensional shape of the device indicating a cross-section by A-A.

Figure 14 illustrates the position of the antenna 109 placed in the outer part of the adhesive device and being connected to the central part of the microelectronic system.

In Figure 15 the third dimension is shown in cross-section along the line A-A in figure 13. The circle B from the rim of the device is further magnified in figure 16 and the circle C of the centre is likewise magnified in figure 17.

Figure 16 shows more in detail the building of the antenna lying embedded in the adhesive. This clearly shows the cover film 103 and the release liner 104 for the adhesive 102.

Figure 17 shows the position of the central part of the microelectronic system 1 with a battery 105, a CPU 106 and protruding the adhesive the electrode 107. The battery and the CPU is enveloped in a transparent silicone rubber 108.

Finally figure 18 illustrates the adhesive device in a perspective.

There are other ways of constructing an adhesive device having an embedded micro electronic system, that fulfils the basic requirement of a three-dimensional construction and the drawings may thus not be construed as limiting.

One special advantage of the invention is the simple and inexpensive way of preparing an adhesive body having a three-dimensional shape from a pressure sensitive adhesive.

As mentioned above, the pressure sensitive adhesives are either a thermoplastic pressure sensitive adhesive or it is a chemically curable adhesive that has the ability to be moulded into a three-dimensional shape.

The thermoplastic pressure sensitive adhesive may typically enter a fluid condition and achieve a moderate viscosity at above 100-120 deg C i.e. above the glass transition temperature of the composition, which makes it easy to mould the adhesive composition to the desired shape. One example may be direct moulding. In a first step the cover layer is provided in the desired shape at temperatures just below the glass transition temperature of the cover film and then the necessary amount of adhesive is filled the into the mould to fill up the mould. The filling of the mould may be in two steps whenever appropriate. This will allow partly filling with the molten adhesive in a second step, placing the electronic parts in a third step and eventually filling and covering the electronic parts

with the remainder of the adhesive in a fourth step. As a last step a release liner is applied and then the adhesive device is punched out of the mould.

Alternatively the adhesive laminated with the cover film may be processed through compression, pressing or moulding into the desired geometry or shape at elevated temperature, but slightly below the glass transition temperature of the adhesive. Optionally the microelectronic system may be placed between two layers of adhesives and then moulded. The moulding is performed in the press at elevated temperature and if desired with the microelectronic system placed in the mould preferably in the centre of the mould.

In the special embodiment where exchangeable or reusable components are a part of the adhesive device, a female and a male part of a moulding shape is required.

In another embodiment of the invention curable pressure sensitive adhesive is cast in the desired shape. The casting may follow the same principles as of above allowing a partial filling step of the mould with the cover film, applying the electronic components and thereafter complete the filling of adhesive in the mould and finally concluding with placing the release liner, curing if necessary and die cutting.

Another method is moulding by compression of adhesives having high or very high viscosity. A primary layer comprising a pressure sensitive adhesive e.g. a hydrocolloid containing block copolymer on a cover film taken from a roll enters the processing equipment as a first step, the pre-assembled, optionally encapsulated micro electronic components is placed with the appropriate distance in a second step, in a third step, a secondary layer of the same or another pressure sensitive adhesive is laminated to the first layer of pressure sensitive adhesive enclosing the microelectronic part between the layers, in a fourth step said laminate is formed in a hydraulic press into a shape containing multiple projections centred upon the microelectronic part and in a fifth step the individual projections are die cut to final devices.

The pressure sensitive adhesive devices can be produced according to a continuously process as described in US 6726791.

Figs. 19, 20 and 21 shows one embodiment 1 of a sensor assembly according to the invention. Figure 19 shows the sensor assembly in an exploded view. Figure 20 shows the assembly seen in section along line XX – XX in Fig. 19 when the sensor assembly is assembled. Fig. 21 shows the sensor assembly seen from the skin side, also referenced to as the proximal side, i.e. the side of the sensor assembly, which is to be attached to the skin.

The sensor assembly 1 consists of a sensor device 2 and housing element 3 which contains a microelectronic circuit 4. The sensor device 2 is made up by an adhesive element 5 and a power source element in the shape of a coin cell battery 6.
The housing element 3 is made up of a distal part 7 and a proximal part 8. A recess 9 is formed in the distal part. The recess has a circumference, which is slightly larger than the circumference of the coin cell battery allowing the coin cell battery to be received in the recess.

In the recess there is provided two electrical contacts 10a,10b for electrically connecting the microelectronic circuit 4 and the battery 6 when the battery is placed in the recess. The microelectronic circuit is made up of a number of components arranged on a print board 11. Every component will not be described herein as the circuit is well known in the art and as such not a part of the invention in itself. In general it can be mentioned that the circuit comprises an antenna 12 formed by a number of windings of a conductive material printed on the print board. The antenna transmits and receives data from a central unit placed within communication range. The central unit may for example be a personal computer which gathers data from the sensor assembly. The data is then processed according to known processes and algorithms.

The antenna 12 is connected to a microprocessor 13, which receives signals from a first transducer 14 and a second transducer 15. The first and second transducer extends from the print board through the proximal part and terminates on the proximal surface of the proximal part. Thus, when the housing is placed on the skin the first and second transducer contacts the skin surface. In order to reduce interference between the first and second transducer a barrier element 16 is placed on the proximal surface of the proximal part between the two transducers. The barrier element is formed of a dielectric material and is a well known measure in order to avoid so-called cross talk, typically causing unwanted interference, between two electronic components.

When used the battery is placed in the recess, whereby the battery is placed in contact with the electrical contacts 10a, 10b and thereby powers the microelectronic circuit. The adhesive element is then applied on the distal side of the distal part of the housing and the distal side of the battery. This secures the battery in the recess and connects the adhesive element, the power source element and the housing element into a sensor assembly. As can be seen the adhesive element has a circumference which is larger than the circumference of the housing which provides an adhesive proximal surface 17 which can be applied to the skin surface of a person or other mammal.

When the sensor assembly later is removed the adhesive element is separated from the housing element the battery is removed along with the adhesive element as the distal surface of the battery is adhesively attached to the adhesive element. The adhesive element and the battery can then be disposed and the housing element may be cleaned and stored for later use.

The adhesive element is covered by a cover layer 18 in order to protect the adhesive element from adhering to unwanted surfaces, such as the inside of worn clothing articles. The cover layer 18 also functions as backing layer whereon the adhesive material 19 is disposed during production.

Fig. 22a shows another embodiment 30 of a device according to the invention. Fig. 22b shows a section of Fig. 22a in an enlarged view. The device is made up by a two-dimensional adhesive element 31 and a power source in the shape of a coin cell battery 32 adhered to the adhesive element.

The adhesive element is formed of a backing layer 33. On the proximal side of the backing layer there is provided a first adhesive layer 34, which is covered by a first release liner 35. The distal side of the backing layer there is provided a second adhesive layer 36 to which the battery is adhered. A second release liner 37 covers the rest of the distal side of the adhesive, whereon the battery is not attached.

When applied to a surface, such as a skin surface of a person, the first release liner 35 is removed. This exposed the first adhesive layer, which may be adhered to the skin surface thereby attaching the device 30 to the skin surface. The second release liner is then

removed exposing the second adhesive layer. Not shown in the drawing, a housing containing a microelectronic system is then attached to the adhesive layer while at the same time an electrical contact on the housing is brought into electrical connection which the battery 32.

Although such a housing as described above do not have any surface contact such as the housing described with reference to Fig. 19, the housing may still comprise sensor technology. Such sensors may simply measure the ambient temperature or the device may be applied under the nose and a sensor for measuring the breathing rhythm through the nose may be applied on the device. Alternatively the sensor may apply skin contacting transducers outside the circumference of the device, while still being adhered thereto.

Fig. 23 shows yet another embodiment 40 of a two-dimensional device according to the invention and Fig. 24 shows a sectional view of the third embodiment along line XXIV – XXIV in Fig. 23. Here the power source element is formed as a thin film battery 41 being an integrated part of a backing layer 42.

On the proximal side of the backing layer there is applied a first adhesive layer 43 which is covered by a first release liner 44. The distal side of the backing layer is covered by a second adhesive layer 45 which is covered by a second release liner 46. The second adhesive layer is interrupted in an area 47 allowing access to contacts 48a and 48b which provides electrical contact to the thin film battery.

When used the device 40 described with reference to Fig. 23 is applied in the same way as the device 30 described with reference to Fig. 22.

It should be understood that different types of adhesives may be used on respectively the proximal side of the backing layer and the distal side of the backing layer. While the proximal side is attached to the skin surface and thus preferably should be skin friendly, the adhesive on the distal side should preferably be of a type which provides optimal attachment to a electronic circuit or a housing containing such circuit while still allowing the device to be separated there from after use.

Although the above embodiments describe releasable attachable means in shape of adhesive attachment for connecting the device to the electronic circuit other types of

release attachable means may be used. Such releasable attachable means can for example be mechanical such as a snap lock arrangement between the battery and the recess in the housing, where the recess is formed with protruding ribs which couples with the battery. Alternatively additional coupling means may be provided on the device for coupling with complementary coupling means on the electronic circuit or the housing containing the electronic circuit, and may for example be in the shape of bayonet coupling, hooks, frictional couplings or threaded couplings.

Experimental Section

Example 1

Three batches of adhesive were produced. The adhesives were prepared by standard hot melt procedure in a Herman Linden z-blade mixer (Machine type LK 110.5), by mixing the components of elastomer (Kraton), one third of the plasticiser (DOA) and the resin (Arkon) at 130 degree C until a homogeneous mixture was achieved (30-50 minutes). The rest of the plasticiser and the hydrocolloid filler (CMC) was added and the mixture was blended for 20 minutes.

	Recipe 1	Recipe 2	Recipe 3
Kraton 1161 (Shell)	18,0	19,0	15,0
Arkon P90 (Arakawa	32,0	36,0	
DOA (Dioctyl adipate)	5,6	7,5	
Vistanex® LM-MH (Exxon)			45,0
CMC: Blanose 9H4XF (Hercules)	44,4	37,5	40,0

Example 2

Moulded bodies of the adhesives of example 1:

Each of the adhesives according to claim 1 were applied on to a 35 micrometer thick cover film of polyethylene and a siliconised polyethylene liner was applied to the opposite side of the adhesive patch and pressed to the desired shape according to any of the illustrations 1-3 in a for the shape designed mould at 90 degree C by altering the non-cavity holding

mould to give the shape of the recess. The centre of the adhesive device was 3.4 mm and the thickness of the outer rim 0.4 mm.

Example 3

Moulded silicone pressure sensitive adhesive body:

Dow Corning 7-9800 A&B (mixing ration between A and B is 1:1 by weight) were used for production of a PDMS based adhesive body. A mould having a triangular shape (each side of the triangular mould having a distance of 300 mm, the center part having a thickness of 0,5 mm and the edge having a thickness of 0,1 mm) was used. The components were thoroughly mixed and applied on a 50 µm cover layer of silicone rubber lining in the female part of a triangular mould and a male mould part was placed on top, said part lined with a low density polyethylene release liner. The adhesive was cured in an oven at 100 degree C for 15 minutes. After curing the adhesive was punched out of the mould and a dent in the centre of the adhesive body device for embedment of an electronic sensing system was punched out.

Example 4

Moulded thermoplastic PSA adhesive body:

The components of recipe 2 in example 1 were mixed in a Herman Linden mixer and while still hot and soft, the resulting dough-like material mass was removed from the mixer and placed on a thermoplastic polyurethane cover film placed in the cavity of a moulding form and a release liner is placed on top. The second part of the mould was plane. The adhesive is compression moulded at approximately 90 degree C and 100 bar. The release liner was removed and an encapsulated microelectronic sensing system was placed at the centre of the adhesive body within the mould, the release liner was reapplied and the moulding step was repeated. Finally the resulting sensor pad was punched out.

Example 5

Moulded thermoplastic PSA adhesive body with integrated RFID-tag:

A pressure sensitive adhesive according to recipe 2 in example 1 were mixed in a Herman Linden mixer and while still hot and soft a minor part of the material was removed from the mixer and placed on a cover film towards the female part of a mould and a release liner was placed on top and thereafter the male part of the mould having a small protrusion

over the area corresponding to the microelectronic system of the product was applied. The whole construction is compression moulded at approximately 90 degree C and 100 bar. Hereafter the release liner was removed and a RFID tag encapsulated in polypropylene was placed in the recess of the pressure sensitive adhesive and the mould was filled up with the remaining adhesive. A release liner is attached again and the whole construction was compression moulded again. The resultant pad was punched out. The thickness of the outer rim was 0.2 mm, the central thickness was 2.5 mm and the shape was circular with a diameter 40 mm.

Example 6

In this example the micro electronic system embedded into the adhesive body consist of both the RFID tag and communication and storage components. In order to protect the micro electronic system the components are encapsulated in polyethylene. The components are integrated in the PSA during a continuous process as described in US 6726791. The primary layer comprises the cover film with pressure sensitive adhesive, the secondary layer is the encapsulated micro electronic part; and the third layer is of a mouldable layer pressure sensitive adhesive; the whole construction is combined in the moulding cavities.

Example 7

Preparation of a Hydrogel adhesive composition:

3.5 grams of PVP K-90, 17.5 grams of PVP K-25, 3.5 grams of Pemulen TR2 and 28 grams of PEG 400 were mixed as a premix. Initially the premix of the plastizicing glycols, the PVP and the cross-linked polyacrylic acid were added and mixed in a Brabender mixer at 100 degrees C for 10 minutes. Then 17.5 grams of the amphiphilic polyurethane (Tecogel 2000) was slowly added in order to ensure complete mixing of the components. After 20 minutes' mixing a macroscopically homogenous mixture was obtained. The hot adhesive from the mixing chamber was moulded into a circular adhesive body (diameter 4 cm) with a dent for a later applied micro electronic system. The thickness of the pad is 3 mm at the centre and the thickness is gradually decreasing to 0,3 mm at the edge of the pad. The adhesive device was compression moulded between a sheet of silicone paper and a 30 μm PU cover film.

Example 8

A microelectronic sensing system for invasive measurement of oxygen:

An adhesive according to example 1 recipe 2 was used embedment of a micro electronic system consisting of an oxygen electrode, a central processing unit, a transmitter and a battery. The shape of the adhesive body is oval (70 x 30 mm) having a centre thickness of 5 mm, an edge of 0,3 mm and an essential linear increase in thickness from the edge to centre of the pad. The adhesive body has a centrally placed through hole and a dent in the skin-contacting part of the surface of the adhesive body for the silicone covered micro electrical components.

The CPU, the battery and the transmitter are as described in the examples 11. The oxygen electrode was oxygen electrode product number 723 (from Diamond General, Development Corp. US).
The CPU, transmitter and battery were electrically connected and thereafter covered with a thin layer of polymeric silicone, only the electrical contact of the CPU to the electrode, remains uncoated.

The tip of the electrode in the sensing device is surrounded with a medical needle with outer diameter of 0,7 mm.

During use the electrode and the needle are positioned in a way where the electrical contacts of the CPU are connected with corresponding contacts of the electrode.

During application of the measuring device the partly silicone covered micro electronic system was firstly applied onto the adhesive body in the dent at the skin contacting side of the device. The device is applied to the skin. The needle is then positioned from the outside through the hole in the adhesive by penetrating the skin in a second step and the electrode partly enveloped in a plug is mounted through the hollow centre of the needle as a third step creating electrical contact to uncoated connections of micro electronic system. The plug part of the electrode fits the smooth curvature of the cover film without introducing recesses.

During use, the electrode may be rinsed and reapplied according to needs for achieving correct signals.

Example 9

Microelctronic hub embedded in adhesive sensor device according to the invention:

An adhesive according to example 1 receipe 1 was moulded in a first layer forming an oval shell (50 x 80 mm) having a smooth surface to one side. This surface is declining in slope towards the outer periphery and is covered with a 30 µm thin film of polyurethane i.e. placed between mould and adhesive. The opposite side of the adhesive body was formed with a centrally soft shaped indentation of approximately 2 x 10 x 15 mm for applying the microelectronic system. A siliconised release liner of polyethylene was placed on the surface with the indentation. In a second step the release liner was removed, an antenna is placed at the outer periphery of the adhesive body and the CPU and the battery was placed in the central indentation. In a final step a second layer of adhesive was applied to embed the antenna at the area of the outer periphery but not the components in the central indentation. A release liner is applied and the complete construct which was die cut to the final size. The antenna is connected to the central microelectronic parts through electrical contacting elements making reuse of the central part possible. The antenna is encapsulated in thin polyethylene terephthalate (PET)-plastic and the central microelectronic parts are encapsulated in silicone rubber.

Example 10

Microelectronic hub:

A construction with microelectronic hub in which the antenna as well as the battery is completely integrated in the pressure sensitive adhesive of previous example 1. This is done by letting the adhesive of the final step in example 9 cover the antenna as well the central microelectronic parts.

Example 11

An adhesive device having embedded a microelectronic system for human temperature sensing and alarm with no remote communication

An adhesive according to example 1 recipe 2 was used for embedment of a micro electronic system consisting of an temperature sensor, a central processing unit, a transmitter, battery and an OLED (Organic Light emitting Diode). The shape of the adhesive body is round (30mm) having a centre thickness of 5 mm, a peripheral edge of 0,2 mm and an essential linear increase in thickness from the edge to centre of the pad.

The adhesive body has a dent in the skin-contacting part of the surface for the silicone covered micro electrical components.

The CPU is a µController ATMEGA 128L, an AVR 8bit RISC processor from ATMEL,
Battery is an Panasonic Coin cell CR3202.
OLED flexible colour display is from OSD (One Stop Display) part #OSCC 130-0.
Temperature sensor is from Pasport Ps-2125

During use the temperature sensor continuously monitors human skin temperature. At certain events determined by the micro-Controller influenced by time of day, temperature gradient compared to stored data, the system will give a visual alarm in form text or lights of relevant information at the flexible display.

The system is integrated into the adhesive and activated when peeling off the release liner and will function until end of battery.

Example 12

An adhesive device having embedded a microelectronic system for human temperature sensing and alarm with no remote communication is constructed according to example 11.

The construction of the adhesive device is identical to the one of example 11 except that instead of the OLED flexible colour display for signalling a temperature change an EL (Electro-lumiscent Lamp) is used as the signalling part in the surface of the device. The part is an EL Lamp Part #: 300210KIT from Being Seen Technologies.

During use the temperature sensor continuously monitors human skin temperature. At certain events determined by the micro-Controller influenced by time of day, temperature gradient compared to stored data, the system will give a visual alarm in the form of a light.

Example 13

In one embodiment illustrated with reference to Figs. 19 – 21 the adhesive material 19 is a pressure sensitive adhesive (PSA) consisting of a hot-melt processable styrenic block copolymer with hydrocolloids, the battery is a metal cased coin cell battery and the housing is coated with a layer of PolyDiMethylSiloxane.

In Example 13 below, the peel forces between the PSA and the surface, the battery and the housing were determined:

The PSA is a hot-melt processable Styrenic block copolymer with hydrocolloids, which is thermo formed into the desired shape. The PSA designated A, has the following composition: 25% Kraton D1107 (Kraton Polymers), 35% Arkon P90 (a hydrogenated polycyclopentadiene from Arkawa Ltd.) 8 % DiOctylAdipate and 32% sodium carboxymethylcellulose.

In order to illustrate the peel force between the different parts the peel force has been determined via use of FINAT; FTM2, 25mm test sample width, 90 degrees peel angle, test speed of 300 mm/min and a resting time of 30 minutes.

With regard to peel force from skin the following test method was utilized:
Strips of adhesive 25 mm wide were cut from slabs of PSA composition A. A strip of adhesive tape (TESA 4124) was attached in order to prevent stretching of the samples. The samples were taped to a clamp. The skin of the volunteer was prepared by washing the underside of the forearm with diluted soap and allowing to dry at least 2 hours before the PSA was attached. The adhesive side of the sample was placed on the prepared skin. The resting time for the adhesive was 30 minutes. The clamp was attached to the hook of the testing device, an Instron Tensile tester Model 5564. The forearm was placed on a movable support of the testing device, taking care to keep the end of the sample directly under the clamp in order to keep a 90-degree peel angle. The forearm was kept still while the tensile strength tester was activated to pull the adhesive up at a rate of 300 mm/min. The peel value of the steady state part of the resulting graph was recorded and it was confirmed that no residue was left on the skin of the forearm.

The battery was a metal cased Manganese Dioxide Lithium coin cell battery CR2330, from Panasonic, and the microelectronic housing was coated with a layer of PolyDiMethylSiloxane (PDMS); MED-1137 from NuSil Technology.

The peel forces have been determined between the adhesive and the following parts with following results and with three repetitions of the test, where s indicates the standard deviation.

Peel force between A and PDMS coated housing	0,1 N/25mm
Peel force between A and steel	22,5 N/25mm (s= 2,3)
Peel force between A and human skin	2,5 N/25mm (s= 0,25)

Furthermore, different types of materials may be used for different parts of the device and the microelectronic circuit and/or the housing whereby different peel forces may be provided. Thus it would be possible to achieve peel forces between the PSA and the skin in the general range of 1 – 5 N/25 mm, peel forces between the PSA and the housing generally below 1 N/25mm and the peel forces between the PSA and the metal casing of the battery generally above 20 N/25mm.

It can thus be understood, that when the sensor assembly 1 has been applied to the skin of a user it may easily be peeled off after use, by pulling the adhesive element with a force above the peel force between the PSA and the skin. The adhesive element 5 may then easily be separated from the housing element 3 containing the microelectronic circuit 4. As the peel force between the adhesive element and the battery 6 is much higher than between the adhesive element and the housing, the battery is practically inseparable from the adhesive element, and thus the battery will be attached to the adhesive when the adhesive is separated from the housing.

Claims:

1. A three-dimensional adhesive device to be attached to the body surface of a mammal comprising an microelectronic system **characterized by**
(a) a three-dimensional adhesive body made of a pressure sensitive adhesive having an upper surface and a bottom surface;
(b) a microelectronic system embedded in the body of the pressure sensitive adhesive;
(c) one or more cover layer(s) attached to the upper surface; and
(d) optionally a release liner releasable attached to the bottom surface of the adhesive device.

2. An adhesive device according to claim 1 wherein the micro electronic system is a microelectronic sensing system.

3. The adhesive device according to any of claims 1-2 wherein the three-dimensional adhesive body has an essentially planar bottom surface adapted to adhere to the body surface of a mammal and an smooth upper surface, the adhesive device being thickest at the central part of the body and thinnest at the periphery of the body.

4. The adhesive device according to any of claims 1-3 wherein the thickness of the adhesive device at the periphery is less than 50 % of the thickness of the adhesive device where it is thickest, suitably the thickness at the periphery is less than 25 % of the thickness of the adhesive device where it is thickest, preferred the thickness at the periphery is less than 10 % of the thickness of the adhesive device where it is thickest , and most preferred the thickness at the periphery is less than 5 % of the thickness of the adhesive device where it is thickest.

5. The adhesive device according to claim 4 wherein the thickness at the periphery of the adhesive device is more than 0.05 mm, suitably between 0.05 and 0.4 mm and the thickness where the adhesive device is thickest, is between 0.5 and 15 mm, suitably between 1 and 5 mm.

6. The adhesive device according to any of claims 1-5 wherein the angle between the bottom surface of the adhesive device and a line drawn from any point on the circumference of the and the point at the upper surface where the adhesive body is

thickest is below 60 degrees, preferably below 45 degrees and most preferably below 30 degrees.

7. The adhesive device according to any of claims 1-6 wherein the pressure sensitive adhesive making up the three-dimensional adhesive body is a mouldable thermoplastic pressure sensitive adhesive having a flexibility enabling the adhesive device to conform to the curvature of body parts while retaining its adhesive properties even under movements.

8. The adhesive device according to any of claims 1-7 wherein the pressure sensitive adhesive is an adhesive based on polymers selected from block-copolymers such as styrene-block-copolymers, and hydrogenated styrene-block-copolymers, amorphous poly-alpha-olefins (APAO), polyacrylics, polyvinylethers, polyurethanes, polyelhylenevinylacetate, silicone, or from the group of hydrogel pressure sensitive adhesives.

9. The adhesive device according to claim 8 wherein the block-copolymers such as styrene-block-copolymers, and hydrogenated styrene-block-copolymers is selected from Styrene/ethylene-Butylene/Styrene (SEBS), Styrene/Isoprene/Styrene (SIS), and Styrene/Ethylene-Propylene/Styrene (SEPS).

10. The adhesive device according to claim 8 wherein the adhesive is a PolyDiMethylSiloxane based adhesive, such as a PolyDiMethylSiloxane gel.

11. The adhesive device according to any of claims 1-10 wherein the pressure sensitive adhesive making up the adhesive body comprises hydrocolloids.

12. The adhesive device according to any of claims 1-10 wherein the pressure sensitive adhesive making up the adhesive body is a foamed adhesive.

13. The adhesive device according to any of claims 1-12 wherein the entire microelectronic system is integrated in the adhesive body and is completely covered by the adhesive body on all sides.

14. The adhesive device according to any of claims 1-12 wherein one or more components of the microelectronic system is integrated into the adhesive body and is covered by the adhesive body on all sides and the rest of the component(s) of the microelectronic system are located elsewhere in the adhesive body, the components of the microelectronic system having the necessary mechanical and electrical connection to each other.

15. The adhesive device according to any of claims 1-12 wherein the entire microelectronic system is contained in one or more recesses provided in the upper surface of the adhesive body facing the cover layer(s).

16. The adhesive device according to claim 14 wherein one or more components of the microelectronic sensing system is integrated into the adhesive body and is covered by the adhesive body on all sides and the rest of the microelectronic system is contained in one or more recesses provided in the upper surface of the adhesive body facing the cover layer(s).

17. The adhesive device according to any of claims 1-12 wherein the entire microelectronic system is contained in one or more recesses provided in the adhesive bottom surface of the adhesive body.

18. The adhesive device according to claim 14 wherein a one or more components of the microelectronic system is integrated into the adhesive body and is covered by the adhesive body at all sides and the rest of the microelectronic sensing system is contained in one or more recesses provided in the adhesive bottom surface of the adhesive body.

19. The adhesive device according to any of claims 1-12 wherein the entire microelectronic system is contained in one or more through hole(s) in the adhesive body and is accessible from both the upper surface facing the cover layer(s) and the adhesive bottom surface.

20. The adhesive device according to claim 14 wherein a one or more components of the microelectronic sensing system is integrated into the adhesive body and is covered by the adhesive body and the rest of the microelectronic system is contained in one or

more through hole(s) in the adhesive body and is accessible from both the upper surface facing the cover layer and the adhesive bottom surface.

21. The adhesive device according to claim 14 wherein one or more components of the microelectronic system is integrated into the adhesive body and is covered by the adhesive body, other components of the microelectronic system is contained in one or more through holes in the adhesive body and is accessible from both the upper surface facing the cover layer and the adhesive bottom surface, and the rest of the microelectronic system is contained in one or more recesses in the upper and/or bottom surface of the adhesive body.

22. The adhesive device according to any of claims 1-12 wherein one or more components of the microelectronic system is contained in one or more through holes in the adhesive body and is accessible from both the upper surface facing the cover layer and the adhesive bottom surface and the rest of the microelectronic system is contained in one or more recesses in the upper and/or bottom surface of the adhesive body.

23. The adhesive device according to claims 1-12 wherein one or more components of the micro electronic system is contained in one or more recesses in the upper surface of the adhesive body and the rest of the microelectronic system is contained in one or more recesses in the bottom surface of the adhesive body.

24. The adhesive device according to any of claims 1 to 23 wherein the microelectronic system or one or more components thereof is encapsulated in a material different from the adhesive body.

25. The adhesive device according to claim 24 wherein the microelectronic system or components thereof is encapsulated in a polymer film, a polymer foil, or a polymer coating or the microelectronic system or components thereof is moulded into a polymer material, or is encapsulated in a glass or ceramic material.

26. The adhesive device according to claim 25 wherein the polymer used for encapsulation is silicone rubber.

27. The adhesive device according to claims 1-26 wherein the one or more components of the microelectronic system is accessible from outside the adhesive body, and may be replaced by a similar component during the life time of the adhesive device.

28. The adhesive device according to claim 27 wherein the component, which may be exchanged, is the energy source, e.g. the battery.

29. The adhesive device according to claims 1-26 wherein the one or more components of the microelectronic system is accessible from outside the adhesive device, and the component(s) may be reused.

30. The adhesive device according to any of claims 27 –29 wherein the replaceable component(s) or the reusable component(s) is encapsulated and form a package, which fit a recess or a through hole in the adhesive body.

31. The adhesive device according to claim 30 wherein the package of encapsulated, replaceable or reusable component(s) is fixed into the adhesive body by a mechanical doubling, suitably snap lock mechanism.

32. The adhesive device according to claim 30 wherein the package of encapsulated, replaceable or reusable component(s) is fixed to the surface of the adhesive in the recess or through hole of the adhesive body.

33. The adhesive device according to claim 30 wherein the package of encapsulated, replaceable or reusable component(s) is fixed in a recess or through hole in the adhesive body, where said recess or trough hole is provided with an inner non-adhesive surface, such as a PDMS coating.

34. The adhesive device according to any of claims 1-33 wherein the microelectronic system comprises components selected from communication component(s), CPU, power source, storage component(s), transducer component(s), actuator component(s) and mechanical and/or electrical interconnection between the components.

35. The adhesive device according to any of claims 1-34 wherein microelectronic system is a system enabling wireless communication.

36. The adhesive device according to claim 34 wherein the transducer has a detecting element selected from electrodes (polar, bipolar), a pressure sensor, a needle with an electrode, an accelerometer, a photo detector, a microphone, ISFET, an NTC resistor, a band gab detector, an ion membrane, an enzyme detector or a condenser .

37. The adhesive device according to claim 36 wherein the transducer has a non-invasive detecting element, such as electrodes, e.g. steel electrodes.

38. The adhesive device according to claim 36 wherein the transducer has an invasive detecting element, such as a needle containing an electrode.

39. The adhesive device according to claims 34-36 where there is no physical contact between the detector and the skin of the mammal.

40. The adhesive device according to claim 34 wherein the microelectronic system comprises a Network HUB, a gateway or a coordinator system.

41. The adhesive device according to claim 34 wherein the microelectronic system includes a GPS.

42. The adhesive device according to claim 34 wherein the microelectronic system includes a RFID tag.

43. The adhesive device according to claim 40 wherein the microelectronic system is a gateway comprising storage and communication components, CPU and a battery encapsulated in plastic and working as a dedicated network coordinator for transmission of data to a central unit (CU).

44. The adhesive device according to claim 41 wherein the microelectronic system is a system selected from:

- a system comprising storage and communication components, CPU, battery, GPS, components for wireless synchronisation of real time clock for data logging of GPS data optionally encapsulated in plastic, and

- a system comprising storage and communication components, CPU, battery, GPS, components for wireless synchronisation of real time clock for data logging of GPS data, mobile net for data logging and transmission of data and position to mobile phones, optionally encapsulated in plastic,

45. The adhesive device according to claim 34 wherein the microelectronic system is useful for nerve stimulation and comprises storage and communication components, CPU, power source and transducer for transmitting data and power to an implant for nerve stimulation.

46. The adhesive device according to claim 34 wherein the microelectronic system is a system useful for electromyography and comprises a transducer, CPU, power source, communication and storage components and an optionally an actuator.

47. The adhesive device according to claim 1-46, wherein the device comprises a power source element for powering said microelectronic system, wherein

- the adhesive body is releasable attached to one or more of the components of the microelectronic system,
- the adhesive body has at least a first area for adhering to the body surface, and

48. The adhesive device according to claim 47, wherein the power source element is attached to the adhesive body and the adhesive body has at least a second area for adhering to one or more of the components of the microelectronic system.

49. The adhesive device according to claim 48 or 47, wherein a first peel force between the second area and the microelectronic circuit is smaller than a second peel force between the power source and the adhesive body.

50. The adhesive device according to claim 47, 48 or 49, wherein the power source element is at least partly contained in the adhesive body.

51. The adhesive device according to claim 47, 48, 49 or 50, wherein the adhesive device is adapted to be releasable connectable to a housing containing the

microelectronic system and that the housing is formed of a proximal housing part and a distal housing part.

52. The adhesive device according to claim 51, wherein the at least one power source is adapted to be received in a recess, the recess is formed in the distal housing part and that at least one electrical contact is provided in the distal housing providing electrical connection between the power source and the microelectronic circuit.

53. A sensor assembly adapted to be attached to the body surface of a mammal, comprising

- a sensor circuit, comprising a number of electrical components,
- at least one power source for powering at least one of the electrical components,
- at least one adhesive for attaching the sensor assembly to the body surface of a mammal, and
- that at least one of the power source and the adhesive is releasable connected to the sensor circuit.

54. A sensor assembly according to claim 53, wherein the sensor circuit is at least partly contained in a housing and that the housing is formed of a proximal housing part and a distal housing part.

55. A sensor assembly according to claim 54, wherein a first peel force between the adhesive and the housing is smaller than a second peel force between the adhesive and the battery.

56. A sensor assembly according to claim 54 or 55, wherein the at least one transducer is attached to the proximal surface of the proximal part.

57. A sensor assembly according to claim 54, 55 or 56, wherein

- a recess is formed in the distal housing part, the recess is adapted to receive the at least one power source, and
- at least one electrical contact is provided in the distal housing providing electrical connection between the at least one power source and the electrical components.

58. A multi-sensor network comprising one or more adhesive devices according to claims 1-52.

59. A multi-sensor network according to claim 58 comprising an adhesive device comprising a network coordinator, at least two adhesive devices comprising a microelectronic system useful for electromyography and comprises a transducer, CPU, power source, communication and storage components and an optionally an actuator and adhesive devices comprising a microelectronic system useful for suitable for measuring heart rate.

60. A method for producing an adhesive device according to claim 1 having embedded a microelectronic system in an adhesive, said device having a cover film and a release liner characterised by the adhesive body being compression moulded.

61. A method for producing an adhesive device according to claim 1 having embedded a microelectronic system in an adhesive, said device having a cover film and a release liner characterised by the adhesive body being injection moulded.

62. A method for producing an adhesive device according to claim 1 having embedded a microelectronic system in an adhesive, said device having a cover film and a release liner characterised by the adhesive body being formed by reaction moulding.

63. An adhesive device according to claim 1 having embedded a microelectronic system in the adhesive body and being connected to other electronic systems by wiring.

64. The use of a device comprising an adhesive element and a power source element, and where the device is used for attaching an electronic circuit to a surface and to power said electronic circuit, wherein said electronic circuit is releasable connectable to the adhesive element and the power source element.

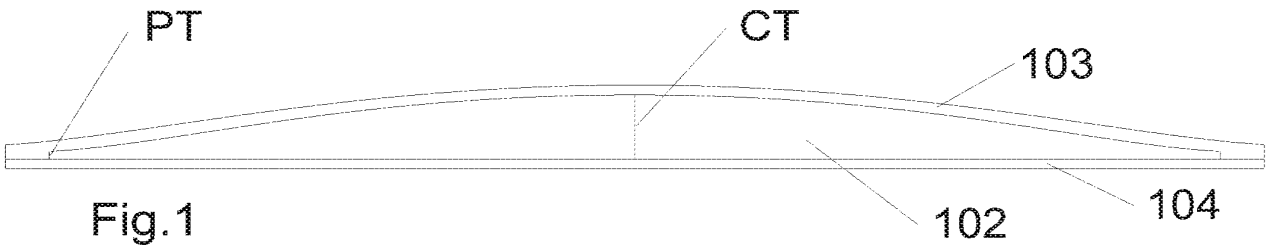


Fig.1

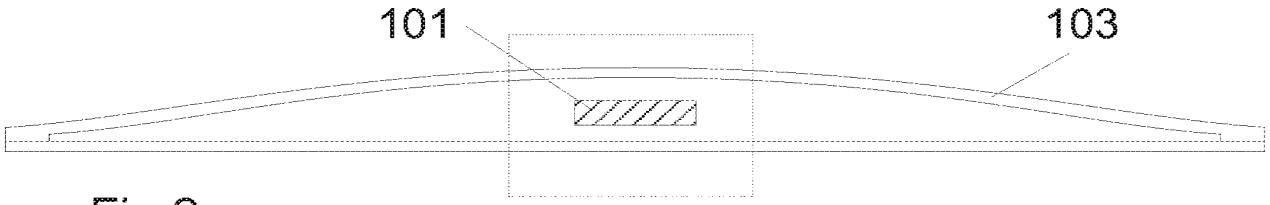


Fig.2

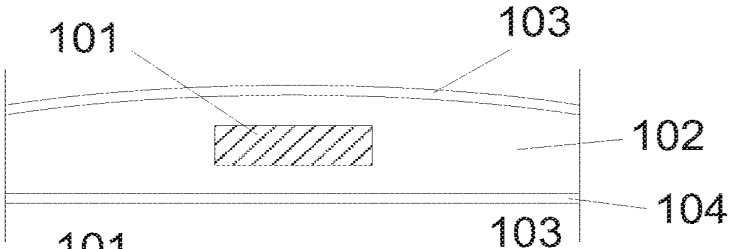


Fig.3

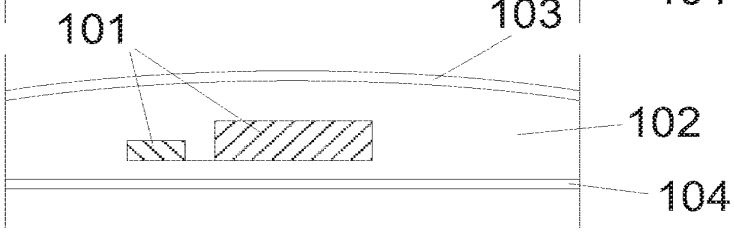


Fig.4

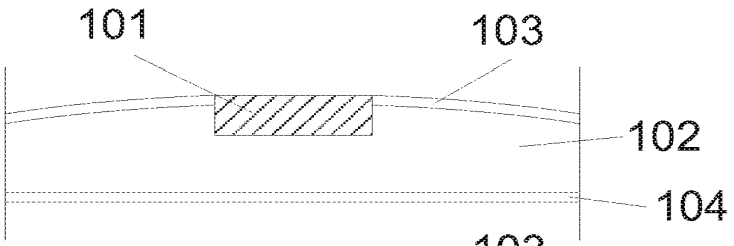


Fig.5

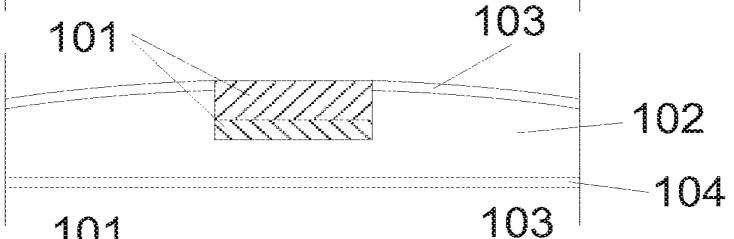


Fig.6

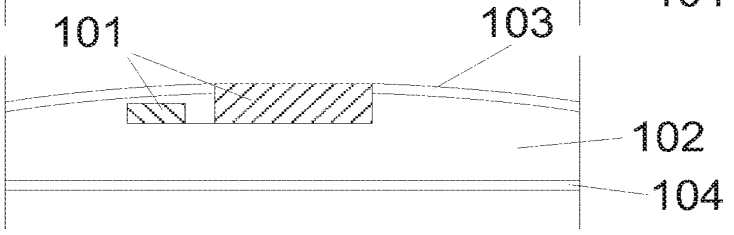


Fig.7

Fig.8

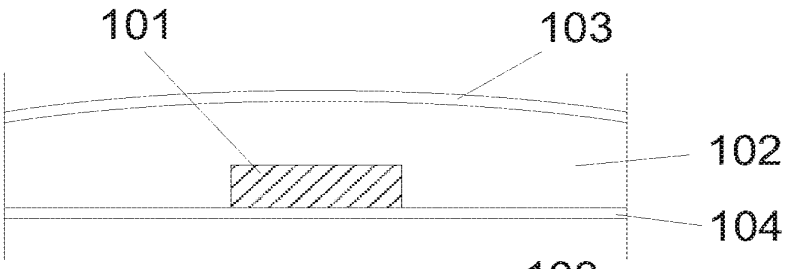


Fig.9

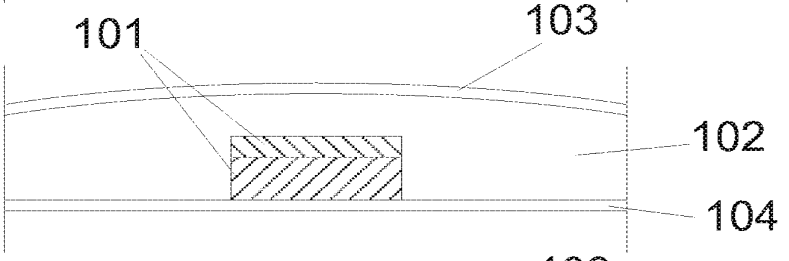


Fig.10

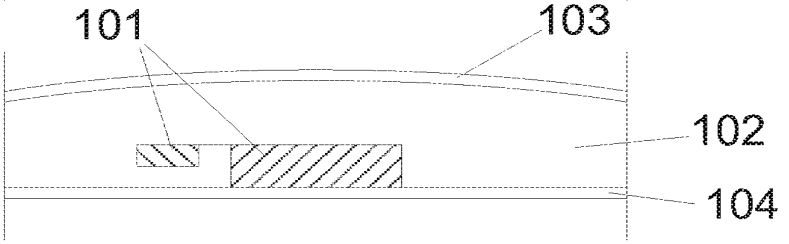


Fig.11

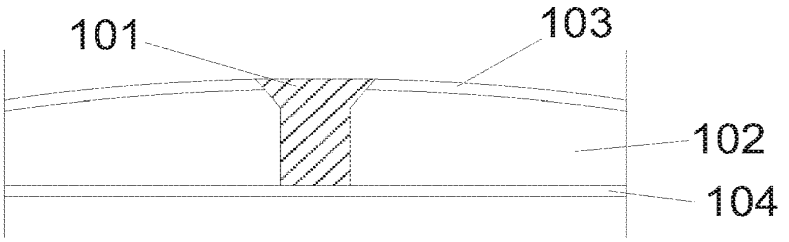


Fig.12

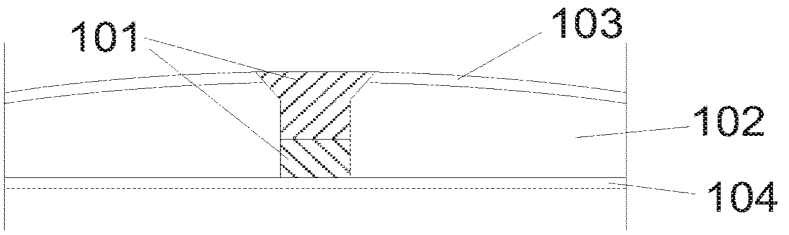


Fig.13

Fig.14

Fig.15

Fig.16

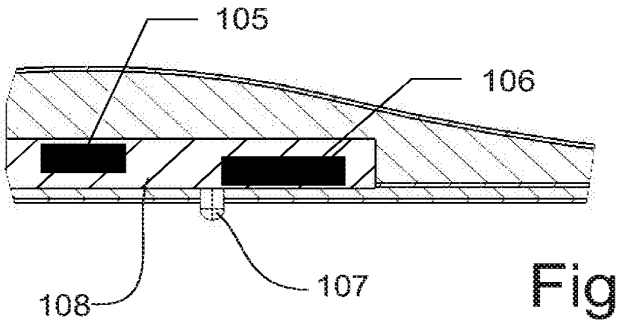


Fig.17

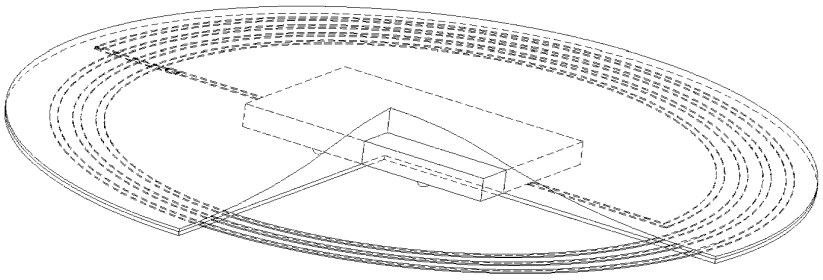


Fig.18

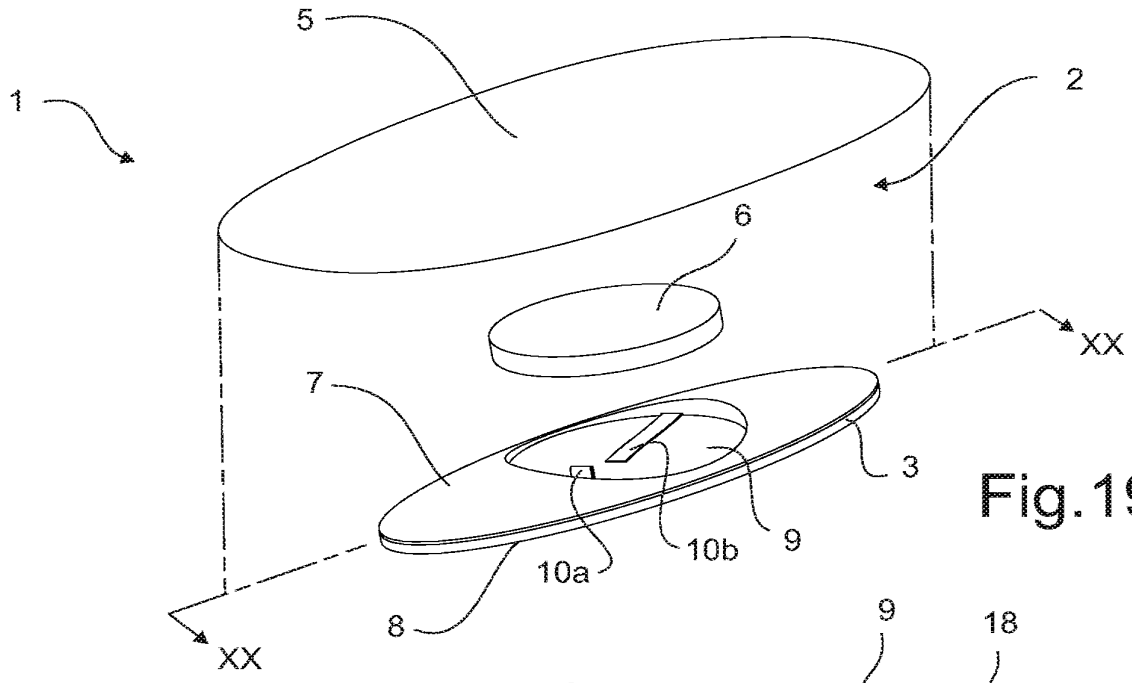


Fig.19

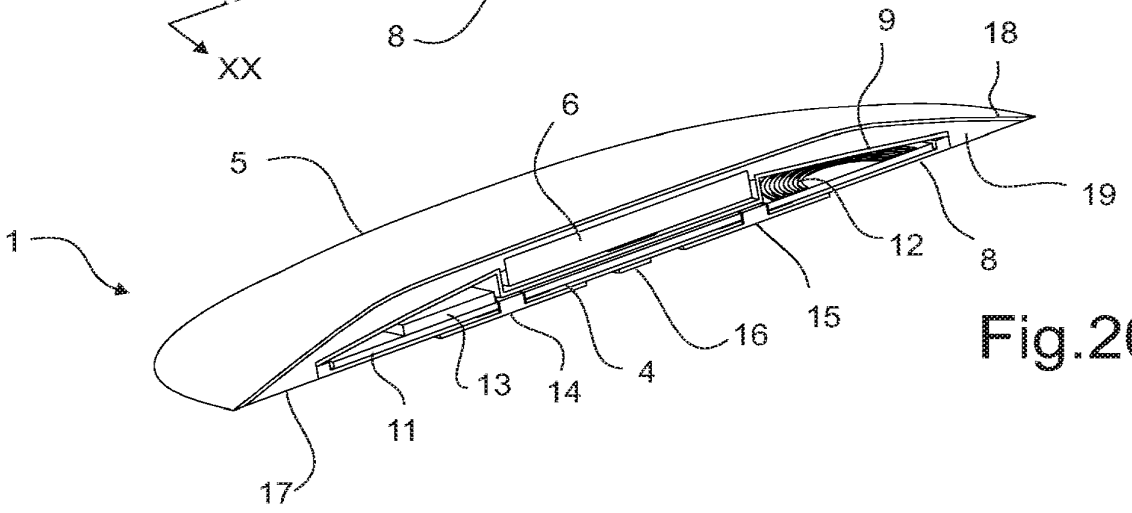


Fig.20

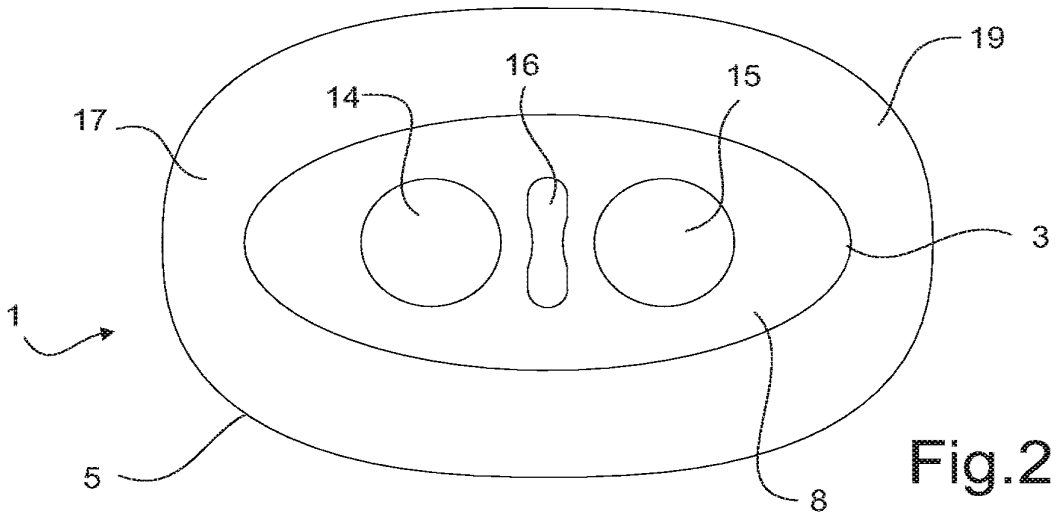


Fig.21

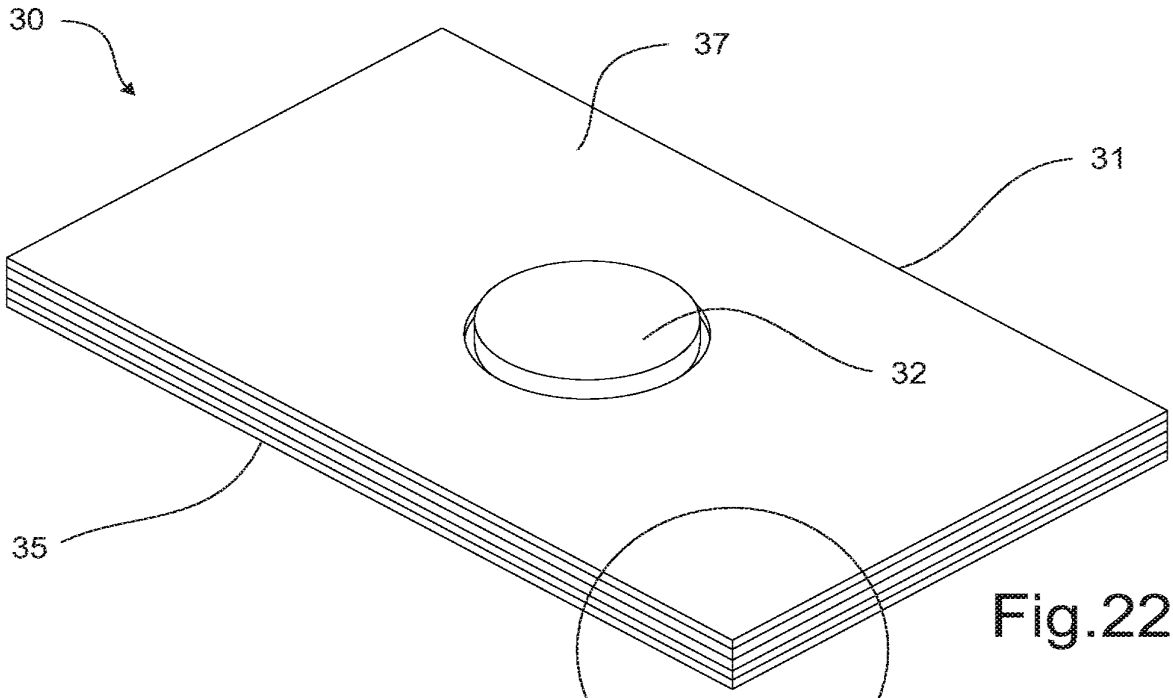


Fig.22a

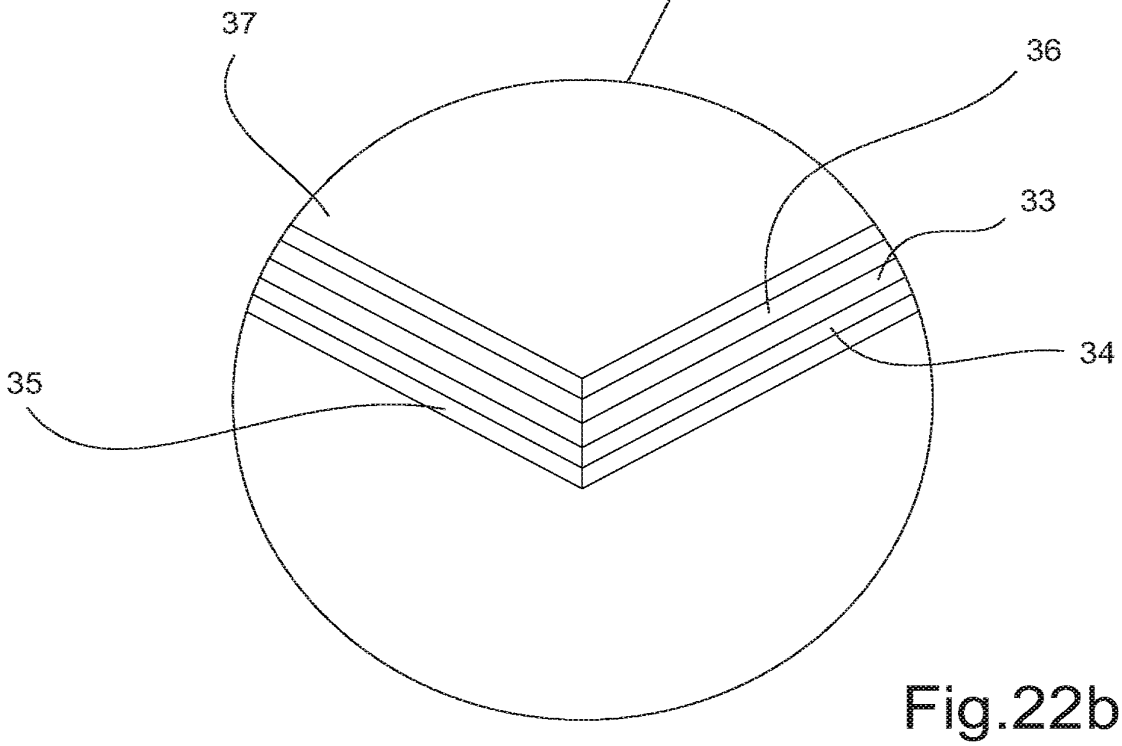


Fig.22b

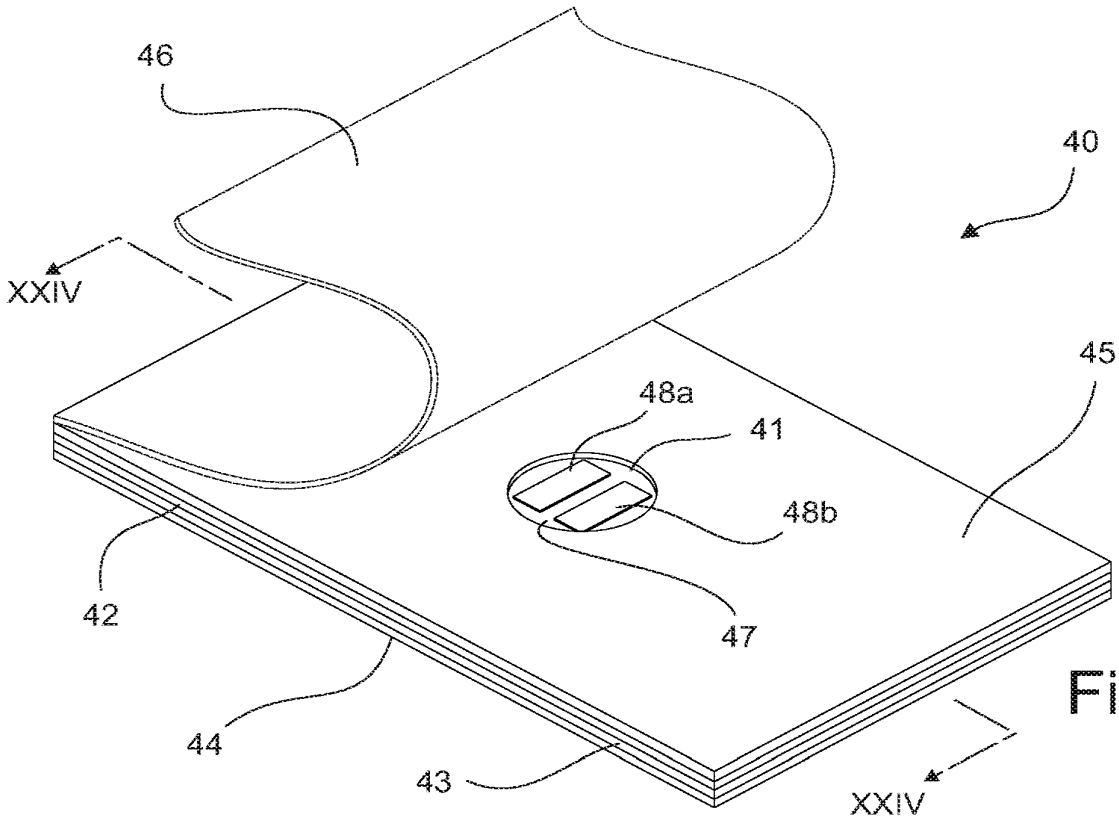

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XXIV

Fig.23

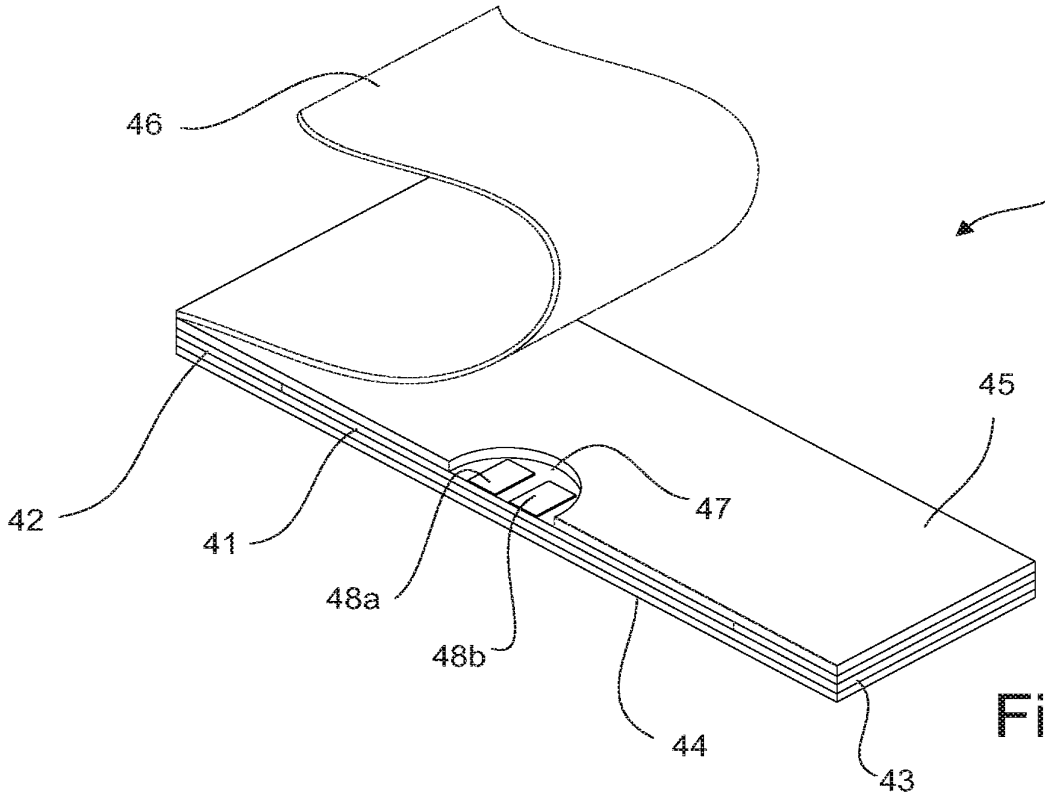

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48a
48b
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Fig.24

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum
Internationales Büro

PCT

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2. November 2006 (02.11.2006)

(10) Internationale Veröffentlichungsnummer
WO 2006/114297 A1

(51) Internationale Patentklassifikation:
A61M 5/00 (2006.01) *A61B 5/00* (2006.01)

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26. April 2006 (26.04.2006)

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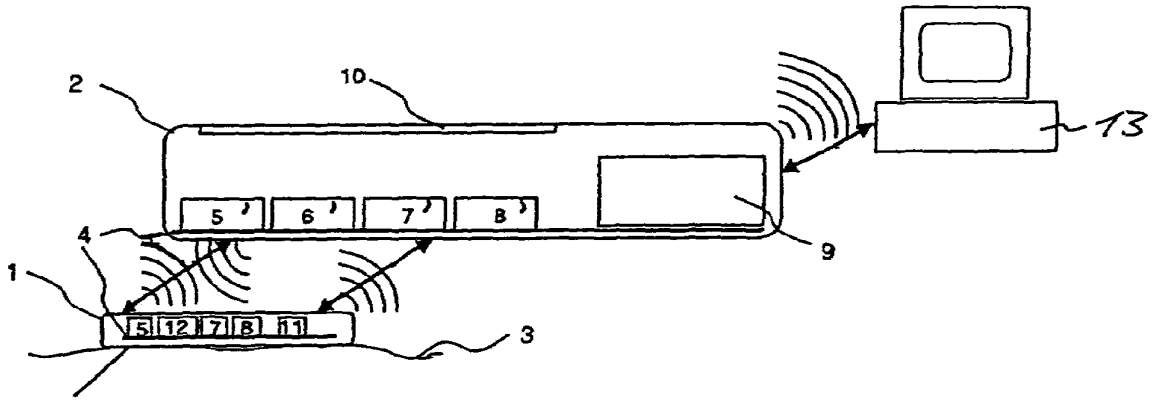
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(54) Title: ENERGY-OPTIMISED DATA TRANSMISSION FOR A MEDICAL APPLIANCE

(54) Bezeichnung: ENERGIEOPTIMIERTE DATENÜBERTRAGUNG EINES MEDIZINISCHEN GERÄTS



(57) Abstract: A medical appliance (1) is disclosed for use on and/or in the body of a user and comprises a transmission unit (5) and an activation switch (6) which is connected to the transmission unit (5) and can activate the transmission unit (5) when an activation signal is received by the activation switch (6). Also disclosed is a process for transmitting data between a medical appliance (1) and an external appliance (2), the external appliance (2) activating the medical appliance (1) prior to data transmission when the latter is in an idle state.

(57) Zusammenfassung: Die vorliegende Erfindung betrifft ein medizinisches Gerät (1) zum Einsatz am und/oder im Körper eines Benutzers mit einer Sendeeinheit (5) und einem Aktivierungsschalter (6), welcher mit der Sendeeinheit (5) verbunden ist und die Sendeeinheit (5) aktivieren kann, wenn ein Aktivierungssignal vom Aktivierungsschalter (6) empfangen wurde, sowie ein Verfahren zum Übertragen von Daten zwischen einem medizinischen Gerät (1) und einem externen Gerät (2), wobei das sich im Ruhezustand befindende medizinische Gerät (1) von dem externen Gerät (2) vor der Datenübertragung aktiviert wird.

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Zur Erklärung der Zweibuchstaben-Codes und der anderen Abkürzungen wird auf die Erklärungen ("Guidance Notes on Codes and Abbreviations") am Anfang jeder regulären Ausgabe der PCT-Gazette verwiesen.

Energieoptimierte Datenübertragung eines medizinischen Geräts

Die Erfindung bezieht sich auf ein medizinisches Gerät, ein System und ein Verfahren zur energieoptimierten Datenübertragung von und/oder zu dem medizinischen Gerät.

Während des Betriebes eines medizinischen Gerätes, wie zum Beispiel einer auf der Haut eines Benutzers angebrachten Infusionspumpe oder eines Sensors, ist es für einen Benutzer von Vorteil, wenn dem medizinischen Gerät zum Beispiel von einer Fernsteuerung Daten für den Betrieb des medizinischen Gerätes übertragen werden können oder wenn zum Beispiel Sensor-Messdaten an ein externes Gerät übertragen werden.

Ein von einer Fernsteuerung ansteuerbares externes Infusionsgerät ist aus der US 6,551,276 B1 bekannt, wobei das externe Infusionsgerät einen Empfänger aufweist, welcher in einem so genannten Standby-Modus sein kann und automatisch ungefähr alle 2,5 Sekunden aktiviert wird, um festzustellen, ob von der Fernsteuerung ein Funksignal ausgesandt wird, sodass die Funkfernsteuerung ein Aktivierungssignal über eine Periode von zum Beispiel ca. 5 Sekunden aussenden sollte, um von dem Empfänger erkannt zu werden.

Die US 4,395,259 beschreibt ein implantierbares Messgerät, welches eine Einheit zur Abgabe einer Dosis aufweist, wobei ein externes Steuergerät induktiv mit diesem Gerät gekoppelt werden kann, um zum Beispiel die Infusionsrate zu verändern.

Es ist eine Aufgabe der vorliegenden Erfindung ein medizinisches Gerät, ein System und ein Verfahren vorzuschlagen, welche eine Datenübertragung bei einem geringen Energieeinsatz ermöglichen.

Diese Aufgabe wird durch die Gegenstände der unabhängigen Ansprüche gelöst. Vorteilhafte Ausführungsformen ergeben sich aus den abhängigen Ansprüchen.

Ein medizinisches Gerät, wie zum Beispiel ein zum Beispiel subkutaner Sensor, insbesondere ein Glukose-Sensor, eine Pumpe, insbesondere eine Insulin-Pumpe, welche zum Beispiel implantiert, minimal invasiv oder nicht invasiv sein können, oder ein Pen zum Einsatz am und/oder im Körper eines Benutzers weist bevorzugt mindestens eine elektrische oder elektronische Funktionseinheit auf, wie zum Beispiel einen Messsensor, einen Prozessor, einen Speicher oder einen Elektromotor, welcher beispielsweise von dem Prozessor angesteuert werden kann und weist eine Sende- und/oder Empfangseinheit zum Übertragen, also zum Senden und/oder Empfangen von Daten auf, wobei erfindungsgemäß ein Aktivierungsschalter vorgesehen ist, der mit der Sende-/Empfangseinheit und/oder mindestens einer elektronischen Funktionseinheit in Verbindung steht, wobei der Aktivierungsschalter durch ein externes Aktivierungssignal aktiviert werden kann, um zum Beispiel die Sende-/Empfangseinheit und/oder mindestens eine elektronische Funktionseinheit zu aktivieren, sodass beispielsweise eine drahtlose Kommunikationsverbindung hergestellt werden kann, um zum Beispiel Messdaten von einem Sensor an ein externes Gerät zu übertragen oder zum Beispiel Steuerdaten zur Einstellung einer Basalrate oder zur Abgabe eines Bolus an eine Insulin-Pumpe zu senden oder die durch die Kommunikationsverbindungen verbundenen Geräte zu synchronisieren. Erfindungsgemäß wird die Kommunikation nur bei Bedarf, also „on demand" aufgenommen, wobei durch die für die Datenübertragung erforderliche Aktivierung des Aktivierungsschalters sichergestellt werden kann, dass nur dann eine Kommunikation aufgebaut oder hergestellt wird, wenn Empfänger und Sender, also das medizinische Gerät und ein externes Gerät, wie zum Beispiel eine Steuervorrichtung oder die jeweiligen Eingabe-/Ausgabeeinheiten davon, entweder in direktem physikalischen Kontakt miteinander stehen oder so relativ zueinander angeordnet sind, dass eine vorgegebene maximale Entfernung zwischen Sender und Empfänger unterschritten wird. Weiterhin kann zum Beispiel der Aktivierungsschalter des medizinischen Gerätes, welcher von einem Aktivierungselement des externen Gerätes aktiviert wird, nur dann ein Anschalt- oder Freigabesignal ausgeben, wenn das medizinische Gerät und ein externes Gerät eine vorgegebene Orientierung zueinander haben, also zum Beispiel Sende- und Empfangseinheiten oder Sende- und Empfangselemente etwa einander gegenüber liegen.

Somit kann der Energiebedarf des medizinischen Gerätes verringert werden, da nur dann elektrische oder elektronische Komponenten zur Übertragung von Daten aktiviert werden, wenn ein entsprechender Sender oder Empfänger eines externen Geräts in Reichweite ist, wobei die Sende- und Empfangseinheiten so dimensioniert oder ausgelegt werden können, dass eine Datenübertragung nur über eine relativ kurze Strecke, wie zum Beispiel 5 cm oder weniger, sichergestellt werden muss, was beispielsweise ausreicht, um Daten von einem externen Gerät, welche auf die Kleidung eines Benutzers aufgelegt wurde, durch diese Kleidung hindurch zu einem darunter auf der Haut des Patienten angebrachten oder implantierten medizinischen Gerätes zu übertragen oder von diesem medizinischen Gerät zu empfangen. Da die Datenübertragungseinheit erfindungsgemäß nur eine relativ geringe Leistungsfähigkeit aufweisen muss, kann diese im Vergleich zu zum Beispiel Datenübertragungseinheiten, welche für Entfernungen im Meterbereich ausgelegt sind, relativ klein ausgestaltet werden, wobei Sende- und Empfangs-Elemente, wie zum Beispiel Antennen, Induktionsspulen, oder andere elektromagnetische Wellen aussendende oder empfangende Elemente, wie zum Beispiel Lampen- oder Fotodioden oder Lautsprecher und Mikrophone nur eine geringe Reichweite und Leistungsfähigkeit besitzen müssen.

Der Aktivierungsschalter kann zum Beispiel auch ein Element oder Bauteil sein, mit welchem eine zum Beispiel von dem externen Gerät zur Verfügung gestellte Energie empfangen oder aufgenommen werden kann, um zum Beispiel mit dem externen Gerät kommunizieren zu können oder um eine zum Beispiel von dem externen Gerät vorgegebene Aktion auszuführen, so dass das medizinische Gerät in diesem Fall keine eigene Energieversorgung aufweisen muss, da diesem die benötigte Energie von dem externen Gerät zur Verfügung gestellt wird. Beispielsweise kann eine Induktionsspule als Aktivierungsschalter vorgesehen sein, wobei ein sich in der Nähe der Induktionsspule befindendes externes Gerät zum Beispiel ebenfalls eine Induktionsspule aufweisen kann, um über die induktive Kopplung der Induktionsspulen Energie an das medizinische Gerät zu übertragen, wodurch dieses aktiviert werden und zum Beispiel eine Messung durchführen kann.

Alternativ oder ergänzend kann ein Aktivierungsschalter auch als Magnetschalter, zum Beispiel als Reed-Kontakt ausgebildet sein, welcher von einem externen Magnetfeld, also

zum Beispiel einem an dem externen Gerät vorgesehenen Permanent-Magneten oder Elektro-Magneten aktiviert wird und zum Beispiel eine Verbindung der in dem medizinischen Gerät vorhandenen elektrischen oder elektronischen Komponenten, wie zum Beispiel der Sende- / Empfangseinheit mit einer ebenfalls in dem medizinischen Gerät vorhandenen Energiequelle zum Beispiel in Form einer Batterie oder eines Akkumulators herstellt. Weiterhin können andere Sensoren, welche zum Beispiel elektromagnetische Felder, Schall oder Licht detektieren können, oder magnetische oder kapazitive Effekte nutzen, als Aktivierungsschalter verwendet werden, wie zum Beispiel eine Fotodiode oder ein Mikrophon.

Dabei kann der Aktivierungsschalter so ausgebildet sein, dass eine nach der Aktivierung durch ein externes Gerät hergestellte Kommunikationsverbindung wieder unterbrochen wird, wenn kein Aktivierungssignal mehr anliegt, also zum Beispiel wenn ein vorgegebener Mindestabstand zum externen Gerät wieder überschritten wird. Alternativ oder ergänzend kann die Aktivierung des medizinischen Gerätes auch nur für einen vorgegebenen Zeitraum erfolgen, welcher zum Beispiel benötigt wird, um Daten zu übertragen oder eine vorgegebene Aktion, wie zum Beispiel das Abgeben eines Bolus und/oder das Aussenden eines Bestätigungssignals, auszuführen.

Ebenso kann auch ein mechanischer Schalter als Aktivierungsschalter zum Beispiel unter einem gummiartigen Oberflächenelement vorgesehen sein, welcher zum Beispiel die Stromversorgung oder eine Sende-/Empfangseinheit des medizinischen Gerätes aktiviert, nachdem ein mechanischer Schaltvorgang, also zum Beispiel ein Druck auf den mechanischen Schalter, durch ein auf das medizinische Gerät aufgelegtes externes Gerät ausgelöst wurde. Dabei kann das medizinische Gerät beispielsweise ein Oberflächenprofil aufweisen, welches einem Gegenprofil des externen Gerätes entspricht, sodass das externe Gerät zum Beispiel in einer durch das Oberflächenprofil bestimmten Orientierung auf das medizinische Gerät aufgelegt werden muss, um dieses zu aktivieren oder um eine Datenverbindung herzustellen. Im Falle eines direkten Kontaktes zwischen dem medizinischen Gerät und dem externen Gerät kann eine Datenverbindung oder auch eine Energieübertragung zum Beispiel auch über eine elektrische Leitung erfolgen, wenn sich

einander entsprechende Kontaktelemente des medizinischen Geräts und des externen Gerätes berühren.

Die Erfindung bezieht sich weiterhin auf ein Steuergerät, wie zum Beispiel eine Fernbedienung oder ein Blutglukose-Messgerät zum Ansteuern eines wie oben beschriebenen medizinischen Gerätes, wobei das Steuergerät als externes Gerät eine Aktivierungseinheit aufweist, mit welcher ein oder mehrere Aktivierungsschalter des medizinischen Gerätes aktiviert oder getätigt werden können. Als Aktivierungseinheit kann am externen Gerät zum Beispiel ein Magnet, insbesondere ein Permanentmagnet oder ein Elektromagnet, eine Induktionsspule zum Übertragen von Energie zu dem medizinischen Gerät, ein Lautsprecher, eine Lampe oder ein bestimmtes Oberflächenprofil zur Betätigung eines mechanischen Schalters vorgesehen sein. Weiterhin weist das Steuergerät eine Sende- und/oder Empfangseinheit auf, um eine Datenverbindung mit dem medizinischen Gerät herstellen zu können, wobei die Sende-/Empfangseinheit zum Beispiel aktiviert werden kann, nachdem ein Aktivierungssignal von der Aktivierungseinheit des Steuergerätes ausgesandt wurde oder vom Steuergerät detektiert wurde, dass eine Verbindung, wie zum Beispiel ein mechanischer Kontakt, eine Funkverbindung und/oder eine induktive Kopplung, mit dem medizinischen Gerät hergestellt wurde, oder besteht.

Das externe Gerät kann eine Eingabeeinheit, zum Beispiel eine Tastatur oder einen Touch-Screen, aufweisen, um es einem Benutzer zu ermöglichen Steuersignale in das Steuergerät einzugeben, welche von diesem an das medizinische Gerät übertragen werden können, um zum Beispiel die Arbeitsweise einer implantierten Insulinpumpe zu steuern, wie zum Beispiel die Basalrate oder einen Bolus einzustellen. Vorzugsweise weist das Steuergerät eine Anzeigeeinheit oder ein Display auf, an welchem zum Beispiel zu übertragende Steuerdaten, von einem Benutzer eingegebene Befehle oder Parameter, oder von dem medizinischen Gerät empfangene Daten, wie zum Beispiel Messdaten eines Sensors, dargestellt werden können.

Bevorzugt weist das Steuergerät eine Schnittstelle für die Kommunikation mit einem anderen elektrischen Gerät auf, wie zum Beispiel eine USB-Schnittstelle, eine Infrarot-Schnittstelle oder eine Bluetooth-Schnittstelle, um Daten zum Beispiel mit einem

Computer, einem Mobiltelefon oder einem PDA austauschen zu können, also eine so genannte „Long-Range" Kommunikation durchführen zu können.

Weiterhin bezieht sich die Erfindung auf ein System zum Übertragen von Daten mit einem wie oben beschriebenen bevorzugt am oder im Körper eines Patienten tragbaren medizinischen Gerät und einem wie oben beschriebenen externen Steuergerät, wobei diese Geräte nach dem Aktivieren der Sende- und/oder Empfangseinheit auch synchronisiert werden können.

Gemäß einem weiteren Aspekt bezieht sich die Erfindung auf ein Verfahren zum Übertragen von Daten zwischen einem medizinischen Gerät und einem externen Gerät, wobei das sich im Ruhezustand befindende medizinische Gerät von dem externen Gerät vor der Datenübertragung aktiviert wird. Somit kann das medizinische Gerät zum Beispiel in einem wenige oder keine Energie verbrauchenden Ruhezustand bleiben, wenn kein externes Gerät vorhanden oder aktiviert ist, um eine Datenverbindung herzustellen, sodass das medizinische Gerät nur dann Energie für die Datenkommunikation verbraucht, wenn es vorher von einem externen oder Steuergerät aktiviert wurde, welches zur Datenübertragung bereit ist.

Vorzugsweise wird das medizinische Gerät berührungslos zum Beispiel durch ein elektrisches, magnetisches oder elektromagnetisches Feld, Schall und/oder Licht aktiviert. Ebenso ist es auch möglich, das medizinische Gerät durch einen direkten physikalischen Kontakt mit dem Steuergerät zu aktivieren. Vorzugsweise erfolgt die Aktivierung des medizinischen Gerätes nur dann, wenn ein vorgegebener Abstand von zum Beispiel 2 bis 10cm, also zum Beispiel 5 cm unterschritten wurde, wobei es möglich ist, dass zum Beispiel ein Aktivierungsschalter des medizinischen Gerätes eine Kommunikation zwischen diesem und einem externen Gerät wieder abbricht, wenn ein vorgegebener Abstand wieder überschritten wird. Die Aktivierung des medizinischen Gerätes kann auch zeitlich begrenzt sein oder mit der Ausführung einer Aktion des medizinischen Gerätes beendet werden, wie zum Beispiel nach dem Transfer von Messdaten aus dem Speicher eines Sensor über die Sende- und Empfangseinheiten zu dem externen Steuergerät, wobei diese Messdaten nach dem Senden an das externe Gerät oder nach dem Empfang eines

Bestätigungssignals über den richtigen Empfang der gesendeten Daten im Speicher des medizinischen Gerätes gelöscht werden können. Bei einer solchen Datenübertragung können zum Beispiel alle Daten, die seit dem letzten Datenaustausch gewonnen wurden, wie zum Beispiel Messwerte mit zugehörigem Erfassungszeitpunkt, übertragen und zum Beispiel gelöscht werden, damit der Speicher des medizinischen Gerätes zur Speicherung neuer Daten zur Verfügung steht.

Vorzugsweise können von dem medizinischen Gerät und/oder dem externen Steuergerät Identifikationscodes gesendet werden, um zu verhindern, dass Daten versehentlich zwischen unterschiedlichen nicht zugeordneten Systemen ausgetauscht werden. Der Identifikationscode kann zum Beispiel Teil eines Funkprotokolls sein und zum Beispiel in einer Systemkomponente fest einprogrammiert sein. Ebenso ist es möglich, dass der Identifikationscode zum Beispiel beim Systemstart frei programmierbar ist und zum Beispiel zwei Komponenten nach Aktivierung durch einen Benutzer miteinander gekoppelt werden können. Weiterhin können bekannte RFID tags zum Beispiel am medizinischen Gerät zusammen mit RFID-Transpondern am Steuergerät zur Identifikation verwendet werden.

Die Erfindung wird nachfolgend anhand bevorzugter Ausführungsbeispiele beschrieben. Es zeigen:

Figur 1 eine erste Ausführungsform eines erfindungsgemäßen Systems zur Aktivierung eines medizinischen Gerätes durch eine Energieübertragung von einem Steuergerät;

Figur 2 eine zweite Ausführungsform eines erfindungsgemäßen Systems zur Aktivierung eines medizinischen Geräts über einen Permanent-Magneten;

Figur 3 eine dritte Ausführungsform eines erfindungsgemäßen Systems mit der Fähigkeit zur „Long-Range“ Kommunikation;

Figur 4 eine vierte Ausführungsform eines erfindungsgemäßen Systems, welches die Übertragung einfacher Signale über größere Entfernungen ermöglicht;

Figur 5 eine fünfte Ausführungsform eines erfindungsgemäßen Systems, welche einen Datenaustausch zwischen einem medizinischen Gerät und einem Steuergerät ermöglicht; und

Figur 6 die Ausführungsform aus Figur 5 während des Datenaustauschs zwischen einem medizinischen Gerät und einem Steuergerät.

Figur 1 zeigt eine erste Ausführungsform eines erfindungsgemäßen Systems mit einem ambulant auf der Haut 3 eines Anwenders tragbaren medizinischen Gerät 1, welches auf der Haut 3 angebracht oder implantiert sein kann und zum Beispiel eine Pumpe oder ein Sensor ist. Das medizinische Gerät 1 weist eine Induktionsspule 6 zum Aufnehmen einer von einer korrespondierenden Induktionsspule 6' eines externen Steuergeräts 2 durch induktive Kopplung übertragenen Energie auf, wobei die Induktionsspule 6 des medizinischen Gerätes 1 als Aktivierungsschalter für die Sende-/Empfangseinheit 5 und den Prozessor 7 des Gerätes 1 dient, welche von der Induktionsspule 6 mit Strom versorgt werden. Der Prozessor 7 ist mit einem Speicher 8 gekoppelt und kann nach der Aktivierung auch die Sende-/Empfangseinheit 5 ansteuern, um zum Beispiel Mess- oder Konfigurationsdaten aus dem Speicher 8 über die Einheit 5 an die korrespondierende Sende-/Empfangseinheit 5' des externen Steuergeräts 2 zu übertragen oder in Gegenrichtung empfangene Daten, wie zum Beispiel Konfigurationsdaten für das medizinische Gerät 1, zu verarbeiten und/oder in dem Speicher 8 zu speichern. Weiterhin kann in dem medizinischen Gerät 1 optional auch eine Batterie 11 vorgesehen sein, welche zum Beispiel nur die für eine Sensor- oder Pump-Funktion des medizinischen Gerätes 1 erforderliche Energie zur Verfügung stellt, so dass zum Beispiel für die Datenkommunikation keine Energieversorgung im medizinischen Gerät 1 benötigt wird.

Das externe Steuergerät 2, wie zum Beispiel ein Blutglukosemessgerät, weist ebenso wie das medizinische Gerät 1 einen Prozessor 7' und einen Speicher 8' auf, um zum Beispiel von einem Benutzer über einen Touch-Screen 10 eingegebene Daten und/oder vom

medizinischen Gerät 1 erhaltene Daten abzuspeichern oder Daten über die Sende-/Empfangseinheiten 5, 5' an das medizinische Gerät zu übertragen. Weiterhin ist eine Batterie oder ein Akkumulator 9 zur Energieversorgung des externen Steuergerätes 2 vorgesehen. Somit kann eine Kommunikation zwischen dem medizinischen Gerät 1 und dem externen Steuergerät 2 nach der Aktivierung über einen Energietransfer durch die Induktionsspulen 6, 6' hergestellt werden, wobei zum Beispiel nach erfolgter Datenübertragung zwischen diesen Geräten der Speicher des Steuergerätes 2 von einem weiteren Gerät, wie zum Beispiel unter Bezugnahme auf die Figuren 3 und 4 beschrieben, ausgelesen werden kann.

Die elektronischen Baugruppen 5 bis 9 und 11 sind in dem gezeigten Beispiel auf einer Platine 4 angeordnet.

Figur 2 zeigt eine zweite Ausführungsform eines erfindungsgemäßen Systems, wobei im Unterschied zur ersten in Figur 1 gezeigten Ausführungsform ein Permanentmagnet 6' im Steuergerät 2 vorgesehen ist, um einen Magnetschalter 12, wie zum Beispiel einen Reed-Kontakt, des medizinischen Gerätes 1 zu aktivieren, so dass der als Aktivierungsschalter dienende Magnetschalter 12 zum Beispiel die Sende-/Empfangseinheit 5 und/oder den Prozessor 7 des medizinischen Gerätes 1 aktivieren und für eine Datenübertragung freigeben kann.

Figur 3 zeigt eine dritte Ausführungsform eines erfindungsgemäßen Systems, wobei eine Aktivierung oder Datenübertragung des medizinischen Gerätes 1 durch das externe Steuergerät 2 zum Beispiel durch eine Induktionsspule 6' oder einen Permanentmagneten 6'' erfolgen kann, welche mit einer Induktionsspule 6 oder einem Magnetschalter 12 des medizinischen Gerätes 1 zusammenwirken. Weiterhin ist das externe Steuergerät 2 so ausgelegt, dass eine Datenverbindung mit einem weiteren externen Gerät 13, wie zum Beispiel mit einem PC, einem Mobiltelefon oder einem PDA, hergestellt werden kann, um Daten von dem Steuergerät 2, welche zum Beispiel an dieses von dem medizinischen Gerät 1 übertragen wurden, an die externe Einheit 13 zu übertragen oder in Gegenrichtung von dieser zu empfangen.

Figur 4 zeigt eine vierte Ausführungsform eines erfindungsgemäßen Systems, wobei zusätzlich zu der in Figur 3 gezeigten dritten Ausführungsform eine Datenkommunikation auch über eine größere Entfernung zwischen dem medizinischen Gerät 1 und dem Steuergerät 2 für bestimmte Signale, wie zum Beispiel kurze Statussignale, möglich ist. Hierzu kann die Sende-/Empfangseinheit 5 des medizinischen Gerätes 1 so ausgelegt sein, dass kurzzeitig unter Einsatz größerer Energie ein zum Beispiel mehrere Meter reichendes Status- oder Requestsignal ausgesandt wird, welches zum Beispiel auch über eine größere Entfernung an das Steuergerät 2 übertragen werden kann, um zum Beispiel einem Benutzer des Steuergerätes 2 zu signalisieren, dass eine Kommunikation mit dem medizinischen Gerät 1 hergestellt werden soll.

Die Figuren 5 und 6 zeigen eine fünfte Ausführungsform eines erfindungsgemäßen Systems, welches einen Datenaustausch zwischen einem ambulant auf der Haut 3 eines Anwenders tragbaren medizinischen Gerät 1, wie einem Sensor oder einer Pumpe oder Infusionspumpe oder einem so genannten Patch Module, und einem externen, insbesondere von einem Anwender tragbaren oder mobilen, Steuergerät 2, wie einem Blutzucker-Messgerät, ermöglicht. Das medizinische Gerät 1, welches auf der Haut 3 angebracht oder implantiert sein kann, weist zum Beispiel eine Nadel 15 auf, mittels welcher geringe Blutmengen des Anwenders abgenommen werden können. Auch kann das medizinische Gerät 1 subkutan oder unter der Haut 3 des Anwenders angeordnet sein oder kann minimal-invasiv geringe Blutmengen des Anwenders abnehmen. Das medizinische Gerät 1 umfasst eine Recheneinheit, wie einen Prozessor oder Mikroprozessor, einen Speicher, eine Sende-/Empfangseinheit, eine Energiequelle, wie eine Batterie und/oder eine zuvor beschriebene Induktionsspule und/oder einen zuvor beschriebenen Magnetschalter, und eine Messeinheit, wie eine elektronische Schaltung, zum Messen oder Ermitteln mindestens eines physiologischen Parameters des Anwenders, insbesondere des Blutzuckerwerts oder Blutglukosespiegels, anhand der abgenommenen Blutmenge. Die Messeinheit kann optisch arbeiten, so dass das abgenommene Blut mit verschiedenen chemischen Stoffen reagiert, was zu einer Farbänderung eines Testfeldes führt. Diese Farbänderung kann von der Messeinheit erfasst werden und es aus der Dauer und Stärke der Änderung kann der Blutzuckerwert bestimmt werden. Auch kann die Messeinheit amperometrisch arbeiten, so

dass durch Messung eines Stromstärke-Verlaufs durch das Blut der Blutzuckerwert bestimmt werden kann.

Das externe Steuergerät 2, wie ein Blutglukosemessgerät oder Datenlogger, weist eine Anzeigevorrichtung 10, insbesondere einen Bildsschirm oder ein Display oder einen Touch-Screen, eine Sende-/Empfangseinheit, einen Speicher, eine Energiequelle, wie eine Batterie, und zumindest eine Recheneinheit, insbesondere einen Prozessor oder Mikroprozessor auf. Weiter kann das externe Steuergerät 2 einen in Bezug auf die Figuren 1 bis 4 beschriebenen Aktivierungsschalter, insbesondere eine Induktionsspule oder einen Permanentmagneten, aufweisen. Das Steuergerät 2 kann so ausgebildet sein, dass es anhand von Messdaten den Blutzuckerwert oder den Blutzuckerwertverlauf des Anwenders ermitteln kann, welcher zum Beispiel durch Ausgabe von Zahlenwerten oder eines grafischen Verlaufs oder Diagrams auf der Anzeigevorrichtung 10 dargestellt werden kann.

Wie in Figur 6 gezeigt, kann das externe Steuergerät 2, wie das Blutzucker-Messgerät, in die Nähe oder in Reichweite des medizinischen Geräts 1, wie dem Patch Module, gebracht werden, um einen Datenaustausch oder eine Datenübertragung zwischen dem Steuergerät 2 und dem medizinischen Gerät 1 zu ermöglichen. Vorzugsweise aktiviert dabei der Aktivierungsschalter des Steuergeräts 2 den Aktivierungsschalter des medizinischen Geräts 1, so dass von dem Aktivierungsschalter des Steuergeräts 2 Energie auf den Aktivierungsschalter des medizinischen Geräts 1 übertragen werden kann, mittels welcher das medizinische Gerät 1 mit Strom versorgt werden kann. Auch kann beispielsweise der Aktivierungsschalter des Steuergeräts 2 die Energiequelle oder Energieversorgung des medizinischen Geräts 1 aktivieren, so dass das medizinische Gerät 1 nach Aktivierung der Energiequelle mit Strom versorgt werden kann.

Mit dem medizinischen Gerät 1 kann aus dem Blut eines Anwenders ein Blutwert bestimmt werden. Dieser Wert kann beispielsweise mit Seiteninformationen, wie der Uhrzeit der Blutabnahme, von der Sende-/Empfangseinheit des medizinischen Geräts 1 an die Send-/Empfangseinheit des Steuergeräts 2 gesendet werden, wenn sich das Steuergerät 2 in ausreichender Nähe des medizinischen Geräts 1 befindet, welche eine Datenübertragung ermöglicht. Aus diesem Blutwert kann in dem Steuergerät 2 von der Recheneinheit des

Steuergeräts 2 der Blutzuckerwert oder Glukosegehalt des Anwenders ermittelt werden und beispielsweise mit den Seiteninformationen in dem Speicher abgespeichert oder auf der Anzeigevorrichtung 10 dargestellt werden.

Auch kann in dem medizinischen Gerät 1 aus dem abgenommenen Blut des Anwenders mittels der Recheneinheit der Blutzuckerwert oder Glukosespiegel des Anwenders ermittelt werden und beispielsweise in der in Figur 6 gezeigten Position oder Anordnung an das Steuergerät 2 beispielsweise mit den Seiteninformationen übertragen werden. Auch können zu verschiedenen Zeitpunkten aufgenommene Blutzuckerwerte mit dem Zeitpunkt oder der Uhrzeit der Abnahme in dem Speicher des medizinischen Geräts 1 gespeichert werden und bei Bedarf von dem externen Steuergerät 2 abgerufen werden. Daten über den ermittelten Blutzuckerspiegel und gegebenenfalls die Seiteninformationen können von der Sende-/Empfangseinheit des medizinischen Geräts 1 an die Sende-/Empfangseinheit des Steuergeräts 2 übertragen werden und können in dem Speicher des Steuergeräts 2 abgespeichert werden oder auf der Anzeigevorrichtung 10 des Steuergeräts 2 als Zahlenwerte oder als Diagram dargestellt werden. Beispielsweise können in dem Steuergerät 2 mehrere zu verschiedenen Zeitpunkten gewonnene Blutzuckerwerte gespeichert und bei Bedarf beispielsweise über der Zeit grafisch dargestellt werden, um ein Blutzuckerspiegel-Diagramm eines Anwenders zu erhalten. Einzelwerte in dem Blutzuckerspiegel-Diagramm können zum Beispiel von dem Anwender mittels des Touch-Screens oder mittels einer anderen Eingabeeinheit ausgewählt werden, welche dann als Zahlenwerte ausgegeben werden können. Insbesondere kann auch unmittelbar nach dem Empfang des von dem medizinischen Gerät ermittelten Blutzuckerwerts der Blutzuckerwert auf der Anzeigevorrichtung 10 des Steuergeräts 2 ausgegeben werden. Auch kann das Steuergerät 2 in Aktivierungs-Reichweite des medizinischen Geräts 1 gehalten werden, so dass die Sende-/Empfangseinheit des Steuergeräts 2 beispielsweise ein Aktivierungssignal an das medizinische Gerät 1 senden kann, worauf das medizinische Gerät 1 aktiviert wird und zum Beispiel eine Blutzuckermessung durchführt und/oder einen ermittelten Blutzuckerwert an das Steuergerät 2 sendet, welcher auf der Anzeigevorrichtung 10 des Steuergeräts 2 ausgegeben werden kann.

Die ermittelten Daten über den Glukosespiegel oder den Glukosespiegelverlauf des Anwenders können über eine an dem Steuergerät 2 angeordnete Schnittstelle, wie einer Infrarot- oder Bluetooth- oder FireWire-Schnittstelle, auf eine externe Recheneinheit, wie einen Computer, übertragen werden und in der Recheneinheit weiterverarbeitet oder ausgegeben oder mit einer Darstellungs- oder Auswertungs-Software dargestellt und/oder ausgewertet werden.

Anwaltsakte: 55 551 XX
Anmelder: Disetronic Licensing AG

Patentansprüche 1 bis 7

1. Medizinisches System umfassend:
   a) ein medizinisches Gerät (1) zum Einsatz am und/oder im Körper eines Benutzers mit einer Sendeeinheit und/oder Empfangseinheit (5) und einem Aktivierungsschalter (6), welcher mit der Sendeeinheit und/oder Empfangseinheit (5) verbunden ist und die Sendeeinheit und/oder Empfangseinheit (5) aktivieren kann, wenn ein Aktivierungssignal vom Aktivierungsschalter (6) empfangen wurde; und
   b) eine Fernbedienung (2) mit einer Dateneingabeeinheit, einer Aktivierungseinheit (6', 6") zum Aktivieren des Aktivierungsschalters (6) des medizinischen Geräts (1) und einer Sende- und/oder Empfangseinheit (5'), welche mit der Sendeeinheit und/oder Empfangseinheit (5) des medizinischen Geräts (1) Daten austauschen kann.

2. Medizinisches System nach Anspruch 1, wobei das medizinische Gerät (1) ein Sensor, ein Glukosesensor, ein Infusionssystem, eine Pumpe, eine Insulin-Pumpe, oder ein Pen ist.

3. Medizinisches System nach Anspruch 1 oder 2, wobei die Fernbedienung (2) ein Glucosemessgerät ist.

4. Medizinisches Gerät nach einem der vorhergehenden Ansprüche, wobei der Aktivierungsschalter (6) eine Induktionsspule, ein Magnetschalter (12), ein Reed-Kontakt, ein Mikrofon oder ein lichtempfindlicher Schalter, eine Fotodiode, oder ein mechanischer Schalter ist.

5. Medizinisches System nach einem der vorhergehenden Ansprüche, wobei die Aktivierungseinheit (6', 6") eine Induktionsspule (6') und/oder ein Permanentmagnet (6") ist.

6. Medizinisches System nach einem der vorhergehenden Ansprüche, wobei die Fernbedienung (2) eine Datenausgabeeinheit (10) aufweist.

7. Medizinisches System nach einem der vorhergehenden Ansprüche, wobei die Fernbedienung (2) eine Schnittstelle zur Kommunikation mit einem elektronischen Gerät, einem PC, Mobiltelefon oder PDA aufweist.

FIG. 1

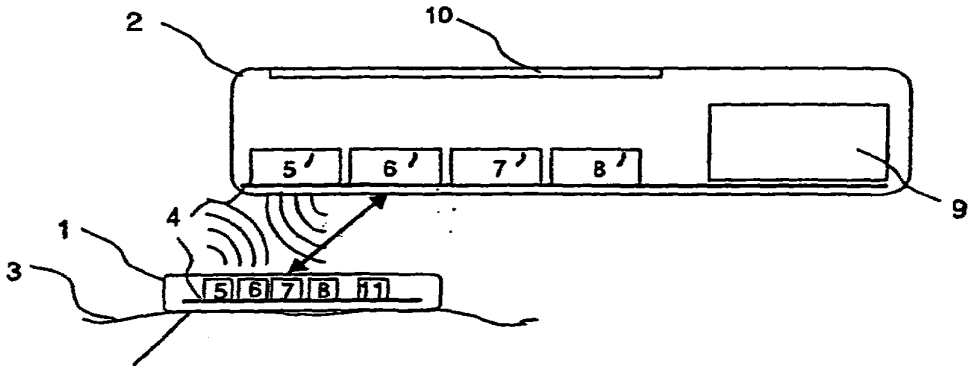


FIG. 2

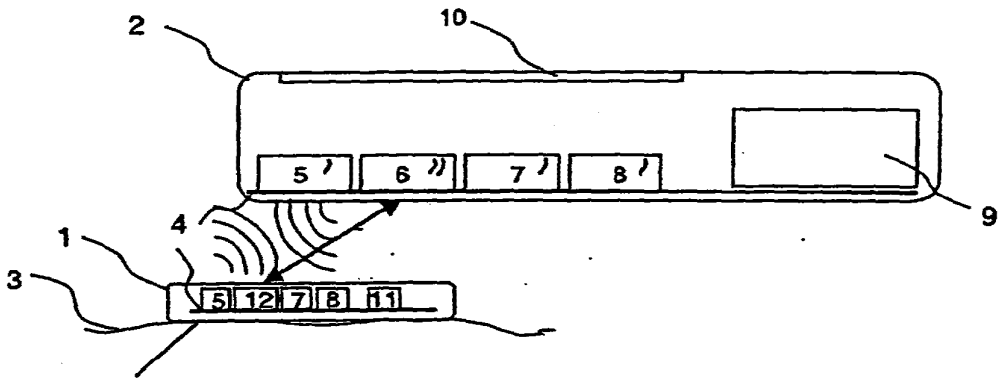


FIG. 3

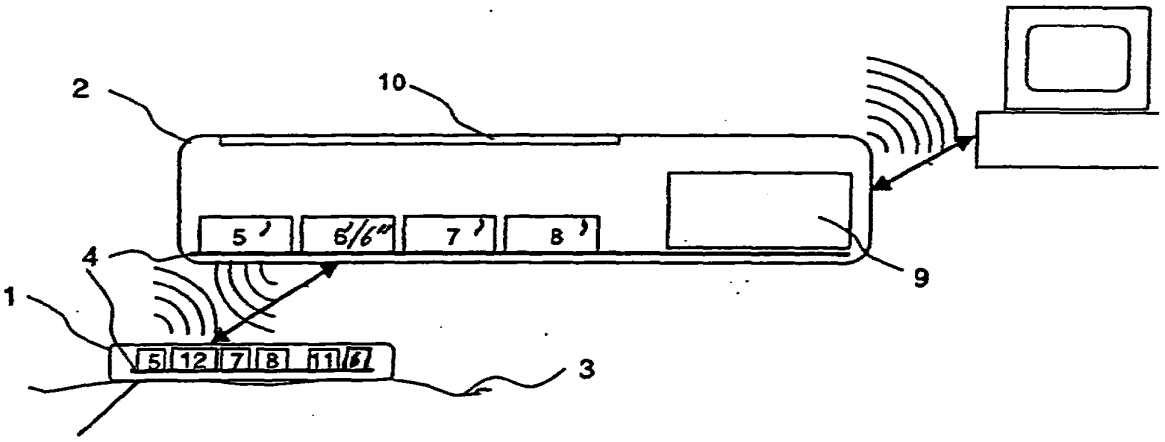
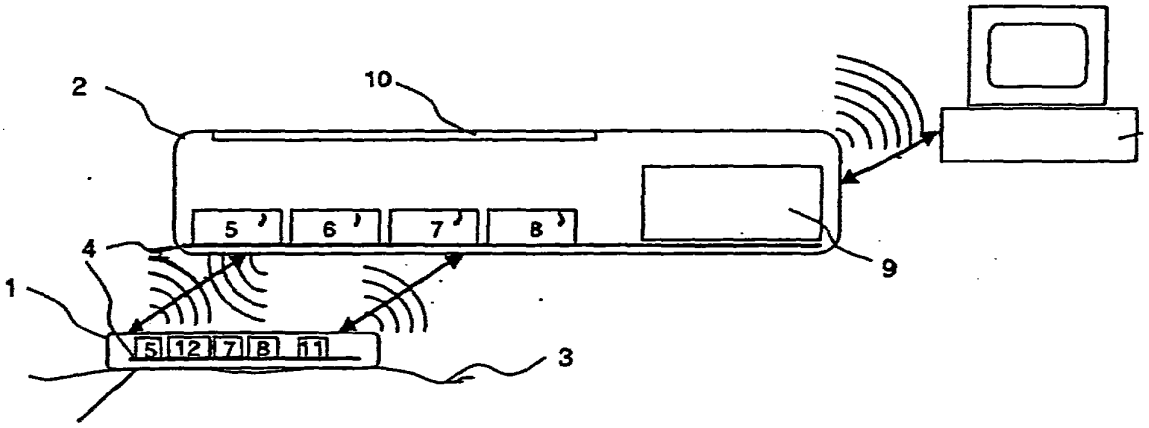


FIG. 4



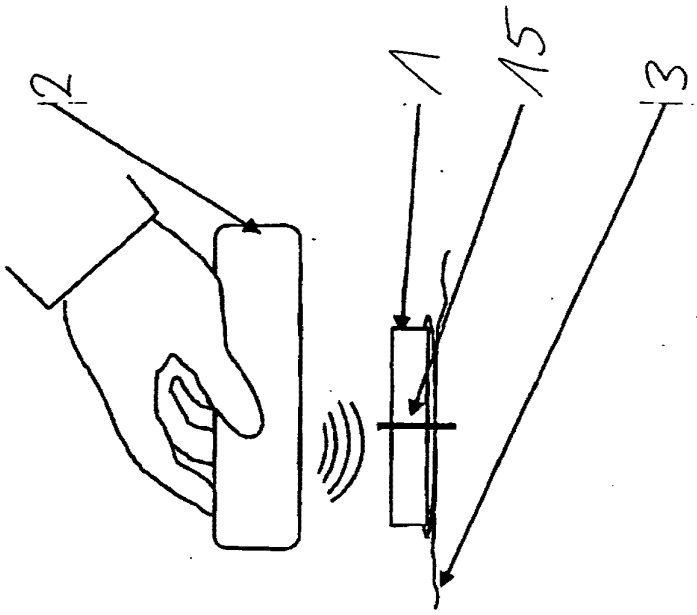


Fig. 6

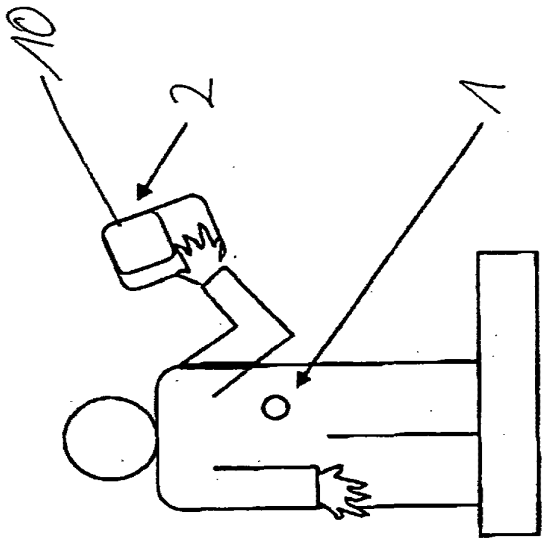


Fig. 5

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2006/003869

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/00 A61B5/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2004/204744 A1 (PENNER AVI ET AL) 14 October 2004 (2004-10-14) figures 1-6 paragraph [0034] - paragraph [0068]	1,2,4-7
X	EP 1 343 112 A (ENDOART S.A) 10 September 2003 (2003-09-10) paragraph [0022] - paragraph [0027]; claim 12; figures 1-4	1,2,4-6
X	US 2002/072784 A1 (SHEPPARD NORMAN F ET AL) 13 June 2002 (2002-06-13) paragraph [0031] - paragraph [0032]; figures 1-3	1,2,4-6

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 July 2006	02/08/2006

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Reinbold, S

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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2006/003869

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/065464 A1 (TALBOT CARY D ET AL) 24 March 2005 (2005-03-24) figures 1-7 paragraph [0044] - paragraph [0049] -----	1,3
X	US 6 239 724 B1 (DORON EYAL ET AL) 29 May 2001 (2001-05-29) figures 1-13 column 8, line 54 - column 11, line 3 -----	1,2,4-6

2

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information on patent family members

International application No
PCT/EP2006/003869

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		WO 2004089465 A1	21-10-2004
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		WO 9934453 A1	08-07-1999
		US 6237398 B1	29-05-2001
		US 6431175 B1	13-08-2002
		US 6198965 B1	06-03-2001
		US 6504286 B1	07-01-2003

INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2006/003869

A. KLASSIFIZIERUNG DES ANMELDUNGSGEGENSTANDES
INV. A61M5/00 A61B5/00

Nach der Internationalen Patentklassifikation (IPC) oder nach der nationalen Klassifikation und der IPC

B. RECHERCHIERTE GEBIETE

Recherchierter Mindestprüfstoff (Klassifikationssystem und Klassifikationssymbole)
A61M A61B

Recherchierte, aber nicht zum Mindestprüfstoff gehörende Veröffentlichungen, soweit diese unter die recherchierten Gebiete fallen

Während der internationalen Recherche konsultierte elektronische Datenbank (Name der Datenbank und evtl. verwendete Suchbegriffe)
EPO-Internal, WPI Data

C. ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	US 2004/204744 A1 (PENNER AVI ET AL) 14. Oktober 2004 (2004-10-14) Abbildungen 1-6 Absatz [0034] - Absatz [0068]	1,2,4-7
X	EP 1 343 112 A (ENDOART S.A) 10. September 2003 (2003-09-10) Absatz [0022] - Absatz [0027]; Anspruch 12; Abbildungen 1-4	1,2,4-6
X	US 2002/072784 A1 (SHEPPARD NORMAN F ET AL) 13. Juni 2002 (2002-06-13) Absatz [0031] - Absatz [0032]; Abbildungen 1-3	1,2,4-6

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[X] Weitere Veröffentlichungen sind der Fortsetzung von Feld C zu entnehmen [X] Siehe Anhang Patentfamilie

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Datum des Abschlusses der internationalen Recherche	Absendedatum des internationalen Recherchenberichts
11. Juli 2006	02/08/2006

Name und Postanschrift der Internationalen Recherchenbehörde	Bevollmächtigter Bediensteter
Europäisches Patentamt, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Reinbold, S

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INTERNATIONALER RECHERCHENBERICHT

Internationales Aktenzeichen
PCT/EP2006/003869

C. (Fortsetzung) ALS WESENTLICH ANGESEHENE UNTERLAGEN

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	US 2005/065464 A1 (TALBOT CARY D ET AL) 24. März 2005 (2005-03-24) Abbildungen 1-7 Absatz [0044] - Absatz [0049]	1,3
X	US 6 239 724 B1 (DORON EYAL ET AL) 29. Mai 2001 (2001-05-29) Abbildungen 1-13 Spalte 8, Zeile 54 - Spalte 11, Zeile 3	1,2,4-6

2

INTERNATIONALER RECHERCHENBERICHT

Angaben zu Veröffentlichungen, die zur selben Patentfamilie gehören

Internationales Aktenzeichen
PCT/EP2006/003869

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		US 6431175 B1	13-08-2002
		US 6198965 B1	06-03-2001
		US 6504286 B1	07-01-2003

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C12M 1/00 (2006.01) *G01N 33/52* (2006.01)
C12M 1/40 (2006.01) *G01N 33/49* (2006.01)
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(71) Applicant *(for all designated States except US)*: **DEXCOM, INC.** [US/US]; 5555 Oberlin Drive, San Diego, CA 92121 (US).

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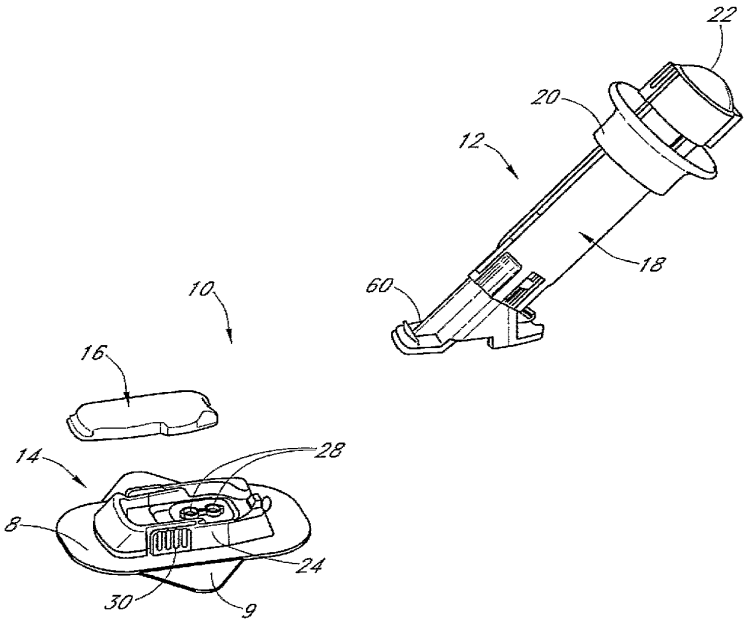
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[Continued on next page]

(54) Title: ANALYTE SENSOR



(57) Abstract: The present invention relates generally to systems and methods for measuring an analyte in a host. More particularly, the present invention relates to systems and methods for transcutaneous measurement of glucose in a host using a transcutaneous analyte sensor system including an applicator (12), a mounting unit (14), an electronics unit (16), a base (24), a sensor (32), and one or more contacts (28) configured to provide secure electrical contact between the sensor and the electronics unit (16).

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ANALYTE SENSOR

FIELD OF THE INVENTION

[0001] The present invention relates generally to systems and methods for measuring an analyte in a host. More particularly, the present invention relates to systems and methods for transcutaneous measurement of glucose in a host.

BACKGROUND OF THE INVENTION

[0002] Diabetes mellitus is a disorder in which the pancreas cannot create sufficient insulin (Type I or insulin dependent) and/or in which insulin is not effective (Type 2 or non–insulin dependent). In the diabetic state, the victim suffers from high blood sugar, which can cause an array of physiological derangements associated with the deterioration of small blood vessels, for example, kidney failure, skin ulcers, or bleeding into the vitreous of the eye. A hypoglycemic reaction (low blood sugar) can be induced by an inadvertent overdose of insulin, or after a normal dose of insulin or glucose-lowering agent accompanied by extraordinary exercise or insufficient food intake.

[0003] Conventionally, a person with diabetes carries a self-monitoring blood glucose (SMBG) monitor, which typically requires uncomfortable finger pricking methods. Due to the lack of comfort and convenience, a person with diabetes normally only measures his or her glucose levels two to four times per day. Unfortunately, such time intervals are so far spread apart that the person with diabetes likely finds out too late of a hyperglycemic or hypoglycemic condition, sometimes incurring dangerous side effects. It is not only unlikely that a person with diabetes will take a timely SMBG value, it is also likely that he or she will not know if his or her blood glucose value is going up (higher) or down (lower) based on conventional method. This inhibits the ability to make educated insulin therapy decisions.

[0004] A variety of sensors are known that use an electrochemical cell to provide output signals by which the presence or absence of an analyte, such as glucose, in a sample can be determined. For example, in an electrochemical cell, an analyte (or a species derived from it) that is electro-active generates a detectable signal at an electrode, and this signal can be used to detect or measure the presence and/or amount within a biological sample. In some conventional sensors, an enzyme is provided that reacts with the analyte to be measured, and

the byproduct of the reaction is qualified or quantified at the electrode. An enzyme has the advantage that it can be very specific to an analyte and also, when the analyte itself is not sufficiently electro-active, can be used to interact with the analyte to generate another species which is electro-active and to which the sensor can produce a desired output. In one conventional amperometric glucose oxidase-based glucose sensor, immobilized glucose oxidase catalyses the oxidation of glucose to form hydrogen peroxide, which is then quantified by amperometric measurement (for example, change in electrical current) through a polarized electrode.

SUMMARY OF THE INVENTION

[0005] In a first aspect, a sensor for transcutaneous measurement of an analyte in a host is provided, the sensor comprising at least one electrode formed from a conductive material; and a membrane disposed on an electroactive portion of the electrode, wherein the membrane is configured to control an influx of the analyte therethrough, and wherein the membrane comprises a substantially non-smooth outer surface.

[0006] In an embodiment of the first aspect, the substantially non-smooth surface appears under magnification to resemble a super-positioning of disc shaped objects.

[0007] In an embodiment of the first aspect, the disc shaped objects comprise a rounded shape.

[0008] In an embodiment of the first aspect, the disc shaped objects have an average diameter of from about 5 microns to about 250 microns.

[0009] In an embodiment of the first aspect, the membrane further comprises an enzyme domain.

[0010] In an embodiment of the first aspect, the membrane further comprises an interference domain.

[0011] In an embodiment of the first aspect, the membrane further comprises an electrode domain.

[0012] In an embodiment of the first aspect, the membrane is at least partially formed by a vapor deposition coating process.

[0013] In an embodiment of the first aspect, the vapor deposition coating process comprises a physical vapor deposition coating process, e.g., ultrasonic vapor deposition.

[0014] In an embodiment of the first aspect, the membrane substantially resists ascorbate flux therethrough.

[0015] In an embodiment of the first aspect, the electrode comprises a wire comprising a conductive material, and wherein the sensor is configured for substantially continuous measurement of glucose in a host.

[0016] In a second aspect, a method for manufacturing a transcutaneous analyte sensor is provided, the method comprising the steps of providing at least one electrode comprising an electroactive portion; and applying a membrane to the electroactive port ion, wherein at least one layer of the membrane is applied by vapor deposition.

[0017] In an embodiment of the second aspect, the vapor deposition comprises physical vapor deposition.

[0018] In an embodiment of the second aspect, the physical vapor deposition comprises ultrasonic vapor deposition.

[0019] In an embodiment of the second aspect, the layer of the membrane is deposited in a vacuum chamber. The layer can be configured to resist flow of the analyte therethrough.

[0020] In an embodiment of the second aspect, at least one layer of the membrane is applied using an ultrasonic nozzle. The layer can be configured to resist flow of the analyte therethrough.

[0021] In an embodiment of the second aspect, the step of applying a membrane comprises applying an enzyme domain. The enzyme domain can be applied by dip coating.

[0022] In an embodiment of the second aspect, the step of applying a membrane comprises applying an electrode domain. The electrode domain can be applied by dip coating.

[0023] In an embodiment of the second aspect, the electrode comprises a wire comprising a conductive material, and wherein the sensor is configured for substantially continuous measurement of glucose in a host.

[0024] In a third aspect, a method for manufacturing a plurality of transcutaneous analyte sensors is provided, the method comprising providing a plurality of electrodes, each

electrode comprising an electroactive portion; placing the plurality of electrodes into a vacuum chamber; and vapor depositing at least one membrane layer thereon.

[0025] In an embodiment of the third aspect, the membrane layer is configured to control influx of an analyte therethrough.

[0026] In an embodiment of the third aspect, wherein an *in vitro* sensitivity of the plurality of sensors deviates from a median *in vitro* sensitivity by less about 20%.

[0027] In an embodiment of the third aspect, an *in vitro* sensitivity of the plurality of sensors deviates from a median *in vitro* sensitivity by less about 16%.

[0028] In an embodiment of the third aspect, an *in vitro* sensitivity of the plurality of sensors deviates from a median *in vitro* sensitivity by less about 12%.

[0029] In an embodiment of the third aspect, the method further comprises curing the membrane layer. The curing step can include placing a plurality of electrodes, each comprising the membrane layer, into a vacuum oven, a convection oven, or a variable frequency microwave oven.

[0030] In an embodiment of the third aspect, each electrode comprises a wire comprising a conductive material, and wherein each sensor is configured for substantially continuous measurement of glucose in a host.

[0031] In a fourth aspect, a method for limiting use of an analyte sensor to a predetermined time period is provided, the method comprising providing a key associated with an analyte sensor, wherein the key is configured to control an amount of time over which information is obtained from the analyte sensor.

[0032] In an embodiment of the fourth aspect, the analyte sensor is a transcutaneous glucose sensor.

[0033] In an embodiment of the fourth aspect, the sensor is operatively connected to a receiver, wherein the receiver is configured to display sensor data.

[0034] In an embodiment of the fourth aspect, the receiver is configured to receive the key.

[0035] In an embodiment of the fourth aspect, the receiver is configured to control an amount of time over which information is displayed on the receiver from the sensor in response to the key.

[0036] In an embodiment of the fourth aspect, the key is a software key.

[0037] In an embodiment of the fourth aspect, the key is a unique code.

[0038] In an embodiment of the fourth aspect, the key is selected from the group consisting of a unique number, a receiver ID, a sensor duration, a number of sensor systems, and combinations thereof.

[0039] In an embodiment of the fourth aspect, the key is configured for use with a plurality of sensors.

[0040] In an embodiment of the fourth aspect, the key is provided by an information tag.

[0041] In a fifth aspect, a method for distributing and controlling use of implantable sensor systems comprising reusable and disposable parts, the method comprising providing a single-use device associated with the sensor system, wherein the single-use device is configured to be inserted into a host's tissue; providing a key associated with the single-use device; and providing a reusable device associated with a sensor system, wherein the reusable device is configured to provide sensor information responsive to receipt of the key.

[0042] In an embodiment of the fifth aspect, the reusable device comprises a receiver configured to receive sensor information.

[0043] In an embodiment of the fifth aspect, the reusable device further comprises an electronics unit configured to releasably mate with the single-use device.

[0044] In an embodiment of the fifth aspect, the method further comprises obtaining a package containing a plurality of single-use devices.

[0045] In an embodiment of the fifth aspect, the single-use device is a transcutaneous analyte sensor configured for insertion into a subcutaneous tissue of a host.

[0046] In an embodiment of the fifth aspect, the key comprises a written license code packaged with the single-use device.

[0047] In an embodiment of the fifth aspect, the step of providing the key comprises providing a license code via at least one communication selected from the group consisting of written communication, voice communication, and electronic communication.

[0048] In an embodiment of the fifth aspect, the reusable device is configured to receive the key via manual entry.

[0049] In an embodiment of the fifth aspect, the reusable device is configured to wirelessly receive the key.

[0050] In an embodiment of the fifth aspect, key comprises sensor duration information configured to enable the sensor system to control an amount of time over which information is obtained from the single-use device or is displayed by the reusable device.

[0051] In an embodiment of the fifth aspect, the single-use device comprises a transcutaneous analyte sensor configured for insertion in a subcutaneous tissue of a host, and wherein the key comprises sensor insertion information configured to enable the sensor system to control a number of sensor insertions.

[0052] In an embodiment of the fifth aspect, the single-use device comprises a transcutaneous analyte sensor configured for insertion in a subcutaneous tissue of a host, and wherein the step of inserting the single-use device into a host comprises using an applicator to insert the sensor into the host.

[0053] In an embodiment of the fifth aspect, the step of obtaining sensor information from the sensor system comprises at least one step selected from the group consisting of measurement of analyte information, digitalizing of sensor information, transmission of sensor information, receiving of sensor information, storing of sensor information, processing of sensor information, and displaying of sensor information.

[0054] In a sixth aspect, a method for limiting use of a glucose sensor system to a predetermined time period is provided, the method comprising inputting a key into a receiver, wherein the key is configured to control an amount of time over which information is obtained from a sensor system, after which time the sensor system is disabled such that glucose information cannot be obtained, wherein the sensor system is a transcutaneous glucose sensor system comprising a sensor configured for insertion into a tissue of a host and an electronics unit operatively connected to the sensor and configured to provide a signal representative of a glucose concentration in the host, and wherein the receiver is configured to receive the signal representative of a glucose concentration in the host and to display corresponding glucose information; and obtaining glucose information from the sensor.

[0055] In an embodiment of the sixth aspect, the step of inputting the key into the receiver is performed before the step of obtaining glucose information from the sensor.

[0056] In a seventh aspect, a device for measuring an analyte in a host is provided, the device comprising a sensor operably connected to sensor electronics, the sensor electronics configured for measuring an analyte in a host; at least one electrical contact configured to connect the sensor to the sensor electronics; and a sealing member, wherein the sealing member at least partially surrounds at least one of the sensor and the electrical contact, wherein the sealing member comprises a material having a durometer hardness of from about 5 Shore A to about 80 Shore A.

[0057] In an embodiment of the seventh aspect, the durometer hardness is from about 10 Shore A to about 50 Shore A.

[0058] In an embodiment of the seventh aspect, the durometer hardness is about 20 Shore A.

[0059] In an embodiment of the seventh aspect, the durometer hardness is about 50 Shore A

[0060] In an embodiment of the seventh aspect, the sensor comprises a wire.

[0061] In an embodiment of the seventh aspect, the sensor comprises a planar substrate.

[0062] In an embodiment of the seventh aspect, the sealing material comprises a silicone.

[0063] In an embodiment of the seventh aspect, the device further comprises a sealant adjacent to the sealing member.

[0064] In an embodiment of the seventh aspect, the sensor electronics are housed within an electronics unit configured to mate with the electrical contact.

[0065] In an embodiment of the seventh aspect, the electronics unit and the sealing member are configured to mate to provide a compression force therebetween.

[0066] In an embodiment of the seventh aspect, the device further comprises at least one raised portion configured to provide a compression force to the sealing member when the electrical contact is connected to the sensor electronics.

[0067] In an eighth embodiment, a device for use in measuring an analyte in a host is provided, the device comprising a sensor operably connected to sensor electronics, the sensor electronics configured for measuring an analyte in a host; at least one electrical contact configured to operably connect the sensor to the sensor electronics; and a sealing member at least partially surrounding at least one of the sensor and the electrical contact, wherein the sealing member is configured to seal the electrical contact from moisture when the sensor is operably connected to the sensor electronics.

[0068] In an embodiment of the eighth aspect, the sealing member comprises a material having a durometer hardness of from about 5 Shore A to about 80 Shore A.

[0069] In an embodiment of the eighth aspect, the device further comprises a sealant adjacent to the sealing member.

[0070] In an embodiment of the eighth aspect, the device further comprises a housing on which the sealing member is disposed, wherein the housing is configured to mechanically or chemically hold the sealing member thereon.

[0071] In an embodiment of the eighth aspect, the device further comprises an adhesive configured to hold the sealing member on the housing.

[0072] In an embodiment of the eighth aspect, the device further comprises at least one protrusion configured to substantially mate with at least one depression, whereby the sealing member is held on the housing.

[0073] In an embodiment of the eighth aspect, the sealing member comprises at least one gap that is maintained when the electrical contact is operably connected to the sensor electronics.

[0074] In an embodiment of the eighth aspect, the sensor at least partially extends through the gap.

[0075] In an embodiment of the eighth aspect, the gap is filled with a sealant.

[0076] In an embodiment of the eighth aspect, the device further comprises at least one channel communicating between a first side of the sealing member and a second side of the sealing member.

[0077] In an embodiment of the eighth aspect, the channel is filled with a sealant.

[0078] In an embodiment of the eighth aspect, substantially no air gaps are adjacent to the electrical contact when the electrical contact is operably connected to the sensor electronics.

[0079] In an embodiment of the eighth aspect, the sealing member comprises a material selected from the group consisting of silicone, silicone/polyurethane hybrid, polyurethane, polysulfide, and mixtures thereof.

[0080] In an embodiment of the eighth aspect, the sealing member is self-lubricating.

[0081] In an embodiment of the eighth aspect, the sealing member comprises a sealant sandwiched between an upper portion of the sealing member and a lower portion of the sealing member.

[0082] In an embodiment of the eighth aspect, the device further comprises a guide tube configured to maintain an opening in the sealing member prior to sensor insertion into the host.

[0083] In an embodiment of the eighth aspect, the device further comprises a lubricant between the sealing member and the guide tube.

[0084] In a ninth aspect, a device for use in measuring an analyte in a host is provided, the device comprising a sensor operably connected to sensor electronics, the sensor electronics configured for measuring an analyte in a host; at least one electrical contact configured to connect the sensor to the sensor electronics, wherein the electrical contact comprises a material having a durometer hardness of from about 5 Shore A to about 80 Shore A; and a sealing member at least partially surrounding at least one of the sensor and the electrical contact, wherein the sealing member comprises a material having a durometer hardness of from about 5 Shore A to about 80 Shore A.

[0085] In an embodiment of the ninth aspect, the durometer hardness of the electrical contact is higher than the durometer hardness of the sealing member.

[0086] In an embodiment of the ninth aspect, the durometer hardness of the electrical contact is about 50 Shore A.

[0087] In an embodiment of the ninth aspect, the durometer hardness of the sealing member is higher than the durometer hardness of the contact.

[0088] In an embodiment of the ninth aspect, the durometer hardness of the sealing member is about 50 Shore A.

[0089] In an embodiment of the ninth aspect, the sealing member comprises a filler material.

[0090] In an embodiment of the ninth aspect, the filler material is configured to stiffen the sealing member.

[0091] In a tenth aspect, a sensor system for measuring an analyte concentration in a host is provided, the system comprising at least one electrode configured for implantation in a host and configured to measure an analyte concentration in a tissue of the host; sensor electronics operably connected to the electrode and configured to provide analyte data representative of an analyte concentration in the host; and an information tag comprising sensor information.

[0092] In an embodiment of the tenth aspect, the information tag comprises a memory.

[0093] In an embodiment of the tenth aspect, the information tag transmits information using at least one connection selected from the group consisting of a serial connection, a radio frequency connection, an acoustic frequency connection, an infrared frequency connection, and a magnetic induction connection.

[0094] In an embodiment of the tenth aspect, the system further comprises a mounting unit configured to maintain the sensor positioned transcutaneously within the tissue of the host.

[0095] In an embodiment of the tenth aspect, the information tag is embedded within the mounting unit.

[0096] In an embodiment of the tenth aspect, the system further comprises a receiver configured to receive the analyte data from the sensor electronics.

[0097] In an embodiment of the tenth aspect, the receiver is configured to read sensor information from the information tag.

[0098] In an embodiment of the tenth aspect, the system further comprises packaging configured to contain at least a portion of a sensor system during transport.

[0099] In an embodiment of the tenth aspect, the information tag is in or on the packaging.

[0100] In an embodiment of the tenth aspect, the sensor information comprises at least one item selected from the group consisting of manufacturing information, calibration information, identification information, expiration information, sensor duration information, and archived data.

[0101] In an embodiment of the tenth aspect, the sensor information comprises a license code.

[0102] In an eleventh aspect, a transcutaneous analyte sensor assembly is provided, the assembly comprising a mounting unit adapted for mounting on a skin of a host; an electronics unit configured to releasably mate with the mounting unit; a sensor configured to measure a concentration of an analyte in the host, wherein the sensor is operably connected to the electronics unit when the electronics unit is mated to the mounting unit; and an information tag comprising sensor information.

[0103] In an embodiment of the eleventh aspect, the sensor information is embedded in an information tag within the mounting unit.

[0104] In an embodiment of the eleventh aspect, the assembly further comprises a receiver, wherein the receiver is configured to read sensor information from the information tag.

[0105] In an embodiment of the eleventh aspect, the information tag comprises a memory.

[0106] In an embodiment of the eleventh aspect, the information tag transmits information using at least one connection selected from the group consisting of a serial connection, a radio frequency connection, an acoustic frequency connection, an infrared frequency connection, and a magnetic induction connection.

[0107] In an embodiment of the eleventh aspect, the sensor information is embedded within the electronics unit.

[0108] In an embodiment of the eleventh aspect, the assembly further comprises packaging configured to contain the sensor assembly during transport, wherein the information tag is provided in or on the packaging.

[0109] In an embodiment of the eleventh aspect, the assembly further comprises a receiver, wherein the receiver is configured to read the sensor information from the information tag.

[0110] In an embodiment of the eleventh aspect, the sensor information comprises information configured to trigger initialization of the sensor.

[0111] In a twelfth aspect, a transcutaneous glucose sensor system is provided, the sensor system comprising a mounting unit adapted for mounting on a skin of a host; a sensor configured to measure an analyte concentration in the host; sensor electronics operably connected to the sensor, wherein the sensor is configured to provide data representative of an analyte concentration in the host; a receiver remote from the mounting unit and configured to receive sensor data from the electronics unit representative of a measured analyte concentration; and an information tag configured to provide sensor information selected from the group consisting of manufacturing information, calibration information, identification information, expiration information, sensor duration information, archived data, license code information, and combinations thereof.

[0112] In an embodiment of the twelfth aspect, the receiver is configured to read sensor information from the information tag.

[0113] In an embodiment of the twelfth aspect, the electronics unit is configured to releasably mate with the mounting unit, and wherein the electronics unit is operably connected to the sensor when the electronics unit is mated to the mounting unit.

[0114] In a thirteenth aspect, a device configured for placement on a skin surface of a host is provided, the device comprising a sensor configured for transcutaneous insertion into a host and operatively connected to sensor electronics for processing data obtained from the sensor; and a housing adapted for placement on a skin surface of the host and coupled to the sensor electronics, wherein at least one of the housing and the sensor electronics comprises a user interface configured to communicate information responsive to processed sensor data.

[0115] In an embodiment of the thirteenth aspect, the user interface comprises a screen configured to display at least one numerical value.

[0116] In an embodiment of the thirteenth aspect, the user interface comprises a screen configured to display trend information.

[0117] In an embodiment of the thirteenth aspect, the user interface comprises a screen configured to display graphical information.

[0118] In an embodiment of the thirteenth aspect, the user interface is configured to communicate information audibly.

[0119] In an embodiment of the thirteenth aspect, the user interface is configured to communicate information tactilely.

[0120] In an embodiment of the thirteenth aspect, the user interface is configured to provide information to the host in response to activation of a button.

[0121] In an embodiment of the thirteenth aspect, the sensor electronics are configured to alert the host when the sensor data is outside a predetermined boundary.

[0122] In an embodiment of the thirteenth aspect, the sensor electronics are configured to filter the sensor data.

[0123] In an embodiment of the thirteenth aspect, the sensor electronics are configured to calibrate the sensor data.

[0124] In an embodiment of the thirteenth aspect, the device further comprises a receiver, wherein the receiver is configured to communicate with the sensor electronics.

[0125] In an embodiment of the thirteenth aspect, the receiver is configured to request information from the sensor electronics.

[0126] In an embodiment of the thirteenth aspect, the sensor electronics are configured to transmit sensor data responsive to a request by the receiver.

[0127] In an embodiment of the thirteenth aspect, the receiver and the sensor electronics are operatively connected by at least one connection selected from the group consisting of a cable, a radio frequency connection, an optical connection, an inductive coupling connection, an infrared connection, and a microwave connection.

[0128] In an embodiment of the thirteenth aspect, the sensor electronics are releasably attachable to the housing.

[0129] In a fourteenth aspect, a transcutaneous glucose sensing device is provided, the device comprising a glucose sensor configured for transcutaneous insertion

through a skin of a host; and an on-skin housing coupled to the sensor, wherein the on-skin housing is adhered to the skin, and wherein the on-skin housing comprises sensor electronics configured to process sensor data and to provide sensor data to the host via a user interface.

[0130] In an embodiment of the fourteenth aspect, the user interface is configured to provide sensor data by at least method selected from the group consisting of visually, audibly, and tactilely.

[0131] In an embodiment of the fourteenth aspect, the user interface is housed on or in the on-skin housing.

[0132] In an embodiment of the fourteenth aspect, the user interface is operatively connected to the on-skin housing via at least one wire.

[0133] In an embodiment of the fourteenth aspect, the user interface is configured to be worn on the host at a location remote from the on-skin housing.

[0134] In an embodiment of the fourteenth aspect, the user interface is configured to be worn on clothing of the host, and wherein the on-skin housing in configured to be worn on the skin of the host.

[0135] In an embodiment of the fourteenth aspect, the user interface is directly wired to the on-skin housing.

[0136] In an embodiment of the fourteenth aspect, the sensor electronics are releasably attachable to the on-skin housing.

[0137] In a fifteenth aspect, a transcutaneous glucose sensor system is provided, the system comprising a glucose sensor configured for transcutaneous insertion through skin of a host; an on-skin device coupled to the sensor and comprising electronics configured to process data obtained from the sensor; and a receiver remote from the on-skin device configured to request information from the on-skin device.

[0138] In an embodiment of the fifteenth aspect, the on-skin device is configured to provide sensor information indicative of a glucose value of the host by at least one method selected from the group consisting of visual, audible, and tactile.

[0139] In an embodiment of the fifteenth aspect, the on-skin device is configured to provide filtered sensor data by at least one method selected from the group consisting of visual, audible, and tactile.

[0140] In an embodiment of the fifteenth aspect, the on-skin device is configured to provide calibrated sensor data by at least one method selected from the group consisting of visual, audible, and tactile.

BRIEF DESCRIPTION OF THE DRAWINGS

[0141] Fig. 1 is a perspective view of a transcutaneous analyte sensor system, including an applicator, a mounting unit, and an electronics unit.

[0142] Fig. 2 is a perspective view of a mounting unit, including the electronics unit in its functional position.

[0143] Fig. 3 is an exploded perspective view of a mounting unit, showing its individual components.

[0144] Fig. 4A is an exploded perspective view of a contact subassembly, showing its individual components.

[0145] Fig. 4B is a perspective view of an alternative contact configuration.

[0146] Fig. 4C is a perspective view of another alternative contact configuration.

[0147] Figs. 4D to 4H are schematic cross-sectional views of a portion of the contact subassembly; namely, a variety of embodiments illustrating alternative sealing member configurations.

[0148] Fig. 5A is an expanded cutaway view of a proximal portion of a sensor.

[0149] Fig. 5B is an expanded cutaway view of a distal portion of a sensor.

[0150] Fig. 5C is a cross-sectional view through the sensor of Fig. 5B on line C-C, showing an exposed electroactive surface of a working electrode surrounded by a membrane system.

[0151] Fig. 6 is an exploded side view of an applicator, showing the components that facilitate sensor insertion and subsequent needle retraction.

[0152] Figs. 7A to 7D are schematic side cross-sectional views that illustrate applicator components and their cooperating relationships.

[0153] Fig. 8A is a perspective view of an applicator and mounting unit in one embodiment including a safety latch mechanism.

[0154] Fig. 8B is a side view of an applicator matingly engaged to a mounting unit in one embodiment, prior to sensor insertion.

[0155] Fig. 8C is a side view of a mounting unit and applicator depicted in the embodiment of Fig. 8B, after the plunger subassembly has been pushed, extending the needle and sensor from the mounting unit.

[0156] Fig. 8D is a side view of a mounting unit and applicator depicted in the embodiment of Fig. 8B, after the guide tube subassembly has been retracted, retracting the needle back into the applicator.

[0157] Fig. 8E is a perspective view of an applicator, in an alternative embodiment, matingly engaged to the mounting unit after to sensor insertion.

[0158] Fig. 8F is a perspective view of the mounting unit and applicator, as depicted in the alternative embodiment of Fig. 8E, matingly engaged while the electronics unit is slidingly inserted into the mounting unit.

[0159] Fig. 8G is a perspective view of the electronics unit, as depicted in the alternative embodiment of Fig. 8E, matingly engaged to the mounting unit after the applicator has been released.

[0160] Figs. 8H and 8I are comparative top views of the sensor system shown in the alternative embodiment illustrated in Figs. 8E to 8G as compared to the embodiments illustrated in Figs. 8B to 8D.

[0161] Figs. 9A to 9C are side views of an applicator and mounting unit, showing stages of sensor insertion.

[0162] Figs. 10A and 10B are perspective and side cross-sectional views, respectively, of a sensor system showing the mounting unit immediately following sensor insertion and release of the applicator from the mounting unit.

[0163] Figs. 11A and 11B are perspective and side cross-sectional views, respectively, of a sensor system showing the mounting unit after pivoting the contact subassembly to its functional position.

[0164] Figs. 12A to 12C are perspective and side views, respectively, of the sensor system showing the sensor, mounting unit, and electronics unit in their functional positions.

[0165] Fig. 13 is an exploded perspective view of one exemplary embodiment of a continuous glucose sensor

[0166] Fig.14A is a block diagram that illustrates electronics associated with a sensor system.

[0167] Fig. 14B is a perspective view of an alternative embodiment, wherein the electronics unit and/or mounting unit, hereinafter referred to as the "on-skin device," is configured to communicate sensor information directly to the user (e.g., host).

[0168] Fig. 15 is a perspective view of a sensor system wirelessly communicating with a receiver.

[0169] Fig. 16A illustrates a first embodiment wherein the receiver shows a numeric representation of the estimated analyte value on its user interface, which is described in more detail elsewhere herein.

[0170] Fig. 16B illustrates a second embodiment wherein the receiver shows an estimated glucose value and one hour of historical trend data on its user interface, which is described in more detail elsewhere herein.

[0171] Fig. 16C illustrates a third embodiment wherein the receiver shows an estimated glucose value and three hours of historical trend data on its user interface, which is described in more detail elsewhere herein.

[0172] Fig. 16D illustrates a fourth embodiment wherein the receiver shows an estimated glucose value and nine hours of historical trend data on its user interface, which is described in more detail elsewhere herein.

[0173] Fig. 17A is a block diagram that illustrates a configuration of a medical device including a continuous analyte sensor, a receiver, and an external device.

[0174] Figs. 17B to 17D are illustrations of receiver liquid crystal displays showing embodiments of screen displays.

[0175] Fig. 18A is a flow chart that illustrates the initial calibration and data output of sensor data.

[0176] Fig. 18B is a graph that illustrates one example of using prior information for slope and baseline. Figs. 18C-G disclose integrated receiver housing **1892** and stylus **1998**.

[0177] Fig. 19A is a flow chart that illustrates evaluation of reference and/or sensor data for statistical, clinical, and/or physiological acceptability.

[0178] Fig. 19B is a graph of two data pairs on a Clarke Error Grid to illustrate the evaluation of clinical acceptability in one exemplary embodiment.

[0179] Fig. 20 is a flow chart that illustrates evaluation of calibrated sensor data for aberrant values.

[0180] Fig. 21 is a flow chart that illustrates self-diagnostics of sensor data.

[0181] Figs. 22A and 22B are graphical representations of glucose sensor data in a human obtained over approximately three days.

[0182] Fig. 23A is a graphical representation of glucose sensor data in a human obtained over approximately seven days.

[0183] Fig. 23B is a flow chart that illustrates a method for distributing and controlling use of sensor systems with disposable and single-use parts.

[0184] Fig. 24A is a bar graph that illustrates the ability of sensors to resist uric acid pre- and post-electron beam exposure in one *in vitro* experiment.

[0185] Fig. 24B is a bar graph that illustrates the ability of sensors to resist ascorbic acid pre- and post-electron beam exposure in one *in vitro* experiment.

[0186] Fig. 24C is a bar graph that illustrates the ability of sensors to resist acetaminophen pre- and post-electron beam exposure in one *in vitro* experiment.

[0187] Fig. 25A is a graphical representation that illustrates the acetaminophen blocking ability of a glucose sensor including a cellulose acetate interference domain that has been treated using electron beam radiation and tested *in vivo*.

[0188] Fig. 25B is a graphical representation that illustrates the acetaminophen blocking ability of a glucose sensor including a cellulose acetate/Nafion® interference domain that has been treated using electron beam radiation and tested *in vivo*.

[0189] Fig. 25C is a graphical representation that illustrates the lack of acetaminophen blocking ability of a control glucose sensor without an interference domain and tested *in vivo*.

[0190] Fig. 26A is a bar graph that represents the break-in time of the test sensors vs. the control sensors.

[0191] Fig. 26B is a graph that represents the response of glucose sensors to a variety of interferents.

[0192] Fig. 26C is a graph that represents an "equivalent glucose signal" caused by the interferents tested.

[0193] Fig. 27 is a photomicrograph obtained by Scanning Electron Microscopy (SEM) at 350X magnification of a sensor including a vapor deposited resistance domain on an outer surface.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0194] The following description and examples illustrate some exemplary embodiments of the disclosed invention in detail. Those of skill in the art will recognize that there are numerous variations and modifications of this invention that are encompassed by its scope. Accordingly, the description of a certain exemplary embodiment should not be deemed to limit the scope of the present invention.

Definitions

[0195] In order to facilitate an understanding of the preferred embodiments, a number of terms are defined below.

[0196] The term "analyte" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to a substance or chemical constituent in a biological fluid (for example, blood, interstitial fluid, cerebral spinal fluid, lymph fluid or urine) that can be analyzed. Analytes can include naturally occurring substances, artificial substances, metabolites, and/or reaction products. In some embodiments, the analyte for measurement by the sensing regions, devices, and methods is glucose. However, other analytes are contemplated as well, including but not limited to acarboxyprothrombin; acylcarnitine; adenine phosphoribosyl transferase; adenosine deaminase; albumin; alpha-fetoprotein; amino acid profiles (arginine (Krebs cycle), histidine/urocanic acid, homocysteine, phenylalanine/tyrosine, tryptophan); andrenostenedione; antipyrine; arabinitol enantiomers; arginase; benzoylecgonine (cocaine); biotinidase; biopterin; c-reactive protein; carnitine; carnosinase; CD4; ceruloplasmin; chenodeoxycholic acid; chloroquine; cholesterol; cholinesterase; conjugated 1-ß hydroxy-cholic acid; cortisol; creatine kinase; creatine kinase MM isoenzyme; cyclosporin A; d-penicillamine; de-ethylchloroquine; dehydroepiandrosterone sulfate; DNA (acetylator

polymorphism, alcohol dehydrogenase, alpha 1-antitrypsin, cystic fibrosis, Duchenne/Becker muscular dystrophy, glucose-6-phosphate dehydrogenase, hemoglobin A, hemoglobin S, hemoglobin C, hemoglobin D, hemoglobin E, hemoglobin F, D-Punjab, beta-thalassemia, hepatitis B virus, HCMV, HIV-1, HTLV-1, Leber hereditary optic neuropathy, MCAD, RNA, PKU, Plasmodium vivax, sexual differentiation, 21-deoxycortisol); desbutylhalofantrine; dihydropteridine reductase; diptheria/tetanus antitoxin; erythrocyte arginase; erythrocyte protoporphyrin; esterase D; fatty acids/acylglycines; free ß-human chorionic gonadotropin; free erythrocyte porphyrin; free thyroxine (FT4); free tri-iodothyronine (FT3); fumarylacetoacetase; galactose/gal-1-phosphate; galactose-1-phosphate uridyltransferase; gentamicin; glucose-6-phosphate dehydrogenase; glutathione; glutathione perioxidase; glycocholic acid; glycosylated hemoglobin; halofantrine; hemoglobin variants; hexosaminidase A; human erythrocyte carbonic anhydrase I; 17-alpha-hydroxyprogesterone; hypoxanthine phosphoribosyl transferase; immunoreactive trypsin; lactate; lead; lipoproteins ((a), B/A-1, ß); lysozyme; mefloquine; netilmicin; phenobarbitone; phenytoin; phytanic/pristanic acid; progesterone; prolactin; prolidase; purine nucleoside phosphorylase; quinine; reverse tri-iodothyronine (rT3); selenium; serum pancreatic lipase; sissomicin; somatomedin C; specific antibodies (adenovirus, anti-nuclear antibody, anti-zeta antibody, arbovirus, Aujeszky's disease virus, dengue virus, Dracunculus medinensis, Echinococcus granulosus, Entamoeba histolytica, enterovirus, Giardia duodenalisa, Helicobacter pylori, hepatitis B virus, herpes virus, HIV-1, IgE (atopic disease), influenza virus, Leishmania donovani, leptospira, measles/mumps/rubella, Mycobacterium leprae, Mycoplasma pneumoniae, Myoglobin, Onchocerca volvulus, parainfluenza virus, Plasmodium falciparum, poliovirus, Pseudomonas aeruginosa, respiratory syncytial virus, rickettsia (scrub typhus), Schistosoma mansoni, Toxoplasma gondii, Trepenoma pallidium, Trypanosoma cruzi/rangeli, vesicular stomatis virus, Wuchereria bancrofti, yellow fever virus); specific antigens (hepatitis B virus, HIV-1); succinylacetone; sulfadoxine; theophylline; thyrotropin (TSH); thyroxine (T4); thyroxine-binding globulin; trace elements; transferrin; UDP-galactose-4-epimerase; urea; uroporphyrinogen I synthase; vitamin A; white blood cells; and zinc protoporphyrin. Salts, sugar, protein, fat, vitamins, and hormones naturally occurring in blood or interstitial fluids can also constitute analytes in certain embodiments. The analyte

can be naturally present in the biological fluid, for example, a metabolic product, a hormone, an antigen, an antibody, and the like. Alternatively, the analyte can be introduced into the body, for example, a contrast agent for imaging, a radioisotope, a chemical agent, a fluorocarbon-based synthetic blood, or a drug or pharmaceutical composition, including but not limited to insulin; ethanol; cannabis (marijuana, tetrahydrocannabinol, hashish); inhalants (nitrous oxide, amyl nitrite, butyl nitrite, chlorohydrocarbons, hydrocarbons); cocaine (crack cocaine); stimulants (amphetamines, methamphetamines, Ritalin, Cylert, Preludin, Didrex, PreState, Voranil, Sandrex, Plegine); depressants (barbituates, methaqualone, tranquilizers such as Valium, Librium, Miltown, Serax, Equanil, Tranxene); hallucinogens (phencyclidine, lysergic acid, mescaline, peyote, psilocybin); narcotics (heroin, codeine, morphine, opium, meperidine, Percocet, Percodan, Tussionex, Fentanyl, Darvon, Talwin, Lomotil); designer drugs (analogs of fentanyl, meperidine, amphetamines, methamphetamines, and phencyclidine, for example, Ecstasy); anabolic steroids; and nicotine. The metabolic products of drugs and pharmaceutical compositions are also contemplated analytes. Analytes such as neurochemicals and other chemicals generated within the body can also be analyzed, such as, for example, ascorbic acid, uric acid, dopamine, noradrenaline, 3-methoxytyramine (3MT), 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA), 5-hydroxytryptamine (5HT), histamine, Advanced Glycation End Products (AGEs) and 5-hydroxyindoleacetic acid (FHIAA).

[0197] The term "host" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to mammals, particularly humans.

[0198] The term "exit-site" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to the area where a medical device (for example, a sensor and/or needle) exits from the host's body.

[0199] The term "continuous (or continual) analyte sensing" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers

without limitation to the period in which monitoring of analyte concentration is continuously, continually, and or intermittently (regularly or irregularly) performed, for example, about every 5 to 10 minutes.

[0200] The term "electrochemically reactive surface" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to the surface of an electrode where an electrochemical reaction takes place. For example, a working electrode measures hydrogen peroxide produced by the enzyme-catalyzed reaction of the analyte detected, which reacts to create an electric current. Glucose analyte can be detected utilizing glucose oxidase, which produces H_2O_2 as a byproduct. H_2O_2 reacts with the surface of the working electrode, producing two protons ($2H^+$), two electrons ($2e^-$) and one molecule of oxygen (O_2), which produces the electronic current being detected.

[0201] The term "electronic connection" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to any electronic connection known to those in the art that can be utilized to interface the sensing region electrodes with the electronic circuitry of a device, such as mechanical (for example, pin and socket) or soldered electronic connections.

[0202] The term "sensing region" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to the region of a monitoring device responsible for the detection of a particular analyte. The sensing region generally comprises a non-conductive body, a working electrode (anode), a reference electrode (optional), and/or a counter electrode (cathode) passing through and secured within the body forming electrochemically reactive surfaces on the body and an electronic connective means at another location on the body, and a multi-domain membrane affixed to the body and covering the electrochemically reactive surface.

[0203] The term "high oxygen solubility domain" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to

a domain composed of a material that has higher oxygen solubility than aqueous media such that it concentrates oxygen from the biological fluid surrounding the membrane system. The domain can act as an oxygen reservoir during times of minimal oxygen need and has the capacity to provide, on demand, a higher oxygen gradient to facilitate oxygen transport across the membrane. Thus, the ability of the high oxygen solubility domain to supply a higher flux of oxygen to critical domains when needed can improve overall sensor function.

[0204] The term "domain" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to a region of the membrane system that can be a layer, a uniform or non-uniform gradient (for example, an anisotropic region of a membrane), or a portion of a membrane.

[0205] The term "distal to" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to the spatial relationship between various elements in comparison to a particular point of reference. In general, the term indicates an element is located relatively far from the reference point than another element.

[0206] The term "proximal to" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to the spatial relationship between various elements in comparison to a particular point of reference. In general, the term indicates an element is located relatively near to the reference point than another element.

[0207] The term "*in vivo* portion" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to the portion of the device (for example, a sensor) adapted for insertion into and/or existence within a living body of a host.

[0208] The term "*ex vivo* portion" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to

be limited to a special or customized meaning), and refers without limitation to the portion of the device (for example, a sensor) adapted to remain and/or exist outside of a living body of a host.

[0209] The terms "raw data stream", "raw data signal", and "data stream" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to an analog or digital signal from the analyte sensor directly related to the measured analyte. For example, the raw data stream is digital data in "counts" converted by an A/D converter from an analog signal (for example, voltage or amps) representative of an analyte concentration. The terms broadly encompass a plurality of time spaced data points from a substantially continuous analyte sensor, each of which comprises individual measurements taken at time intervals ranging from fractions of a second up to, for example, 1, 2, or 5 minutes or longer.

[0210] The term "count" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to a unit of measurement of a digital signal. For example, a raw data stream or raw data signal measured in counts is directly related to a voltage (for example, converted by an A/D converter), which is directly related to current from the working electrode.

[0211] The term "physiologically feasible" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to one or more physiological parameters obtained from continuous studies of glucose data in humans and/or animals. For example, a maximal sustained rate of change of glucose in humans of about 4 mg/dL/min to about 6 mg/dL/min and a maximum acceleration of the rate of change of about 0.1 mg/dL/min/min to about 0.2 mg/dL/min/min are deemed physiologically feasible limits. Values outside of these limits are considered non-physiological and are likely a result of, *e.g.*, signal error.

[0212] The term "ischemia" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be

limited to a special or customized meaning), and refers without limitation to local and temporary deficiency of blood supply due to obstruction of circulation to a part (for example, a sensor). Ischemia can be caused, for example, by mechanical obstruction (for example, arterial narrowing or disruption) of the blood supply.

[0213] The term "matched data pairs" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to reference data (for example, one or more reference analyte data points) matched with substantially time corresponding sensor data (for example, one or more sensor data points).

[0214] The term "Clarke Error Grid" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to an error grid analysis, for example, an error grid analysis used to evaluate the clinical significance of the difference between a reference glucose value and a sensor generated glucose value, taking into account 1) the value of the reference glucose measurement, 2) the value of the sensor glucose measurement, 3) the relative difference between the two values, and 4) the clinical significance of this difference. See Clarke *et al.*, "Evaluating Clinical Accuracy of Systems for Self-Monitoring of Blood Glucose" Diabetes Care, Volume 10, Number 5, September-October 1987.

[0215] The term "Consensus Error Grid" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to an error grid analysis that assigns a specific level of clinical risk to any possible error between two time corresponding measurements, *e.g.*, glucose measurements. The Consensus Error Grid is divided into zones signifying the degree of risk posed by the deviation. See Parkes *et al.*, "A New Consensus Error Grid to Evaluate the Clinical Significance of Inaccuracies in the Measurement of Blood Glucose" Diabetes Care, Volume 23, Number 8, August 2000.

[0216] The term "clinical acceptability" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to

determination of the risk of an inaccuracy to a patient. Clinical acceptability considers a deviation between time corresponding analyte measurements (for example, data from a glucose sensor and data from a reference glucose monitor) and the risk (for example, to the decision making of a person with diabetes) associated with that deviation based on the analyte value indicated by the sensor and/or reference data. An example of clinical acceptability can be 85% of a given set of measured analyte values within the "A" and "B" region of a standard Clarke Error Grid when the sensor measurements are compared to a standard reference measurement.

[0217] The terms "sensor" and "sensor system" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to the component or region of a device by which an analyte can be quantified.

[0218] The term "needle" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to a slender hollow instrument for introducing material into or removing material from the body.

[0219] The terms "operatively connected," "operatively linked," "operably connected," and "operably linked" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to one or more components linked to one or more other components. The terms can refer to a mechanical connection, an electrical connection, or a connection that allows transmission of signals between the components. For example, one or more electrodes can be used to detect the amount of analyte in a sample and to convert that information into a signal; the signal can then be transmitted to a circuit. In such an example, the electrode is "operably linked" to the electronic circuitry.

[0220] The term "baseline" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to the component of an analyte sensor signal that is not related to the analyte concentration. In one example of

a glucose sensor, the baseline is composed substantially of signal contribution due to factors other than glucose (for example, interfering species, non-reaction-related hydrogen peroxide, or other electroactive species with an oxidation potential that overlaps with hydrogen peroxide). In some embodiments wherein a calibration is defined by solving for the equation $y=mx+b$, the value of b represents the baseline of the signal.

[0221] The terms "sensitivity" and "slope" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to an amount of electrical current produced by a predetermined amount (unit) of the measured analyte. For example, in one preferred embodiment, a sensor has a sensitivity (or slope) of about 3.5 to about 7.5 picoAmps of current for every 1 mg/dL of glucose analyte.

[0222] The term "membrane system" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to a permeable or semi-permeable membrane that can be comprised of two or more domains and is typically constructed of materials of one or more microns in thickness, which is permeable to oxygen and is optionally permeable to, *e.g.*, glucose or another analyte. In one example, the membrane system comprises an immobilized glucose oxidase enzyme, which enables a reaction to occur between glucose and oxygen whereby a concentration of glucose can be measured.

[0223] The terms "processor module" and "microprocessor" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to a computer system, state machine, processor, or the like designed to perform arithmetic or logic operations using logic circuitry that responds to and processes the basic instructions that drive a computer.

[0224] The terms "smoothing" and "filtering" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to modification of a set of data to make it smoother and more continuous or to remove or

diminish outlying points, for example, by performing a moving average of the raw data stream.

[0225] The term "algorithm" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to a computational process (for example, programs) involved in transforming information from one state to another, for example, by using computer processing.

[0226] The term "regression" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to finding a line for which a set of data has a minimal measurement (for example, deviation) from that line. Regression can be linear, non-linear, first order, second order, or the like. One example of regression is least squares regression.

[0227] The term "calibration" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to the process of determining the relationship between the sensor data and the corresponding reference data, which can be used to convert sensor data into meaningful values substantially equivalent to the reference data. In some embodiments, namely, in continuous analyte sensors, calibration can be updated or recalibrated over time as changes in the relationship between the sensor data and reference data occur, for example, due to changes in sensitivity, baseline, transport, metabolism, or the like.

[0228] The terms "interferents" and "interfering species" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to effects and/or species that interfere with the measurement of an analyte of interest in a sensor to produce a signal that does not accurately represent the analyte concentration. In one example of an electrochemical sensor, interfering species are compounds with an oxidation potential that overlap that of the analyte to be measured, thereby producing a false positive signal.

[0229] The terms "chloridization" and "chloridizing" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to treatment or preparation with chloride. The term "chloride" as used herein, is a broad term and is used in its ordinary sense, including, without limitation, to refer to Cl^- ions, sources of Cl^- ions, and salts of hydrochloric acid. Chloridization and chloridizing methods include, but are not limited to, chemical and electrochemical methods.

[0230] The term "R-value" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to one conventional way of summarizing the correlation of data; that is, a statement of what residuals (*e.g.*, root mean square deviations) are to be expected if the data are fitted to a straight line by the a regression.

[0231] The terms "data association" and "data association function" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to a statistical analysis of data and particularly its correlation to, or deviation from, from a particular curve. A data association function is used to show data association. For example, the data that forms that calibration set as described herein can be analyzed mathematically to determine its correlation to, or deviation from, a curve (*e.g.*, line or set of lines) that defines the conversion function; this correlation or deviation is the data association. A data association function is used to determine data association. Examples of data association functions include, but are not limited to, linear regression, non-linear mapping/regression, rank (*e.g.*, non-parametric) correlation, least mean square fit, mean absolute deviation (MAD), mean absolute relative difference. In one such example, the correlation coefficient of linear regression is indicative of the amount of data association of the calibration set that forms the conversion function, and thus the quality of the calibration.

[0232] The term "quality of calibration" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to the

statistical association of matched data pairs in the calibration set used to create the conversion function. For example, an R-value can be calculated for a calibration set to determine its statistical data association, wherein an R-value greater than 0.79 determines a statistically acceptable calibration quality, while an R-value less than 0.79 determines statistically unacceptable calibration quality.

[0233] The term "congruence" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to the quality or state of agreeing, coinciding, or being concordant. In one example, congruence can be determined using rank correlation.

[0234] The term "concordant" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to being in agreement or harmony, and/or free from discord.

[0235] The phrase "continuous glucose sensing" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to the period in which monitoring of plasma glucose concentration is continuously or continually performed, for example, at time intervals ranging from fractions of a second up to, for example, 1, 2, or 5 minutes, or longer.

[0236] The term "single point glucose monitor" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to a device that can be used to measure a glucose concentration within a host at a single point in time, for example, some embodiments utilize a small volume in vitro glucose monitor that includes an enzyme membrane such as described with reference to U.S. Patent 4,994,167 and U.S. Patent 4,757,022. It should be understood that single point glucose monitors can measure multiple samples (for example, blood or interstitial fluid); however only one sample is measured at a time and typically requires some user initiation and/or interaction.

[0237] The term "biological sample" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to sample of a host body, for example blood, interstitial fluid, spinal fluid, saliva, urine, tears, sweat, or the like.

[0238] The terms "substantial" and "substantially" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to a sufficient amount that provides a desired function. For example, the interference domain of the preferred embodiments is configured to resist a sufficient amount of interfering species such that tracking of glucose levels can be achieved, which may include an amount greater than 50 percent, an amount greater than 60 percent, an amount greater than 70 percent, an amount greater than 80 percent, and an amount greater than 90 percent of interfering species.

[0239] The terms "cellulosic derivatives" and "cellulosic polymers" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to derivatives of cellulose formed by reaction with carboxylic acid anhydrides. Examples of cellulosic derivatives include cellulose acetate, 2-hydroxyethyl cellulose, cellulose acetate phthalate, cellulose acetate propionate, cellulose acetate butyrate, cellulose acetate trimellitate, and the like.

[0240] The term "cellulose acetate" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to any of several compounds obtained by treating cellulose with acetic anhydride.

[0241] The term "cellulose acetate butyrate" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to any of several compounds obtained by treating cellulose with acetic anhydride and butyric anhydride.

[0242] The term "Nafion®" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to DuPont's trademark of a sulfonated tetrafluorethylene polymer modified from Teflon® developed in the late 1960s. In general, Nafion® is a perfluorinated polymer that contains small proportions of sulfonic or carboxylic ionic functional groups.

[0243] The terms "crosslink" and "crosslinking" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to joining (adjacent chains of a polymer or protein) by creating covalent bonds. Crosslinking can be accomplished by techniques such as thermal reaction, chemical reaction or by providing ionizing radiation (for example, electron beam radiation, UV radiation, or gamma radiation). In preferred embodiments, crosslinking utilizes a technique that forms free radicals, for example, electron beam exposure.

[0244] The term "ionizing radiation" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to radiation consisting of particles, X-ray beams, electron beams, UV beams, or gamma ray beams, which produce ions in the medium through which it passes.

[0245] The term "casting" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to a process where a fluid material is applied to a surface or surfaces and allowed to cure or dry. The term is broad enough to encompass a variety of coating techniques, for example, using a draw-down machine (*i.e.*, drawing-down), dip coating, spray coating, spin coating, or the like.

[0246] The term "dip coating" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to coating which involves dipping an object or material into a liquid coating substance.

[0247] The term "spray coating" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to coating which involves spraying a liquid coating substance onto an object or material.

[0248] The term "spin coating" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to a coating process in which a thin film is created by dropping a raw material solution onto a substrate while it is rotating.

[0249] The terms "solvent" and "solvent systems" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to substances (e.g., liquids) capable of dissolving or dispersing one or more other substances. Solvents and solvent systems can include compounds and/or solutions that include components in addition to the solvent itself.

[0250] The term "baseline" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to the component of an analyte sensor signal that is not related to the analyte concentration. In one example of a glucose sensor, the baseline is composed substantially of signal contribution due to factors other than glucose (for example, interfering species, non-reaction-related hydrogen peroxide, or other electroactive species with an oxidation potential that overlaps with hydrogen peroxide). In some embodiments wherein a calibration is defined by solving for the equation $y=mx+b$, the value of b represents the baseline of the signal.

[0251] The terms "sensitivity" and "slope" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to an amount of electrical current produced by a predetermined amount (unit) of the measured analyte. For example, in one preferred embodiment, a sensor has a sensitivity (or slope) of about 3.5 to about 7.5 picoAmps of current for every 1 mg/dL of glucose analyte.

[0252] The terms "baseline and/or sensitivity shift," "baseline and/or sensitivity drift," "shift," and "drift" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to a change in the baseline and/or sensitivity of the sensor signal over time. While the term "shift" generally refers to a substantially distinct change over a relatively short time period, and the term "drift" generally refers to a substantially gradual change over a relatively longer time period, the terms can be used interchangeably and can also be generally referred to as "change" in baseline and/or sensitivity.

[0253] The terms "sealant" and "lubricant" as used herein are broad terms, and are to be given their ordinary and customary meaning to a person of ordinary skill in the art (and are not to be limited to a special or customized meaning), and refer without limitation to a material with a low surface tension that repels and/or blocks moisture, for example, oil, grease, or gel. Sealants or lubricants can be used to fill gaps and/or to repel or block water. One exemplary sealant is petroleum jelly.

Sensor System

[0254] The preferred embodiments relate to the use of an analyte sensor that measures a concentration of analyte of interest or a substance indicative of the concentration or presence of the analyte. In some embodiments, the sensor is a continuous device, for example a subcutaneous, transdermal (*e.g.*, transcutaneous), or intravascular device. In some embodiments, the device can analyze a plurality of intermittent blood samples. The analyte sensor can use any method of analyte-sensing, including enzymatic, chemical, physical, electrochemical, spectrophotometric, polarimetric, calorimetric, radiometric, or the like.

[0255] The analyte sensor uses any method, including invasive, minimally invasive, and non-invasive sensing techniques, to provide an output signal indicative of the concentration of the analyte of interest. The output signal is typically a raw signal that is used to provide a useful value of the analyte of interest to a user, such as a patient or physician, who can be using the device. Accordingly, appropriate smoothing, calibration, and evaluation methods can be applied to the raw signal and/or system as a whole to provide relevant and acceptable estimated analyte data to the user.

[0256] The methods and devices of preferred embodiments can be employed in a continuous glucose sensor that measures a concentration of glucose or a substance indicative of a concentration or a presence of glucose. However, certain methods and devices of preferred embodiments are also suitable for use in connection with non-continuous (e.g., single point measurement or finger stick) monitors, such as the OneTouch® system manufactured by LifeScan, Inc., or monitors as disclosed in U.S. Pat. Nos. 5,418,142; 5,515,170; 5,526,120; 5,922,530; 5,968,836; and 6,335,203. In some embodiments, the glucose sensor is an invasive, minimally-invasive, or non-invasive device, for example a subcutaneous, transdermal, or intravascular device. In some embodiments, the device can analyze a plurality of intermittent biological samples, such as blood, interstitial fluid, or the like. The glucose sensor can use any method of glucose-measurement, including colorimetric, enzymatic, chemical, physical, electrochemical, spectrophotometric, polarimetric, calorimetric, radiometric, or the like. In alternative embodiments, the sensor can be any sensor capable of determining the level of an analyte in the body, for example oxygen, lactase, hormones, cholesterol, medicaments, viruses, or the like.

[0257] The glucose sensor uses any method to provide an output signal indicative of the concentration of the glucose. The output signal is typically a raw data stream that is used to provide a value indicative of the measured glucose concentration to a patient or doctor, for example.

[0258] One exemplary embodiment described in detail below utilizes an implantable glucose sensor. Another exemplary embodiment described in detail below utilizes a transcutaneous glucose sensor.

[0259] In one alternative embodiment, the continuous glucose sensor comprises a transcutaneous sensor such as described in U.S. Patent 6,565,509 to Say *et al.* In another alternative embodiment, the continuous glucose sensor comprises a subcutaneous sensor such as described with reference to U.S. Patent 6,579,690 to Bonnecaze *et al.* or U.S. Patent 6,484,046 to Say *et al.* In another alternative embodiment, the continuous glucose sensor comprises a refillable subcutaneous sensor such as described with reference to U.S. Patent 6,512,939 to Colvin *et al.* In another alternative embodiment, the continuous glucose sensor comprises an intravascular sensor such as described with reference to U.S. Patent 6,477,395

to Schulman *et al.* In another alternative embodiment, the continuous glucose sensor comprises an intravascular sensor such as described with reference to U.S. Patent 6,424,847 to Mastrototaro *et al.* All of the above patents are incorporated in their entirety herein by reference.

[0260] Although a few exemplary embodiments of continuous glucose sensors are illustrated and described herein, it should be understood that the disclosed embodiments are applicable to any device capable of single analyte, substantially continual or substantially continuous measurement of a concentration of analyte of interest and providing an output signal that represents the concentration of that analyte.

[0261] In a first exemplary embodiment, a transcutaneous analyte sensor system is provided that includes an applicator for inserting the transdermal analyte sensor under a host's skin. The sensor system includes a sensor for sensing the analyte, wherein the sensor is associated with a mounting unit adapted for mounting on the skin of the host. The mounting unit houses the electronics unit associated with the sensor and is adapted for fastening to the host's skin. In certain embodiments, the system further includes a receiver for receiving and/or processing sensor data.

[0262] Fig. 1 is a perspective view of a transcutaneous analyte sensor system **10.** In the preferred embodiment of a system as depicted in Fig. 1, the sensor includes an applicator **12**, a mounting unit **14**, and an electronics unit **16**. The system can further include a receiver **158**, such as is described in more detail with reference to Fig. 15.

[0263] The mounting unit (housing) **14** includes a base **24** adapted for mounting on the skin of a host, a sensor adapted for transdermal insertion through the skin of a host (see Fig. 4A), and one or more contacts **28** configured to provide secure electrical contact between the sensor and the electronics unit **16**. The mounting unit **14** is designed to maintain the integrity of the sensor in the host so as to reduce or eliminate translation of motion between the mounting unit, the host, and/or the sensor.

[0264] In one embodiment, an applicator **12** is provided for inserting the sensor **32** through the host's skin at the appropriate insertion angle with the aid of a needle (see Figs. 6 through 8), and for subsequent removal of the needle using a continuous push-pull action. Preferably, the applicator comprises an applicator body **18** that guides the applicator

components (see Figs. 6 through 8) and includes an applicator body base **60** configured to mate with the mounting unit **14** during insertion of the sensor into the host. The mate between the applicator body base **60** and the mounting unit **14** can use any known mating configuration, for example, a snap-fit, a press-fit, an interference-fit, or the like, to discourage separation during use. One or more release latches **30** enable release of the applicator body base **60**, for example, when the applicator body base **60** is snap fit into the mounting unit **14**.

[0265] The electronics unit **16** includes hardware, firmware, and/or software that enable measurement of levels of the analyte via the sensor. For example, the electronics unit **16** can comprise a potentiostat, a power source for providing power to the sensor, other components useful for signal processing, and preferably an RF module for transmitting data from the electronics unit **16** to a receiver (see Figs. 14 to 16). Electronics can be affixed to a printed circuit board (PCB), or the like, and can take a variety of forms. For example, the electronics can take the form of an integrated circuit (IC), such as an Application-Specific Integrated Circuit (ASIC), a microcontroller, or a processor. Preferably, electronics unit **16** houses the sensor electronics, which comprise systems and methods for processing sensor analyte data. Examples of systems and methods for processing sensor analyte data are described in more detail in U.S. Publication No. US-2005-0027463-A1.

[0266] After insertion of the sensor using the applicator **12**, and subsequent release of the applicator **12** from the mounting unit **14** (see Figs. 8B to 8D), the electronics unit **16** is configured to releasably mate with the mounting unit **14** in a manner similar to that described above with reference to the applicator body base **60**. The electronics unit **16** includes contacts on its backside (not shown) configured to electrically connect with the contacts **28**, such as are described in more detail with reference to Figs. 2 through 4. In one embodiment, the electronics unit **16** is configured with programming, for example initialization, calibration reset, failure testing, or the like, each time it is initially inserted into the mounting unit **14** and/or each time it initially communicates with the sensor **32**.

Mounting Unit

[0267] Fig. 2 is a perspective view of a sensor system of a preferred embodiment, shown in its functional position, including a mounting unit and an electronics unit matingly

engaged therein. Figs. 12A to 12C illustrate the sensor is its functional position for measurement of an analyte concentration in a host.

[0268] In preferred embodiments, the mounting unit **14**, also referred to as a housing, comprises a base **24** adapted for fastening to a host's skin. The base can be formed from a variety of hard or soft materials, and preferably comprises a low profile for minimizing protrusion of the device from the host during use. In some embodiments, the base **24** is formed at least partially from a flexible material, which is believed to provide numerous advantages over conventional transcutaneous sensors, which, unfortunately, can suffer from motion-related artifacts associated with the host's movement when the host is using the device. For example, when a transcutaneous analyte sensor is inserted into the host, various movements of the sensor (for example, relative movement between the *in vivo* portion and the *ex vivo* portion, movement of the skin, and/or movement within the host (dermis or subcutaneous)) create stresses on the device and can produce noise in the sensor signal. It is believed that even small movements of the skin can translate to discomfort and/or motion-related artifact, which can be reduced or obviated by a flexible or articulated base. Thus, by providing flexibility and/or articulation of the device against the host's skin, better conformity of the sensor system **10** to the regular use and movements of the host can be achieved. Flexibility or articulation is believed to increase adhesion (with the use of an adhesive pad) of the mounting unit **14** onto the skin, thereby decreasing motion-related artifact that can otherwise translate from the host's movements and reduced sensor performance.

[0269] Fig. 3 is an exploded perspective view of a sensor system of a preferred embodiment, showing a mounting unit, an associated contact subassembly, and an electronics unit. In some embodiments, the contacts **28** are mounted on or in a subassembly hereinafter referred to as a contact subassembly **26** (see Fig. 4A), which includes a contact holder **34** configured to fit within the base **24** of the mounting unit **14** and a hinge **38** that allows the contact subassembly **26** to pivot between a first position (for insertion) and a second position (for use) relative to the mounting unit **14**, which is described in more detail with reference to Figs. 10 and 11. The term "hinge" as used herein is a broad term and is used in its ordinary sense, including, without limitation, to refer to any of a variety of pivoting, articulating,

and/or hinging mechanisms, such as an adhesive hinge, a sliding joint, and the like; the term hinge does not necessarily imply a fulcrum or fixed point about which the articulation occurs.

[0270] In certain embodiments, the mounting unit **14** is provided with an adhesive pad **8**, preferably disposed on the mounting unit's back surface and preferably including a releasable backing layer **9**. Thus, removing the backing layer **9** and pressing the base portion **24** of the mounting unit onto the host's skin adheres the mounting unit **14** to the host's skin. Additionally or alternatively, an adhesive pad can be placed over some or all of the sensor system after sensor insertion is complete to ensure adhesion, and optionally to ensure an airtight seal or watertight seal around the wound exit-site (or sensor insertion site) (not shown). Appropriate adhesive pads can be chosen and designed to stretch, elongate, conform to, and/or aerate the region (*e.g.*, host's skin).

[0271] In preferred embodiments, the adhesive pad **8** is formed from spun-laced, open- or closed-cell foam, and/or non-woven fibers, and includes an adhesive disposed thereon, however a variety of adhesive pads appropriate for adhesion to the host's skin can be used, as is appreciated by one skilled in the art of medical adhesive pads. In some embodiments, a double-sided adhesive pad is used to adhere the mounting unit to the host's skin. In other embodiments, the adhesive pad includes a foam layer, for example, a layer wherein the foam is disposed between the adhesive pad's side edges and acts as a shock absorber.

[0272] In some embodiments, the surface area of the adhesive pad **8** is greater than the surface area of the mounting unit's back surface. Alternatively, the adhesive pad can be sized with substantially the same surface area as the back surface of the base portion. Preferably, the adhesive pad has a surface area on the side to be mounted on the host's skin that is greater than about 1, 1.25, 1.5, 1.75, 2, 2.25, or 2.5, times the surface area of the back surface **25** of the mounting unit base **24**. Such a greater surface area can increase adhesion between the mounting unit and the host's skin, minimize movement between the mounting unit and the host's skin, and/or protect the wound exit-site (sensor insertion site) from environmental and/or biological contamination. In some alternative embodiments, however, the adhesive pad can be smaller in surface area than the back surface assuming a sufficient adhesion can be accomplished.

[0273] In some embodiments, the adhesive pad **8** is substantially the same shape as the back surface **25** of the base **24**, although other shapes can also be advantageously employed, for example, butterfly-shaped, round, square, or rectangular. The adhesive pad backing can be designed for two-step release, for example, a primary release wherein only a portion of the adhesive pad is initially exposed to allow adjustable positioning of the device, and a secondary release wherein the remaining adhesive pad is later exposed to firmly and securely adhere the device to the host's skin once appropriately positioned. The adhesive pad is preferably waterproof. Preferably, a stretch-release adhesive pad is provided on the back surface of the base portion to enable easy release from the host's skin at the end of the useable life of the sensor, as is described in more detail with reference to Figs. 9A to 9C.

[0274] In some circumstances, it has been found that a conventional bond between the adhesive pad and the mounting unit may not be sufficient, for example, due to humidity that can cause release of the adhesive pad from the mounting unit. Accordingly, in some embodiments, the adhesive pad can be bonded using a bonding agent activated by or accelerated by an ultraviolet, acoustic, radio frequency, or humidity cure. In some embodiments, a eutectic bond of first and second composite materials can form a strong adhesion. In some embodiments, the surface of the mounting unit can be pretreated utilizing ozone, plasma, chemicals, or the like, in order to enhance the bondability of the surface.

[0275] A bioactive agent is preferably applied locally at the insertion site (exit-site) prior to or during sensor insertion. Suitable bioactive agents include those which are known to discourage or prevent bacterial growth and infection, for example, anti-inflammatory agents, antimicrobials, antibiotics, or the like. It is believed that the diffusion or presence of a bioactive agent can aid in prevention or elimination of bacteria adjacent to the exit-site. Additionally or alternatively, the bioactive agent can be integral with or coated on the adhesive pad, or no bioactive agent at all is employed.

[0276] Fig. 4A is an exploded perspective view of the contact subassembly **26** in one embodiment, showing its individual components. Preferably, a watertight (waterproof or water-resistant) sealing member **36**, also referred to as a sealing material or seal, fits within a contact holder **34** and provides a watertight seal configured to surround the electrical connection at the electrode terminals within the mounting unit in order to protect the

electrodes (and the respective operable connection with the contacts of the electronics unit **16**) from damage due to moisture, humidity, dirt, and other external environmental factors. In one embodiment, the sealing member **36** is formed from an elastomeric material, such as silicone; however, a variety of other elastomeric or sealing materials can also be used, for example, silicone-polyurethane hybrids, polyurethanes, and polysulfides. Preferably, the sealing member is configured to compress within the contact subassembly when the electronics unit is mated to the mounting unit. In some embodiments, the sealing member **36** comprises a self-lubricating material, for example, self-lubricating silicone or other materials impregnated with or otherwise comprising a lubricant configured to be released during use. In some embodiments, the sealing member **36** includes a self-sealing material, for example, one that leaches out a sealant such as a silicone oil. In some embodiments, bumps, ridges, or other raised portions (not shown), can be added to a component of the sensor system, such as to the contact subassembly **26** (e.g., housing adjacent to the sealing member), electronics unit **16** and/or sealing member **36** to provide additional compression and improve the seal formed around the contacts **28** and/or sensor **32** when the contacts **28** are mated to the sensor electronics.

[0277] Preferably, the sealing member is selected using a durometer. A durometer is an instrument used for measuring the indentation hardness of rubber, plastics, and other materials. Durometers are built to various standards from ASTM, DIN, JIS, and ISO. The hardness of plastics is most commonly measured by the Shore (Durometer) test or Rockwell hardness test. Both methods measure the resistance of plastics toward indentation and provide an empirical hardness value. Shore Hardness, using either the Shore A or Shore D scale, is the preferred method for rubbers/elastomers and is also commonly used for softer plastics such as polyolefins, fluoropolymers, and vinyls. The Shore A scale is used for softer rubbers while the Shore D scale is used for harder ones. In preferred embodiments, the Shore A scale is employed in connection with selection of a sealing member.

[0278] The Shore hardness is measured with a Durometer and sometimes referred to as "Durometer hardness." The hardness value is determined by the penetration of the Durometer indenter foot into the sample. Because of the resilience of rubbers and plastics, the indentation reading may change over time, so the indentation time is sometimes reported

along with the hardness number. The ASTM test method designation for the Shore Durometer hardness test is ASTM D2240. The results obtained from this test are a useful measure of relative resistance to indentation of various grades of polymers.

[0279] Using a durometer in the selection of a sealing member enables selection of a material with optimal durometer hardness that balances the advantages of a lower durometer hardness with the advantages of a higher durometer hardness. For example, when a guide tube (e.g., cannula) is utilized to maintain an opening in a silicone sealing member prior to sensor insertion, a compression set (e.g., some retention of a compressed shape caused by compression of the material over time) within the silicone can result due to compression over time of the sealing member by the guide tube. Compression set can also result from certain sterilization procedures (e.g., radiation sterilization such as electron beam or gamma radiation). Unfortunately, in some circumstances, the compression set of the sealing member may cause gaps or incompleteness of contact between the sealing member and the contacts and/or sensor. In general, a lower durometer hardness provides a better conformation (e.g., seal) surrounding the contacts and/or sensor as compared to a higher durometer hardness. Additionally, a lower durometer hardness enables a design wherein less force is required to create the seal (e.g., to snap the electronics unit into the mounting unit, for example, as in the embodiment illustrated in Fig. 4A) as compared to a higher durometer hardness, thereby increasing the ease of use of the device. However, the benefits of a lower durometer hardness silicone material must be balanced with potential disadvantages in manufacturing. For example, lower durometer hardness silicones are often produced by compounding with a silicone oil. In some circumstances, it is believed that some silicone oil may leach or migrate during manufacture and/or sterilization, which may corrupt aspects of the manufacturing process (e.g., adhesion of glues and/or effectiveness of coating processes). Additionally, a higher durometer hardness material generally provides greater stability of the material, which may reduce or avoid damage to the sealing member cause by pressure or other forces.

[0280] It is generally preferred that a sealing member **36** with a durometer hardness of from about 5 to about 80 Shore A is employed, more preferably a durometer hardness of from about 10 to about 50 Shore A, and even more preferably from about 20 to

about 50 Shore A. In one embodiment, of a transcutaneous analyte sensor, the sealing member is fabricated using a silicone of about 20 Shore A to maximize the conformance of the seal around the contacts and/or sensor while minimizing the force required to compress the silicone for that conformance. In another embodiment, the sealing member is formed from a silicone of about 50 Shore A so as to provide increased strength of the sealing member (e.g., its resistance to compression). While a few representative examples have been provided above, one skilled in the art appreciates that higher or lower durometer hardness sealing material may also be suitable for use.

[0281] In one alternative embodiment, a sealing member **36** with a durometer hardness of about 10 Shore A is used. In this embodiment, the sealing material tends to "weep" out, further increasing conformance of the seal against the adjacent parts. In another alternative embodiment, a sealing material with a durometer hardness of about 0 (zero) Shore A is used as a sealant and/or in combination with a sealant, also referred to as a lubricant, which in some embodiments is a hydrophobic fluid filling material such as a grease, silicone, petroleum jelly, or the like. Preferably, the sensor and/or contacts are encased in a housing that contains the sealant, causing the material to "squeeze" around contacts and/or sensor. Any suitable hydrophobic fluid filling material can be employed. Especially preferred are synthetic or petroleum hydrocarbon-based materials, silicone-based materials, ester-based greases, and other pharmaceutical-grade materials.

[0282] In some embodiments, the sealing member can comprise a material that has been modified to enhance the desirable properties of the sealing member **36**. For example, one or more filler materials or stiffening agents such as glass beads, polymer beads, composite beads, beads comprising various inert materials, carbon black, talc, titanium oxide, silicone dioxide, and the like. In some embodiments, the filler material is incorporated into the sealing member material to mechanically stiffen the sealing member. In general, however, use of a filler material or stiffening agent in the sealing member material can provide a variety of enhanced properties including increased modulus of elasticity, crosslink density, hardness, and stiffness, and decreased creep, for example. In some alternative embodiments, gases are chemically (or otherwise) injected into the sealing member material. For example, the sealing material can comprise a polymeric foam (e.g., a polyurethane foam,

a latex foam, a styrene-butadiene foam, and the like), or a dispersion of gas bubbles in a grease or jelly.

[0283] In alternative embodiments, the seal **36** is designed to form an interference fit with the electronics unit and can be formed from a variety of materials, for example, flexible plastics, or noble metals. One of ordinary skill in the art appreciates that a variety of designs can be employed to provide a seal surrounding electrical contacts such as described herein. For example, the contact holder **34** can be integrally designed as a part of the mounting unit, rather than as a separate piece thereof. Additionally or alternatively, a sealant can be provided in or around the sensor (*e.g.*, within or on the contact subassembly or sealing member), such as is described in more detail with reference to Figs 11A and 11B. In general, sealing materials with durometer hardnesses in the described ranges can provide improved sealing in a variety of sensor applications. For example, a sealing member as described in the preferred embodiments (e.g., selected using a durometer to ensure optimal durometer hardness, and the like) can be implemented adjacent to and/or to at least partially surrounding the sensor in a variety of sensor designs, including, for example, the sensor designs of the preferred embodiments, as well as a planar substrate such as described in U.S. Patent Number 6,175,752.

[0284] In the illustrated embodiment of Fig. 4A, the sealing member **36** is formed with a raised portion **37** surrounding the contacts **28**. The raised portion **37** enhances the interference fit surrounding the contacts **28** when the electronics unit **16** is mated to the mounting unit **14**. Namely, the raised portion surrounds each contact and presses against the electronics unit **16** to form a tight seal around the electronics unit. However, a variety of alternative sealing member configurations are described with reference to Figs. 4D to 4H, below.

[0285] Contacts **28** fit within the seal **36** and provide for electrical connection between the sensor **32** and the electronics unit **16**. In general, the contacts are designed to ensure a stable mechanical and electrical connection of the electrodes that form the sensor **32** (see Fig. 5A to 5C) to mutually engaging contacts **28** thereon. A stable connection can be provided using a variety of known methods, for example, domed metallic contacts, cantilevered fingers, pogo pins, or the like, as is appreciated by one skilled in the art.

[0286] In preferred embodiments, the contacts **28** are formed from a conductive elastomeric material, such as a carbon black elastomer, through which the sensor **32** extends (see Figs. 10B and 11B). Conductive elastomers are advantageously employed because their resilient properties create a natural compression against mutually engaging contacts, forming a secure press fit therewith. In some embodiments, conductive elastomers can be molded in such a way that pressing the elastomer against the adjacent contact performs a wiping action on the surface of the contact, thereby creating a cleaning action during initial connection. Additionally, in preferred embodiments, the sensor **32** extends through the contacts **28** wherein the sensor is electrically and mechanically secure by the relaxation of elastomer around the sensor (see Figs. 7A to 7D).

[0287] In an alternative embodiment, a conductive, stiff plastic forms the contacts, which are shaped to comply upon application of pressure (for example, a leaf-spring shape). Contacts of such a configuration can be used instead of a metallic spring, for example, and advantageously avoid the need for crimping or soldering through compliant materials; additionally, a wiping action can be incorporated into the design to remove contaminants from the surfaces during connection. Non-metallic contacts can be advantageous because of their seamless manufacturability, robustness to thermal compression, non-corrosive surfaces, and native resistance to electrostatic discharge (ESD) damage due to their higher-than-metal resistance.

[0288] Figs. 4B and 4C are perspective views of alternative contact configurations. Fig. 4B is an illustration of a narrow contact configuration. Fig. 4C is an illustration of a wide contact configuration. One skilled in the art appreciates that a variety of configurations are suitable for the contacts of the preferred embodiments, whether elastomeric, stiff plastic or other materials are used. In some circumstances, it can be advantageous to provide multiple contact configurations (such as illustrated in Figs. 4A to 4C) to differentiate sensors from each other. In other words, the architecture of the contacts can include one or more configurations each designed (keyed) to fit with a particular electronics unit. See section entitled "Differentiation of Sensor Systems" below, which describes systems and methods for differentiating (keying) sensor systems.

[0289] Figs. 4D to 4H are schematic cross-sectional views of a portion of the contact subassembly; namely, a variety of alternative embodiments of the sealing member **36** are illustrated. In each of these embodiments (e.g., Figs. 4D to 4H), a sensor **32** is shown, which is configured for operable connection to sensor electronics for measuring an analyte in a host such as described in more detail elsewhere herein. Additionally, two electrical contacts **28**, as described in more detail elsewhere herein, are configured to operably connect the sensor to the sensor electronics. Thus, the sealing member **36** in each of these alternative configurations (e.g., Figs. 4D to 4H) at least partially surrounds the sensor and/or the electrical contacts to seal the electrical contacts from moisture when the sensor is operably connected to the sensor electronics.

[0290] Fig. 4D is a schematic cross-sectional view of the sealing member **36** in an embodiment similar to Fig. 4A, including gaps **400** that are maintained when the one or more electrical contacts are operably connected to the sensor electronics. Preferably, these air gaps provide for some flexibility of the sealing member **36** to deform or compress to seal the electrical contacts **28** from moisture or other environmental effects.

[0291] In certain circumstances, such as during sensor insertion or needle/guide tube retraction (see Figs. 7A to 7D), a sealing member with a certain elasticity can be compressed or deformed by the insertion and/or retraction forces applied thereto. Accordingly in some embodiments, the sealing member is configured to be maintained (e.g., held substantially in place) on the housing (e.g., contact subassembly **26** or base **34**) without substantial translation, deformation, and/or compression (e.g., during sensor insertion). Fig. 4D illustrates one such implementation, wherein one or more depressions **402** are configured to receive mating protrusions (e.g., on the base **34** of the contact subassembly **26**, not shown). A variety of male-female or other such mechanical structures can be implemented to hold the sealing member in place, as is appreciated by one skilled in the art. In one alternative embodiment, an adhesive (not shown) is configured to adhere the sealing member **36** to the housing (e.g., base **34** of the contact subassembly **26**) to provide substantially the same benefit of holding the sealing member during sensor insertion/retraction without substantial deformation, as described in more detail, above. In another embodiment, the base **34** of the contact subassembly **26** (or equivalent structure) comprises reinforcing mechanical supports

configured to hold the sealing member as described above. One skilled in the art appreciates a variety of mechanical and/or chemical methods that can be implemented to maintain a sealing member substantially stationary (e.g., without substantial translation, deformation and/or compression) when compression and/or deformation forces are applied thereto. Although one exemplary embodiment is illustrated with reference to Fig. 4D, a wide variety of systems and methods for holding the sealing member can be implemented with a sealing member of any particular design.

[0292] Fig. 4E is a schematic cross-sectional view of the sealing member **36** in an alternative embodiment without gaps. In certain circumstances, full contact between mating members may be preferred.

[0293] In certain circumstances moisture may "wick" along the length of the sensor (e.g., from an exposed end) through the sealing member **36** to the contacts **28**. Fig. 4F is a schematic cross-sectional view of a sealing member **36** in an alternative embodiment wherein one or more gaps **400** are provided. In this embodiment, the gaps **400** extend into the sealing member and encompass at least a portion of the sensor **32**. The gaps **400** or "deep wells" of Fig. 4F are designed to interrupt the path that moisture may take, avoiding contact of the moisture at the contacts **28**. If moisture is able to travel along the path of the sensor, the abrupt change of surface tension at the opening **404** of the gap **400** in the sealing member **36** substantially deters the moisture from traveling to the contacts **28**.

[0294] Fig. 4G is a schematic cross-sectional view of the sealing member **36** in another alternative embodiment wherein one or more gaps **400** are provided. In this embodiment, the gaps extend from the bottom side of the sealing member **36**, which can be helpful in maintaining a stable position of the contacts **28** and/or reduces "pumping" of air gaps in some situations.

[0295] In some embodiments, gaps **400** can be filled by a sealant, which also may be referred to as a lubricant, for example, oil, grease, or gel. In one exemplary embodiment, the sealant includes petroleum jelly and is used to provide a moisture barrier surrounding the sensor. Referring to Fig. 4F, filling the gaps **400** with a sealant provides an additional moisture barrier to reduce or avoid moisture from traveling to the contacts **28**. Sealant can be used to fill gaps or crevices in any sealing member configuration.

[0296] In some sealing member configurations, it can be advantageous to provide a channel **406** through the sealing member **36** in order to create an additional pathway for sealant (e.g. lubricant) in order to expel air and/or to provide a path for excess sealant to escape. In some embodiments, more than one channel is provided.

[0297] Fig. 4H is a schematic cross-sectional view of a sealing member **36** in an alternative embodiment wherein a large gap **400** is provided between the sealing member upper portion **408** and the sealing member lower portion **410**. These portions **408**, **410** may or may not be connected; however, they are configured to sandwich the sensor and sealant (e.g., grease) therebetween. The sealing member **36** illustrated with reference to Fig. 4H can provide ease of manufacture and/or product assembly with a comprehensive sealing ability. Additional gaps (with or without sealant) can be provided in a variety of locations throughout the sealing member **36**; these additional gaps, for example, provide space for excess sealant.

Sensor

[0298] Preferably, the sensor **32** includes a distal portion **42**, also referred to as the *in vivo* portion, adapted to extend out of the mounting unit for insertion under the host's skin, and a proximal portion **40**, also referred to as an *ex vivo* portion, adapted to remain above the host's skin after sensor insertion and to operably connect to the electronics unit **16** via contacts **28**. Preferably, the sensor **32** includes two or more electrodes: a working electrode **44** and at least one additional electrode, which can function as a counter electrode and/or reference electrode, hereinafter referred to as the reference electrode **46**. A membrane system is preferably deposited over the electrodes, such as described in more detail with reference to Figs. 5A to 5C, below.

[0299] Fig. 5A is an expanded cutaway view of a proximal portion **40** of the sensor in one embodiment, showing working and reference electrodes. In the illustrated embodiments, the working and reference electrodes **44**, **46** extend through the contacts **28** to form electrical connection therewith (see Figs. 10B and 11B). Namely, the working electrode **44** is in electrical contact with one of the contacts **28** and the reference electrode **46** is in electrical contact with the other contact **28**, which in turn provides for electrical connection with the electronics unit **16** when it is mated with the mounting unit **14**. Mutually engaging electrical contacts permit operable connection of the sensor **32** to the electronics unit **16** when

connected to the mounting unit **14**; however other methods of electrically connecting the electronics unit **16** to the sensor **32** are also possible. In some alternative embodiments, for example, the reference electrode can be configured to extend from the sensor and connect to a contact at another location on the mounting unit (*e.g.*, non-coaxially). Detachable connection between the mounting unit **14** and electronics unit **16** provides improved manufacturability, namely, the relatively inexpensive mounting unit **14** can be disposed of when replacing the sensor system after its usable life, while the relatively more expensive electronics unit **16** can be reused with multiple sensor systems.

[0300] In alternative embodiments, the contacts **28** are formed into a variety of alternative shapes and/or sizes. For example, the contacts **28** can be discs, spheres, cuboids, and the like. Furthermore, the contacts **28** can be designed to extend from the mounting unit in a manner that causes an interference fit within a mating cavity or groove of the electronics unit, forming a stable mechanical and electrical connection therewith.

[0301] Fig. 5B is an expanded cutaway view of a distal portion of the sensor in one embodiment, showing working and reference electrodes. In preferred embodiments, the sensor is formed from a working electrode **44** and a reference electrode **46** helically wound around the working electrode **44**. An insulator **45** is disposed between the working and reference electrodes to provide necessary electrical insulation therebetween. Certain portions of the electrodes are exposed to enable electrochemical reaction thereon, for example, a window **43** can be formed in the insulator to expose a portion of the working electrode **44** for electrochemical reaction.

[0302] In preferred embodiments, each electrode is formed from a fine wire with a diameter of from about 0.001 or less to about 0.010 inches or more, for example, and is formed from, *e.g.*, a plated insulator, a plated wire, or bulk electrically conductive material. Although the illustrated electrode configuration and associated text describe one preferred method of forming a transcutaneous sensor, a variety of known transcutaneous sensor configurations can be employed with the transcutaneous analyte sensor system of the preferred embodiments, such as U.S. Patent No. 5,711,861 to Ward *et al.*, U.S. Patent No. 6,642,015 to Vachon *et al.*, U.S. Patent No. 6,654,625 to Say *et al.*, U.S. Patent 6,565,509 to Say *et al.* , U.S. Patent No. 6,514,718 to Heller, U.S. Patent No. 6,465,066 to Essenpreis *et*

al., U.S. Patent No. 6,214,185 to Offenbacher *et al.*, U.S. Patent No. 5,310,469 to Cunningham *et al.*, and U.S. Patent No. 5,683,562 to Shaffer *et al.*, U.S. Patent 6,579,690 to Bonnecaze *et al.*, U.S. Patent 6,484,046 to Say *et al.*, U.S. Patent 6,512,939 to Colvin *et al.*, U.S. Patent 6,424,847 to Mastrototaro *et al.*, U.S. Patent 6,424,847 to Mastrototaro et al, for example. All of the above patents are incorporated in their entirety herein by reference and are not inclusive of all applicable analyte sensors; in general, it should be understood that the disclosed embodiments are applicable to a variety of analyte sensor configurations. It is noted that much of the description of the preferred embodiments, for example the membrane system described below, can be implemented not only with *in vivo* sensors, but also with *in vitro* sensors, such as blood glucose meters (SMBG).

[0303] In preferred embodiments, the working electrode comprises a wire formed from a conductive material, such as platinum, platinum-iridium, palladium, graphite, gold, carbon, conductive polymer, alloys, or the like. Although the electrodes can by formed by a variety of manufacturing techniques (bulk metal processing, deposition of metal onto a substrate, or the like), it can be advantageous to form the electrodes from plated wire (*e.g.*, platinum on steel wire) or bulk metal (*e.g.*, platinum wire). It is believed that electrodes formed from bulk metal wire provide superior performance (*e.g.*, in contrast to deposited electrodes), including increased stability of assay, simplified manufacturability, resistance to contamination (*e.g.*, which can be introduced in deposition processes), and improved surface reaction (*e.g.*, due to purity of material) without peeling or delamination.

[0304] The working electrode **44** is configured to measure the concentration of an analyte. In an enzymatic electrochemical sensor for detecting glucose, for example, the working electrode measures the hydrogen peroxide produced by an enzyme catalyzed reaction of the analyte being detected and creates a measurable electronic current For example, in the detection of glucose wherein glucose oxidase produces hydrogen peroxide as a byproduct, hydrogen peroxide reacts with the surface of the working electrode producing two protons ($2H^+$), two electrons ($2e^-$) and one molecule of oxygen (O_2), which produces the electronic current being detected.

[0305] In preferred embodiments, the working electrode **44** is covered with an insulating material **45**, for example, a non-conductive polymer. Dip-coating, spray-coating,

vapor-deposition, or other coating or deposition techniques can be used to deposit the insulating material on the working electrode. In one embodiment, the insulating material comprises parylene, which can be an advantageous polymer coating for its strength, lubricity, and electrical insulation properties. Generally, parylene is produced by vapor deposition and polymerization of para-xylylene (or its substituted derivatives). While not wishing to be bound by theory, it is believed that the lubricious (e.g., smooth) coating (*e.g.*, parylene) on the sensors of the preferred embodiments contributes to minimal trauma and extended sensor life. Fig. 23 shows transcutaneous glucose sensor data and corresponding blood glucose values over approximately seven days in a human, wherein the transcutaneous glucose sensor data was formed with a parylene coating on at least a portion of the device. While parylene coatings are generally preferred, any suitable insulating material can be used, for example, fluorinated polymers, polyethyleneterephthalate, polyurethane, polyimide, other nonconducting polymers, or the like. Glass or ceramic materials can also be employed. Other materials suitable for use include surface energy modified coating systems such as are marketed under the trade names AMC18, AMC148, AMC141, and AMC321 by Advanced Materials Components Express of Bellafonte, PA. In some alternative embodiments, however, the working electrode may not require a coating of insulator.

[0306] The reference electrode **46**, which can function as a reference electrode alone, or as a dual reference and counter electrode, is formed from silver, silver/silver chloride, or the like. Preferably, the reference electrode **46** is juxtapositioned and/or twisted with or around the working electrode **44**; however other configurations are also possible (*e.g.*, an intradermal or on-skin reference electrode). In the illustrated embodiments, the reference electrode **46** is helically wound around the working electrode **44**. The assembly of wires is then optionally coated or adhered together with an insulating material, similar to that described above, so as to provide an insulating attachment.

[0307] In some embodiments, a silver wire is formed onto the sensor as described above, and subsequently chloridized to form silver/silver chloride reference electrode. Advantageously, chloridizing the silver wire as described herein enables the manufacture of a reference electrode with optimal *in vivo* performance. Namely, by controlling the quantity and amount of chloridization of the silver to form silver/silver chloride, improved break-in

time, stability of the reference electrode, and extended life has been shown with the preferred embodiments (see Figs. 22 and 23). Additionally, use of silver chloride as described above allows for relatively inexpensive and simple manufacture of the reference electrode.

[0308] In embodiments wherein an outer insulator is disposed, a portion of the coated assembly structure can be stripped or otherwise removed, for example, by hand, excimer lasing, chemical etching, laser ablation, grit-blasting (*e.g.*, with sodium bicarbonate or other suitable grit), or the like, to expose the electroactive surfaces. Alternatively, a portion of the electrode can be masked prior to depositing the insulator in order to maintain an exposed electroactive surface area. In one exemplary embodiment, grit blasting is implemented to expose the electroactive surfaces, preferably utilizing a grit material that is sufficiently hard to ablate the polymer material, while being sufficiently soft so as to minimize or avoid damage to the underlying metal electrode (*e.g.*, a platinum electrode). Although a variety of "grit" materials can be used (*e.g.*, sand, talc, walnut shell, ground plastic, sea salt, and the like), in some preferred embodiments, sodium bicarbonate is an advantageous grit-material because it is sufficiently hard to ablate, *e.g.*, a parylene coating without damaging, *e.g.*, an underlying platinum conductor. One additional advantage of sodium bicarbonate blasting includes its polishing action on the metal as it strips the polymer layer, thereby eliminating a cleaning step that might otherwise be necessary.

[0309] In the embodiment illustrated in Fig. 5B, a radial window **43** is formed through the insulating material **45** to expose a circumferential electroactive surface of the working electrode. Additionally, sections **41** of electroactive surface of the reference electrode are exposed. For example, the **41** sections of electroactive surface can be masked during deposition of an outer insulating layer or etched after deposition of an outer insulating layer.

[0310] In some applications, cellular attack or migration of cells to the sensor can cause reduced sensitivity and/or function of the device, particularly after the first day of implantation. However, when the exposed electroactive surface is distributed circumferentially about the sensor (*e.g.*, as in a radial window), the available surface area for reaction can be sufficiently distributed so as to minimize the effect of local cellular invasion of the sensor on the sensor signal. Alternatively, a tangential exposed electroactive window

can be formed, for example, by stripping only one side of the coated assembly structure. In other alternative embodiments, the window can be provided at the tip of the coated assembly structure such that the electroactive surfaces are exposed at the tip of the sensor. Other methods and configurations for exposing electroactive surfaces can also be employed.

[0311] In some embodiments, the working electrode has a diameter of from about 0.001 inches or less to about 0.010 inches or more, preferably from about 0.002 inches to about 0.008 inches, and more preferably from about 0.004 inches to about 0.005 inches. The length of the window can be from about 0.1 mm (about 0.004 inches) or less to about 2 mm (about 0.078 inches) or more, and preferably from about 0.5 mm (about 0.02 inches) to about 0.75 mm (0.03 inches). In such embodiments, the exposed surface area of the working electrode is preferably from about 0.000013 in^2 (0.0000839cm^2) or less to about 0.0025 in^2 (0.016129 cm^2) or more (assuming a diameter of from about 0.001 inches to about 0.010 inches and a length of from about 0.004 inches to about 0.078 inches). The preferred exposed surface area of the working electrode is selected to produce an analyte signal with a current in the picoAmp range, such as is described in more detail elsewhere herein. However, a current in the picoAmp range can be dependent upon a variety of factors, for example the electronic circuitry design (*e.g.*, sample rate, current draw, A/D converter bit resolution, etc.), the membrane system (*e.g.*, permeability of the analyte through the membrane system), and the exposed surface area of the working electrode. Accordingly, the exposed electroactive working electrode surface area can be selected to have a value greater than or less than the above-described ranges taking into consideration alterations in the membrane system and/or electronic circuitry. In preferred embodiments of a glucose sensor, it can be advantageous to minimize the surface area of the working electrode while maximizing the diffusivity of glucose in order to optimize the signal-to-noise ratio while maintaining sensor performance in both high and low glucose concentration ranges.

[0312] In some alternative embodiments, the exposed surface area of the working (and/or other) electrode can be increased by altering the cross-section of the electrode itself. For example, in some embodiments the cross-section of the working electrode can be defined by a cross, star, cloverleaf, ribbed, dimpled, ridged, irregular, or other non-circular configuration; thus, for any predetermined length of electrode, a specific increased surface

area can be achieved (as compared to the area achieved by a circular cross-section). Increasing the surface area of the working electrode can be advantageous in providing an increased signal responsive to the analyte concentration, which in turn can be helpful in improving the signal-to-noise ratio, for example.

[0313] In some alternative embodiments, additional electrodes can be included within the assembly, for example, a three-electrode system (working, reference, and counter electrodes) and/or an additional working electrode (*e.g.*, an electrode which can be used to generate oxygen, which is configured as a baseline subtracting electrode, or which is configured for measuring additional analytes). U.S. Publication No. US-2005-0161346-A1 and U.S. Publication No. US-2005-0143635-A1 describe some systems and methods for implementing and using additional working, counter, and/or reference electrodes. In one implementation wherein the sensor comprises two working electrodes, the two working electrodes are juxtapositioned (*e.g.*, extend parallel to each other), around which the reference electrode is disposed (*e.g.*, helically wound). In some embodiments wherein two or more working electrodes are provided, the working electrodes can be formed in a double-, triple-, quad-, etc. helix configuration along the length of the sensor (for example, surrounding a reference electrode, insulated rod, or other support structure). The resulting electrode system can be configured with an appropriate membrane system, wherein the first working electrode is configured to measure a first signal comprising glucose and baseline and the additional working electrode is configured to measure a baseline signal consisting of baseline only (*e.g.*, configured to be substantially similar to the first working electrode without an enzyme disposed thereon). In this way, the baseline signal can be subtracted from the first signal to produce a glucose-only signal that is substantially not subject to fluctuations in the baseline and/or interfering species on the signal.

[0314] Although the preferred embodiments illustrate one electrode configuration including one bulk metal wire helically wound around another bulk metal wire, other electrode configurations are also contemplated. In an alternative embodiment, the working electrode comprises a tube with a reference electrode disposed or coiled inside, including an insulator therebetween. Alternatively, the reference electrode comprises a tube with a working electrode disposed or coiled inside, including an insulator therebetween. In another

alternative embodiment, a polymer (*e.g.*, insulating) rod is provided, wherein the electrodes are deposited (*e.g.*, electro-plated) thereon. In yet another alternative embodiment, a metallic (*e.g.*, steel) rod is provided, coated with an insulating material, onto which the working and reference electrodes are deposited. In yet another alternative embodiment, one or more working electrodes are helically wound around a reference electrode.

[0315] Preferably, the electrodes and membrane systems of the preferred embodiments are coaxially formed, namely, the electrodes and/or membrane system all share the same central axis. While not wishing to be bound by theory, it is believed that a coaxial design of the sensor enables a symmetrical design without a preferred bend radius. Namely, in contrast to prior art sensors comprising a substantially planar configuration that can suffer from regular bending about the plane of the sensor, the coaxial design of the preferred embodiments do not have a preferred bend radius and therefore are not subject to regular bending about a particular plane (which can cause fatigue failures and the like). However, non-coaxial sensors can be implemented with the sensor system of the preferred embodiments.

[0316] In addition to the above-described advantages, the coaxial sensor design of the preferred embodiments enables the diameter of the connecting end of the sensor (proximal portion) to be substantially the same as that of the sensing end (distal portion) such that the needle is able to insert the sensor into the host and subsequently slide back over the sensor and release the sensor from the needle, without slots or other complex multi-component designs.

[0317] In one such alternative embodiment, the two wires of the sensor are held apart and configured for insertion into the host in proximal but separate locations. The separation of the working and reference electrodes in such an embodiment can provide additional electrochemical stability with simplified manufacture and electrical connectivity. It is appreciated by one skilled in the art that a variety of electrode configurations can be implemented with the preferred embodiments.

[0318] In some embodiments, the sensor includes an antimicrobial portion configured to extend through the exit-site when the sensor is implanted in the host. Namely, the sensor is designed with *in vivo* and *ex vivo* portions as described in more detail elsewhere

herein; additionally, the sensor comprises a transition portion, also referred to as an antimicrobial portion, located between the *in vivo* and *ex vivo* portions **42**, **40**. The antimicrobial portion is designed to provide antimicrobial effects to the exit-site and adjacent tissue when implanted in the host.

[0319] In some embodiments, the antimicrobial portion comprises silver, *e.g.*, the portion of a silver reference electrode that is configured to extend through the exit-site when implanted. Although exit-site infections are a common adverse occurrence associated with some conventional transcutaneous medical devices, the devices of preferred embodiments are designed at least in part to minimize infection, to minimize irritation, and/or to extend the duration of implantation of the sensor by utilizing a silver reference electrode to extend through the exit-site when implanted in a patient. While not wishing to be bound by theory, it is believed that the silver may reduce local tissue infections (within the tissue and at the exit-site); namely, steady release of molecular quantities of silver is believed to have an antimicrobial effect in biological tissue (*e.g.*, reducing or preventing irritation and infection), also referred to as passive antimicrobial effects. Although one example of passive antimicrobial effects is described herein, one skilled in the art can appreciate a variety of passive anti-microbial systems and methods that can be implemented with the preferred embodiments. Additionally, it is believed that antimicrobial effects can contribute to extended life of a transcutaneous analyte sensor, enabling a functional lifetime past a few days, *e.g.*, seven days or longer. Fig. 23 shows transcutaneous glucose sensor data and corresponding blood glucose values over approximately seven days in a human, wherein the transcutaneous glucose sensor data was formed with a silver transition portion that extended through the exit-site after sensor implantation.

[0320] In some embodiments, active antimicrobial systems and methods are provided in the sensor system in order to further enhance the antimicrobial effects at the exit-site. In one such embodiment, an auxiliary silver wire is disposed on or around the sensor, wherein the auxiliary silver wire is connected to electronics and configured to pass a current sufficient to enhance its antimicrobial properties (active antimicrobial effects), as is appreciated by one skilled in the art. The current can be passed continuously or intermittently, such that sufficient antimicrobial properties are provided. Although one

example of active antimicrobial effects is described herein, one skilled in the art can appreciate a variety of active anti-microbial systems and methods that can be implemented with the preferred embodiments.

Anchoring Mechanism

[0321] It is preferred that the sensor remains substantially stationary within the tissue of the host, such that migration or motion of the sensor with respect to the surrounding tissue is minimized. Migration or motion is believed to cause inflammation at the sensor implant site due to irritation, and can also cause noise on the sensor signal due to motion-related artifact, for example. Therefore, it can be advantageous to provide an anchoring mechanism that provides support for the sensor's *in vivo* portion to avoid the above-mentioned problems. Combining advantageous sensor geometry with an advantageous anchoring minimizes additional parts and allows for an optimally small or low profile design of the sensor. In one embodiment the sensor includes a surface topography, such as the helical surface topography provided by the reference electrode surrounding the working electrode. In alternative embodiments, a surface topography could be provided by a roughened surface, porous surface (*e.g.* porous parylene), ridged surface, or the like. Additionally (or alternatively), the anchoring can be provided by prongs, spines, barbs, wings, hooks, a bulbous portion (for example, at the distal end), an S-bend along the sensor, a rough surface topography, a gradually changing diameter, combinations thereof, or the like, which can be used alone or in combination with the helical surface topography to stabilize the sensor within the subcutaneous tissue.

Variable Stiffness

[0322] As described above, conventional transcutaneous devices are believed to suffer from motion artifact associated with host movement when the host is using the device. For example, when a transcutaneous analyte sensor is inserted into the host, various movements on the sensor (for example, relative movement within and between the subcutaneous space, dermis, skin, and external portions of the sensor) create stresses on the device, which is known to produce artifacts on the sensor signal. Accordingly, there are different design considerations (for example, stress considerations) on various sections of the sensor. For example, the distal portion **42** of the sensor can benefit in general from greater

flexibility as it encounters greater mechanical stresses caused by movement of the tissue within the patient and relative movement between the *in vivo* and *ex vivo* portions of the sensor. On the other hand, the proximal portion **40** of the sensor can benefit in general from a stiffer, more robust design to ensure structural integrity and/or reliable electrical connections. Additionally, in some embodiments wherein a needle is retracted over the proximal portion **40** of the device (see Figs. 6 to 8), a stiffer design can minimize crimping of the sensor and/or ease in retraction of the needle from the sensor. Thus, by designing greater flexibility into the *in vivo* (distal) portion **42**, the flexibility is believed to compensate for patient movement, and noise associated therewith. By designing greater stiffness into the *ex vivo* (proximal) portion **40**, column strength (for retraction of the needle over the sensor), electrical connections, and integrity can be enhanced. In some alternative embodiments, a stiffer distal end and/or a more flexible proximal end can be advantageous as described in U.S. Publication No. US-2006-0015024-A1.

[0323] The preferred embodiments provide a distal portion **42** of the sensor **32** designed to be more flexible than a proximal portion **40** of the sensor. The variable stiffness of the preferred embodiments can be provided by variable pitch of any one or more helically wound wires of the device, variable cross-section of any one or more wires of the device, and/or variable hardening and/or softening of any one or more wires of the device, such as is described in more detail with reference to U.S. Publication No. US-2006-0015024-A1.

Membrane System

[0324] Fig. 5C is a cross-sectional view through the sensor on line C-C of Fig. 5B showing the exposed electroactive surface of the working electrode surrounded by the membrane system in one embodiment. Preferably, a membrane system is deposited over at least a portion of the electroactive surfaces of the sensor **32** (working electrode and optionally reference electrode) and provides protection of the exposed electrode surface from the biological environment, diffusion resistance (limitation) of the analyte if needed, a catalyst for enabling an enzymatic reaction, limitation or blocking of interferents, and/or hydrophilicity at the electrochemically reactive surfaces of the sensor interface. Some examples of suitable membrane systems are described in U.S. Publication No. US-2005-0245799-A1.

[0325] In general, the membrane system includes a plurality of domains, for example, an electrode domain **47**, an interference domain **48**, an enzyme domain **49** (for example, including glucose oxidase), and a resistance domain **50**, as shown in Fig. 5C, and can include a high oxygen solubility domain, and/or a bioprotective domain (not shown), such as is described in more detail in U.S. Publication No. US-2005-0245799-A1, and such as is described in more detail below. The membrane system can be deposited on the exposed electroactive surfaces using known thin film techniques (for example, vapor deposition, spraying, electro-depositing, dipping, or the like). In alternative embodiments, however, other vapor deposition processes (e.g., physical and/or chemical vapor deposition processes) can be useful for providing one or more of the insulating and/or membrane layers, including ultrasonic vapor deposition, electrostatic deposition, evaporative deposition, deposition by sputtering, pulsed laser deposition, high velocity oxygen fuel deposition, thermal evaporator deposition, electron beam evaporator deposition, deposition by reactive sputtering molecular beam epitaxy, atmospheric pressure chemical vapor deposition (CVD), atomic layer CVD, hot wire CVD, low-pressure CVD, microwave plasma-assisted CVD, plasma-enhanced CVD, rapid thermal CVD, remote plasma-enhanced CVD, and ultra-high vacuum CVD, for example. However, the membrane system can be disposed over (or deposited on) the electroactive surfaces using any known method, as will be appreciated by one skilled in the art.

[0326] In some embodiments, one or more domains of the membrane systems are formed from materials such as described above in connection with the porous layer, such as silicone, polytetrafluoroethylene, polyethylene-co-tetrafluoroethylene, polyolefin, polyester, polycarbonate, biostable polytetrafluoroethylene, homopolymers, copolymers, terpolymers of polyurethanes, polypropylene (PP), polyvinylchloride (PVC), polyvinylidene fluoride (PVDF), polybutylene terephthalate (PBT), polymethylmethacrylate (PMMA), polyether ether ketone (PEEK), polyurethanes, cellulosic polymers, polysulfones and block copolymers thereof including, for example, di-block, tri-block, alternating, random and graft copolymers. U.S. Publication No. US-2005-0245799-A1 describes biointerface and membrane system configurations and materials that may be applied to the preferred embodiments.

Electrode Domain

[0327] In selected embodiments, the membrane system comprises an electrode domain. The electrode domain **47** is provided to ensure that an electrochemical reaction occurs between the electroactive surfaces of the working electrode and the reference electrode, and thus the electrode domain **47** is preferably situated more proximal to the electroactive surfaces than the interference and/or enzyme domain. Preferably, the electrode domain includes a coating that maintains a layer of water at the electrochemically reactive surfaces of the sensor. In other words, the electrode domain is present to provide an environment between the surfaces of the working electrode and the reference electrode which facilitates an electrochemical reaction between the electrodes. For example, a humectant in a binder material can be employed as an electrode domain; this allows for the full transport of ions in the aqueous environment. The electrode domain can also assist in stabilizing the operation of the sensor by accelerating electrode start-up and drifting problems caused by inadequate electrolyte. The material that forms the electrode domain can also provide an environment that protects against pH-mediated damage that can result from the formation of a large pH gradient due to the electrochemical activity of the electrodes.

[0328] In one embodiment, the electrode domain **47** includes a flexible, water-swellable, hydrogel film having a "dry film" thickness of from about 0.05 micron or less to about 20 microns or more, more preferably from about 0.05, 0.1, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45, 0.5, 1, 1.5, 2, 2.5, 3, or 3.5 microns to about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 19.5 microns, and more preferably still from about 2, 2.5 or 3 microns to about 3.5, 4, 4.5, or 5 microns. "Dry film" thickness refers to the thickness of a cured film cast from a coating formulation by standard coating techniques.

[0329] In certain embodiments, the electrode domain **47** is formed of a curable mixture of a urethane polymer and a hydrophilic polymer. Particularly preferred coatings are formed of a polyurethane polymer having carboxylate or hydroxyl functional groups and non-ionic hydrophilic polyether segments, wherein the polyurethane polymer is crosslinked with a water soluble carbodiimide (*e.g.*, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC)) in the presence of polyvinylpyrrolidone and cured at a moderate temperature of about 50°C.

[0330] In some preferred embodiments, the electrode domain **47** is formed from a hydrophilic polymer such as polyvinylpyrrolidone (PVP). An electrode domain formed from

PVP has been shown to reduce break-in time of analyte sensors; for example, a glucose sensor utilizing a cellulosic-based interference domain such as described in more detail below.

[0331] Preferably, the electrode domain is deposited by vapor deposition, spray coating, dip coating, or other thin film techniques on the electroactive surfaces of the sensor. In one preferred embodiment, the electrode domain is formed by dip-coating the electroactive surfaces in an electrode layer solution and curing the domain for a time of from about 15 minutes to about 30 minutes at a temperature of from about 40°C to about 55°C (and can be accomplished under vacuum (*e.g.*, 20 to 30 mmHg)). In embodiments wherein dip-coating is used to deposit the electrode domain, a preferred insertion rate of from about 1 to about 3 inches per minute into the electrode layer solution, with a preferred dwell time of from about 0.5 to about 2 minutes in the electrode layer solution, and a preferred withdrawal rate of from about 0.25 to about 2 inches per minute from the electrode layer solution provide a functional coating. However, values outside of those set forth above can be acceptable or even desirable in certain embodiments, for example, depending upon solution viscosity and solution surface tension, as is appreciated by one skilled in the art. In one embodiment, the electroactive surfaces of the electrode system are dip-coated one time (one layer) and cured at 50°C under vacuum for 20 minutes.

[0332] Although an independent electrode domain **47** is described herein, in some embodiments sufficient hydrophilicity can be provided in the interference domain and/or enzyme domain (the domain adjacent to the electroactive surfaces) so as to provide for the full transport of ions in the aqueous environment (*e.g.* without a distinct electrode domain). In these embodiments, an electrode domain is not necessary.

Interference Domain

[0333] Interferents are molecules or other species that are reduced or oxidized at the electrochemically reactive surfaces of the sensor, either directly or via an electron transfer agent, to produce a false positive analyte signal. In preferred embodiments, an interference domain **48** is provided that substantially restricts, resists, or blocks the flow of one or more interfering species. Some known interfering species for a glucose sensor, as described in more detail above, include acetaminophen, ascorbic acid, bilirubin, cholesterol, creatinine,

dopamine, ephedrine, ibuprofen, L-dopa, methyl dopa, salicylate, tetracycline, tolazamide, tolbutamide, triglycerides, and uric acid. In general, the interference domain of the preferred embodiments is less permeable to one or more of the interfering species than to the analyte, e.g., glucose.

[0334] In one embodiment, the interference domain **48** is formed from one or more cellulosic derivatives. In general, cellulosic derivatives include polymers such as cellulose acetate, cellulose acetate butyrate, 2-hydroxyethyl cellulose, cellulose acetate phthalate, cellulose acetate propionate, cellulose acetate trimellitate, and the like.

[0335] In one preferred embodiment, the interference domain **48** is formed from cellulose acetate butyrate. Cellulose acetate butyrate with a molecular weight of about 10,000 daltons to about 75,000 daltons, preferably from about 15,000, 20,000, or 25,000 daltons to about 50,000, 55,000, 60,000, 65,000, or 70,000 daltons, and more preferably about 20,000 daltons is employed. In certain embodiments, however, higher or lower molecular weights can be preferred. Additionally, a casting solution or dispersion of cellulose acetate butyrate at a weight percent of about 15% to about 25%, preferably from about 15%, 16%, 17%, 18%, 19% to about 20%, 21%, 22%, 23%, 24% or 25%, and more preferably about 18% is preferred. Preferably, the casting solution includes a solvent or solvent system, for example an acetone:ethanol solvent system. Higher or lower concentrations can be preferred in certain embodiments. A plurality of layers of cellulose acetate butyrate can be advantageously combined to form the interference domain in some embodiments, for example, three layers can be employed. It can be desirable to employ a mixture of cellulose acetate butyrate components with different molecular weights in a single solution, or to deposit multiple layers of cellulose acetate butyrate from different solutions comprising cellulose acetate butyrate of different molecular weights, different concentrations, and/or different chemistries (e.g., functional groups). It can also be desirable to include additional substances in the casting solutions or dispersions, e.g., functionalizing agents, crosslinking agents, other polymeric substances, substances capable of modifying the hydrophilicity/hydrophobicity of the resulting layer, and the like.

[0336] In one alternative embodiment, the interference domain **48** is formed from cellulose acetate. Cellulose acetate with a molecular weight of about 30,000 daltons or less

to about 100,000 daltons or more, preferably from about 35,000, 40,000, or 45,000 daltons to about 55,000, 60,000, 65,000, 70,000, 75,000, 80,000, 85,000, 90,000, or 95,000 daltons, and more preferably about 50,000 daltons is preferred. Additionally, a casting solution or dispersion of cellulose acetate at a weight percent of about 3% to about 10%, preferably from about 3.5%, 4.0%, 4.5%, 5.0%, 5.5%, 6.0%, or 6.5% to about 7.5%, 8.0%, 8.5%, 9.0%, or 9.5%, and more preferably about 8% is preferred. In certain embodiments, however, higher or lower molecular weights and/or cellulose acetate weight percentages can be preferred. It can be desirable to employ a mixture of cellulose acetates with molecular weights in a single solution, or to deposit multiple layers of cellulose acetate from different solutions comprising cellulose acetates of different molecular weights, different concentrations, or different chemistries (e.g., functional groups). It can also be desirable to include additional substances in the casting solutions or dispersions such as described in more detail above.

[0337] Layer(s) prepared from combinations of cellulose acetate and cellulose acetate butyrate, or combinations of layer(s) of cellulose acetate and layer(s) of cellulose acetate butyrate can also be employed to form the interference domain **48**.

[0338] In some alternative embodiments, additional polymers, such as Nafion®, can be used in combination with cellulosic derivatives to provide equivalent and/or enhanced function of the interference domain **48**. As one example, a 5 wt % Nafion® casting solution or dispersion can be used in combination with a 8 wt % cellulose acetate casting solution or dispersion, e.g., by dip coating at least one layer of cellulose acetate and subsequently dip coating at least one layer Nafion® onto a needle-type sensor such as described with reference to the preferred embodiments. Any number of coatings or layers formed in any order may be suitable for forming the interference domain of the preferred embodiments.

[0339] In some alternative embodiments, more than one cellulosic derivative can be used to form the interference domain **48** of the preferred embodiments. In general, the formation of the interference domain on a surface utilizes a solvent or solvent system in order to solvate the cellulosic derivative (or other polymer) prior to film formation thereon. In preferred embodiments, acetone and ethanol are used as solvents for cellulose acetate; however one skilled in the art appreciates the numerous solvents that are suitable for use with cellulosic derivatives (and other polymers). Additionally, one skilled in the art appreciates

that the preferred relative amounts of solvent can be dependent upon the cellulosic derivative (or other polymer) used, its molecular weight, its method of deposition, its desired thickness, and the like. However, a percent solute of from about 1% to about 25% is preferably used to form the interference domain solution so as to yield an interference domain having the desired properties. The cellulosic derivative (or other polymer) used, its molecular weight, method of deposition, and desired thickness can be adjusted, depending upon one or more other of the parameters, and can be varied accordingly as is appreciated by one skilled in the art.

[0340] In some alternative embodiments, other polymer types that can be utilized as a base material for the interference domain **48** including polyurethanes, polymers having pendant ionic groups, and polymers having controlled pore size, for example. In one such alternative embodiment, the interference domain includes a thin, hydrophobic membrane that is non-swellable and restricts diffusion of low molecular weight species. The interference domain **48** is permeable to relatively low molecular weight substances, such as hydrogen peroxide, but restricts the passage of higher molecular weight substances, including glucose and ascorbic acid. Other systems and methods for reducing or eliminating interference species that can be applied to the membrane system of the preferred embodiments are described in U.S. Publication No. US-2005-0115832-A1, U.S. Publication No. US-2005-0176136-A1, U.S. Publication No. US-2005-0161346-A1, and U.S. Publication No. US-2005-0143635-A1. In some alternative embodiments, a distinct interference domain is not included.

[0341] In preferred embodiments, the interference domain **48** is deposited directly onto the electroactive surfaces of the sensor for a domain thickness of from about 0.05 micron or less to about 20 microns or more, more preferably from about 0.05, 0.1, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45, 0.5, 1, 1.5, 2, 2.5, 3, or 3.5 microns to about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 19.5 microns, and more preferably still from about 1, 1.5 or 2 microns to about 2.5 or 3 microns. Thicker membranes can also be desirable in certain embodiments, but thinner membranes are generally preferred because they have a lower impact on the rate of diffusion of hydrogen peroxide from the enzyme membrane to the electrodes.

[0342] In general, the membrane systems of the preferred embodiments can be formed and/or deposited on the exposed electroactive surfaces (*e.g.*, one or more of the working and reference electrodes) using known thin film techniques (for example, casting, spray coating, drawing down, electro-depositing, dip coating, and the like), however casting or other known application techniques can also be utilized. Preferably, the interference domain is deposited by vapor deposition, spray coating, or dip coating. In one exemplary embodiment of a needle-type (transcutaneous) sensor such as described herein, the interference domain is formed by dip coating the sensor into an interference domain solution using an insertion rate of from about 20 inches/min to about 60 inches/min, preferably 40 inches/min, a dwell time of from about 0 minute to about 5 seconds, preferably 0 seconds, and a withdrawal rate of from about 20 inches/minute to about 60 inches/minute, preferably about 40 inches/minute, and curing (drying) the domain from about 1 minute to about 30 minutes, preferably from about 3 minutes to about 15 minutes (and can be accomplished at room temperature or under vacuum (*e.g.*, 20 to 30 mmHg)). In one exemplary embodiment including cellulose acetate butyrate interference domain, a 3-minute cure (i.e., dry) time is preferred between each layer applied. In another exemplary embodiment employing a cellulose acetate interference domain, a 15 minute cure (i.e., dry) time is preferred between each layer applied.

[0343] The dip process can be repeated at least one time and up to 10 times or more. The preferred number of repeated dip processes depends upon the cellulosic derivative(s) used, their concentration, conditions during deposition (e.g., dipping) and the desired thickness (*e.g.*, sufficient thickness to provide functional blocking of (or resistance to) certain interferents), and the like. In some embodiments, 1 to 3 microns may be preferred for the interference domain thickness; however, values outside of these can be acceptable or even desirable in certain embodiments, for example, depending upon viscosity and surface tension, as is appreciated by one skilled in the art. In one exemplary embodiment, an interference domain is formed from three layers of cellulose acetate butyrate. In another exemplary embodiment, an interference domain is formed from 10 layers of cellulose acetate. In alternative embodiments, the interference domain can be formed using any known method

and combination of cellulose acetate and cellulose acetate butyrate, as will be appreciated by one skilled in the art.

[0344] In some embodiments, the electroactive surface can be cleaned prior to application of the interference domain **48**. In some embodiments, the interference domain **48** of the preferred embodiments can be useful as a bioprotective or biocompatible domain, namely, a domain that interfaces with host tissue when implanted in an animal (*e.g.*, a human) due to its stability and biocompatibility.

Enzyme Domain

[0345] In preferred embodiments, the membrane system further includes an enzyme domain **49** disposed more distally from the electroactive surfaces than the interference domain 48; however other configurations can be desirable. In the preferred embodiments, the enzyme domain provides an enzyme to catalyze the reaction of the analyte and its co-reactant, as described in more detail below. In the preferred embodiments of a glucose sensor, the enzyme domain includes glucose oxidase; however other oxidases, for example, galactose oxidase or uricase oxidase, can also be used.

[0346] For an enzyme-based electrochemical glucose sensor to perform well, the sensor's response is preferably limited by neither enzyme activity nor co-reactant concentration. Because enzymes, including glucose oxidase, are subject to deactivation as a function of time even in ambient conditions, this behavior is compensated for in forming the enzyme domain. Preferably, the enzyme domain is constructed of aqueous dispersions of colloidal polyurethane polymers including the enzyme. However, in alternative embodiments the enzyme domain is constructed from an oxygen enhancing material, for example, silicone, or fluorocarbon, in order to provide a supply of excess oxygen during transient ischemia. Preferably, the enzyme is immobilized within the domain. See, e.g., U.S. Patent Application Number 10/896,639 filed on July 21, 2004 and entitled "Oxygen Enhancing Membrane Systems for Implantable Device."

[0347] In preferred embodiments, the enzyme domain is deposited onto the interference domain for a domain thickness of from about 0.05 micron or less to about 20 microns or more, more preferably from about 0.05, 0.1, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45, 0.5, 1, 1.5, 2, 2.5, 3, or 3.5 microns to about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,

19, or 19.5 microns, and more preferably still from about 2, 2.5 or 3 microns to about 3.5, 4, 4.5, or 5 microns. However in some embodiments, the enzyme domain can be deposited directly onto the electroactive surfaces. Preferably, the enzyme domain is deposited by spray or dip coating. In one embodiment of needle-type (transcutaneous) sensor such as described herein, the enzyme domain is formed by dip coating the interference domain coated sensor into an enzyme domain solution and curing the domain for from about 15 to about 30 minutes at a temperature of from about 40°C to about 55°C (and can be accomplished under vacuum (*e.g.*, 20 to 30 mmHg)). In embodiments wherein dip coating is used to deposit the enzyme domain at room temperature, a preferred insertion rate of from about 0.25 inch per minute to about 3 inches per minute, with a preferred dwell time of from about 0.5 minutes to about 2 minutes, and a preferred withdrawal rate of from about 0.25 inch per minute to about 2 inches per minute provides a functional coating. However, values outside of those set forth above can be acceptable or even desirable in certain embodiments, for example, depending upon viscosity and surface tension, as is appreciated by one skilled in the art. In one embodiment, the enzyme domain is formed by dip coating two times (namely, forming two layers) in an enzyme domain solution and curing at 50°C under vacuum for 20 minutes. However, in some embodiments, the enzyme domain can be formed by dip coating and/or spray coating one or more layers at a predetermined concentration of the coating solution, insertion rate, dwell time, withdrawal rate, and/or desired thickness.

Resistance Domain

[0348] In preferred embodiments, the membrane system includes a resistance domain **50** disposed more distal from the electroactive surfaces than the enzyme domain. Although the following description is directed to a resistance domain for a glucose sensor, the resistance domain can be modified for other analytes and co-reactants as well.

[0349] There exists a molar excess of glucose relative to the amount of oxygen in blood; that is, for every free oxygen molecule in extracellular fluid, there are typically more than 100 glucose molecules present (see Updike *et al.*, Diabetes Care 5:207-21(1982)). However, an immobilized enzyme-based glucose sensor employing oxygen as co-reactant is preferably supplied with oxygen in non-rate-limiting excess in order for the sensor to respond linearly to changes in glucose concentration, while not responding to changes in oxygen

concentration. Specifically, when a glucose-monitoring reaction is oxygen limited, linearity is not achieved above minimal concentrations of glucose. Without a semipermeable membrane situated over the enzyme domain to control the flux of glucose and oxygen, a linear response to glucose levels can be obtained only for glucose concentrations of up to about 40 mg/dL. However, in a clinical setting, a linear response to glucose levels is desirable up to at least about 400 mg/dL.

[0350] The resistance domain includes a semipermeable membrane that controls the flux of oxygen and glucose to the underlying enzyme domain, preferably rendering oxygen in a non-rate-limiting excess. As a result, the upper limit of linearity of glucose measurement is extended to a much higher value than that which is achieved without the resistance domain. In one embodiment, the resistance domain exhibits an oxygen to glucose permeability ratio of from about 50:1 or less to about 400:1 or more, preferably about 200:1. As a result, one-dimensional reactant diffusion is adequate to provide excess oxygen at all reasonable glucose and oxygen concentrations found in the subcutaneous matrix (See Rhodes *et al.*, Anal. Chem., 66:1520-1529 (1994)).

[0351] In alternative embodiments, a lower ratio of oxygen-to-glucose can be sufficient to provide excess oxygen by using a high oxygen solubility domain (for example, a silicone or fluorocarbon-based material or domain) to enhance the supply/transport of oxygen to the enzyme domain. If more oxygen is supplied to the enzyme, then more glucose can also be supplied to the enzyme without creating an oxygen rate-limiting excess. In alternative embodiments, the resistance domain is formed from a silicone composition, such as is described in U.S. Publication No. US-2005-0090607-A1.

[0352] In a preferred embodiment, the resistance domain includes a polyurethane membrane with both hydrophilic and hydrophobic regions to control the diffusion of glucose and oxygen to an analyte sensor, the membrane being fabricated easily and reproducibly from commercially available materials. A suitable hydrophobic polymer component is a polyurethane, or polyetherurethaneurea. Polyurethane is a polymer produced by the condensation reaction of a diisocyanate and a difunctional hydroxyl-containing material. A polyurethaneurea is a polymer produced by the condensation reaction of a diisocyanate and a difunctional amine-containing material. Preferred diisocyanates include aliphatic

diisocyanates containing from about 4 to about 8 methylene units. Diisocyanates containing cycloaliphatic moieties can also be useful in the preparation of the polymer and copolymer components of the membranes of preferred embodiments. The material that forms the basis of the hydrophobic matrix of the resistance domain can be any of those known in the art as appropriate for use as membranes in sensor devices and as having sufficient permeability to allow relevant compounds to pass through it, for example, to allow an oxygen molecule to pass through the membrane from the sample under examination in order to reach the active enzyme or electrochemical electrodes. Examples of materials which can be used to make non-polyurethane type membranes include vinyl polymers, polyethers, polyesters, polyamides, inorganic polymers such as polysiloxanes and polycarbosiloxanes, natural polymers such as cellulosic and protein based materials, and mixtures or combinations thereof.

[0353] In a preferred embodiment, the hydrophilic polymer component is polyethylene oxide. For example, one useful hydrophobic-hydrophilic copolymer component is a polyurethane polymer that includes about 20% hydrophilic polyethylene oxide. The polyethylene oxide portions of the copolymer are thermodynamically driven to separate from the hydrophobic portions of the copolymer and the hydrophobic polymer component. The 20% polyethylene oxide-based soft segment portion of the copolymer used to form the final blend affects the water pick-up and subsequent glucose permeability of the membrane.

[0354] In preferred embodiments, the resistance domain is deposited onto the enzyme domain to yield a domain thickness of from about 0.05 microns or less to about 20 microns or more, more preferably from about 0.05, 0.1, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45, 0.5, 1, 1.5, 2, 2.5, 3, or 3.5 microns to about 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 19.5 microns, and more preferably still from about 2, 2.5 or 3 microns to about 3.5, 4, 4.5, or 5 microns. Preferably, the resistance domain is deposited onto the enzyme domain by vapor deposition, spray coating, or dip coating. In one preferred embodiment, spray coating is the preferred deposition technique. The spraying process atomizes and mists the solution, and therefore most or all of the solvent is evaporated prior to the coating material settling on the underlying domain, thereby minimizing contact of the solvent with the enzyme.

[0355] In another preferred embodiment, physical vapor deposition (e.g., ultrasonic vapor deposition) is used for coating one or more of the membrane domain(s) onto the electrodes, wherein the vapor deposition apparatus and process include an ultrasonic nozzle that produces a mist of micro-droplets in a vacuum chamber. In these embodiments, the micro-droplets move turbulently within the vacuum chamber, isotropically impacting and adhering to the surface of the substrate. Advantageously, vapor deposition as described above can be implemented to provide high production throughput of membrane deposition processes (e.g., at least about 20 to about 200 or more electrodes per chamber), greater consistency of the membrane on each sensor, and increased uniformity of sensor performance, for example, as described below.

[0356] In some embodiments, depositing the resistance domain (for example, as described in the preferred embodiments above) includes formation of a membrane system that substantially blocks or resists ascorbate (a known electrochemical interferant in hydrogen peroxide-measuring glucose sensors). While not wishing to be bound by theory, it is believed that during the process of depositing the resistance domain as described in the preferred embodiments, a structural morphology is formed that is characterized in that ascorbate does not substantially permeate therethrough.

[0357] In a preferred embodiment, the resistance domain is deposited on the enzyme domain by spray coating a solution of from about 1 wt. % to about 5 wt. % polymer and from about 95 wt. % to about 99 wt. % solvent. In spraying a solution of resistance domain material, including a solvent, onto the enzyme domain, it is desirable to mitigate or substantially reduce any contact with enzyme of any solvent in the spray solution that can deactivate the underlying enzyme of the enzyme domain. Tetrahydrofuran (THF) is one solvent that minimally or negligibly affects the enzyme of the enzyme domain upon spraying. Other solvents can also be suitable for use, as is appreciated by one skilled in the art.

[0358] Although a variety of spraying or deposition techniques can be used, spraying the resistance domain material and rotating the sensor at least one time by 180° can typically provide adequate coverage by the resistance domain. Spraying the resistance domain material and rotating the sensor at least two times by 120° provides even greater

coverage (one layer of 360° coverage), thereby ensuring resistivity to glucose, such as is described in more detail above.

[0359] In preferred embodiments, the resistance domain is spray coated and subsequently cured for a time of from about 15 minutes to about 90 minutes at a temperature of from about 40°C to about 60°C (and can be accomplished under vacuum (*e.g.*, from 20 to 30 mmHg)). A cure time of up to about 90 minutes or more can be advantageous to ensure complete drying of the resistance domain.

[0360] In one embodiment, the resistance domain is formed by spray coating at least six layers (namely, rotating the sensor seventeen times by 120° for at least six layers of 360° coverage) and curing at 50°C under vacuum for 60 minutes. However, the resistance domain can be formed by dip coating or spray coating any layer or plurality of layers, depending upon the concentration of the solution, insertion rate, dwell time, withdrawal rate, and/or the desired thickness of the resulting film. Additionally, curing in a convention oven can also be employed.

[0361] In certain embodiments, a variable frequency microwave oven can be used to cure the membrane domains/layers. In general, microwave ovens directly excite the rotational mode of solvents. Consequently, microwave ovens cure coatings from the inside out rather than from the outside in as with conventional convection ovens. This direct rotational mode excitation is responsible for the typically observed "fast" curing within a microwave oven. In contrast to conventional microwave ovens, which rely upon a fixed frequency of emission that can cause arcing of dielectric (metallic) substrates if placed within a conventional microwave oven, Variable Frequency Microwave (VFM) ovens emit thousands of frequencies within 100 milliseconds, which substantially eliminates arcing of dielectric substrates. Consequently, the membrane domains/layers can be cured even after deposition on metallic electrodes as described herein. While not wishing to be bound by theory, it is believe that VFM curing can increase the rate and completeness of solvent evaporation from a liquid membrane solution applied to a sensor, as compared to the rate and completeness of solvent evaporation observed for curing in conventional convection ovens.

[0362] In certain embodiments, VFM is can be used together with convection oven curing to further accelerate cure time. In some sensor applications wherein the

membrane is cured prior to application on the electrode (see, for example, U.S. Publication No. US-2005-0245799-A1, which is incorporated herein by reference in its entirety), conventional microwave ovens (e.g., fixed frequency microwave ovens) can be used to cure the membrane layer.

Treatment of Interference Domain/Membrane System

[0363] Although the above-described methods generally include a curing step in formation of the membrane system, including the interference domain, the preferred embodiments further include an additional treatment step, which can be performed directly after the formation of the interference domain and/or some time after the formation of the entire membrane system (or anytime in between). In some embodiments, the additional treatment step is performed during (or in combination with) sterilization of the sensor.

[0364] In some embodiments, the membrane system (or interference domain) is treated by exposure to ionizing radiation, for example, electron beam radiation, UV radiation, X-ray radiation, gamma radiation, and the like. Alternatively, the membrane can be exposed to visible light when suitable photoinitiators are incorporated into the interference domain. While not wishing to be bound by theory, it is believed that exposing the interference domain to ionizing radiation substantially crosslinks the interference domain and thereby creates a tighter, less permeable network than an interference domain that has not been exposed to ionizing radiation.

[0365] In some embodiments, the membrane system (or interference domain) is crosslinked by forming free radicals, which may include the use of ionizing radiation, thermal initiators, chemical initiators, photoinitiators (e.g., UV and visible light), and the like. Any suitable initiator or any suitable initiator system can be employed, for example, α-hydroxyketone, α-aminoketone, ammonium persulfate (APS), redox systems such as APS/bisulfite, or potassium permanganate. Suitable thermal initiators include but are not limited to potassium persulfate, ammonium persulfate, sodium persulfate, and mixtures thereof.

[0366] In embodiments wherein electron beam radiation is used to treat the membrane system (or interference domain), a preferred exposure time is from about 6k or 12kGy to about 25 or 50 kGy, more preferably about 25kGy. However, one skilled in the art

appreciates that choice of molecular weight, composition of cellulosic derivative (or other polymer), and/or the thickness of the layer can affect the preferred exposure time of membrane to radiation. Preferably, the exposure is sufficient for substantially crosslinking the interference domain to form free radicals, but does not destroy or significantly break down the membrane or does not significantly damage the underlying electroactive surfaces.

[0367] In embodiments wherein UV radiation is employed to treat the membrane, UV rays from about 200 nm to about 400 nm are preferred; however values outside of this range can be employed in certain embodiments, dependent upon the cellulosic derivative and/or other polymer used.

[0368] In some embodiments, for example, wherein photoinitiators are employed to crosslink the interference domain, one or more additional domains can be provided adjacent to the interference domain for preventing delamination that may be caused by the crosslinking treatment. These additional domains can be "tie layers" (*i.e.*, film layers that enhance adhesion of the interference domain to other domains of the membrane system). In one exemplary embodiment, a membrane system is formed that includes the following domains: resistance domain, enzyme domain, electrode domain, and cellulosic-based interference domain, wherein the electrode domain is configured to ensure adhesion between the enzyme domain and the interference domain. In embodiments wherein photoinitiators are employed to crosslink the interference domain, UV radiation of greater than about 290 nm is preferred. Additionally, from about 0.01 to about 1 wt % photoinitiator is preferred weight-to-weight with a preselected cellulosic polymer (*e.g.*, cellulose acetate); however values outside of this range can be desirable dependent upon the cellulosic polymer selected.

[0369] In general, sterilization of the transcutaneous sensor can be completed after final assembly, utilizing methods such as electron beam radiation, gamma radiation, glutaraldehyde treatment, or the like. The sensor can be sterilized prior to or after packaging. In an alternative embodiment, one or more sensors can be sterilized using variable frequency microwave chamber(s), which can increase the speed and reduce the cost of the sterilization process. In another alternative embodiment, one or more sensors can be sterilized using ethylene oxide (EtO) gas sterilization, for example, by treating with 100% ethylene oxide, which can be used when the sensor electronics are not detachably connected to the sensor

and/or when the sensor electronics must undergo a sterilization process. In one embodiment, one or more packaged sets of transcutaneous sensors (e.g., 1, 2, 3, 4, or 5 sensors or more) are sterilized simultaneously.

Signal Response

[0370] Advantageously, sensors with the membrane system of the preferred embodiments, including an electrode domain **47** and/or interference domain **48**, an enzyme domain **49**, and a resistance domain **50**, provide stable signal response to increasing glucose levels of from about 40 to about 400 mg/dL, and sustained function (at least 90% signal strength) even at low oxygen levels (for example, at about 0.6 mg/L O_2). While not wishing to be bound by theory, it is believed that the resistance domain provides sufficient resistivity, or the enzyme domain provides sufficient enzyme, such that oxygen limitations are seen at a much lower concentration of oxygen as compared to prior art sensors.

[0371] In preferred embodiments, a sensor signal with a current in the picoAmp range is preferred, which is described in more detail elsewhere herein. However, the ability to produce a signal with a current in the picoAmp range can be dependent upon a combination of factors, including the electronic circuitry design (*e.g.*, A/D converter, bit resolution, and the like), the membrane system (*e.g.*, permeability of the analyte through the resistance domain, enzyme concentration, and/or electrolyte availability to the electrochemical reaction at the electrodes), and the exposed surface area of the working electrode. For example, the resistance domain can be designed to be more or less restrictive to the analyte depending upon to the design of the electronic circuitry, membrane system, and/or exposed electroactive surface area of the working electrode.

[0372] Accordingly, in preferred embodiments, the membrane system is designed with a sensitivity of from about 1 pA/mg/dL to about 100 pA/mg/dL, preferably from about 5 pA/mg/dL to 25 pA/mg/dL, and more preferably from about 3.5 to about 7.5 pA/mg/dL. While not wishing to be bound by any particular theory, it is believed that membrane systems designed with a sensitivity in the preferred ranges permit measurement of the analyte signal in low analyte and/or low oxygen situations. Namely, conventional analyte sensors have shown reduced measurement accuracy in low analyte ranges due to lower availability of the analyte to the sensor and/or have shown increased signal noise in high analyte ranges due to

insufficient oxygen necessary to react with the amount of analyte being measured. While not wishing to be bound by theory, it is believed that the membrane systems of the preferred embodiments, in combination with the electronic circuitry design and exposed electrochemical reactive surface area design, support measurement of the analyte in the picoAmp range, which enables an improved level of resolution and accuracy in both low and high analyte ranges not seen in the prior art.

Mutarotase Enzyme

[0373] In some embodiments, mutarotase, an enzyme that converts α D-glucose to β D-glucose, is incorporated into the membrane system. Mutarotase can be incorporated into the enzyme domain and/or can be incorporated into another domain of the membrane system. In general, glucose exists in two distinct isomers, α and β, which are in equilibrium with one another in solution and in the blood or interstitial fluid. At equilibrium, α is present at a relative concentration of about 35.5% and β is present in the relative concentration of about 64.5% (see Okuda *et. al.*, *Anal Biochem*. 1971 Sep; 43(1):312-5). Glucose oxidase, which is a conventional enzyme used to react with glucose in glucose sensors, reacts with β D-glucose and not with α D-glucose. Since only the β D-glucose isomer reacts with the glucose oxidase, errant readings may occur in a glucose sensor responsive to a shift of the equilibrium between the α D-glucose and the β D-glucose. Many compounds, such as calcium, can affect equilibrium shifts of α D-glucose and β D-glucose. For example, as disclosed in U.S. Patent No. 3,964,974 to Banaugh *et al.*, compounds that exert a mutarotation accelerating effect on α D-glucose include histidine, aspartic acid, imidazole, glutamic acid, α hydroxyl pyridine, and phosphate.

[0374] Accordingly, a shift in α D-glucose and β D-glucose equilibrium can cause a glucose sensor based on glucose oxidase to err high or low. To overcome the risks associated with errantly high or low sensor readings due to equilibrium shifts, the sensor of the preferred embodiments can be configured to measure total glucose in the host, including α D-glucose and β D-glucose by the incorporation of the mutarotase enzyme, which converts α D-glucose to β D-glucose.

[0375] Although sensors of some embodiments described herein include an interference domain in order to block or reduce one or more interferents, sensors with the

membrane systems of the preferred embodiments, including an electrode domain **47**, an enzyme domain **48**, and a resistance domain **49**, have been shown to inhibit ascorbate without an additional interference domain. Namely, the membrane system of the preferred embodiments, including an electrode domain **47**, an enzyme domain **48**, and a resistance domain **49**, has been shown to be substantially non-responsive to ascorbate in physiologically acceptable ranges. While not wishing to be bound by theory, it is believed that the processing process of spraying the depositing the resistance domain by spray coating, as described herein, forms results in a structural morphology that is substantially resistance resistant to ascorbate.

Oxygen Conduit

[0376] As described above, certain sensors depend upon an enzyme within the membrane system through which the host's bodily fluid passes and in which the analyte (for example, glucose) within the bodily fluid reacts in the presence of a co-reactant (for example, oxygen) to generate a product. The product is then measured using electrochemical methods, and thus the output of an electrode system functions as a measure of the analyte. For example, when the sensor is a glucose oxidase based glucose sensor, the species measured at the working electrode is H_2O_2. An enzyme, glucose oxidase, catalyzes the conversion of oxygen and glucose to hydrogen peroxide and gluconate according to the following reaction:

$$\text{Glucose} + O_2 \rightarrow \text{Gluconate} + H_2O_2$$

[0377] Because for each glucose molecule reacted there is a proportional change in the product, H_2O_2, one can monitor the change in H_2O_2 to determine glucose concentration. Oxidation of H_2O_2 by the working electrode is balanced by reduction of ambient oxygen, enzyme generated H_2O_2 and other reducible species at a counter electrode, for example. See Fraser, D.M., "An Introduction to *In Vivo* Biosensing: Progress and Problems." In "Biosensors and the Body," D.M. Fraser, ed., 1997, pp. 1-56 John Wiley and Sons, New York))

[0378] *In vivo,* glucose concentration is generally about one hundred times or more that of the oxygen concentration. Consequently, oxygen is a limiting reactant in the electrochemical reaction, and when insufficient oxygen is provided to the sensor, the sensor is unable to accurately measure glucose concentration. Thus, depressed sensor function or

inaccuracy is believed to be a result of problems in availability of oxygen to the enzyme and/or electroactive surface(s).

[0379] Accordingly, in an alternative embodiment, an oxygen conduit (for example, a high oxygen solubility domain formed from silicone or fluorochemicals) is provided that extends from the *ex vivo* portion of the sensor to the *in vivo* portion of the sensor to increase oxygen availability to the enzyme. The oxygen conduit can be formed as a part of the coating (insulating) material or can be a separate conduit associated with the assembly of wires that forms the sensor.

Porous Biointerface Materials

[0380] In alternative embodiments, the distal portion **42** includes a porous material disposed over some portion thereof, which modifies the host's tissue response to the sensor. In some embodiments, the porous material surrounding the sensor advantageously enhances and extends sensor performance and lifetime in the short term by slowing or reducing cellular migration to the sensor and associated degradation that would otherwise be caused by cellular invasion if the sensor were directly exposed to the *in vivo* environment. Alternatively, the porous material can provide stabilization of the sensor via tissue ingrowth into the porous material in the long term. Suitable porous materials include silicone, polytetrafluoroethylene, expanded polytetrafluoroethylene, polyethylene-co-tetrafluoroethylene, polyolefin, polyester, polycarbonate, biostable polytetrafluoroethylene, homopolymers, copolymers, terpolymers of polyurethanes, polypropylene (PP), polyvinylchloride (PVC), polyvinylidene fluoride (PVDF), polyvinyl alcohol (PVA), polybutylene terephthalate (PBT), polymethylmethacrylate (PMMA), polyether ether ketone (PEEK), polyamides, polyurethanes, cellulosic polymers, polysulfones and block copolymers thereof including, for example, di-block, tri-block, alternating, random and graft copolymers, as well as metals, ceramics, cellulose, hydrogel polymers, poly (2-hydroxyethyl methacrylate, pHEMA), hydroxyethyl methacrylate, (HEMA), polyacrylonitrile-polyvinyl chloride (PAN-PVC), high density polyethylene, acrylic copolymers, nylon, polyvinyl difluoride, polyanhydrides, poly(l-lysine), poly (L-lactic acid), hydroxyethylmethacrylate, hydroxyapeptite, alumina, zirconia, carbon fiber, aluminum, calcium phosphate, titanium,

titanium alloy, nintinol, stainless steel, and CoCr alloy, or the like, such as are described in U.S. Publication No. US-2005-0031689-A1 and U.S. Publication No. US-2005-0112169-A1.

[0381] In some embodiments, the porous material surrounding the sensor provides unique advantages in the short term (*e.g.*, one to 30 days) that can be used to enhance and extend sensor performance and lifetime. However, such materials can also provide advantages in the long term too (*e.g.*, greater than 30 days). Particularly, the *in vivo* portion of the sensor (the portion of the sensor that is implanted into the host's tissue) is encased (partially or fully) in a porous material. The porous material can be wrapped around the sensor (for example, by wrapping the porous material around the sensor or by inserting the sensor into a section of porous material sized to receive the sensor). Alternately, the porous material can be deposited on the sensor (for example, by electrospinning of a polymer directly thereon). In yet other alternative embodiments, the sensor is inserted into a selected section of porous biomaterial. Other methods for surrounding the *in vivo* portion of the sensor with a porous material can also be used as is appreciated by one skilled in the art.

[0382] The porous material surrounding the sensor advantageously slows or reduces cellular migration to the sensor and associated degradation that would otherwise be caused by cellular invasion if the sensor were directly exposed to the *in vivo* environment. Namely, the porous material provides a barrier that makes the migration of cells towards the sensor more tortuous and therefore slower (providing short term advantages). It is believed that this reduces or slows the sensitivity loss normally observed in a short-term sensor over time.

[0383] In an embodiment wherein the porous material is a high oxygen solubility material, such as porous silicone, the high oxygen solubility porous material surrounds some of or the entire *in vivo* portion **42** of the sensor. High oxygen solubility materials are materials that dynamically retain a high availability of oxygen that can be used to compensate for the local oxygen deficit during times of transient ischemia (*e.g.*, silicone and fluorocarbons). It is believed that some signal noise normally seen by a conventional sensor can be attributed to an oxygen deficit. In one exemplary embodiment, porous silicone surrounds the sensor and thereby effectively increases the concentration of oxygen local (proximal) to the sensor. Thus, an increase in oxygen availability proximal to the sensor as

achieved by this embodiment ensures that an excess of oxygen over glucose is provided to the sensor; thereby reducing the likelihood of oxygen limited reactions therein. Accordingly, by providing a high oxygen solubility material (*e.g.*, porous silicone) surrounding the *in vivo* portion of the sensor, it is believed that increased oxygen availability, reduced signal noise, longevity, and ultimately enhanced sensor performance can be achieved.

Bioactive Agents

[0384] In some alternative embodiments, a bioactive agent is incorporated into the above described porous material and/or membrane system, which diffuses out into the environment adjacent to the sensing region, such as is described in U.S. Publication No. US-2005-0031689-A1. Additionally or alternately, a bioactive agent can be administered locally at the exit-site or implantation-site. Suitable bioactive agents are those that modify the host's tissue response to the sensor, for example anti-inflammatory agents, anti-infective agents, anesthetics, inflammatory agents, growth factors, immunosuppressive agents, antiplatelet agents, anti-coagulants, anti-proliferates, ACE inhibitors, cytotoxic agents, anti-barrier cell compounds, vascularization-inducing compounds, anti-sense molecules, or mixtures thereof, such as are described in more detail in co-pending U.S. Patent Publication No. US-2005-0031689-A1.

[0385] In embodiments wherein the porous material is designed to enhance short-term (*e.g.*, from about 1 to about 30 days) lifetime or performance of the sensor, a suitable bioactive agent can be chosen to ensure that tissue ingrowth does not substantially occur within the pores of the porous material. Namely, by providing a tissue modifying bioactive agent, such as an anti-inflammatory agent (for example, Dexamethasone), substantially tissue ingrowth can be inhibited, at least in the short term, in order to maintain sufficient glucose transport through the pores of the porous material to maintain a stable sensitivity.

[0386] In embodiments wherein the porous material is designed to enhance long-term (*e.g.*, from about a day to about a year or more) lifetime or performance of the sensor, a suitable bioactive agent, such as a vascularization-inducing compound or anti-barrier cell compound, can be chosen to encourage tissue ingrowth without barrier cell formation.

[0387] In some alternative embodiments, the *in vivo* portion of the sensor is designed with porosity therethrough, for example, a design wherein the sensor wires are

configured in a mesh, loose helix configuration (namely, with spaces between the wires), or with micro-fabricated holes therethrough. Porosity within the sensor modifies the host's tissue response to the sensor, because tissue ingrowth into and/or through the *in vivo* portion of the sensor increases stability of the sensor and/or improves host acceptance of the sensor, thereby extending the lifetime of the sensor *in vivo*.

Sensor Manufacture

[0388] In some embodiments, the sensor is manufactured partially or wholly using a continuous reel-to-reel process, wherein one or more manufacturing steps are automated. In such embodiments, a manufacturing process can be provided substantially without the need for manual mounting and fixing steps and substantially without the need human interaction. A process can be utilized wherein a plurality of sensors of the preferred embodiments, including the electrodes, insulator, and membrane system, are continuously manufactured in a semi-automated or automated process.

[0389] In one embodiment, a plurality of twisted pairs is continuously formed into a coil, wherein a working electrode is coated with an insulator material around which a plurality of reference electrodes is wound. The plurality of twisted pairs are preferably indexed and subsequently moved from one station to the next whereby the membrane system is serially deposited according to the preferred embodiments. Preferably, the coil is continuous and remains as such during the entire sensor fabrication process, including winding of the electrodes, insulator application, and membrane coating processes. After drying of the membrane system, each individual sensor is cut from the continuous coil.

[0390] A continuous reel-to-reel process for manufacturing the sensor eliminates possible sensor damage due to handling by eliminating handling steps, and provides faster manufacturing due to faster trouble shooting by isolation when a product fails. Additionally, a process run can be facilitated because of elimination of steps that would otherwise be required (*e.g.*, steps in a manual manufacturing process). Finally, increased or improved product consistency due to consistent processes within a controlled environment can be achieved in a machine or robot driven operation.

[0391] In certain embodiments, vapor deposition (e.g., physical vapor deposition) is utilized to deposit one or more of the membrane domains onto the sensor. Vapor

deposition can be used to coat one or more insulating layers onto the electrodes and one or more of the domains of the membrane system onto the electrochemically reactive surfaces. The vapor deposition process can be a part of a continuous manufacturing process, for example, a semi-automated or fully-automated manufacturing process. Physical vapor deposition processes are generally preferred. In such physical vapor deposition processes in the gas phase for forming a thin film, source material is physically transferred in a vacuum to the substrate without any chemical reaction(s) involved. Physical vapor deposition processes include evaporation (e.g., by thermal or e-beam) and sputtering processes. In alternative embodiments, chemical vapor deposition can be used. In chemical vapor deposition processes for depositing a thin film, the substrate is exposed to one or more volatile precursors, which react and/or decompose on the substrate surface to produce the desired deposit. Advantageously, vapor deposition processes can be implemented to provide high production throughput of membrane deposition processes (e.g., deposition on at least about 20 to about 200 or more electrodes per chamber), greater consistency of the membrane on each sensor, and increased uniformity of sensor performance, as described below.

Applicator

[0392] Fig. 6 is an exploded side view of an applicator, showing the components that enable sensor and needle insertion. In this embodiment, the applicator **12** includes an applicator body **18** that aides in aligning and guiding the applicator components. Preferably, the applicator body **18** includes an applicator body base **60** that matingly engages the mounting unit **14** and an applicator body cap **62** that enables appropriate relationships (for example, stops) between the applicator components.

[0393] The guide tube subassembly **20** includes a guide tube carrier **64** and a guide tube **66**. In some embodiments, the guide tube is a cannula. The guide tube carrier **64** slides along the applicator body **18** and maintains the appropriate relative position of the guide tube **66** during insertion and subsequent retraction. For example, prior to and during insertion of the sensor, the guide tube **66** extends through the contact subassembly **26** to maintain an opening that enables easy insertion of the needle therethrough (see Figs. 7A to 7D). During retraction of the sensor, the guide tube subassembly **20** is pulled back, engaging with and causing the needle and associated moving components to retract back into the

applicator **12** (See Figs. 7C and 7D). In some embodiments, a lubricant (e.g., petroleum jelly) is placed within the sealing member **36** of the contact subassembly such that it surrounds the guide tube (e.g., cannula), thereby allowing the guide tube to easily retract back into the applicator, for example, without causing compression or deformation of the sealing member **36**.

[0394] A needle subassembly **68** is provided that includes a needle carrier **70** and needle **72**. The needle carrier **70** cooperates with the other applicator components and carries the needle **72** between its extended and retracted positions. The needle can be of any appropriate size that can encompass the sensor **32** and aid in its insertion into the host. Preferred sizes include from about 32 gauge or less to about 18 gauge or more, more preferably from about 28 gauge to about 25 gauge, to provide a comfortable insertion for the host. Referring to the inner diameter of the needle, approximately 0.006 inches to approximately 0.023 inches is preferable, and 0.013 inches is most preferable. The needle carrier **70** is configured to engage with the guide tube carrier **64**, while the needle **72** is configured to slidably nest within the guide tube **66**, which allows for easy guided insertion (and retraction) of the needle through the contact subassembly **26**.

[0395] A push rod subassembly **74** is provided that includes a push rod carrier **76** and a push rod **78**. The push rod carrier **76** cooperates with other applicator components to ensure that the sensor is properly inserted into the host's skin, namely the push rod carrier **76** carries the push rod **78** between its extended and retracted positions. In this embodiment, the push rod **78** is configured to slidably nest within the needle **72**, which allows for the sensor **32** to be pushed (released) from the needle **72** upon retraction of the needle, which is described in more detail with reference to Figs. 7A through 7D. In some embodiments, a slight bend or serpentine shape is designed into or allowed in the sensor in order to maintain the sensor within the needle by interference. While not wishing to be bound by theory, it is believed that a slight friction fit of the sensor within the needle minimizes motion of the sensor during withdrawal of the needle and maintains the sensor within the needle prior to withdrawal of the needle.

[0396] A plunger subassembly **22** is provided that includes a plunger **80** and plunger cap **82**. The plunger subassembly **22** cooperates with other applicators components

to ensure proper insertion and subsequent retraction of the applicator components. In this embodiment, the plunger **80** is configured to engage with the push rod to ensure the sensor remains extended (namely, in the host) during retraction, such as is described in more detail with reference to Fig. 7C.

Sensor Insertion

[0397] Figs. 7A through 7D are schematic side cross-sectional views that illustrate the applicator components and their cooperating relationships at various stages of sensor insertion. Fig. 7A illustrates the needle and sensor loaded prior to sensor insertion. Fig. 7B illustrates the needle and sensor after sensor insertion. Fig. 7C illustrates the sensor and needle during needle retraction. Fig. 7D illustrates the sensor remaining within the contact subassembly after needle retraction. Although the embodiments described herein suggest manual insertion and/or retraction of the various components, automation of one or more of the stages can also be employed. For example, spring-loaded mechanisms that can be triggered to automatically insert and/or retract the sensor, needle, or other cooperative applicator components can be implemented.

[0398] Referring to Fig. 7A, the sensor **32** is shown disposed within the needle **72**, which is disposed within the guide tube **66**. In this embodiment, the guide tube **66** is provided to maintain an opening within the contact subassembly **26** and/or contacts **28** to provide minimal friction between the needle **72** and the contact subassembly **26** and/or contacts **28** during insertion and retraction of the needle **72**. However, the guide tube is an optional component, which can be advantageous in some embodiments wherein the contact subassembly **26** and/or the contacts **28** are formed from an elastomer or other material with a relatively high friction coefficient, and which can be omitted in other embodiments wherein the contact subassembly **26** and or the contacts **28** are formed from a material with a relatively low friction coefficient (for example, hard plastic or metal). A guide tube, or the like, can be preferred in embodiments wherein the contact subassembly **26** and/or the contacts **28** are formed from a material designed to frictionally hold the sensor **32** (see Fig. 7D), for example, by the relaxing characteristics of an elastomer, or the like. In these embodiments, the guide tube is provided to ease insertion of the needle through the contacts, while allowing for a frictional hold of the contacts on the sensor **32** upon subsequent needle

retraction. Stabilization of the sensor in or on the contacts **28** is described in more detail with reference to Fig. 7D and following. Although Fig. 7A illustrates the needle and sensor inserted into the contacts subassembly as the initial loaded configuration, alternative embodiments contemplate a step of loading the needle through the guide tube **66** and/or contacts **28** prior to sensor insertion.

[0399] Referring to Fig. 7B, the sensor **32** and needle **72** are shown in an extended position. In this stage, the pushrod **78** has been forced to a forward position, for example by pushing on the plunger shown in Fig. 6, or the like. The plunger **22** (Fig. 6) is designed to cooperate with other of the applicator components to ensure that sensor **32** and the needle **72** extend together to a forward position (as shown); namely, the push rod **78** is designed to cooperate with other of the applicator components to ensure that the sensor **32** maintains the forward position simultaneously within the needle **72**.

[0400] Referring to Fig. 7C, the needle **72** is shown during the retraction process. In this stage, the push rod **78** is held in its extended (forward) position in order to maintain the sensor **32** in its extended (forward) position until the needle **72** has substantially fully retracted from the contacts **28**. Simultaneously, the cooperating applicator components retract the needle **72** and guide tube **66** backward by a pulling motion (manual or automated) thereon. In preferred embodiments, the guide tube carrier **64** (Fig. 6) engages with cooperating applicator components such that a backward (retraction) motion applied to the guide tube carrier retracts the needle **72** and guide tube **66**, without (initially) retracting the push rod **78**. In an alternative embodiment, the push rod **78** can be omitted and the sensor **32** held it its forward position by a cam, elastomer, or the like, which is in contact with a portion of the sensor while the needle moves over another portion of the sensor. One or more slots can be cut in the needle to maintain contact with the sensor during needle retraction.

[0401] Referring to Fig. 7D, the needle **72**, guide tube **66**, and push rod **78** are all retracted from contact subassembly **26**, leaving the sensor **32** disposed therein. The cooperating applicator components are designed such that when the needle **72** has substantially cleared from the contacts **28** and/or contact subassembly **26**, the push rod **78** is retracted along with the needle **72** and guide tube **66**. The applicator **12** can then be released

(manually or automatically) from the contacts **28**, such as is described in more detail elsewhere herein, for example with reference to Figs. 8D and 9A.

[0402] The preferred embodiments are generally designed with elastomeric contacts to ensure a retention force that retains the sensor **32** within the mounting unit **14** and to ensure stable electrical connection of the sensor **32** and its associated contacts **28**. Although the illustrated embodiments and associated text describe the sensor **32** extending through the contacts **28** to form a friction fit therein, a variety of alternatives are contemplated. In one alternative embodiment, the sensor is configured to be disposed adjacent to the contacts (rather than between the contacts). The contacts can be constructed in a variety of known configurations, for example, metallic contacts, cantilevered fingers, pogo pins, or the like, which are configured to press against the sensor after needle retraction.

[0403] It is generally preferred that a contact **28** is formed from a material with a durometer hardness of from about 5 to about 80 Shore A, more preferably from about 10 to about 50 Shore A, and even more preferably from about 20 to about 50 Shore A. In one implementation of a transcutaneous analyte sensor as described with reference to the preferred embodiments, the contact **28** is formed from a material with a durometer hardness of about 20 Shore A to maximize conformance (e.g., compression) of the contact around the sensor and/or within the sealing member. In another implementation of a transcutaneous analyte sensor as described with reference to the preferred embodiments, the contact **28** is formed from a material with a durometer hardness of about 50 Shore A to increase the strength of the contact **28** (e.g., increase resistance to compression). While a few examples have been provided above, one skilled in the art will appreciate that higher or lower durometer hardness sealing materials can also be advantageously employed.

[0404] In some embodiments, the durometer hardness of the elastomeric contacts **28** is higher than the durometer hardness of the sealing member **36**. In one example, the durometer hardness of the contacts is about 50 Shore A and the durometer hardness of the sealing member is about 20 Shore A; however, a variety of durometer hardness materials within the preferred range (typically, from about 5 Shore A to about 80 Shore A) can be chosen. In these embodiments, the higher durometer hardness contacts generally provide

greater stability while the lower durometer hardness sealing member generally provides superior compression and/or seal around the contacts.

[0405] In some embodiments, the durometer hardness of the sealing member **36** is higher than the durometer hardness of the elastomeric contacts **28**. In one example, the durometer hardness of the sealing member is about 50 Shore A and the durometer hardness of the contacts is about 20 Shore A, however a variety of durometer hardness materials within the preferred range (typically, from about 5 Shore A to about 80 Shore A) can be chosen. In these embodiments, the higher durometer hardness sealing member provides greater stability while the lower durometer hardness contacts provide superior compression and/or seal.

[0406] The illustrated embodiments are designed with coaxial contacts **28**; namely, the contacts **28** are configured to contact the working and reference electrodes **44**, **46** axially along the distal portion **42** of the sensor **32** (see Fig. 5A). As shown in Fig. 5A, the working electrode **44** extends farther than the reference electrode **46**, which allows coaxial connection of the electrodes **44**, **46** with the contacts **28** at locations spaced along the distal portion of the sensor (see also Figs. 9B and 10B). Although the illustrated embodiments employ a coaxial design, other designs are contemplated within the scope of the preferred embodiments. For example, the reference electrode can be positioned substantially adjacent to (but spaced apart from) the working electrode at the distal portion of the sensor. In this way, the contacts **28** can be designed side-by-side rather than co-axially along the axis of the sensor.

[0407] Fig. 8A is a perspective view of an applicator and mounting unit in one embodiment including a safety latch mechanism **84**. The safety latch mechanism **84** is configured to lock the plunger subassembly **22** in a stationary position such that it cannot be accidentally pushed prior to release of the safety latch mechanism. In this embodiment, the sensor system **10** is preferably packaged (*e.g.*, shipped) in this locked configuration, wherein the safety latch mechanism **84** holds the plunger subassembly **22** in its extended position, such that the sensor **32** cannot be prematurely inserted (*e.g.*, accidentally released). The safety latch mechanism **84** is configured such that a pulling force shown in the direction of the arrow (see Fig. 8A) releases the lock of the safety latch mechanism on the plunger subassembly, thereby allowing sensor insertion. Although one safety latch mechanism that

locks the plunger subassembly is illustrated and described herein, a variety of safety latch mechanism configurations that lock the sensor to prevent it from prematurely releasing (*i.e.*, that lock the sensor prior to release of the safety latch mechanism) are contemplated, as can be appreciated by one skilled in the art, and fall within the scope of the preferred embodiments.

[0408] Fig. 8A additionally illustrates a force-locking mechanism **86** included in certain alternative embodiments of the sensor system, wherein the force-locking mechanism **86** is configured to ensure a proper mate between the electronics unit **16** and the mounting unit **14** (see Fig. 12A, for example). In embodiments wherein a seal is formed between the mounting unit and the electronics unit, as described in more detail elsewhere herein, an appropriate force may be required to ensure a seal has sufficiently formed therebetween; in some circumstances, it can be advantageous to ensure the electronics unit has been properly mated (*e.g.*, snap-fit or sealingly mated) to the mounting unit. Accordingly, upon release of the applicator **12** from the mounting unit **14** (after sensor insertion), and after insertion of the electronics unit **16** into the mounting unit **14**, the force-locking mechanism **86** allows the user to ensure a proper mate and/or seal therebetween. In practice, a user pivots (e.g., lifts or twists) the force-locking mechanism such that it provides force on the electronics unit **16** by pulling up on the circular tab illustrated in Fig. 8A; the force-locking mechanism is preferably released thereafter. Although one system and one method for providing a secure and/or sealing fit between the electronics unit and the mounting unit are illustrated, various other force-locking mechanisms can be employed that utilize a variety of systems and methods for providing a secure and/or sealing fit between the electronics unit and the mounting unit (housing).

[0409] Figs. 8B to 8D are side views of an applicator and mounting unit in one embodiment, showing various stages of sensor insertion. Fig. 8B is a side view of the applicator matingly engaged to the mounting unit prior to sensor insertion. Fig. 8C is a side view of the mounting unit and applicator after the plunger subassembly has been pushed, extending the needle and sensor from the mounting unit (namely, through the host's skin). Fig. 8D is a side view of the mounting unit and applicator after the guide tube subassembly has been retracted, retracting the needle back into the applicator. Although the drawings and

associated text illustrate and describe embodiments wherein the applicator is designed for manual insertion and/or retraction, automated insertion and/or retraction of the sensor/needle, for example, using spring-loaded components, can alternatively be employed.

[0410] The preferred embodiments advantageously provide a system and method for easy insertion of the sensor and subsequent retraction of the needle in a single push-pull motion. Because of the mechanical latching system of the applicator, the user provides a continuous force on the plunger cap **82** and guide tube carrier **64** that inserts and retracts the needle in a continuous motion. When a user grips the applicator, his or her fingers grasp the guide tube carrier **64** while his or her thumb (or another finger) is positioned on the plunger cap **82**. The user squeezes his or her fingers and thumb together continuously, which causes the needle to insert (as the plunger slides forward) and subsequently retract (as the guide tube carrier slides backward) due to the system of latches located within the applicator (Figs. 6 to 8) without any necessary change of grip or force, leaving the sensor implanted in the host. In some embodiments, a continuous torque, when the applicator components are configured to rotatingly engage one another, can replace the continuous force. Some prior art sensors, in contrast to the sensors of the preferred embodiments, suffer from complex, multi-step, or multi-component insertion and retraction steps to insert and remove the needle from the sensor system.

[0411] Fig. 8B shows the mounting unit and applicator in the ready position. The sensor system can be shipped in this configuration, or the user can be instructed to mate the applicator **12** with the mounting unit **14** prior to sensor insertion. The insertion angle α is preferably fixed by the mating engagement of the applicator **12**. In the illustrated embodiment, the insertion angle α is fixed in the applicator **12** by the angle of the applicator body base **60** with the shaft of the applicator body **18**. However, a variety of systems and methods of ensuring proper placement can be implemented. Proper placement ensures that at least a portion of the sensor **32** extends below the dermis of the host upon insertion. In alternative embodiments, the sensor system **10** is designed with a variety of adjustable insertion angles. A variety of insertion angles can be advantageous to accommodate a variety of insertion locations and/or individual dermis configurations (for example, thickness of the dermis). In preferred embodiments, the insertion angle α is from about 0 to about 90 degrees,

more preferably from about 30 to about 60 degrees, and even more preferably about 45 degrees.

[0412] In practice, the mounting unit is placed at an appropriate location on the host's skin, for example, the skin of the arm, thigh, or abdomen. Thus, removing the backing layer **9** from the adhesive pad **8** and pressing the base portion of the mounting unit on the skin adheres the mounting unit to the host's skin.

[0413] Fig. 8C shows the mounting unit and applicator after the needle **72** has been extended from the mounting unit **14** (namely, inserted into the host) by pushing the push rod subassembly **22** into the applicator **12**. In this position, the sensor **32** is disposed within the needle **72** (namely, in position within the host), and held by the cooperating applicator components. In alternative embodiments, the mounting unit and/or applicator can be configured with the needle/sensor initially extended. In this way, the mechanical design can be simplified and the plunger-assisted insertion step can be eliminated or modified. The needle can be simply inserted by a manual force to puncture the host's skin, and only one (pulling) step is required on the applicator, which removes the needle from the host's skin.

[0414] Fig. 8D shows the mounting unit and applicator after the needle **72** has been retracted into the applicator **12**, exposing the sensor **32** to the host's tissue. During needle retraction, the push rod subassembly maintains the sensor in its extended position (namely, within the host). In preferred embodiments, retraction of the needle irreversibly locks the needle within the applicator so that it cannot be accidentally and/or intentionally released, reinserted, or reused. The applicator is preferably configured as a disposable device to reduce or eliminate a possibility of exposure of the needle after insertion into the host. However a reusable or reloadable applicator is also contemplated in some alternative embodiments. After needle retraction, the applicator **12** can be released from the mounting unit, for example, by pressing the release latch(es) **30**, and the applicator disposed of appropriately. In alternative embodiments, other mating and release configurations can be implemented between the mounting unit and the applicator, or the applicator can automatically release from the mounting unit after sensor insertion and subsequent needle retraction. In one alternative embodiment, a retention hold (*e.g.,* ball and detent configuration) holds and releases the electronics unit (or applicator).

[0415] In one alternative embodiment, the mounting unit is configured to releasably mate with the applicator and electronics unit in a manner such that when the applicator is releasably mated to the mounting unit (*e.g.*, after sensor insertion), the electronics unit is configured to slide into the mounting unit, thereby triggering release of the applicator and simultaneous mating of the electronics unit to the mounting unit. Cooperating mechanical components, for example, sliding ball and detent type configurations, can be used to accomplish the simultaneous mating of electronics unit and release of the applicator.

[0416] Figs. 8E to 8G are perspective views of a sensor system 310 of an alternative embodiment, including an applicator **312**, electronics unit **316**, and mounting unit **314**, showing various stages of applicator release and/or electronic unit mating. Fig. 8E is a perspective view of the applicator matingly engaged to the mounting unit after sensor insertion. Fig. 8F is a perspective view of the mounting unit and applicator matingly engaged while the electronics unit is slidingly inserted into the mounting unit. Fig. 8G is a perspective view of the electronics unit matingly engaged with the mounting unit after the applicator has been released.

[0417] In general, the sensor system **310** comprises a sensor adapted for transcutaneous insertion into a host's skin; a housing **314** adapted for placement adjacent to the host's skin; an electronics unit **316** releasably attachable to the housing; and an applicator **312** configured to insert the sensor through the housing **314** and into the skin of the host, wherein the applicator **312** is adapted to releasably mate with the housing **314**, and wherein the system **310** is configured to release the applicator **312** from the housing when the electronics unit **316** is attached to the housing **314**.

[0418] Fig. 8E shows the sensor system **310** after the sensor has been inserted and prior to release of the applicator **312**. In this embodiment, the electronics unit **316** is designed to slide into the mounting unit **314**. Preferably, the electronics unit **316** is configured and arranged to slide into the mounting unit **314** in only one orientation. In the illustrated embodiment, the insertion end is slightly tapered and dovetailed in order to guide insertion of the electronics unit **316** into the housing **314**; however other self-alignment configurations are possible. In this way, the electronics unit **316** self-aligns and orients the

electronics unit **316** in the housing, ensuring a proper fit and a secure electronic connection with the sensor.

[0419] Fig. 8F shows the sensor system **310** after the electronics unit **316** has been inserted therein. Preferably, the electronic unit **316** slide-fits into the mounting unit. In some embodiments, the sensor system **310** can be designed to allow the electronics unit **316** to be attached to the mounting unit **314** (*i.e.*, operably connected to the sensor) before the sensor system **310** is affixed to the host. Advantageously, this design provides mechanical stability for the sensor during transmitter insertion.

[0420] Fig. 8G shows the sensor system **310** upon release of the applicator **312** from the mounting unit **314** and electronics unit **316**. In this embodiment, the sensor system **310** is configured such that mating the electronics unit to the mounting unit triggers the release of the applicator **312** from the mounting unit **314**.

[0421] Thus, the above described sensor system **310**, also referred to as the slide-in system, allows for self-alignment of the electronics unit, creates an improved seal around the contacts due to greater holding force, provides mechanical stability for the sensor during insertion of the electronics unit, and causes automatic release of the applicator and simultaneous lock of the electronics unit into the mounting unit.

[0422] Although the overall design of the sensor system **10** results in a miniaturized volume as compared to numerous conventional devices, as described in more detail below; the sensor system **310** further enables a reduction in volume, as compared to, for example, the sensor system **10** described above.

[0423] Figs. 8H and 8I are comparative top views of the sensor system shown in the alternative embodiment illustrated in Figs. 8E to 8G and compared to the embodiments illustrated elsewhere (see Figs. 1 to 3 and 10 to 12, for example). Namely, the alternative embodiment described with reference to Figs. 8E to 8G further enables reduced size (*e.g.*, mass, volume, and the like) of the device as compared to certain other devices. It has been discovered that the size (including volume and/or surface area) of the device can affect the function of the device. For example, motion of the mounting unit/electronics unit caused by external influences (*e.g.*, bumping or other movement on the skin) is translated to the sensor *in vivo*, causing motion artifact (*e.g.*, an effect on the signal, or the like). Accordingly, by

enabling a reduction of size, a more stable signal with overall improved patient comfort can be achieved.

[0424] Accordingly, slide-in system **310** described herein, including the systems and methods for inserting the sensor and connecting the electronics unit to the mounting unit, enables the mounting unit **316**/electronics unit **314** subassembly to have a volume of less than about 10 cm^3, more preferably less than about 8 cm^3, and even more preferably less than about 6 cm^3, 5 cm^3, or 4 cm^3 or less. In general, the mounting unit **316**/electronics unit **314** subassembly comprises a first major surface and a second major surface opposite the first major surface. The first and second major surfaces together preferably account for at least about 50% of the surface area of the device; the first and second major surfaces each define a surface area, wherein the surface area of each major surface is less than or equal to about 10 cm^2, preferably less than or equal to about 8 cm^2, and more preferably less than or equal to about 6.5 cm^2, 6 cm^2, 5.5 cm^2, 5 cm^2, 4.5 cm^2, or 4 cm^2 or less. Typically, the mounting unit **316**/electronics unit **314** subassembly has a length **320** of less than about 40 mm by a width **322** of less than about 20 mm and a thickness of less than about 10 mm, and more preferably a length **320** less than or equal to about 35 mm by a width **322** less than or equal to about 18 mm by a thickness of less than or equal to about 9 mm.

[0425] In some embodiments, the mounting unit **14**/electronics unit **16** assembly has the following dimensional properties: preferably a length of about 6 cm or less, more preferably about 5 cm or less, more preferably still about 4.6 cm or less, even more preferably 4 cm or less, and most preferably about 3 cm or less; preferably a width of about 5 cm or less, more preferably about 4 cm or less, even more preferably 3 cm or less, even more preferably still about 2 cm or less, and most preferably about 1.5 cm or less; and/or preferably a thickness of about 2 cm or less, more preferably about 1.3 cm or less, more preferably still about 1 cm or less, even more preferably still about 0.7cm or less, and most preferably about 0.5 cm or less. The mounting unit **14**/electronics unit **16** assembly preferably has a volume of about 20 cm^3 or less, more preferably about 10 cm^3 or less, more preferably still about 5 cm^3 or less, and most preferably about 3 cm^3 or less; and preferably weighs 12 g or less, more preferably about 9 g or less, and most preferably about 6 g or less, although in some

embodiments the electronics unit may weigh more than about 12 g, e.g., up to about 25 g, 45g, or 90 g.

[0426] In some embodiments, the sensor **32** exits the base of the mounting unit **14** at a location distant from an edge of the base. In some embodiments, the sensor **32** exits the base of the mounting unit **14** at a location substantially closer to the center than the edges thereof. While not wishing to be bound by theory, it is believed that by providing an exit port for the sensor **32** located away from the edges, the sensor **32** can be protected from motion between the body and the mounting unit, snagging of the sensor by an external source, and/or environmental contaminants (*e.g.*, microorganisms) that can migrate under the edges of the mounting unit. In some embodiments, the sensor exits the mounting unit away from an outer edge of the device. Fig. 23 shows transcutaneous glucose sensor data and corresponding blood glucose values obtained over approximately seven days in a human, wherein the transcutaneous glucose sensor data was configured with an exit port situated at a location substantially closer to the center than the edges of the base.

[0427] In some alternative embodiments, however, the sensor exits the mounting unit **14** at an edge or near an edge of the device. In some embodiments, the mounting unit is configured such that the exit port (location) of the sensor is adjustable; thus, in embodiments wherein the depth of the sensor insertion is adjustable, six-degrees of freedom can thereby be provided.

Extensible Adhesive Pad

[0428] In certain embodiments, an adhesive pad is used with the sensor system. A variety of design parameters are desirable when choosing an adhesive pad for the mounting unit. For example: 1) the adhesive pad can be strong enough to maintain full contact at all times and during all movements (devices that release even slightly from the skin have a greater risk of contamination and infection), 2) the adhesive pad can be waterproof or water permeable such that the host can wear the device even while heavily perspiring, showering, or even swimming in some cases, 3) the adhesive pad can be flexible enough to withstand linear and rotational forces due to host movements, 4) the adhesive pad can be comfortable for the host, 5) the adhesive pad can be easily releasable to minimize host pain, 6) and/or the adhesive pad can be easily releasable so as to protect the sensor during release. Unfortunately,

these design parameters are difficult to simultaneously satisfy using known adhesive pads, for example, strong medical adhesive pads are available but are usually non-precise (for example, requiring significant "ripping" force during release) and can be painful during release due to the strength of their adhesion.

[0429] Therefore, the preferred embodiments provide an adhesive pad **8'** for mounting the mounting unit onto the host, including a sufficiently strong medical adhesive pad that satisfies one or more strength and flexibility requirements described above, and further provides a for easy, precise and pain-free release from the host's skin. Fig. 9A is a side view of the sensor assembly, illustrating the sensor implanted into the host with mounting unit adhered to the host's skin via an adhesive pad in one embodiment. Namely, the adhesive pad **8'** is formed from an extensible material that can be removed easily from the host's skin by stretching it lengthwise in a direction substantially parallel to (or up to about 35 degrees from) the plane of the skin. It is believed that this easy, precise, and painless removal is a function of both the high extensibility and easy stretchability of the adhesive pad.

[0430] In one embodiment, the extensible adhesive pad includes a polymeric foam layer or is formed from adhesive pad foam. It is believed that the conformability and resiliency of foam aids in conformation to the skin and flexibility during movement of the skin. In another embodiment, a stretchable solid adhesive pad, such as a rubber-based or an acrylate-based solid adhesive pad can be used. In another embodiment, the adhesive pad comprises a film, which can aid in increasing load bearing strength and rupture strength of the adhesive pad

[0431] Figs. 9B to 9C illustrate initial and continued release of the mounting unit from the host's skin by stretching the extensible adhesive pad in one embodiment. To release the device, the backing adhesive pad is pulled in a direction substantially parallel to (or up to about 35 degrees from) the plane of the device. Simultaneously, the extensible adhesive pad stretches and releases from the skin in a relatively easy and painless manner.

[0432] In one implementation, the mounting unit is bonded to the host's skin via a single layer of extensible adhesive pad **8'**, which is illustrated in Figs. 9A to 9C. The extensible adhesive pad includes a substantially non-extensible pull-tab **52**, which can

include a light adhesive pad layer that allows it to be held on the mounting unit **14** prior to release. Additionally, the adhesive pad can further include a substantially non-extensible holding tab **54**, which remains attached to the mounting unit during release stretching to discourage complete and/or uncontrolled release of the mounting unit from the skin.

[0433] In one alternative implementation, the adhesive pad **8'** includes two-sides, including the extensible adhesive pad and a backing adhesive pad (not shown). In this embodiment, the backing adhesive pad is bonded to the mounting unit's back surface **25** while the extensible adhesive pad **8'** is bonded to the host's skin. Both adhesive pads provide sufficient strength, flexibility, and waterproof or water permeable characteristics appropriate for their respective surface adhesion. In some embodiments, the backing and extensible adhesive pads are particularly designed with an optimized bond for their respective bonding surfaces (namely, the mounting unit and the skin).

[0434] In another alternative implementation, the adhesive pad **8'** includes a double-sided extensible adhesive pad surrounding a middle layer or backing layer (not shown). The backing layer can comprise a conventional backing film or can be formed from foam to enhance comfort, conformability, and flexibility. Preferably, each side of the double-sided adhesive pad is respectively designed for appropriate bonding surface (namely, the mounting unit and skin). A variety of alternative stretch-release configurations are possible. Controlled release of one or both sides of the adhesive pad can be facilitated by the relative lengths of each adhesive pad side, by incorporation of a non-adhesive pad zone, or the like.

[0435] Figs. 10A and 10B are perspective and side cross-sectional views, respectively, of the mounting unit immediately following sensor insertion and release of the applicator from the mounting unit. In one embodiment, such as illustrated in Figs. 10A and 10B, the contact subassembly **26** is held in its insertion position, substantially at the insertion angle α of the sensor. Maintaining the contact subassembly **26** at the insertion angle α during insertion enables the sensor **32** to be easily inserted straight through the contact subassembly **26**. The contact subassembly **26** further includes a hinge **38** that allows movement of the contact subassembly **26** from an angled to a flat position. The term "hinge," as used herein, is a broad term and is used in its ordinary sense, including, without limitation, a mechanism

that allows articulation of two or more parts or portions of a device. The term is broad enough to include a sliding hinge, for example, a ball and detent type hinging mechanism.

[0436] Although the illustrated embodiments describe a fixed insertion angle designed into the applicator, alternative embodiments can design the insertion angle into other components of the system. For example, the insertion angle can be designed into the attachment of the applicator with the mounting unit, or the like. In some alternative embodiments, a variety of adjustable insertion angles can be designed into the system to provide for a variety of host dermis configurations.

[0437] Fig. 10B illustrates the sensor **32** extending from the mounting unit **14** by a preselected distance, which defines the depth of insertion of the sensor into the host. The dermal and subcutaneous make-up of animals and humans is variable and a fixed depth of insertion may not be appropriate for all implantations. Accordingly, in an alternative embodiment, the distance that the sensor extends from the mounting unit is adjustable to accommodate a variety of host body-types. For example, the applicator **12** can be designed with a variety of adjustable settings, which control the distance that the needle **72** (and therefore the sensor **32**) extends upon sensor insertion. One skilled in the art appreciates a variety of means and mechanisms can be employed to accommodate adjustable sensor insertion depths, which are considered within the scope of the preferred embodiments. The preferred insertion depth is from about 0.1 mm or less to about 2 cm or more, preferably from about 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, or 0.45 mm to about 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, or 1.9 cm.

[0438] Figs. 11A and 11B are perspective and side cross-sectional views, respectively, of the mounting unit after articulating the contact subassembly to its functional position (which is also referred to as an inserted, implanted, or sensing position). The hinge **38** enables the contact subassembly **26** to tilt from its insertion position (Fig. 10) to its functional position (Fig. 11) by pressing downward on the contact subassembly, for example. Certain embodiments provide this pivotal movement via two separate pieces (the contact subassembly **26** and the mounting unit **14** connected by a hinge, for example, a mechanical or adhesive pad joint or hinge. A variety of pivoting, articulating, and/or hinging mechanisms can be employed with the sensors of preferred embodiments. For example, the hinge can be

formed as a part of the contact subassembly **26**. The contact subassembly can be formed from a flexible piece of material (such as silicone, urethane rubber, or other flexible or elastomeric material), wherein the material is sufficiently flexible to enable bending or hinging of the contact subassembly from an angle appropriate for insertion (Figs. 10A and 10B) to a lower functional configuration (Figs. 11A and 11B).

[0439] The relative pivotal movement of the contact subassembly is advantageous, for example, for enabling the design of a low profile device while providing support for an appropriate needle insertion angle. In its insertion position, the sensor system is designed for easy sensor insertion while forming a stable electrical connection with the associated contacts **28**. In its functional position, the sensor system maintains a low profile for convenience, comfort, and discreetness during use. Thus, the sensor systems of preferred embodiments are advantageously designed with a hinging configuration to provide an optimum guided insertion angle while maintaining a low profile device during sensor use.

[0440] In some embodiments, a shock-absorbing member or feature is incorporated into the design of the sensor and configured to absorb movement of the *in vivo* and/or *ex vivo* portion of the sensor. Conventional analyte sensors can suffer from motion-related artifact associated with host movement when the host is using the device. For example, when a transcutaneous analyte sensor is inserted into the host, various movements on the sensor (for example, relative movement between the *in vivo* portion and the *ex vivo* portion and/or movement within the host) create stresses on the device and can produce noise in the sensor signal. Accordingly in some embodiments, a shock-absorbing member is located on the sensor/mounting unit in a location that absorbs stresses associated with the above-described movement.

[0441] In the preferred embodiments, the sensor **32** bends from a substantially straight to substantially bent configuration upon pivoting of the contact subassembly from the insertion to functional position. The substantially straight sensor configuration during insertion advantageously provides ease of sensor insertion, while the substantial bend in the sensor in its functional position advantageously provides stability on the proximal end of the sensor with flexibility/mobility on the distal end of the sensor. Additionally, motion within the mounting unit (*e.g.*, caused by external forces to the mounting unit, movement of the

skin, and the like) does not substantially translate to the *in vivo* portion of the sensor. Namely, the bend formed within the sensor **32** functions to break column strength, causing flexion that effectively absorbs movements on the sensor during use. Additionally, the sensor can be designed with a length such that when the contact subassembly **26** is pivoted to its functional position (Fig. 10B), the sensor pushes forward and flexes, allowing it to absorb motion between the *in vivo* and *ex vivo* portions of the sensor. It is believed that both of the above advantages minimize motion artifact on the sensor signal and/or minimize damage to the sensor caused by movement, both of which (motion artifact and damage) have been observed in conventional transcutaneous sensors.

[0442] In some alternative embodiments, the shock-absorbing member can be an expanding and contracting member, such as a spring, accordion, telescoping, or bellows-type device. In general, the shock absorbing member can be located such that relative movement between the sensor, the mounting unit, and the host is absorbed without (or minimally) affecting the connection of the sensor to the mounting unit and/or the sensor stability within the implantation site; for example, the shock-absorbing member can be formed as a part of or connected to the sensor **32**.

[0443] Figs. 12A to 12C are perspective and side views of a sensor system including the mounting unit **14** and electronics unit **16** attached thereto. After sensor insertion, the transcutaneous analyte sensor system **10** measures a concentration of an analyte or a substance indicative of the concentration or presence of the analyte as described above. Although the examples are directed to a glucose sensor, the analyte sensor can be a sensor capable of determining the level of any suitable analyte in the body, for example, oxygen, lactase, insulin, hormones, cholesterol, medicaments, viruses, or the like. Once the electronics unit **16** is connected to the mounting unit **14**, the sensor **32** is able to measure levels of the analyte in the host.

[0444] Detachable connection between the mounting unit **14** and electronics unit **16** provides improved manufacturability, namely, the relatively inexpensive mounting unit **14** can be disposed of when replacing the sensor system after its usable life, while the relatively more expensive electronics unit **16** can be reusable with multiple sensor systems. In certain embodiments, the electronics unit **16** is configured with programming, for example,

initialization, calibration reset, failure testing, or the like, each time it is initially inserted into the cavity and/or each time it initially communicates with the sensor **32**. However, an integral (non-detachable) electronics unit can be configured as is appreciated by one skilled in the art.

[0445] Referring to the mechanical fit between the mounting unit **14** and the electronics unit **16** (and/or applicator **12**), a variety of mechanical joints are contemplated, for example, snap fit, interference fit, or slide fit. In the illustrated embodiment of Figs. 12A to 12C, tabs **120** are provided on the mounting unit **14** and/or electronics unit **16** that enable a secure connection therebetween. The tabs **120** of the illustrated embodiment can improve ease of mechanical connection by providing alignment of the mounting unit and electronics unit and additional rigid support for force and counter force by the user (*e.g.*, fingers) during connection. However, other configurations with or without guiding tabs are contemplated, such as illustrated in Figs. 10 and 11, for example.

[0446] In some circumstances, a drift of the sensor signal can cause inaccuracies in sensor performance and/or require re-calibration of the sensor. Accordingly, it can be advantageous to provide a sealant, whereby moisture (*e.g.*, water and water vapor) cannot substantially penetrate to the sensor and its connection to the electrical contacts. The sealant described herein can be used alone or in combination with the sealing member **36** described in more detail above, to seal the sensor from moisture in the external environment.

[0447] Preferably, the sealant fills in holes, crevices, or other void spaces between the mounting unit **14** and electronics unit **16** and/or around the sensor **32** within the mounting unit **32**. For example, the sealant can surround the sensor in the portion of the sensor **32** that extends through the contacts **28**. Additionally, the sealant can be disposed within the additional void spaces, for example a hole **122** that extends through the sealing member **36**.

[0448] Preferably, the sealant comprises a water impermeable material or compound, for example, oil, grease, or gel. In one exemplary embodiment, the sealant, which also can be referred to as a lubricant in certain embodiments, comprises petroleum jelly and is used to provide a moisture barrier surrounding the sensor **32**. In one experiment, petroleum jelly was liquefied by heating, after which a sensor **32** was immersed into the liquefied petroleum jelly to coat the outer surfaces thereof. The sensor was then assembled

into a housing and inserted into a host, during which deployment the sensor was inserted through the electrical contacts **28** and the petroleum jelly conforming therebetween. Sensors incorporating petroleum jelly, such as described above, when compared to sensors without the petroleum jelly moisture barrier exhibited less or no signal drift over time when studied in a humid or submersed environment. While not wishing to be bound by theory, it is believed that incorporation of a moisture barrier surrounding the sensor, especially between the sensor and its associated electrical contacts, reduces or eliminates the effects of humidity on the sensor signal. The viscosity of grease or oil-based moisture barriers allows penetration into and through even small cracks or crevices within the sensor and mounting unit, displacing moisture and thereby increasing the sealing properties thereof. U.S. Patent No. 4,259,540 and U.S. Patent No. 5,285,513 disclose materials suitable for use as a water impermeable material (sealant).

[0449] Referring to the electrical fit between the sensor **32** and the electronics unit **16**, contacts **28** (through which the sensor extends) are configured to electrically connect with mutually engaging contacts on the electronics unit **16**. A variety of configurations are contemplated; however, the mutually engaging contacts operatively connect upon detachable connection of the electronics unit **16** with the mounting unit **14**, and are substantially sealed from external moisture by sealing member **36**. Even with the sealing member, some circumstances can exist wherein moisture can penetrate into the area surrounding the sensor **32** and or contacts, for example, exposure to a humid or wet environment (*e.g.*, caused by sweat, showering, or other environmental causes). It has been observed that exposure of the sensor to moisture can be a cause of baseline signal drift of the sensor over time. For example in a glucose sensor, the baseline is the component of a glucose sensor signal that is not related to glucose (the amount of signal if no glucose is present), which is ideally constant over time. However, some circumstances my exist wherein the baseline can fluctuate over time, also referred to as drift, which can be caused, for example, by changes in a host's metabolism, cellular migration surrounding the sensor, interfering species, humidity in the environment, and the like.

[0450] In some embodiments, the mounting unit is designed to provide ventilation (*e.g.*, a vent hole **124**) between the exit-site and the sensor. In certain embodiments, a filter

(not shown) is provided in the vent hole **124** that allows the passage of air, while preventing contaminants from entering the vent hole **124** from the external environment. While not wishing to be bound by theory, it is believed that ventilation to the exit-site (or to the sensor **32**) can reduce or eliminate trapped moisture or bacteria, which can otherwise increase the growth and/or lifetime of bacteria adjacent to the sensor.

[0451] In some alternative embodiments, a sealing material is provided, which seals the needle and/or sensor from contamination of the external environment during and after sensor insertion. For example, one problem encountered in conventional transcutaneous devices is infection of the exit-site of the wound. For example, bacteria or contaminants can migrate from *ex vivo*, for example, any *ex vivo* portion of the device or the *ex vivo* environment, through the exit-site of the needle/sensor, and into the subcutaneous tissue, causing contamination and infection. Bacteria and/or contaminants can originate from handling of the device, exposed skin areas, and/or leakage from the mounting unit (external to) on the host. In many conventional transcutaneous devices, there exists some path of migration for bacteria and contaminants to the exit-site, which can become contaminated during sensor insertion or subsequent handling or use of the device. Furthermore, in some embodiments of a transcutaneous analyte sensor, the insertion-aiding device (for example, needle) is an integral part of the mounting unit; namely, the device stores the insertion device after insertion of the sensor, which is isolated from the exit-site (namely, point-of-entry of the sensor) after insertion.

[0452] Accordingly, these alternative embodiments provide a sealing material on the mounting unit, interposed between the housing and the skin, wherein the needle and/or sensor are adapted to extend through, and be sealed by, the sealing material. The sealing material is preferably formed from a flexible material that substantially seals around the needle/sensor. Appropriate flexible materials include malleable materials, elastomers, gels, greases, or the like (*e.g.*, see U.S. Patent No. 4,259,540 and U.S. Patent No. 5,285,513). However, not all embodiments include a sealing material, and in some embodiments a clearance hole or other space surrounding the needle and/or sensor is preferred.

[0453] In one embodiment, the base **24** of the mounting unit **14** is formed from a flexible material, for example silicone, which by its elastomeric properties seals the needle

and/or sensor at the exit port **126**, such as is illustrated in Figs. 11A and 11B. Thus, sealing material can be formed as a unitary or integral piece with the back surface **25** of the mounting unit **14**, or with an adhesive pad **8** on the back surface of the mounting unit, however alternatively can be a separate part secured to the device. In some embodiments, the sealing material can extend through the exit port **126** above or below the plane of the adhesive pad surface, or the exit port **126** can comprise a septum seal such as those used in the medical storage and disposal industries (for example, silica gel sandwiched between upper and lower seal layers, such as layers comprising chemically inert materials such as PTFE). A variety of known septum seals can be implemented into the exit port of the preferred embodiments described herein. Whether the sealing material is integral with or a separate part attached to the mounting unit **14**, the exit port **126** is advantageously sealed so as to reduce or eliminate the migration of bacteria or other contaminants to or from the exit-site of the wound and/or within the mounting unit.

[0454] During use, a host or caretaker positions the mounting unit at the appropriate location on or near the host's skin and prepares for sensor insertion. During insertion, the needle aids in sensor insertion, after which the needle is retracted into the mounting unit leaving the sensor in the subcutaneous tissue. In this embodiment, the exit-port **126** includes a layer of sealing material, such as a silicone membrane, that encloses the exit-port in a configuration that protects the exit-site from contamination that can migrate from the mounting unit or spacing external to the exit-site. Thus, when the sensor **32** and/or needle **72** extend through, for example, an aperture or a puncture in the sealing material, to provide communication between the mounting unit and subcutaneous space, a seal is formed therebetween. Elastomeric sealing materials can be advantageous in some embodiments because the elasticity provides a conforming seal between the needle/sensor and the mounting unit and/or because the elasticity provides shock-absorbing qualities allowing relative movement between the device and the various layers of the host's tissue, for example.

[0455] In some alternative embodiments, the sealing material includes a bioactive agent incorporated therein. Suitable bioactive agents include those which are known to discourage or prevent bacteria and infection, for example, anti-inflammatory, antimicrobials,

antibiotics, or the like. It is believed that diffusion or presence of a bioactive agent can aid in prevention or elimination of bacteria adjacent to the exit-site.

[0456] In practice, after the sensor **32** has been inserted into the host's tissue, and an electrical connection formed by mating the electronics unit **16** to the mounting unit **14**, the sensor measures an analyte concentration continuously or continually, for example, at an interval of from about fractions of a second to about 10 minutes or more.

[0457] Fig. 13 is an exploded perspective view of one exemplary embodiment of a continuous glucose sensor **1310A**. In this embodiment, the sensor is preferably wholly implanted into the subcutaneous tissue of a host, such as described in co-pending Patent Application No. 10/885,476 filed July 6, 2004 and entitled "SYSTEMS AND METHODS FOR MANUFACTURE OF AN ANALYTE-MEASURING DEVICE INCLUDING A MEMBRANE SYSTEM"; U.S. Publication No. US-2005-0245799-A1; U.S. Publication No. US-2005-0192557-A1; U.S. Publication No. US-2004-0199059-A1; U.S. Publication No. US-2005-0027463-A1; and U.S. Patent Number 6,001,067. In this exemplary embodiment, a body **1320** and a sensing region **1321** house the electrodes **1322** and sensor electronics (see Fig. 14). The three electrodes **1322** are operably connected to the sensor electronics (see Fig. 14) and are covered by a sensing membrane **1323** and a biointerface membrane **1324**, which are attached by a clip **1325**.

[0458] In one embodiment, the three electrodes **1322** include a platinum working electrode, a platinum counter electrode, and a silver/silver chloride reference electrode. The top ends of the electrodes are in contact with an electrolyte phase (not shown), which is a free-flowing fluid phase disposed between the sensing membrane **1323** and the electrodes **1322**. The sensing membrane **1323** includes an enzyme, for example, glucose oxidase, and covers the electrolyte phase. The biointerface membrane **1324** covers the sensing membrane **1323** and serves, at least in part, to protect the sensor **1310A** from external forces that can result in environmental stress cracking of the sensing membrane **1323**. U.S. Publication No. US-2005-0112169-A1 describes a biointerface membrane that can be used in conjunction with the preferred embodiments.

[0459] In one embodiment, the biointerface membrane **1324** generally includes a cell disruptive domain most distal from the electrochemically reactive surfaces and a cell

impermeable domain less distal from the electrochemically reactive surfaces than the cell disruptive domain. The cell disruptive domain is preferably designed to support tissue ingrowth, disrupt contractile forces typically found in a foreign body response, encourage vascularity within the membrane, and disrupt the formation of a barrier cell layer. The cell impermeable domain is preferably resistant to cellular attachment, impermeable to cells, and composed of a biostable material.

[0460] In one embodiment, the sensing membrane **1323** generally provides one or more of the following functions: 1) protection of the exposed electrode surface from the biological environment, 2) diffusion resistance (limitation) of the analyte, 3) a catalyst for enabling an enzymatic reaction, 4) limitation or blocking of interfering species, and 5) hydrophilicity at the electrochemically reactive surfaces of the sensor interface, such as described in U.S. Publication No. US-2005-0245799-A1. Accordingly, the sensing membrane **1323** preferably includes a plurality of domains or layers, for example, an electrolyte domain, an interference domain, an enzyme domain (for example, glucose oxidase), a resistance domain, and can additionally include an oxygen domain (not shown), and/or a bioprotective domain (not shown), such as described in more detail herein and in U.S. Publication No. US-2005-0245799-A1. However, it is understood that a sensing membrane modified for other devices, for example, by including fewer or additional domains is within the scope of the preferred embodiments.

[0461] In some embodiments, the domains of the biointerface and sensing membranes are formed from materials such as silicone, polytetrafluoroethylene, polyethylene-co-tetrafluoroethylene, polyolefin, polyester, polycarbonate, biostable polytetrafluoroethylene, homopolymers, copolymers, terpolymers of polyurethanes, polypropylene (PP), polyvinylchloride (PVC), polyvinylidene fluoride (PVDF), polybutylene terephthalate (PBT), polymethylmethacrylate (PMMA), polyether ether ketone (PEEK), polyurethanes, cellulosic polymers, polysulfones and block copolymers thereof including, for example, di-block, tri-block, alternating, random and graft copolymers. U.S. Publication No. US-2005-0245799-A1 describes biointerface and sensing membrane configurations and materials that can be applied to the preferred embodiments.

[0462] In the illustrated embodiment, the counter electrode is provided to balance the current generated by the species being measured at the working electrode. In the case of a glucose oxidase based glucose sensor, the species being measured at the working electrode is H_2O_2. Glucose oxidase catalyzes the conversion of oxygen and glucose to hydrogen peroxide and gluconate according to the following reaction:

$$\text{Glucose} + O_2 \rightarrow \text{Gluconate} + H_2O_2$$

[0463] The change in H_2O_2 can be monitored to determine glucose concentration because for each glucose molecule metabolized, there is a proportional change in the product H_2O_2. Oxidation of H_2O_2 by the working electrode is balanced by reduction of ambient oxygen, enzyme generated H_2O_2, or other reducible species at the counter electrode. The H_2O_2 produced from the glucose oxidase reaction further reacts at the surface of working electrode and produces two protons ($2H^+$), two electrons ($2e^-$), and one oxygen molecule (O_2).

[0464] In one embodiment, a potentiostat is employed to monitor the electrochemical reaction at the electrochemical cell. The potentiostat applies a constant potential to the working and reference electrodes to determine a current value. The current that is produced at the working electrode (and flows through the circuitry to the counter electrode) is substantially proportional to the amount of H_2O_2 that diffuses to the working electrode. Accordingly, a raw signal can be produced that is representative of the concentration of glucose in the user's body, and therefore can be utilized to estimate a meaningful glucose value, such as is described herein.

Sensor Electronics

[0465] The following description of sensor electronics associated with the electronics unit is applicable to a variety of continuous analyte sensors, such as non-invasive, minimally invasive, and/or invasive (*e.g.*, transcutaneous and wholly implantable) sensors. For example, the sensor electronics and data processing as well as the receiver electronics and data processing described below can be incorporated into the wholly implantable glucose sensor disclosed in U.S. Publication No. US-2005-0245799-A1 and U.S. Patent Application No. 10/885,476 filed July 6, 2004 and entitled, "SYSTEMS AND METHODS FOR

MANUFACTURE OF AN ANALYTE-MEASURING DEVICE INCLUDING A MEMBRANE SYSTEM."

[0466] Fig. 14 is a block diagram that illustrates the electronics **132** associated with the sensor system **10** in one embodiment. In this embodiment, a potentiostat **134** is shown, which is operably connected to an electrode system (such as described above) and provides a voltage to the electrodes, which biases the sensor to enable measurement of an current signal indicative of the analyte concentration in the host (also referred to as the analog portion). In some embodiments, the potentiostat includes a resistor (not shown) that translates the current into voltage. In some alternative embodiments, a current to frequency converter is provided that is configured to continuously integrate the measured current, for example, using a charge counting device.

[0467] An A/D converter **136** digitizes the analog signal into a digital signal, also referred to as "counts" for processing. Accordingly, the resulting raw data stream in counts, also referred to as raw sensor data, is directly related to the current measured by the potentiostat **134**.

[0468] A processor module **138** includes the central control unit that controls the processing of the sensor electronics **132**. In some embodiments, the processor module includes a microprocessor, however a computer system other than a microprocessor can be used to process data as described herein, for example an ASIC can be used for some or all of the sensor's central processing. The processor typically provides semi-permanent storage of data, for example, storing data such as sensor identifier (ID) and programming to process data streams (for example, programming for data smoothing and/or replacement of signal artifacts such as is described in U.S. Publication No. US-2005-0043598-A1). The processor additionally can be used for the system's cache memory, for example for temporarily storing recent sensor data. In some embodiments, the processor module comprises memory storage components such as ROM, RAM, dynamic-RAM, static-RAM, non-static RAM, EEPROM, rewritable ROMs, flash memory, or the like.

[0469] In some embodiments, the processor module comprises a digital filter, for example, an infinite impulse response (IIR) or finite impulse response (FIR) filter, configured to smooth the raw data stream from the A/D converter. Generally, digital filters are

programmed to filter data sampled at a predetermined time interval (also referred to as a sample rate). In some embodiments, wherein the potentiostat is configured to measure the analyte at discrete time intervals, these time intervals determine the sample rate of the digital filter. In some alternative embodiments, wherein the potentiostat is configured to continuously measure the analyte, for example, using a current-to-frequency converter as described above, the processor module can be programmed to request a digital value from the A/D converter at a predetermined time interval, also referred to as the acquisition time. In these alternative embodiments, the values obtained by the processor are advantageously averaged over the acquisition time due the continuity of the current measurement. Accordingly, the acquisition time determines the sample rate of the digital filter. In preferred embodiments, the processor module is configured with a programmable acquisition time, namely, the predetermined time interval for requesting the digital value from the A/D converter is programmable by a user within the digital circuitry of the processor module. An acquisition time of from about 2 seconds to about 512 seconds is preferred; however any acquisition time can be programmed into the processor module. A programmable acquisition time is advantageous in optimizing noise filtration, time lag, and processing/battery power.

[0470] Preferably, the processor module is configured to build the data packet for transmission to an outside source, for example, an RF transmission to a receiver as described in more detail below. Generally, the data packet comprises a plurality of bits that can include a preamble, a unique identifier identifying the electronics unit, the receiver, or both, (e.g., sensor ID code), data (e.g., raw data, filtered data, and/or an integrated value) and/or error detection or correction. Preferably, the data (transmission) packet has a length of from about 8 bits to about 128 bits, preferably about 48 bits; however, larger or smaller packets can be desirable in certain embodiments. The processor module can be configured to transmit any combination of raw and/or filtered data. In one exemplary embodiment, the transmission packet contains a fixed preamble, a unique ID of the electronics unit, a single five-minute average (e.g., integrated) sensor data value, and a cyclic redundancy code (CRC).

[0471] In some embodiments, the processor module further comprises a transmitter portion that determines the transmission interval of the sensor data to a receiver, or the like. In some embodiments, the transmitter portion, which determines the interval of

transmission, is configured to be programmable. In one such embodiment, a coefficient can be chosen (*e.g.*, a number of from about 1 to about 100, or more), wherein the coefficient is multiplied by the acquisition time (or sampling rate), such as described above, to define the transmission interval of the data packet. Thus, in some embodiments, the transmission interval is programmable from about 2 seconds to about 850 minutes, more preferably from about 30 second to about 5 minutes; however, any transmission interval can be programmable or programmed into the processor module. However, a variety of alternative systems and methods for providing a programmable transmission interval can also be employed. By providing a programmable transmission interval, data transmission can be customized to meet a variety of design criteria (*e.g.*, reduced battery consumption, timeliness of reporting sensor values, etc.)

[0472] Conventional glucose sensors measure current in the nanoAmp range. In contrast to conventional glucose sensors, the preferred embodiments are configured to measure the current flow in the picoAmp range, and in some embodiments, femtoAmps. Namely, for every unit (mg/dL) of glucose measured, at least one picoAmp of current is measured. Preferably, the analog portion of the A/D converter **136** is configured to continuously measure the current flowing at the working electrode and to convert the current measurement to digital values representative of the current. In one embodiment, the current flow is measured by a charge counting device (*e.g.*, a capacitor). Preferably, a charge counting device provides a value (e.g., digital value) representative of the current flow integrated over time (e.g., integrated value). In some embodiments, the value is integrated over a few seconds, a few minutes, or longer. In one exemplary embodiment, the value is integrated over 5 minutes; however, other integration periods can be chosen. Thus, a signal is provided, whereby a high sensitivity maximizes the signal received by a minimal amount of measured hydrogen peroxide (*e.g.*, minimal glucose requirements without sacrificing accuracy even in low glucose ranges), reducing the sensitivity to oxygen limitations *in vivo* (*e.g.*, in oxygen-dependent glucose sensors).

[0473] In some embodiments, the electronics unit is programmed with a specific ID, which is programmed (automatically or by the user) into a receiver to establish a secure wireless communication link between the electronics unit and the receiver. Preferably, the

transmission packet is Manchester encoded; however, a variety of known encoding techniques can also be employed.

[0474] A battery **144** is operably connected to the sensor electronics **132** and provides the power for the sensor. In one embodiment, the battery is a lithium manganese dioxide battery; however, any appropriately sized and powered battery can be used (for example, AAA, nickel-cadmium, zinc-carbon, alkaline, lithium, nickel-metal hydride, lithium-ion, zinc-air, zinc-mercury oxide, silver-zinc, and/or hermetically-sealed). In some embodiments, the battery is rechargeable, and/or a plurality of batteries can be used to power the system. The sensor can be transcutaneously powered via an inductive coupling, for example. In some embodiments, a quartz crystal **96** is operably connected to the processor **138** and maintains system time for the computer system as a whole, for example for the programmable acquisition time within the processor module.

[0475] Optional temperature probe **140** is shown, wherein the temperature probe is located on the electronics assembly or the glucose sensor itself. The temperature probe can be used to measure ambient temperature in the vicinity of the glucose sensor. This temperature measurement can be used to add temperature compensation to the calculated glucose value.

[0476] An RF module **148** is operably connected to the processor **138** and transmits the sensor data from the sensor to a receiver within a wireless transmission **150** via antenna **152**. In some embodiments, a second quartz crystal **154** provides the time base for the RF carrier frequency used for data transmissions from the RF transceiver. In some alternative embodiments, however, other mechanisms, such as optical, infrared radiation (IR), ultrasonic, or the like, can be used to transmit and/or receive data.

[0477] In the RF telemetry module of the preferred embodiments, the hardware and software are designed for low power requirements to increase the longevity of the device (for example, to enable a life of from about 3 to about 24 months, or more) with maximum RF transmittance from the *in vivo* environment to the *ex vivo* environment for wholly implantable sensors (for example, a distance of from about one to ten meters or more). Preferably, a high frequency carrier signal of from about 402 MHz to about 433 MHz is employed in order to maintain lower power requirements. In some embodiments, the RF

module employs a one-way RF communication link to provide a simplified ultra low power data transmission and receiving scheme. The RF transmission can be OOK or FSK modulated, preferably with a radiated transmission power (EIRP) fixed at a single power level of typically less than about 100 microwatts, preferably less than about 75 microwatts, more preferably less than about 50 microwatts, and most preferably less than about 25 microwatts.

[0478] Additionally, in wholly implantable devices, the carrier frequency is adapted for physiological attenuation levels, which is accomplished by tuning the RF module in a simulated *in vivo* environment to ensure RF functionality after implantation; accordingly, the preferred glucose sensor can sustain sensor function for 3 months, 6 months, 12 months, or 24 months or more.

[0479] When a sensor is first implanted into host tissue, the sensor and receiver are initialized. This is referred to as start-up mode, and involves optionally resetting the sensor data and calibrating the sensor **32**. In selected embodiments, mating the electronics unit **16** to the mounting unit triggers a start-up mode. In other embodiments, the start-up mode is triggered by the receiver, which is described in more detail with reference to Fig. 21, below.

[0480] Preferably, the electronics unit **16** indicates to the receiver (Figs. 15 and 17) that calibration is to be initialized (or re-initialized). The electronics unit **16** transmits a series of bits within a transmitted data packet wherein a sensor code can be included in the periodic transmission of the device. The status code is used to communicate sensor status to the receiving device. The status code can be inserted into any location in the transmitted data packet, with or without other sensor information. In one embodiment, the status code is designed to be unique or near unique to an individual sensor, which can be accomplished using a value that increments, decrements, or changes in some way after the transmitter detects that a sensor has been removed and/or attached to the transmitter. In an alternative embodiment, the status code can be configured to follow a specific progression, such as a BCD interpretation of a Gray code.

[0481] In some embodiments, the sensor electronics **132** are configured to detect a current drop to zero in the working electrode **44** associated with removal of a sensor **32**

from the host (or the electronics unit **16** from the mounting unit **14**), which can be configured to trigger an increment of the status code. If the incremented value reaches a maximum, it can be designed to roll over to 0. In some embodiments, the sensor electronics are configured to detect a voltage change cycle associated with removal and/or re-insertion of the sensor, which can be sensed in the counter electrode (*e.g.*, of a three-electrode sensor), which can be configured to trigger an increment of the status code.

[0482] In some embodiments, the sensor electronics **132** can be configured to send a special value (for example, 0) that indicates that the electronics unit is not attached when removal of the sensor (or electronics unit) is detected. This special value can be used to trigger a variety of events, for example, to halt display of analyte values. Incrementing or decrementing routines can be used to skip this special value.

Information Tag

[0483] In certain embodiments, it can be useful to provide readable information in or on the sensor system (e.g., the mounting unit and/or sensor packaging) to identify characteristics about the sensor. Although the following description is mostly drawn to providing sensor information on the mounting unit or the packaging, other parts of the sensor system can house the information tag, for example, the tag can be embedded within the electronics unit. Additionally, when implemented in a wholly implantable sensor (see, e.g., U.S. Publication No. US-2005-0245799-A1), the information tag can be embedded in any portion of the implantable device (e.g., electronics or on a chip within the body of the implantable device).

[0484] In general, the information tag includes information about the sensor manufacture, calibration, identification, expiration, intended sensor duration (e.g., insertion time period), archived data (e.g., most recent 1 hour of analyte data), license code/key information, and the like. In one embodiment, the information tag is provided on a single-use portion of the device (e.g., the mounting unit) and the sensor information is related to the single-use device, for example, information such as license code, sensor duration, and expiration information that can be useful to an associated reusable device (e.g., receiver). Preferably, the information tag is readable by a device or person in a manner that permits easy data transfer (e.g., of the license code or intended sensor duration) with minimal user

interaction. Preferably, the information tag has an electronic component including a memory for storing the sensor information; however, visual information tags (e.g., barcodes) can also be employed. In some embodiments, the information tag comprises a readable chip, wherein the chip transmits information using one or more of the following technologies: radio frequency, infrared, optical, acoustic, magnetic induction, and the like.

[0485] In one embodiment, the information tag includes a serial identification chip (e.g., a serial memory product such as manufactured by Maxim Integrated Products, Inc. of Sunnyvale, CA), also referred to as a one-wire interface. In this embodiment, a port is provided on the sensor system (e.g., the receiver) that receives the serial identification chip and reads the information thereon. In practice, a user inserts the serial identification chip into the sensor system (e.g., a port on the receiver), which allows transmission of the sensor information therein. In some embodiments, the information tag is provided in or on the sensor system packaging.

[0486] In one alternative embodiment, the information tag includes a Radio Frequency Identification (RFID) chip. RFID is a wireless data collection technology that uses electronic tags for storing data. RFID tags (or chips) are read when they are within the proximity of a transmitted radio signal. Because RFID tags can hold substantial amounts of data, the RFID tag can be used for tracking individual items. There are two types of RFID tags: passive and active. "Passive" tags have no power source but use the electromagnetic waves from a reader (e.g., the receiver) up to approximately 15 feet away to transmit back their contents. "Active" tags use a battery to transmit up to about 1,500 feet.

[0487] In some embodiments, an information tag is embedded in or on the on-skin housing (e.g., mounting unit and/or transmitter). Preferably, the receiver is configured to interrogate the information tag to obtain particular information; however, an information tag with two-way communication can also be employed. In one embodiment, the information tag includes a serial number or other identification information for the sensor. In another embodiment, the information tag is configured to initialize the sensor/receiver. In another embodiment, the information tag includes a calibration code that is used by the receiver during calibration of the sensor. In another embodiment, the information tag includes expiration information. In yet another embodiment, the information tag includes a key or

license code. In alternative embodiments, the information tag uniquely identifies the sensor **32** and allows the transmitter to adjust the sensor ID code accordingly and/or to transmit the unique identifier to the receiver **158**. The information tag can be configured to include various combinations of the above-referenced information, or additional information useful to operation of the sensor.

[0488] In some embodiments, the electronics unit **16** is configured to include additional contacts, which are designed to sense a specific resistance, or passive value, in the sensor system while the electronics unit is attached to the mounting unit. Preferably, these additional contacts are configured to detect information about a sensor, for example, whether the sensor is operatively connected to the mounting unit, the sensor's ID, a calibration code, or the like. For example, subsequent to sensing the passive value, the sensor electronics can be configured to change the sensor ID code by either mapping the value to a specific code, or internally detecting that the code is different and adjusting the sensor ID code in a predictable manner. As another example, the passive value can include information on parameters specific to a sensor (such as *in vitro* sensitivity information as described elsewhere herein).

[0489] In some embodiments, the electronics unit **16** includes additional contacts configured to communicate with a chip disposed in the mounting unit **14**. In this embodiment, the chip is designed with a unique or near-unique signature that can be detected by the electronics unit **16** and noted as different, and/or transmitted to the receiver **158** as the sensor ID code.

[0490] In some situations, it can be desirable to wait an amount of time after insertion of the sensor to allow the sensor to equilibrate *in vivo*, also referred to as "break-in." Accordingly, the sensor electronics can be configured to aid in decreasing the break-in time of the sensor by applying different voltage settings (for example, starting with a higher voltage setting and then reducing the voltage setting) to speed the equilibration process.

[0491] In some situations, the sensor may not properly deploy, connect to, or otherwise operate as intended. Accordingly, the sensor electronics can be configured such that if the current obtained from the working electrode, or the subsequent conversion of the current into digital counts, for example, is outside of an acceptable threshold, then the sensor

is marked with an error flag, or the like. The error flag can be transmitted to the receiver to instruct the user to reinsert a new sensor, or to implement some other error correction.

[0492] The above-described detection and transmission methods can be advantageously employed to minimize or eliminate human interaction with the sensor, thereby minimizing human error and/or inconvenience. Additionally, the sensors of preferred embodiments do not require that the receiver be in proximity to the transmitter during sensor insertion. Any one or more of the above described methods of detecting and transmitting insertion of a sensor and/or electronics unit can be combined or modified, as is appreciated by one skilled in the art.

On-Skin Device

[0493] Fig. 14B is a perspective view of an alternative embodiment, wherein the electronics unit and/or mounting unit, hereinafter referred to as the "on-skin device," is configured to communicate sensor information directly to the user (host). The electronics unit can be detachable from the mounting unit in certain embodiments. In other embodiments, the electronics unit is not detachable from the mounting unit. Fig. 14B shows an embodiment wherein the electronics unit **16** and mounting unit **14** collectively form the on-skin device. The on-skin device further includes a user interface **156**, which in the illustrated embodiment includes a readable screen that displays sensor information; however, other user interface configurations can also be employed.

[0494] In some embodiments, the user interface **156** of the on-skin device is configured to vibrate or audibly sound in order to attract the attention of the host, e.g., when a glucose level has risen beyond a set threshold. Although in the illustrated embodiment, the user interface of the on-skin device is configured with an LCD screen, other methods of data communication are possible, e.g., computer-generated audible information, tactile signals, or other user interface types. The term "user interface" as used herein is a broad term, and is to be given its ordinary and customary meaning to a person of ordinary skill in the art (and is not to be limited to a special or customized meaning), and refers without limitation to any method of communication to the user. In embodiments wherein the user interface is a visible display, the display can include one or more of: a number representing the analyte value, trend information (e.g., arrows that represent a speed and/or direction of the rising or falling

of the analyte levels), a color-metric reading (e.g., green, red, or one or more other colors), a graph that represents historical and/or present analyte information, and the like. A variety of displays and/or interface types can be user selectable in some embodiments.

[0495] In one alternative embodiment, the on-skin device is configured to provide a signal, for example, one- two- or three beeps, long- or short-beeps, or vibrations representative of a certain condition, for example, one-beep to indicate a glucose level within the target range, two-beeps to indicate a glucose level in the target range that is rising or falling quickly, and three-beeps to indicate a glucose level that is outside target range. In some embodiments, the signal is responsive to a user's request for information, for example, by pressing a button. In such an embodiment, an "info" button is provided (not shown), which is configured to provide these signals (or other communication) responsive to a user activating (pressing) the button.

[0496] In these embodiments, the on-skin device preferably houses the sensor electronics, which provide systems and methods for measuring, processing, and/or displaying of the sensor data. The sensor electronics generally include hardware, firmware, and/or software that enable measurement of levels of the analyte via the sensor and that enable audible, tactile, or visible communication or display of the sensor data. Accordingly, the sensor electronics preferably enable processing of and displaying of sensor data, for example, the sensor electronics include programming for retrospectively and/or prospectively initiating a calibration, converting sensor data, updating the calibration, and/or evaluating the calibration for the analyte sensor, for example, such as is described in more detail herein with reference to the sensor electronics and/or receiver electronics.

[0497] The electronics can be affixed to a printed circuit board (PCB), or the like, and can take a variety of forms. For example, the electronics can take the form of an integrated circuit (IC), such as an Application-Specific Integrated Circuit (ASIC), a microcontroller, or a processor, such as described in more detail herein with reference to sensor electronics and/or receiver electronics. In some embodiments, the sensor electronics comprise a digital filter, for example, an IIR or FIR filter, configured to smooth the raw data stream from the A/D converter.

[0498] In an embodiment wherein the sensor electronics are at least partially removably attached to the on-skin device, a system can be provided to enable docking of the electronics, and thereby downloading and viewing of the sensor data on a remote device, e.g., a sensor receiver, PDA, computer system, docking station, insulin pump, or the like. In one such embodiment, the on-skin device provides numerical sensor information; however, a user can dock the removable sensor electronics of the on-skin device onto the remote device to view additional information (e.g., graphical sensor information). Alternatively, the on-skin device can be used instead of the receiver to store and process all of the necessary data until a receiver is available for the transfer of data (or enabling a system that does not require a separate receiver). In some alternative embodiments, the on-skin device communicates with the receiver via a cable, radio frequency, optical, inductive coupling, infrared, microwave or other known methods of data transmission. In one such exemplary embodiment, the on-skin device is configured to communicate with the receiver when "requested" by the receiver. For example, when the receiver is held in close proximity (e.g., within 3 meters) of the device, transmission of sensor data can be requested (e.g., using data transmission methods such as inductive coupling, optical, infrared, or the like.)

[0499] In some alternative embodiments, a user interface is provided with the on-skin device; however, such a user interface is located in a remote site from the on-skin device (e.g., via wiring). In one such embodiment, the on-skin device is configured to be worn (e.g., adhered) on the skin (e.g., under clothing) of the host and the user interface is configured to be visible to the user (e.g., worn on clothing or a belt loop, or clipped to the host's clothing). In some embodiments, the user interface is a miniature LCD and/or is configured to provide numerical or audible values.

[0500] An on-skin device with data communication directly therefrom can provide improved convenience to the patient (e.g., there is no need for the patient to keep track of the receiver and maintain it within a predetermined range of the sensor at all times) and increased ease of use (e.g., fewer parts for the patient to understand, program, and/or carry). Additionally, circumstances exist (e.g., on airplanes, while swimming, etc.) where a patient may not be able to carry a receiver or during which time certain wireless

transmissions may not be permitted; however, with an on-skin user-communicating device, the patient will not be without critical sensor data.

[0501] Additionally, the on-skin device as described in the preferred embodiments is sufficiently miniature so as to enable adhesion of the device to a discreet insertion location (e.g., under the user's clothing in certain embodiments). Preferably, the on-skin device has a length of less than about 40 mm and a width of less than about 20 mm and a thickness of less than about 10 mm, and more preferably a length less than or equal to about 35 mm and a width less than or equal to about 18 mm and a thickness of less than or equal to about 9 mm. The dimensions associated with the electronics unit/mounting unit subassembly are described in greater detail elsewhere herein.

Receiver

[0502] Fig. 15 is a perspective view of a sensor system, including wireless communication between a sensor and a receiver. Preferably the electronics unit **16** is wirelessly connected to a receiver **158** via one- or two-way RF transmissions or the like. However, a wired connection is also contemplated. The receiver **158** provides much of the processing and display of the sensor data, and can be selectively worn and/or removed at the host's convenience. Thus, the sensor system **10** can be discreetly worn, and the receiver **158**, which provides much of the processing and display of the sensor data, can be selectively worn and/or removed at the host's convenience. Particularly, the receiver **158** includes programming for retrospectively and/or prospectively initiating a calibration, converting sensor data, updating the calibration, evaluating received reference and sensor data, and evaluating the calibration for the analyte sensor, such as described in more detail with reference to U.S. Publication No. US-2005-0027463-A1.

[0503] Figures 16A to 16D are schematic views of a receiver in first, second, third, and fourth embodiments, respectively. A receiver **1640** comprises systems necessary to receive, process, and display sensor data from an analyte sensor, such as described elsewhere herein. Particularly, the receiver **1640** can be a pager-sized device, for example, and comprise a user interface that has a plurality of buttons **1642** and a liquid crystal display (LCD) screen **1644**, and which can include a backlight. In some embodiments the user

interface can also include a keyboard, a speaker, and a vibrator such as described with reference to Fig. 17A.

[0504] In some embodiments a user is able to toggle through some or all of the screens shown in Figs. 16A to 16D using a toggle button on the receiver. In some embodiments, the user is able to interactively select the type of output displayed on their user interface. In some embodiments, the sensor output can have alternative configurations.

Receiver Electronics

[0505] Fig. 17A is a block diagram that illustrates the configuration of the medical device in one embodiment, including a continuous analyte sensor, a receiver, and an external device. In general, the analyte sensor system is any sensor configuration that provides an output signal indicative of a concentration of an analyte (*e.g.*, invasive, minimally-invasive, and/or non-invasive sensors as described above). The output signal is sent to a receiver **158** and received by an input module **174**, which is described in more detail below. The output signal is typically a raw data stream that is used to provide a useful value of the measured analyte concentration to a patient or a doctor, for example. In some embodiments, the raw data stream can be continuously or periodically algorithmically smoothed or otherwise modified to diminish outlying points that do not accurately represent the analyte concentration, for example due to signal noise or other signal artifacts, such as described in U.S. Patent No. 6,931,327.

[0506] Referring again to Fig. 17A, the receiver **158**, which is operatively linked to the sensor system **10**, receives a data stream from the sensor system **10** via the input module **174**. In one embodiment, the input module includes a quartz crystal operably connected to an RF transceiver (not shown) that together function to receive and synchronize data streams from the sensor system **10**. However, the input module **174** can be configured in any manner that is capable of receiving data from the sensor. Once received, the input module **174** sends the data stream to a processor **176** that processes the data stream, such as is described in more detail below.

[0507] The processor **176** is the central control unit that performs the processing, such as storing data, analyzing data streams, calibrating analyte sensor data, estimating analyte values, comparing estimated analyte values with time corresponding measured

analyte values, analyzing a variation of estimated analyte values, downloading data, and controlling the user interface by providing analyte values, prompts, messages, warnings, alarms, or the like. The processor includes hardware and software that performs the processing described herein, for example flash memory provides permanent or semi-permanent storage of data, storing data such as sensor ID, receiver ID, and programming to process data streams (for example, programming for performing estimation and other algorithms described elsewhere herein) and random access memory (RAM) stores the system's cache memory and is helpful in data processing.

[0508] Preferably, the input module **174** or processor module **176** performs a Cyclic Redundancy Check (CRC) to verify data integrity, with or without a method of recovering the data if there is an error. In some embodiments, error correction techniques such as those that use Hamming codes or Reed-Solomon encoding/decoding methods are employed to correct for errors in the data stream. In one alternative embodiment, an iterative decoding technique is employed, wherein the decoding is processed iteratively (*e.g.*, in a closed loop) to determine the most likely decoded signal. This type of decoding can allow for recovery of a signal that is as low as 0.5 dB above the noise floor, which is in contrast to conventional non-iterative decoding techniques (such as Reed-Solomon), which requires approximately 3 dB or about twice the signal power to recover the same signal (*e.g.*, a turbo code).

[0509] An output module **178**, which is integral with and/or operatively connected with the processor **176**, includes programming for generating output based on the data stream received from the sensor system **10** and its processing incurred in the processor **176**. In some embodiments, output is generated via a user interface **160**.

[0510] The user interface **160** comprises a keyboard **162**, speaker **164**, vibrator **166**, backlight **168**, liquid crystal display (LCD) screen **170**, and one or more buttons **172**. The components that comprise the user interface **160** include controls to allow interaction of the user with the receiver. The keyboard **162** can allow, for example, input of user information about himself/herself, such as mealtime, exercise, insulin administration, customized therapy recommendations, and reference analyte values. The speaker **164** can produce, for example, audible signals or alerts for conditions such as present and/or estimated

hyperglycemic or hypoglycemic conditions in a person with diabetes. The vibrator **166** can provide, for example, tactile signals or alerts for reasons such as described with reference to the speaker, above. The backlight **168** can be provided, for example, to aid the user in reading the LCD **170** in low light conditions. The LCD **170** can be provided, for example, to provide the user with visual data output, such as is described in U.S. Publication No. US-2005-0203360-A1. Figs. 17B to 17D illustrate some additional visual displays that can be provided on the screen 170. In some embodiments, the LCD is a touch-activated screen, enabling each selection by a user, for example, from a menu on the screen. The buttons **172** can provide for toggle, menu selection, option selection, mode selection, and reset, for example. In some alternative embodiments, a microphone can be provided to allow for voice-activated control.

[0511] In some embodiments, prompts or messages can be displayed on the user interface to convey information to the user, such as reference outlier values, requests for reference analyte values, therapy recommendations, deviation of the measured analyte values from the estimated analyte values, or the like. Additionally, prompts can be displayed to guide the user through calibration or trouble-shooting of the calibration.

[0512] In some embodiments, the receiver and/or a device connected to the receiver is configured to audibly output the user's analyte value(s), trend information (increasing or decreasing analyte values), and the like, hereinafter referred to as the audible output module. In some embodiments, the audible output module additionally includes: high and low blood glucose limits at which the module will audibly output the user's analyte value and/or trend information; English and non-English language versions; and choice of male or female voice. In some embodiments, the audible output is transmitted to an earbud worn by the patient for use where privacy is required or by a patient who is somewhat audibly impaired. The audible output module can be particularly advantageous in applications wherein the user is visually and/or hearing impaired, or is unable to visually check their receiver due to other circumstances (e.g., operating a motor vehicle or machinery, engaged in a business meeting or social event, or the like).

[0513] Additionally, data output from the output module **178** can provide wired or wireless, one- or two-way communication between the receiver **158** and an external device

180. The external device **180** can be any device that wherein interfaces or communicates with the receiver **158**. In some embodiments, the external device **180** is a computer, and the receiver **158** is able to download historical data for retrospective analysis by the patient or physician, for example. In some embodiments, the external device **180** is a modem or other telecommunications station, and the receiver **158** is able to send alerts, warnings, emergency messages, or the like, via telecommunication lines to another party, such as a doctor or family member. In some embodiments, the external device **180** is an insulin pen, and the receiver **158** is able to communicate therapy recommendations, such as insulin amount and time to the insulin pen. In some embodiments, the external device **180** is an insulin pump, and the receiver **158** is able to communicate therapy recommendations, such as insulin amount and time to the insulin pump. The external device **180** can include other technology or medical devices, for example pacemakers, implanted analyte sensor patches, other infusion devices, telemetry devices, or the like.

[0514] The user interface **160**, including keyboard **162**, buttons **172**, a microphone (not shown), and the external device **180**, can be configured to allow input of data. Data input can be helpful in obtaining information about the patient (for example, meal time, exercise, or the like), receiving instructions from a physician (for example, customized therapy recommendations, targets, or the like), and downloading software updates, for example. Keyboard, buttons, touch-screen, and microphone are all examples of mechanisms by which a user can input data directly into the receiver. A server, personal computer, personal digital assistant, insulin pump, and insulin pen are examples of external devices that can provide useful information to the receiver. Other devices internal or external to the sensor that measure other aspects of a patient's body (for example, temperature sensor, accelerometer, heart rate monitor, oxygen monitor, or the like) can be used to provide input helpful in data processing. In one embodiment, the user interface can prompt the patient to select an activity most closely related to their present activity, which can be helpful in linking to an individual's physiological patterns, or other data processing. In another embodiment, a temperature sensor and/or heart rate monitor can provide information helpful in linking activity, metabolism, and glucose excursions of an individual. While a few examples of data

input have been provided here, a variety of information can be input, which can be helpful in data processing.

[0515] Fig. 17B is an illustration of an LCD screen **170** showing continuous and single point glucose information in the form of a trend graph **184** and a single numerical value **186**. The trend graph shows upper and lower boundaries **182** representing a target range between which the host should maintain his/her glucose values. Preferably, the receiver is configured such that these boundaries **182** can be configured or customized by a user, such as the host or a care provider. By providing visual boundaries **182**, in combination with continuous analyte values over time (*e.g.*, a trend graph 184), a user can better learn how to control his/her analyte concentration (*e.g.*, a person with diabetes can better learn how to control his/her glucose concentration) as compared to single point (single numerical value **186**) alone. Although Fig. 17B illustrates a 1 hour trend graph (*e.g.*, depicted with a time range **188** of 1 hour), a variety of time ranges can be represented on the screen **170**, for example, 3 hour, 9 hour, 1 day, and the like.

[0516] Fig. 17C is an illustration of an LCD screen **170** showing a low alert screen that can be displayed responsive to a host's analyte concentration falling below a lower boundary (see boundaries **182**). In this exemplary screen, a host's glucose concentration has fallen to 55 mg/dL, which is below the lower boundary set in Fig. 17B, for example. The arrow **190** represents the direction of the analyte trend, for example, indicating that the glucose concentration is continuing to drop. The annotation **192** ("LOW") is helpful in immediately and clearly alerting the host that his/her glucose concentration has dropped below a preset limit, and what may be considered to be a clinically safe value, for example. Fig. 17D is an illustration of an LCD screen **170** showing a high alert screen that can be displayed responsive to a host's analyte concentration rising above an upper boundary (see boundaries **182**). In this exemplary screen, a host's glucose concentration has risen to 200 mg/dL, which is above a boundary set by the host, thereby triggering the high alert screen. The arrow **190** represents the direction of the analyte trend, for example, indicating that the glucose concentration is continuing to rise. The annotation **192** ("HIGH") is helpful in immediately and clearly alerting the host that his/her glucose concentration has above a preset limit, and what may be considered to be a clinically safe value, for example.

[0517] Although a few exemplary screens are depicted herein, a variety of screens can be provided for illustrating any of the information described in the preferred embodiments, as well as additional information. A user can toggle between these screens (*e.g.*, using buttons **172**) and/or the screens can be automatically displayed responsive to programming within the receiver **158**, and can be simultaneously accompanied by another type of alert (audible or tactile, for example).

[0518] In some embodiments the receiver **158** can have a length of from about 8 cm to about 15 cm, a width of from about 3.5 cm to about 10 cm, and/or a thickness of from about 1 cm to about 3.5 cm. In some embodiments the receiver **158** can have a volume of from about 120 cm^3 to about 180 cm^3, and can have a weight of from about 70 g to 130 g. The dimensions and volume can be higher or lower, depending, e.g., on the type of devices integrated (e.g., finger stick devices, pumps, PDAs, and the like.), the type of user interface employed, and the like.

[0519] In some embodiments, the receiver **158** is an application-specific device. In some embodiments the receiver **158** can be a device used for other functions, such as are described in U.S. Patent 6,558,320. For example, the receiver **158** can be integrated into a personal computer (PC), a personal digital assistant (PDA), a cell phone, or another fixed or portable computing device. The integration of the receiver **158** function into a more general purpose device can comprise the addition of software and/or hardware to the device. Communication between the sensor electronics **16** and the receiver **158** function of the more general purpose device can be implemented with wired or wireless technologies. For example, a PDA can be configured with a data communications port and/or a wireless receiver. After the user establishes a communication link between the electronics unit **16** and the PDA, the electronics unit **16** transmits data to the PDA which then processes the data according to software which has been loaded thereon so as to display.

Algorithms

[0520] Fig. 18A provides a flow chart **200** that illustrates the initial calibration and data output of the sensor data in one embodiment, wherein calibration is responsive to reference analyte data. Initial calibration, also referred to as start-up mode, occurs at the initialization of a sensor, for example, the first time an electronics unit is used with a

particular sensor. In certain embodiments, start-up calibration is triggered when the system determines that it can no longer remain in normal or suspended mode, which is described in more detail with reference to Fig. 21.

[0521] Calibration of an analyte sensor comprises data processing that converts sensor data signal into an estimated analyte measurement that is meaningful to a user. Accordingly, a reference analyte value is used to calibrate the data signal from the analyte sensor.

[0522] At block **202**, a sensor data receiving module, also referred to as the sensor data module, receives sensor data (*e.g.*, a data stream), including one or more time-spaced sensor data points, from the sensor **32** via the receiver **158**, which can be in wired or wireless communication with the sensor **32**. The sensor data point(s) can be smoothed (filtered) in certain embodiments using a filter, for example, a finite impulse response (FIR) or infinite impulse response (IIR) filter. During the initialization of the sensor, prior to initial calibration, the receiver receives and stores the sensor data, however it can be configured to not display any data to the user until initial calibration and, optionally, stabilization of the sensor has been established. In some embodiments, the data stream can be evaluated to determine sensor break-in (equilibration of the sensor *in vitro* or *in vivo*).

[0523] At block **204**, a reference data receiving module, also referred to as the reference input module, receives reference data from a reference analyte monitor, including one or more reference data points. In one embodiment, the reference analyte points can comprise results from a self-monitored blood analyte test (*e.g.*, finger stick test). For example, the user can administer a self-monitored blood analyte test to obtain an analyte value (*e.g.*, point) using any known analyte sensor, and then enter the numeric analyte value into the computer system. Alternatively, a self-monitored blood analyte test is transferred into the computer system through a wired or wireless connection to the receiver (*e.g.* computer system) so that the user simply initiates a connection between the two devices, and the reference analyte data is passed or downloaded between the self-monitored blood analyte test and the receiver.

[0524] In yet another embodiment, the self-monitored analyte monitor (*e.g.*, SMBG) is integral with the receiver so that the user simply provides a blood sample to the

receiver, and the receiver runs the analyte test to determine a reference analyte value, such as is described in more detail herein and with reference to U.S. Publication No. US-2005-0154271-A1 which describes some systems and methods for integrating a reference analyte monitor into a receiver for a continuous analyte sensor.

[0525] In some embodiments, the integrated receiver comprises a microprocessor which can be programmed to process sensor data to perform the calibration. Such programming, which is stored in a computer readable memory, can also comprise data acceptability testing using criteria such as that discussed above with reference to Fig. 18A. For example the microprocessor can be programmed so as to determine the rate of change of glucose concentration based on the continuous sensor data, and perform calibration only if the rate of change is below a predetermined threshold, such as 2 mg/dL/min. In some embodiments the receiver can also comprise modules to perform a calibration procedure such as is described herein. Such modules include, but are not limited to an input module, a data matching module, a calibration module, a conversion function module, a sensor data transformation module, a calibration evaluation module, a clinical module, a stability module, and a user interface, each of which have been described herein.

[0526] The monitor can be of any suitable configuration. For example, in one embodiment, the reference analyte points can comprise results from a self-monitored blood analyte test (e.g., from a finger stick test), such as those described in U.S. Pat. Nos. 6,045,567; 6,156,051; 6,197,040; 6,284,125; 6,413,410; and 6,733,655. In one such embodiment, the user can administer a self-monitored blood analyte test to obtain an analyte value (e.g., point) using any suitable analyte sensor, and then enter the numeric analyte value into the computer system (e.g., the receiver). In another such embodiment, a self-monitored blood analyte test comprises a wired or wireless connection to the receiver (e.g. computer system) so that the user simply initiates a connection between the two devices, and the reference analyte data is passed or downloaded between the self-monitored blood analyte test and the receiver. In yet another such embodiment, the self-monitored analyte test is integral with the receiver so that the user simply provides a blood sample to the receiver, and the receiver runs the analyte test to determine a reference analyte value.

[0527] The monitor can be of another configuration, for example, such as described in U.S. Patent No. 4,994,167, U.S. Patent No. 4,757,022, U.S. Patent No. 6,551,494. In alternative embodiments, the single point glucose monitor of this modular embodiment can be configured as described with reference to U.S. Publication No. US-2005-0154271-A1. In yet alternative embodiments, the monitor (e.g., integrated receiver) can be configured using other glucose meter configurations, for example, such as described in U.S. Patent No. 6,641,533 to Causey III, et al. Numerous advantages associated with the integrated receiver, such as ensuring accurate time stamping of the single point glucose test at the receiver and other advantages described herein, can be provided by an integrated continuous glucose receiver and single point glucose monitor, such as described herein.

[0528] In some alternative embodiments, the reference data is based on sensor data from another substantially continuous analyte sensor, *e.g.*, a transcutaneous analyte sensor described herein, or another type of suitable continuous analyte sensor. In an embodiment employing a series of two or more transcutaneous (or other continuous) sensors, the sensors can be employed so that they provide sensor data in discrete or overlapping periods. In such embodiments, the sensor data from one continuous sensor can be used to calibrate another continuous sensor, or be used to confirm the validity of a subsequently employed continuous sensor.

[0529] In some embodiments, reference data can be subjected to "outlier detection" wherein the accuracy of a received reference analyte data is evaluated as compared to time-corresponding sensor data. In one embodiment, the reference data is compared to the sensor data on a modified Clarke Error Grid (*e.g.*, a test similar to the Clarke Error Grid except the boundaries between the different regions are modified slightly) to determine if the data falls within a predetermined threshold. If the data is not within the predetermined threshold, then the receiver can be configured to request additional reference analyte data. If the additional reference analyte data confirms (*e.g.*, closely correlates to) the first reference analyte data, then the first and second reference values are assumed to be accurate and calibration of the sensor is adjusted or re-initialized. Alternatively, if the second reference analyte value falls within the predetermined threshold, then the first reference analyte value is assumed to be an outlier and the second reference analyte value is used by the algorithm(s)

instead. In one alternative embodiments of outlier detection, projection is used to estimate an expected analyte value, which is compared with the actual value and a delta evaluated for substantial correspondence. However, other methods of outlier detection are possible.

[0530] Certain acceptability parameters can be set for reference values received from the user. In some embodiments, the calibration process monitors the continuous analyte sensor data stream to determine a preferred time for capturing reference analyte concentration values for calibration of the continuous sensor data stream. In an example wherein the analyte sensor is a continuous glucose sensor, when data (for example, observed from the data stream) changes too rapidly, the reference glucose value may not be sufficiently reliable for calibration due to unstable glucose changes in the host. In contrast, when sensor glucose data are relatively stable (for example, relatively low rate of change), a reference glucose value can be taken for a reliable calibration. For example, in one embodiment, the receiver can be configured to only accept reference analyte values of from about 40 mg/dL to about 400 mg/dL. As another example, the receiver can be configured to only accept reference analyte values when the rate of change is less than a predetermined maximum, such as 1, 1.5, 2, 2.5, 3, or 3.5, mg/dL/min. As yet another example, the receiver can be configured to only accept reference analyte values when the rate of acceleration (or deceleration) is less than a predetermined maximum, such as 0.01 mg/dL/min^2, 0.02 mg/dL/min^2, 0.03 mg/dL/min^2, 0.04 mg/dL/min^2, or 0.05 mg/dL/min^2 or more.

[0531] In some embodiments, the reference data is pre-screened according to environmental and/or physiological issues, such as time of day, oxygen concentration, postural effects, and patient-entered environmental data. In one example embodiment, wherein the sensor comprises an implantable glucose sensor, an oxygen sensor within the glucose sensor is used to determine if sufficient oxygen is being provided to successfully complete the necessary enzyme and electrochemical reactions for glucose sensing. In another example wherein the sensor comprises an implantable glucose sensor, the counter electrode could be monitored for a "rail-effect," that is, when insufficient oxygen is provided at the counter electrode causing the counter electrode to reach operational (*e.g.*, circuitry) limits. In some embodiments the receiver is configured such that when conditions for accepting reference analyte values are not met, the user is notified. Such notice can include an

indication as to the cause of the unacceptability, such as low oxygen or high rate of analyte value change. In some embodiments the indication can also include an indication of suggested corrective action, such as moderately increasing muscular activity so as to increase oxygen levels or to wait until the rate of analyte value change reduces to an acceptable value.

[0532] In one embodiment, the calibration process can prompt the user via the user interface to "calibrate now" when the reference analyte values are considered acceptable. In some embodiments, the calibration process can prompt the user via the user interface to obtain a reference analyte value for calibration at intervals, for example when analyte concentrations are at high and/or low values. In some additional embodiments, the user interface can prompt the user to obtain a reference analyte value for calibration based at least in part upon certain events, such as meals, exercise, large excursions in analyte levels, faulty or interrupted data readings, or the like. In some embodiments, the algorithms can provide information useful in determining when to request a reference analyte value. For example, when analyte values indicate approaching clinical risk, the user interface can prompt the user to obtain a reference analyte value.

[0533] In yet another example embodiment, the patient is prompted to enter data into the user interface, such as meal times and/or amount of exercise, which can be used to determine likelihood of acceptable reference data. Evaluation data, such as described in the paragraphs above, can be used to evaluate an optimum time for reference analyte measurement. Correspondingly, the user interface can then prompt the user to provide a reference data point for calibration within a given time period. Consequently, because the receiver proactively prompts the user during optimum calibration times, the likelihood of error due to environmental and physiological limitations can decrease and consistency and acceptability of the calibration can increase.

[0534] At block **206**, a data matching module, also referred to as the processor module, matches reference data (*e.g.*, one or more reference analyte data points) with substantially time corresponding sensor data (*e.g.*, one or more sensor data points) to provide one or more matched data pairs. One reference data point can be matched to one time corresponding sensor data point to form a matched data pair. Alternatively, a plurality of reference data points can be averaged (*e.g.*, equally or non-equally weighted average, mean-

value, median, or the like) and matched to one time corresponding sensor data point to form a matched data pair, one reference data point can be matched to a plurality of time corresponding sensor data points averaged to form a matched data pair, or a plurality of reference data points can be averaged and matched to a plurality of time corresponding sensor data points averaged to form a matched data pair.

[0535] In one embodiment, time corresponding sensor data comprises one or more sensor data points that occur from about 0 minutes to about 20 minutes after the reference analyte data time stamp (*e.g.*, the time that the reference analyte data is obtained). In one embodiment, a 5-minute time delay is chosen to compensate for a system time-lag (*e.g.*, the time necessary for the analyte to diffusion through a membrane(s) of an analyte sensor). In alternative embodiments, the time corresponding sensor value can be greater than or less than that of the above-described embodiment, for example ± 60 minutes. Variability in time correspondence of sensor and reference data can be attributed to, for example, a longer or shorter time delay introduced by the data smoothing filter, or if the configuration of the analyte sensor incurs a greater or lesser physiological time lag.

[0536] In some implementations of the sensor, the reference analyte data is obtained at a time that is different from the time that the data is input into the receiver. Accordingly, the "time stamp" of the reference analyte (*e.g.*, the time at which the reference analyte value was obtained) is not the same as the time at which the receiver obtained the reference analyte data. Therefore, some embodiments include a time stamp requirement that ensures that the receiver stores the accurate time stamp for each reference analyte value, that is, the time at which the reference value was actually obtained from the user.

[0537] In certain embodiments, tests are used to evaluate the best-matched pair using a reference data point against individual sensor values over a predetermined time period (*e.g.*, about 30 minutes). In one such embodiment, the reference data point is matched with sensor data points at 5-minute intervals and each matched pair is evaluated. The matched pair with the best correlation can be selected as the matched pair for data processing. In some alternative embodiments, matching a reference data point with an average of a plurality of sensor data points over a predetermined time period can be used to form a matched pair.

[0538] In certain embodiments, the data matching module only forms matched pairs when a certain analyte value condition is satisfied. Such a condition can include any of the conditions discussed above with reference to embodiments pre-screening or conditionally accepting reference analyte value data at block 204.

[0539] At block **208**, a calibration set module, also referred to as the calibration module or processor module, forms an initial calibration set from a set of one or more matched data pairs, which are used to determine the relationship between the reference analyte data and the sensor analyte data. The matched data pairs, which make up the initial calibration set, can be selected according to predetermined criteria. The criteria for the initial calibration set can be the same as, or different from, the criteria for the updated calibration sets. In certain embodiments, the number (n) of data pair(s) selected for the initial calibration set is one. In other embodiments, n data pairs are selected for the initial calibration set wherein n is a function of the frequency of the received reference data points. In various embodiments, two data pairs make up the initial calibration set or six data pairs make up the initial calibration set. In an embodiment wherein a substantially continuous analyte sensor provides reference data, numerous data points are used to provide reference data from more than 6 data pairs (*e.g.*, dozens or even hundreds of data pairs). In one exemplary embodiment, a substantially continuous analyte sensor provides 288 reference data points per day (every five minutes for twenty-four hours), thereby providing an opportunity for a matched data pair 288 times per day, for example. While specific numbers of matched data pairs are referred to in the preferred embodiments, any suitable number of matched data pairs per a given time period can be employed.

[0540] In certain embodiments, the data pairs are selected only when a certain analyte value condition is satisfied. Such a condition can include any of the conditions discussed above with reference to embodiments pre-screening or conditionally accepting reference analyte value data at block 204. In certain embodiments, the data pairs that form the initial calibration set are selected according to their time stamp, for example, by waiting a predetermined "break-in" time period after implantation, the stability of the sensor data can be increased. In certain embodiments, the data pairs that form the initial calibration set are spread out over a predetermined time period, for example, a period of two hours or more. In

certain embodiments, the data pairs that form the initial calibration set are spread out over a predetermined glucose range, for example, spread out over a range of at least 90 mg/dL or more.

[0541] At block **210**, a conversion function module, also referred to as the conversion module or processor module, uses the calibration set to create a conversion function. The conversion function substantially defines the relationship between the reference analyte data and the analyte sensor data.

[0542] A variety of known methods can be used with the preferred embodiments to create the conversion function from the calibration set. In one embodiment, wherein a plurality of matched data points form the calibration set, a linear least squares regression is used to calculate the conversion function; for example, this regression calculates a slope and an offset using the equation $y=mx+b$. A variety of regression or other conversion schemes can be implemented herein.

[0543] In certain embodiments, the conversion function module only creates a conversion function when a certain analyte value condition is satisfied. Such a condition can include any of the conditions discussed above with reference to embodiments pre-screening or conditionally accepting reference analyte value data at block **204** or with reference to selecting data pairs at block **208**.

[0544] In some alternative embodiments, the sensor is calibrated with a single-point through the use of a dual-electrode system to simplify sensor calibration. In one such dual-electrode system, a first electrode functions as a hydrogen peroxide sensor including a membrane system containing glucose-oxidase disposed thereon, which operates as described herein. A second electrode is a hydrogen peroxide sensor that is configured similar to the first electrode, but with a modified membrane system (with the enzyme domain removed, for example). This second electrode provides a signal composed mostly of the baseline signal, b.

[0545] In some dual-electrode systems, the baseline signal is (electronically or digitally) subtracted from the glucose signal to obtain a glucose signal substantially without baseline. Accordingly, calibration of the resultant difference signal can be performed by solving the equation $y = mx$ with a single paired measurement. Calibration of the implanted sensor in this alternative embodiment can be made less dependent on the values/range of the

paired measurements, less sensitive to error in manual blood glucose measurements, and can facilitate the sensor's use as a primary source of glucose information for the user. U.S. Publication No. US-2005-0143635-A1 describes systems and methods for subtracting the baseline from a sensor signal.

[0546] In some alternative dual-electrode system embodiments, the analyte sensor is configured to transmit signals obtained from each electrode separately (*e.g.*, without subtraction of the baseline signal). In this way, the receiver can process these signals to determine additional information about the sensor and/or analyte concentration. For example, by comparing the signals from the first and second electrodes, changes in baseline and/or sensitivity can be detected and/or measured and used to update calibration (*e.g.*, without the use of a reference analyte value). In one such example, by monitoring the corresponding first and second signals over time, an amount of signal contributed by baseline can be measured. In another such example, by comparing fluctuations in the correlating signals over time, changes in sensitivity can be detected and/or measured.

[0547] In some alternative embodiments, a regression equation $y=mx+b$ is used to calculate the conversion function; however, prior information can be provided for m and/or b, thereby enabling calibration to occur with fewer paired measurements. In one calibration technique, prior information (*e.g.*, obtained from *in vivo* or *in vitro* tests) determines a sensitivity of the sensor and/or the baseline signal of the sensor by analyzing sensor data from measurements taken by the sensor (*e.g.*, prior to inserting the sensor). For example, if there exists a predictive relationship between *in vitro* sensor parameters and *in vivo* parameters, then this information can be used by the calibration procedure. For example, if a predictive relationship exists between *in vitro* sensitivity and *in vivo* sensitivity, $m \approx f(m_{in\ vitro})$, then the predicted m can be used, along with a single matched pair, to solve for b ($b = y - mx$). If, in addition, b can be assumed = 0, for example with a dual-electrode configuration that enables subtraction of the baseline from the signal such as described above, then both m and b are known *a priori*, matched pairs are not needed for calibration, and the sensor can be completely calibrated *e.g.* without the need for reference analyte values (*e.g.* values obtained after implantation *in vivo*.)

[0548] In another alternative embodiment, prior information can be provided to guide or validate the baseline (*b*) and/or sensitivity (*m*) determined from the regression analysis. In this embodiment, boundaries can be set for the regression line that defines the conversion function such that working sensors are calibrated accurately and easily (with two points), and non-working sensors are prevented from being calibrated. If the boundaries are drawn too tightly, a working sensor may not enter into calibration. Likewise, if the boundaries are drawn too loosely, the scheme can result in inaccurate calibration or can permit non-working sensors to enter into calibration. For example, subsequent to performing regression, the resulting slope and/or baseline are tested to determine whether they fall within a predetermined acceptable threshold (boundaries). These predetermined acceptable boundaries can be obtained from *in vivo* or *in vitro* tests (*e.g.*, by a retrospective analysis of sensor sensitivities and/or baselines collected from a set of sensors/patients, assuming that the set is representative of future data).

[0549] If the slope and/or baseline fall within the predetermined acceptable boundaries, then the regression is considered acceptable and processing continues to the next step (*e.g.*, block **212**). Alternatively, if the slope and/or baseline fall outside the predetermined acceptable boundaries, steps can be taken to either correct the regression or fail-safe such that a system will not process or display errant data. This can be useful in situations wherein regression results in errant slope or baseline values. For example, when points (matched pairs) used for regression are too close in value, the resulting regression statistically is less accurate than when the values are spread farther apart. As another example, a sensor that is not properly deployed or is damaged during deployment can yield a skewed or errant baseline signal.

[0550] In some alternative embodiments, the sensor system does not require initial and/or update calibration by the host; in these alternative embodiments, also referred to as "zero-point calibration" embodiments, use of the sensor system without requiring a reference analyte measurement for initial and/or update calibration is enabled. In general, the systems and methods of the preferred embodiments provide for stable and repeatable sensor manufacture, particularly when tightly controlled manufacturing processes are utilized. Namely, a batch of sensors of the preferred embodiments can be designed with substantially

the same baseline (*b*) and/or sensitivity (*m*) (+/- 10%) when tested *in vitro*. Additionally, the sensor of the preferred embodiments can be designed for repeatable *m* and *b in vivo*. Thus, an initial calibration factor (conversion function) can be programmed into the sensor (sensor electronics and/or receiver electronics) that enables conversion of raw sensor data into calibrated sensor data solely using information obtained prior to implantation (namely, initial calibration does not require a reference analyte value). Additionally, to obviate the need for recalibration (update calibration) during the life of the sensor, the sensor is designed to minimize drift of the sensitivity and/or baseline over time *in vivo*. Accordingly, the preferred embodiments can be manufactured for zero point calibration.

[0551] Fig. 18B is a graph that illustrates one example of using prior information for slope and baseline. The x-axis represents reference glucose data (blood glucose) from a reference glucose source in mg/dL; the y-axis represents sensor data from a transcutaneous glucose sensor of the preferred embodiments in counts. An upper boundary line **215** is a regression line that represents an upper boundary of "acceptability" in this example; the lower boundary line **216** is a regression line that represents a lower boundary of "acceptability" in this example. The boundary lines **215**, **216** were obtained from retrospective analysis of *in vivo* sensitivities and baselines of glucose sensors as described in the preferred embodiments.

[0552] A plurality of matched data pairs **217** represents data pairs in a calibration set obtained from a glucose sensor as described in the preferred embodiments. The matched data pairs are plotted according to their sensor data and time-corresponding reference glucose data. A regression line **218** represents the result of regressing the matched data pairs **217** using least squares regression. In this example, the regression line falls within the upper and lower boundaries **215**, **216** indicating that the sensor calibration is acceptable.

[0553] However, if the slope and/or baseline had fallen outside the predetermined acceptable boundaries, which would be illustrated in this graph by a line that crosses the upper and/or lower boundaries **215**, **216**, then the system is configured to assume a baseline value and re-run the regression (or a modified version of the regression) with the assumed baseline, wherein the assumed baseline value is derived from *in vivo* or *in vitro* testing. Subsequently, the newly derived slope and baseline are again tested to determine whether they fall within the predetermined acceptable boundaries. Similarly, the processing continues

in response to the results of the boundary test. In general, for a set of matched pairs (*e.g.*, calibration set), regression lines with higher slope (sensitivity) have a lower baseline and regression lines with lower slope (sensitivity) have a higher baseline. Accordingly, the step of assuming a baseline and testing against boundaries can be repeated using a variety of different assumed baselines based on the baseline, sensitivity, *in vitro* testing, and/or *in vivo* testing. For example, if a boundary test fails due to high sensitivity, then a higher baseline is assumed and the regression re-run and boundary-tested. It is preferred that after about two iterations of assuming a baseline and/or sensitivity and running a modified regression, the system assumes an error has occurred (if the resulting regression lines fall outside the boundaries) and fail-safe. The term "fail-safe" includes modifying the system processing and/or display of data responsive to a detected error avoid reporting of inaccurate or clinically irrelevant analyte values.

[0554] In these various embodiments utilizing an additional electrode, prior information (*e.g.*, *in vitro* or *in vivo* testing), signal processing, or other information for assisting in the calibration process can be used alone or in combination to reduce or eliminate the dependency of the calibration on reference analyte values obtained by the host.

[0555] At block **212**, a sensor data transformation module, also referred to as the calibration module, conversion module, or processor module, uses the conversion function to transform sensor data into substantially real-time analyte value estimates, also referred to as calibrated data, or converted sensor data, as sensor data is continuously (or intermittently) received from the sensor. For example, the sensor data, which can be provided to the receiver in "counts," is translated in to estimate analyte value(s) in mg/dL. In other words, the offset value at any given point in time can be subtracted from the raw value (*e.g.*, in counts) and divided by the slope to obtain the estimate analyte value:

$$mg/dL = \frac{(rawvalue - offset)}{slope}$$

[0556] In some alternative embodiments, the sensor and/or reference analyte values are stored in a database for retrospective analysis.

[0557] In certain embodiments, the sensor data transformation module only converts sensor data points into calibrated data points when a certain analyte value condition is satisfied. Such a condition can include any of the conditions discussed above with

reference to embodiments pre-screening or conditionally accepting reference analyte value data at block **204**, with reference to selecting data pairs at block **208**, or with reference to creating a conversion function at block **210**.

[0558] At block **214**, an output module provides output to the user via the user interface. The output is representative of the estimated analyte value, which is determined by converting the sensor data into a meaningful analyte value. User output can be in the form of a numeric estimated analyte value, an indication of directional trend of analyte concentration, and/or a graphical representation of the estimated analyte data over a period of time, for example. Other representations of the estimated analyte values are also possible, for example audio and tactile.

[0559] In some embodiments, annotations are provided on the graph; for example, bitmap images are displayed thereon, which represent events experienced by the host. For example, information about meals, insulin, exercise, sensor insertion, sleep, and the like, can be obtained by the receiver (by user input or receipt of a transmission from another device) and displayed on the graphical representation of the host's glucose over time. It is believed that illustrating a host's life events matched with a host's glucose concentration over time can be helpful in educating the host to his or her metabolic response to the various events.

[0560] In yet another alternative embodiment, the sensor utilizes one or more additional electrodes to measure an additional analyte. Such measurements can provide a baseline or sensitivity measurement for use in calibrating the sensor. Furthermore, baseline and/or sensitivity measurements can be used to trigger events such as digital filtering of data or suspending display of data, all of which are described in more detail in U.S. Publication No. US-2005-0143635-A1.

[0561] Fig. 19A provides a flow chart **220** that illustrates a process which, for example, a stability module can use in the evaluation of reference and/or sensor data for stability, and/or for statistical, clinical, and/or physiological acceptability. Although some acceptability tests are disclosed herein, any known statistical, clinical, physiological standards and methodologies can be applied to evaluate the acceptability of reference and sensor analyte data.

[0562] In some embodiments, a stability determination module is provided, also referred to as the start-up module or processor module, which determines the stability of the analyte sensor over a period of time. Some analyte sensors can have an initial instability time period during which the analyte sensor is unstable for environmental, physiological, or other reasons. Initial sensor instability can occur, for example, when the analyte sensor is implanted subcutaneously; stabilization of the analyte sensor can be dependent upon the maturity of the tissue ingrowth around and within the sensor. Initial sensor instability can also occur when the analyte sensor is implemented transdermally; stabilization of the analyte sensor can be dependent upon electrode stabilization and/or the presence of sweat, for example.

[0563] Accordingly, in some embodiments, achieving sensor stability can include waiting a predetermined time period (*e.g.*, an implantable subcutaneous sensor can require a time period for tissue growth, and a transcutaneous sensor can require time to equilibrate the sensor with the user's skin). In some embodiments, this predetermined waiting period is from about one minute to about six days, from about 1 day to about five days, or from about two days to about four days for a transcutaneous sensor and from about 1 day to about six weeks, from about 1 week to about five weeks, or about from two weeks to about four weeks for a subcutaneous sensor. In other embodiments for a transcutaneous sensor the waiting period is preferably from about 30 minutes to about 24 hours, or more preferably from about one hour to about 12 hours, or from about 2 hours to about 10 hours. In some embodiments, the sensitivity (*e.g.*, sensor signal strength with respect to analyte concentration) can be used to determine the stability of the sensor; for example, amplitude and/or variability of sensor sensitivity can be evaluated to determine the stability of the sensor. In alternative embodiments, detection of pH levels, oxygen, hypochlorite, interfering species (*e.g.*, ascorbate, urea, and/or acetaminophen), correlation between sensor and reference values (*e.g.*, R-value), baseline drift, and/or offset, and the like can be used to determine the stability of the sensor. In one exemplary embodiment, wherein the sensor is a glucose sensor, a signal can be provided that is associated with interfering species (*e.g.*, ascorbate, urea, acetaminophen and/or the like), which can be used to evaluate sensor stability. In another exemplary embodiment, wherein the sensor is a glucose sensor, the counter electrode can be

monitored for oxygen deprivation, which can be used to evaluate sensor stability or functionality.

[0564] In some embodiments, the system (*e.g.*, microprocessor) determines whether the analyte sensor is sufficiently stable according to certain criteria, such as are described above with reference to Fig. 18A. In one embodiment wherein the sensor is an implantable glucose sensor, the system waits a predetermined time period for sufficient tissue ingrowth and evaluates the sensor sensitivity (*e.g.*, from about one minute to six weeks). In another embodiment, the receiver determines sufficient stability based on oxygen concentration near the sensor head. In yet another embodiment, the sensor determines sufficient stability based on a reassessment of baseline drift and/or offset. In yet another alternative embodiment, the system evaluates stability by monitoring the frequency content of the sensor data stream over a predetermined amount of time (*e.g.*, 24 hours); in this alternative embodiment, a template (or templates) are provided that reflect acceptable levels of glucose physiology and are compared with the actual sensor data, wherein a predetermined degree of agreement between the template and the actual sensor data is indicative of sensor stability. A few examples of determinations of sufficient stability are described herein; however, a variety of known tests and parameters can be used to determine sensor stability without departing from the spirit and scope of the preferred embodiments. If the stability is determined to be insufficient, additional sensor data can be repeatedly taken at predetermined intervals until a sufficient degree of stability is achieved.

[0565] In some embodiments, a clinical acceptability evaluation module, also referred to as clinical module, evaluates the clinical acceptability of newly received reference data and/or time corresponding sensor data. In some embodiments clinical acceptability criteria can include any of the conditions discussed above with reference to Fig. 18A as to pre-screening or conditionally accepting reference analyte value data. In some embodiments of evaluating clinical acceptability, the rate of change of the reference data as compared to previously obtained data is assessed for clinical acceptability. That is, the rate of change and acceleration (or deceleration) of the concentration of many analytes *in vivo* have certain physiological limits within the body. Accordingly, a limit can be set to determine if the new matched pair is within a physiologically feasible range, indicated by a rate of change from the

previous data that is within known physiological and/or statistical limits. Similarly, in some embodiments an algorithm that predicts a future value of an analyte can be used to predict and then compare an actual value to a time corresponding predicted value to determine if the actual value falls within a clinically acceptable range based on the predictive algorithm, for example.

[0566] In one exemplary embodiment, the clinical acceptability evaluation module matches the reference data with a substantially time corresponding converted sensor value, and plots the matched data on a Clarke Error Grid. Such a Clarke Error Grid is described in more detail with reference to Fig. 19B, which is a graph of two data pairs on a Clarke Error Grid that illustrates the evaluation of clinical acceptability in one exemplary embodiment. The Clarke Error Grid can be used by the clinical acceptability evaluation module to evaluate the clinical acceptability of the disparity between a reference glucose value and a sensor glucose (*e.g.*, estimated glucose) value, if any, in an embodiment wherein the sensor is a glucose sensor. The x-axis represents glucose reference glucose data and the y-axis represents estimated glucose sensor data. Matched data pairs are plotted accordingly to their reference and sensor values, respectively. In this embodiment, matched pairs that fall within the A and B regions of the Clarke Error Grid are considered clinically acceptable, while matched pairs that fall within the C, D, and E regions of the Clarke Error Grid are not considered clinically acceptable. Particularly, Fig. 19B shows a first matched pair **1992** is shown which falls within the A region of the Clarke Error Grid, and therefore is considered clinically acceptable. A second matched pair **1994** is shown which falls within the C region of the Clarke Error Grid, and therefore is not considered clinically acceptable.

[0567] A variety of other known methods of evaluating clinical acceptability can be utilized. In one alternative embodiment, the Consensus Grid is used to evaluate the clinical acceptability of reference and sensor data. In another alternative embodiment, a mean absolute difference calculation can be used to evaluate the clinical acceptability of the reference data. In another alternative embodiment, the clinical acceptability can be evaluated using any relevant clinical acceptability test, such as a known grid (*e.g.*, Clarke Error or Consensus), and can include additional parameters such as time of day and/or an increasing or decreasing trend of the analyte concentration. In another alternative embodiment, a rate of

change calculation can be used to evaluate clinical acceptability. In yet another alternative embodiment, wherein the reference data is received in substantially real time, the conversion function can be used to predict an estimated glucose value at a time corresponding to the time stamp of the reference analyte value (*e.g.* when there is a time lag of the sensor data such as described elsewhere herein). Accordingly, a threshold can be set for the predicted estimated glucose value and the reference analyte value disparity, if any.

[0568] The conventional analyte meters (*e.g.*, self-monitored blood analyte tests) are known to have a ±20% error in analyte values. Gross errors in analyte readings are known to occur due to patient error in self-administration of the blood analyte test. For example, if the user has traces of sugar on his/her finger while obtaining a blood sample for a glucose concentration test, then the measured glucose value is likely to be much higher than the actual glucose value in the blood. Additionally, it is known that self-monitored analyte tests (*e.g.*, test strips) are occasionally subject to manufacturing defects.

[0569] Another cause for error includes infrequency and time delay that may occur if a user does not self-test regularly, or if a user self-tests regularly but does not enter the reference value at the appropriate time or with the appropriate time stamp. Therefore, it can be advantageous to validate the acceptability of reference analyte values prior to accepting them as valid entries. Accordingly, the receiver evaluates the clinical acceptability of received reference analyte data prior to their acceptance as a valid reference value.

[0570] In one embodiment, the reference analyte data (and/or sensor analyte data) is evaluated with respect to substantially time corresponding sensor data (and/or substantially time corresponding reference analyte data) to determine the clinical acceptability of the reference analyte and/or sensor analyte data. A determination of clinical acceptability considers a deviation between time corresponding glucose measurements (*e.g.*, data from a glucose sensor and data from a reference glucose monitor) and the risk (*e.g.*, to the decision making of a diabetic patient) associated with that deviation based on the glucose value indicated by the sensor and/or reference data. Evaluating the clinical acceptability of reference and sensor analyte data, and controlling the user interface dependent thereon, can minimize clinical risk.

[0571] In one embodiment, the receiver evaluates clinical acceptability each time reference data is obtained. In another embodiment, the receiver evaluates clinical acceptability after the initial calibration and stabilization of the sensor. In some embodiments, the receiver evaluates clinical acceptability as an initial pre-screen of reference analyte data, for example after determining if the reference glucose measurement is from about 40 to about 400 mg/dL. In other embodiments, other methods of pre-screening data can be used, for example by determining if a reference analyte data value is physiologically feasible based on previous reference analyte data values (*e.g.*, below a maximum rate of change).

[0572] In some embodiments, a calibration evaluation module evaluates the new matched pair(s) for selective inclusion into the calibration set. In some embodiments, the receiver simply adds the updated matched data pair into the calibration set, displaces the oldest and/or least concordant matched pair from the calibration set, and proceeds to recalculate the conversion function accordingly.

[0573] In some embodiments, the calibration evaluation includes evaluating only the new matched data pair. In some embodiments, the calibration evaluation includes evaluating all of the matched data pairs in the existing calibration set and including the new matched data pair; in such embodiments not only is the new matched data pair evaluated for inclusion (or exclusion), but additionally each of the data pairs in the calibration set are individually evaluated for inclusion (or exclusion). In some alternative embodiments, the calibration evaluation includes evaluating all possible combinations of matched data pairs from the existing calibration set and including the new matched data pair to determine which combination best meets the inclusion criteria. In some additional alternative embodiments, the calibration evaluation includes a combination of at least two of the above-described evaluation method.

[0574] Inclusion criteria include at least one criterion that defines a set of matched data pairs that form a substantially optimal calibration set. Such criteria can include any of the conditions discussed above with reference to Fig. 18A concerning methods of pre-screening or conditionally accepting reference analyte value data. One inclusion criterion involves the time stamp of the matched data pairs (that make up the calibration set) spanning

at least a predetermined time period (*e.g.*, three hours). Another inclusion criterion involves the time stamps of the matched data pairs not being more than a predetermined age (*e.g.*, one week old). Another inclusion criterion involves the matched pairs of the calibration set having a substantially evenly distributed amount of high and low raw sensor data, estimated sensor analyte values, and/or reference analyte values. Another criterion involves all raw sensor data, estimated sensor analyte values, and/or reference analyte values being within a predetermined range (*e.g.*, 40 to 400 mg/dL for glucose values). Another criterion involves a rate of change of the analyte concentration (*e.g.*, from sensor data) during the time stamp of the matched pair(s). For example, sensor and reference data obtained during the time when the analyte concentration is undergoing a slow rate of change is typically less susceptible to inaccuracies caused by time lag and other physiological and non-physiological effects. Another criterion involves the congruence of respective sensor and reference data in each matched data pair; the matched pairs with the most congruence are chosen. Another criterion involves physiological changes (*e.g.*, low oxygen due to a user's posture that may effect the function of a subcutaneously implantable analyte sensor) to ascertain a likelihood of error in the sensor value. Evaluation of calibration set criteria can involve evaluating one, some, or all of the above described inclusion criteria. It is contemplated that additional embodiments can comprise additional inclusion criteria not explicitly described herein.

[0575] In some embodiments, a quality evaluation module evaluates the quality of the calibration. In one embodiment, the quality of the calibration is based on the association of the calibration set data using statistical analysis. Statistical analysis can include any known cost function, such as linear regression, non-linear mapping/regression, rank (*e.g.*, non-parametric) correlation, least mean square fit, mean absolute deviation (MAD), mean absolute relative difference, and the like. The result of the statistical analysis provides a measure of the association of data used in calibrating the system. A threshold of data association can be set to determine if sufficient quality is exhibited in a calibration set.

[0576] In another embodiment, the quality of the calibration is determined by evaluating the calibration set for clinical acceptability, such as, for example using a Clarke Error Grid, Consensus Grid, or clinical acceptability test. As an example, the matched data pairs that form the calibration set can be plotted on a Clarke Error Grid, such that when all

matched data pairs fall within the A and B regions of the Clarke Error Grid, then the calibration is determined to be clinically acceptable.

[0577] In yet another alternative embodiment, the quality of the calibration is determined based initially on the association of the calibration set data using statistical analysis, and then by evaluating the calibration set for clinical acceptability. If the calibration set fails the statistical and/or the clinical test, the calibration processing recalculates the conversion function with a new (*e.g.*, optimized) set of matched data pairs. In this embodiment, the processing loop iterates until the quality evaluation module: 1) determines clinical acceptability; 2) determines sufficient statistical data association; 3) determines both clinical acceptability and sufficient statistical data association; or 4) surpasses a threshold of iterations.

[0578] Calibration of analyte sensors can be variable over time; that is, the conversion function suitable for one point in time may not be suitable for another point in time (*e.g.*, hours, days, weeks, or months later). For example, in an embodiment wherein the analyte sensor is subcutaneously implantable, the maturation of tissue ingrowth over time can cause variability in the calibration of the analyte sensor. As another example, physiological changes in the user (*e.g.*, metabolism, interfering blood constituents, and lifestyle changes) can cause variability in the calibration of the sensor. Accordingly, a continuously updating calibration algorithm that includes reforming the calibration set, and thus recalculating the conversion function, over time according to a set of inclusion criteria is advantageous.

[0579] One cause for discrepancies in reference and sensor data is a sensitivity drift that can occur over time, when a sensor is inserted into a host and cellular invasion of the sensor begins to block transport of the analyte to the sensor, for example. Therefore, it can be advantageous to validate the acceptability of converted sensor data against reference analyte data, to determine if a drift of sensitivity has occurred and whether the calibration should be updated.

[0580] In one embodiment, the reference analyte data is evaluated with respect to substantially time corresponding converted sensor data to determine the acceptability of the matched pair. For example, clinical acceptability considers a deviation between time corresponding analyte measurements (for example, data from a glucose sensor and data from

a reference glucose monitor) and the risk (for example, to the decision making of a person with diabetes) associated with that deviation based on the glucose value indicated by the sensor and/or reference data. Evaluating the clinical acceptability of reference and sensor analyte data, and controlling the user interface dependent thereon, can minimize clinical risk. Preferably, the receiver evaluates clinical acceptability each time reference data is obtained.

[0581] After initial calibration, such as is described in more detail with reference to Fig. 18, the sensor data receiving module **222** receives substantially continuous sensor data (*e.g.*, a data stream) via a receiver and converts that data into estimated analyte values. As used herein, the term "substantially continuous" is a broad term and is used in its ordinary sense, without limitation, to refer to a data stream of individual measurements taken at time intervals (*e.g.*, time-spaced) ranging from fractions of a second up to, *e.g.*, 1, 2, or 5 minutes or more. As sensor data is continuously converted, it can be occasionally recalibrated in response to changes in sensor sensitivity (drift), for example. Initial calibration and re-calibration of the sensor require a reference analyte value. Accordingly, the receiver can receive reference analyte data at any time for appropriate processing.

[0582] At block **222**, the reference data receiving module, also referred to as the reference input module, receives reference analyte data from a reference analyte monitor. In one embodiment, the reference data comprises one analyte value obtained from a reference monitor. In some alternative embodiments however, the reference data includes a set of analyte values entered by a user into the interface and averaged by known methods, such as are described elsewhere herein. In some alternative embodiments, the reference data comprises a plurality of analyte values obtained from another continuous analyte sensor.

[0583] The reference data can be pre-screened according to environmental and physiological issues, such as time of day, oxygen concentration, postural effects, and patient-entered environmental data. In one exemplary embodiment, wherein the sensor comprises an implantable glucose sensor, an oxygen sensor within the glucose sensor is used to determine if sufficient oxygen is being provided to successfully complete the necessary enzyme and electrochemical reactions for accurate glucose sensing. In another exemplary embodiment, the patient is prompted to enter data into the user interface, such as meal times and/or amount of exercise, which can be used to determine likelihood of acceptable reference data. In yet

another exemplary embodiment, the reference data is matched with time-corresponding sensor data, which is then evaluated on a modified clinical error grid to determine its clinical acceptability.

[0584] Some evaluation data, such as described in the paragraph above, can be used to evaluate an optimum time for reference analyte measurement. Correspondingly, the user interface can then prompt the user to provide a reference data point for calibration within a given time period. Consequently, because the receiver proactively prompts the user during optimum calibration times, the likelihood of error due to environmental and physiological limitations can decrease and consistency and acceptability of the calibration can increase.

[0585] At block **224**, the evaluation module, also referred to as acceptability module, evaluates newly received reference data. In one embodiment, the evaluation module evaluates the clinical acceptability of newly received reference data and time corresponding converted sensor data (new matched data pair). In one embodiment, a clinical acceptability evaluation module **224** matches the reference data with a substantially time corresponding converted sensor value, and determines the Clarke Error Grid coordinates. In this embodiment, matched pairs that fall within the A and B regions of the Clarke Error Grid are considered clinically acceptable, while matched pairs that fall within the C, D, and E regions of the Clarke Error Grid are not considered clinically acceptable.

[0586] A variety of other known methods of evaluating clinical acceptability can be utilized. In one alternative embodiment, the Consensus Grid is used to evaluate the clinical acceptability of reference and sensor data. In another alternative embodiment, a mean absolute difference calculation can be used to evaluate the clinical acceptability of the reference data. In another alternative embodiment, the clinical acceptability can be evaluated using any relevant clinical acceptability test, such as a known grid (*e.g.*, Clarke Error or Consensus), and additional parameters, such as time of day and/or the increase or decreasing trend of the analyte concentration. In another alternative embodiment, a rate of change calculation can be used to evaluate clinical acceptability. In yet another alternative embodiment, wherein the received reference data is in substantially real time, the conversion function could be used to predict an estimated glucose value at a time corresponding to the time stamp of the reference analyte value (this can be required due to a time lag of the sensor

data such as described elsewhere herein). Accordingly, a threshold can be set for the predicted estimated glucose value and the reference analyte value disparity, if any. In some alternative embodiments, the reference data is evaluated for physiological and/or statistical acceptability as described in more detail elsewhere herein.

[0587] At decision block **226**, results of the evaluation are assessed. If acceptability is determined, then processing continues to block **228** to re-calculate the conversion function using the new matched data pair in the calibration set.

[0588] At block **228**, the conversion function module re-creates the conversion function using the new matched data pair associated with the newly received reference data. In one embodiment, the conversion function module adds the newly received reference data (*e.g.*, including the matched sensor data) into the calibration set, and recalculates the conversion function accordingly. In alternative embodiments, the conversion function module displaces the oldest, and/or least concordant matched data pair from the calibration set, and recalculates the conversion function accordingly.

[0589] At block **230**, the sensor data transformation module uses the new conversion function (from block **228**) to continually (or intermittently) convert sensor data into estimated analyte values, also referred to as calibrated data, or converted sensor data, such as is described in more detail above.

[0590] At block **232**, an output module provides output to the user via the user interface. The output is representative of the estimated analyte value, which is determined by converting the sensor data into a meaningful analyte value. User output can be in the form of a numeric estimated analyte value, an indication of directional trend of analyte concentration, and/or a graphical representation of the estimated analyte data over a period of time, for example. Other representations of the estimated analyte values are also possible, for example audio and tactile.

[0591] If, however, acceptability is determined at decision block **226** as negative (unacceptable), then the processing progresses to block **234** to adjust the calibration set. In one embodiment of a calibration set adjustment, the conversion function module removes one or more oldest matched data pair(s) and recalculates the conversion function accordingly. In an alternative embodiment, the conversion function module removes the least concordant

matched data pair from the calibration set, and recalculates the conversion function accordingly.

[0592] At block **236**, the conversion function module re-creates the conversion function using the adjusted calibration set. While not wishing to be bound by theory, it is believed that removing the least concordant and/or oldest matched data pair(s) from the calibration set can reduce or eliminate the effects of sensor sensitivity drift over time, adjusting the conversion function to better represent the current sensitivity of the sensor.

[0593] At block **224**, the evaluation module re-evaluates the acceptability of newly received reference data with time corresponding converted sensor data that has been converted using the new conversion function (block **236**). The flow continues to decision block **238** to assess the results of the evaluation, such as described with reference to decision block **226**, above. If acceptability is determined, then processing continues to block **230** to convert sensor data using the new conversion function and continuously display calibrated sensor data on the user interface.

[0594] If, however, acceptability is determined at decision block **226** as negative, then the processing loops back to block **234** to adjust the calibration set once again. This process can continue until the calibration set is no longer sufficient for calibration, for example, when the calibration set includes only one or no matched data pairs with which to create a conversion function. In this situation, the system can return to the initial calibration or start-up mode, which is described in more detail with reference to Figs. 18 and 21, for example. Alternatively, the process can continue until inappropriate matched data pairs have been sufficiently purged and acceptability is positively determined.

[0595] In alternative embodiments, the acceptability is determined by a quality evaluation, for example, calibration quality can be evaluated by determining the statistical association of data that forms the calibration set, which determines the confidence associated with the conversion function used in calibration and conversion of raw sensor data into estimated analyte values. See, *e.g.*, U.S. Publication No. US-2005-0027463-A1.

[0596] Alternatively, each matched data pair can be evaluated based on clinical or statistical acceptability such as described above; however, when a matched data pair does not pass the evaluation criteria, the system can be configured to ask for another matched data pair

from the user. In this way, a secondary check can be used to determine whether the error is more likely due to the reference glucose value or to the sensor value. If the second reference glucose value substantially correlates to the first reference glucose value, it can be presumed that the reference glucose value is more accurate and the sensor values are errant. Some reasons for errancy of the sensor values include a shift in the baseline of the signal or noise on the signal due to low oxygen, for example. In such cases, the system can be configured to re-initiate calibration using the secondary reference glucose value. If, however, the reference glucose values do not substantially correlate, it can be presumed that the sensor glucose values are more accurate and the reference glucose values eliminated from the algorithm.

[0597] Fig. 20 provides is a flow chart **250** that illustrates the evaluation of calibrated sensor data for aberrant values in one embodiment. Although sensor data are typically accurate and reliable, it can be advantageous to perform a self-diagnostic check of the calibrated sensor data prior to displaying the analyte data on the user interface.

[0598] One reason for anomalies in calibrated sensor data includes transient events, such as local ischemia at the implant site, which can temporarily cause erroneous readings caused by insufficient oxygen to react with the analyte. Accordingly, the flow chart **190** illustrates one self-diagnostic check that can be used to catch erroneous data before displaying it to the user.

[0599] At block **252**, a sensor data receiving module, also referred to as the sensor data module, receives new sensor data from the sensor.

[0600] At block **254**, the sensor data transformation module continuously (or intermittently) converts new sensor data into estimated analyte values, also referred to as calibrated data.

[0601] At block **256**, a self-diagnostic module compares the new calibrated sensor data with previous calibrated sensor data, for example, the most recent calibrated sensor data value. In comparing the new and previous sensor data, a variety of parameters can be evaluated. In one embodiment, the rate of change and/or acceleration (or deceleration) of change of various analytes, which have known physiological limits within the body, and sensor data can be evaluated accordingly. For example, a limit can be set to determine if the new sensor data is within a physiologically feasible range, indicated by a rate of change from

the previous data that is within known physiological (and/or statistical) limits. Similarly, any algorithm that predicts a future value of an analyte can be used to predict and then compare an actual value to a time corresponding predicted value to determine if the actual value falls within a statistically and/or clinically acceptable range based on the predictive algorithm, for example. In certain embodiments, identifying a disparity between predicted and measured analyte data can be used to identify a shift in signal baseline responsive to an evaluated difference between the predicted data and time-corresponding measured data. In some alternative embodiments, a shift in signal baseline and/or sensitivity can be determined by monitoring a change in the conversion function; namely, when a conversion function is re-calculated using the equation $y=mx+b$, a change in the values of m (sensitivity) or b (baseline) above a pre-selected "normal" threshold, can be used to trigger a fail-safe or further diagnostic evaluation.

[0602] Although the above-described self-diagnostics are generally employed with calibrated sensor data, some alternative embodiments are contemplated that check for aberrancy of consecutive sensor values prior to sensor calibration, for example, on the raw data stream and/or after filtering of the raw data stream. In certain embodiments, an intermittent or continuous signal-to-noise measurement can be evaluated to determine aberrancy of sensor data responsive to a signal-to-noise ratio above a set threshold. In certain embodiments, signal residuals (*e.g.,* by comparing raw and filtered data) can be intermittently or continuously analyzed for noise above a set threshold. In certain embodiments, pattern recognition can be used to identify noise associated with physiological conditions, such as low oxygen (see, *e.g.*, U.S. Publication No. US-2005-0043598-A1), or other known signal aberrancies. Accordingly, in these embodiments, the system can be configured, in response to aberrancies in the data stream, to trigger signal estimation, adaptively filter the data stream according to the aberrancy, or the like, as described in more detail in the above cited U.S. Publication No. US-2005-0043598-A1.

[0603] In another embodiment, reference analyte values are processed to determine a level of confidence, wherein reference analyte values are compared to their time-corresponding calibrated sensor values and evaluated for clinical or statistical accuracy. In yet another alternative embodiment, new and previous reference analyte data are compared in

place of or in addition to sensor data. In general, there exist known patterns and limitations of analyte values that can be used to diagnose certain anomalies in raw or calibrated sensor and/or reference analyte data.

[0604] Block **193** describes additional systems and methods that can by utilized by the self-diagnostics module of the preferred embodiments.

[0605] At decision block **258**, the system determines whether the comparison returned aberrant values. In one embodiment, the slope (rate of change) between the new and previous sensor data is evaluated, wherein values greater than +/-10, 15, 20, 25, or 30% or more change and/or +/-2, 3, 4, 5, 6 or more mg/dL/min, more preferably +/-4 mg/dL/min, rate of change are considered aberrant. In certain embodiments, other known physiological parameters can be used to determine aberrant values. However, a variety of comparisons and limitations can be set.

[0606] At block **260**, if the values are not found to be aberrant, the sensor data transformation module continuously (or intermittently) converts received new sensor data into estimated analyte values, also referred to as calibrated data.

[0607] At block **262**, if the values are found to be aberrant, the system goes into a suspended mode, also referred to as fail-safe mode in some embodiments, which is described in more detail below with reference to Fig. 21. In general, suspended mode suspends display of calibrated sensor data and/or insertion of matched data pairs into the calibration set. Preferably, the system remains in suspended mode until received sensor data is not found to be aberrant. In certain embodiments, a time limit or threshold for suspension is set, after which system and/or user interaction can be required, for example, requesting additional reference analyte data, replacement of the electronics unit, and/or reset.

[0608] In some alternative embodiments, in response to a positive determination of aberrant value(s), the system can be configured to estimate one or more glucose values for the time period during which aberrant values exist. Signal estimation generally refers to filtering, data smoothing, augmenting, projecting, and/or other methods for estimating glucose values based on historical data, for example. In one implementation of signal estimation, physiologically feasible values are calculated based on the most recent glucose data, and the aberrant values are replaced with the closest physiologically feasible glucose

values. See also U.S. Publication No. US-2005-0027463-A1, U.S. Publication No. US-2005-0043598-A1, and U.S. Publication No. US-2005-0203360-A1.

[0609] Fig. 21 provides a flow chart **280** that illustrates a self-diagnostic of sensor data in one embodiment. Although reference analyte values can useful for checking and calibrating sensor data, self-diagnostic capabilities of the sensor provide for a fail-safe for displaying sensor data with confidence and enable minimal user interaction (for example, requiring reference analyte values only as needed).

[0610] At block **282**, a sensor data receiving module, also referred to as the sensor data module, receives new sensor data from the sensor.

[0611] At block **284**, the sensor data transformation module continuously (or intermittently) converts received new sensor data into estimated analyte values, also referred to as calibrated data.

[0612] At block **286**, a self-diagnostics module, also referred to as a fail-safe module, performs one or more calculations to determine the accuracy, reliability, and/or clinical acceptability of the sensor data. Some examples of the self-diagnostics module are described above, with reference block **256**. The self-diagnostics module can be further configured to run periodically (*e.g.*, intermittently or in response to a trigger), for example, on raw data, filtered data, calibrated data, predicted data, and the like.

[0613] In certain embodiments, the self-diagnostics module evaluates an amount of time since sensor insertion into the host, wherein a threshold is set for the sensor's usable life, after which time period the sensor is considered to be unreliable. In certain embodiments, the self-diagnostics module counts the number of times a failure or reset is required (for example, how many times the system is forced into suspended or start-up mode), wherein a count threshold is set for a predetermined time period, above which the system is considered to be unreliable. In certain embodiments, the self-diagnostics module compares newly received calibrated sensor data with previously calibrated sensor data for aberrant values, such as is described in more detail with reference to Fig. 5, above. In certain embodiments, the self-diagnostics module evaluates clinical acceptability, such as is described in more detail with reference to Fig. 20, above. In certain embodiments, diagnostics, such as are described in U.S. Publication No. US-2005-0161346-A1 and U.S.

Publication No. US-2005-0143635-A1, can be incorporated into the systems of preferred embodiments for system diagnosis, for example, for identifying interfering species on the sensor signal and for identifying drifts in baseline and sensitivity of the sensor signal.

[0614] In some embodiments, an interface control module, also referred to as the fail-safe module, controls the user interface based upon the clinical acceptability of the reference data received. If the reference data is not considered clinically acceptable, then a fail-safe module begins the initial stages of fail-safe mode. In some embodiments, the initial stages of fail-safe mode include altering the user interface so that estimated sensor data is not displayed to the user. In some embodiments, the initial stages of fail-safe mode include prompting the user to repeat the reference analyte test and provide another reference analyte value. The repeated analyte value is then evaluated for clinical acceptability.

[0615] If the results of the repeated analyte test are determined to be clinically unacceptable, then the fail-safe module can alter the user interface to reflect full fail-safe mode. In one embodiment, full fail-safe mode includes discontinuing sensor analyte display output on the user interface. In other embodiments, color-coded information, trend information, directional information (*e.g.*, arrows or angled lines), gauges, and/or other fail-safe information can be displayed, for example.

[0616] The initial stages of fail-safe mode and full fail safe mode can include user interface control, for example. Additionally, it is contemplated herein that a variety of different modes between initial and full fail-safe mode can be provided, depending on the relative quality of the calibration. In other words, the confidence level of the calibration quality can control a plurality of different user interface screens providing error bars, ± values, and the like. Similar screens can be implemented in various clinical acceptability embodiments.

[0617] At block **288** of Fig. 21, a mode determination module, which can be a part of the sensor evaluation module **224**, determines in which mode the sensor is set (or remains in). In some embodiments, the system is programmed with three modes: 1) start-up mode; 2) normal mode; and 3) suspended mode. Although three modes are described herein, the preferred embodiments are not limited to the number or types of modes with which the system can be programmed. In some embodiments, the system is defined as "in-

cal" (in calibration) in normal mode; otherwise, the system is defined as "out-of-cal' (out of calibration) in start-up and suspended mode. The terms as used herein are meant to describe the functionality and are not limiting in their definitions.

[0618] Preferably, a start-up mode is provided wherein the start-up mode is set when the system determines that it can no longer remain in suspended or normal mode (for example, due to problems detected by the self-diagnostics module, such as described in more detail above) and/or when the system is notified that a new sensor has been inserted. Upon initialization of start-up mode, the system ensures that any old matched data pairs and/or calibration information is purged. In start-up mode, the system initializes the calibration set, such as is described in more detail with reference to Fig. 14, above. Once the calibration set has been initialized, sensor data is ready for conversion and the system is set to normal mode.

[0619] Preferably, a normal mode is provided wherein the normal mode is set when the system is accurately and reliably converting sensor data, for example, wherein clinical acceptability is positively determined, aberrant values are negatively determined, and/or the self-diagnostics modules confirms reliability of data. In normal mode, the system continuously (or intermittently) converts (or calibrates) sensor data. Additionally, reference analyte values received by the system are matched with sensor data points and added to the calibration set.

[0620] In certain embodiments, the calibration set is limited to a predetermined number of matched data pairs, after which the systems purges old or less desirable matched data pairs when a new matched data pair is added to the calibration set. Less desirable matched data pairs can be determined by inclusion criteria, which include one or more criteria that define a set of matched data pairs that form a substantially optimal calibration set.

[0621] Unfortunately, some circumstances can exist wherein a system in normal mode is changed to start-up or suspended mode. In general, the system is programmed to change to suspended mode when a failure of clinical acceptability, aberrant value check, and/or other self-diagnostic evaluation is determined, such as described in more detail above, and wherein the system requires further processing to determine whether a system re-start is required (*e.g.*, start-up mode). In general, the system changes to start-up mode when the

system is unable to resolve itself in suspended mode and/or when the system detects that a new sensor has been inserted (*e.g.*, via system trigger or user input).

[0622] Preferably, a suspended mode is provided wherein the suspended mode is set when a failure of clinical acceptability, aberrant value check, and/or other self-diagnostic evaluation determines unreliability of sensor data. In certain embodiments, the system enters suspended mode when a predetermined time period passes without receiving a reference analyte value. In suspended mode, the calibration set is not updated with new matched data pairs, and sensor data can optionally be converted, but not displayed on the user interface. The system can be changed to normal mode upon resolution of a problem (positive evaluation of sensor reliability from the self-diagnostics module, for example). The system can be changed to start-up mode when the system is unable to resolve itself in suspended mode and/or when the system detects a new sensor has been inserted (via system trigger or user input).

[0623] The systems of preferred embodiments, including a transcutaneous analyte sensor, mounting unit, electronics unit, applicator, and receiver for inserting the sensor, and measuring, processing, and displaying sensor data, provide improved convenience and accuracy because of their designed stability within the host's tissue with minimum invasive trauma, while providing a discreet and reliable data processing and display, thereby increasing overall host comfort, confidence, safety, and convenience. Namely, the geometric configuration, sizing, and material of the sensor of the preferred embodiments enable the manufacture and use of an atraumatic device for continuous measurement of analytes, in contrast to conventional continuous glucose sensors available to persons with diabetes, for example. Additionally, the sensor systems of preferred embodiments provide a comfortable and reliable system for inserting a sensor and measuring an analyte level for up to 30 days or more without surgery. The sensor systems of the preferred embodiments are designed for host comfort, with chemical and mechanical stability that provides measurement accuracy. Furthermore, the mounting unit is designed with a miniaturized and reusable electronics unit that maintains a low profile during use. The usable life of the sensor can be extended by incorporation of a bioactive agent into the sensor that provides local release of an anti-

inflammatory, for example, in order to slow the subcutaneous foreign body response to the sensor.

[0624] After the usable life of the sensor (for example, due to a predetermined expiration, potential infection, or level of inflammation), the host can remove the transcutaneous sensor and mounting from the skin, and dispose of the sensor and mounting unit (preferably saving the electronics unit for reuse). Another transcutaneous sensor system can be inserted with the reusable electronics unit and thus provide continuous sensor output for long periods of time.

Examples

[0625] Fig. 22A is a graphical representation showing transcutaneous glucose sensor data and corresponding blood glucose values over time in a human. The x-axis represents time, the first y-axis represents current in picoAmps, and the second y-axis represents blood glucose in mg/dL. As depicted on the legend, the small diamond points represent the current measured from the working electrode of a transcutaneous glucose sensor of a preferred embodiment; while the larger points represent blood glucose values of blood withdrawn from a finger stick and analyzed using an *in vitro* self-monitoring blood glucose meter (SMBG).

[0626] A transcutaneous glucose sensor was built according to the preferred embodiments and implanted in a human host where it remained over a period of time. Namely, the sensor was built by providing a platinum wire, vapor-depositing the platinum with Parylene to form an insulating coating, helically winding a silver wire around the insulated platinum wire (to form a "twisted pair"), masking sections of the electroactive surface of the silver wire, vapor-depositing Parylene on the twisted pair, chloridizing the silver electrode to form silver chloride reference electrode, and removing a radial window on the insulated platinum wire to expose a circumferential electroactive working electrode surface area thereon, this assembly also referred to as a "parylene-coated twisted pair assembly."

[0627] An interference domain was formed on the parylene-coated twisted pair assembly by dip coating in an interference domain solution (7 weight percent of a 50,000 molecular weight cellulose acetate (Sigma-Aldrich, St. Louis, MO) in a 2:1 acetone/ethanol

solvent solution), followed by drying at room temperature for 3 minutes. This interference domain solution dip coating step was repeated two more times to form an interference domain comprised of 3 layers of cellulose acetate on the assembly. The dip length (insertion depth) was adjusted to ensure that the cellulose acetate covered from the tip of the working electrode, over the exposed electroactive working electrode window, to cover a distal portion of the exposed electroactive reference electrode.

[0628] An enzyme domain was formed over the interference domain by subsequently dip coating the assembly in an enzyme domain solution and drying in a vacuum oven for 20 minutes at 50°C. This dip coating process was repeated once more to form an enzyme domain having two layers. A resistance domain was formed over the interference domain by subsequently spray coating the assembly with a resistance domain solution and drying the assembly in a vacuum oven for 60 minutes at 50°C. Additionally, the sensors were exposed to electron beam radiation at a dose of 25 kGy, while others (control sensors) were not exposed to electron beam radiation.

[0629] The graph of Fig. 22A illustrates approximately 3 days of data obtained by the electronics unit operably connected to the sensor implanted in the human host. Finger-prick blood samples were taken periodically and glucose concentration measured by a blood glucose meter (SMBG). The graphs show the subcutaneous sensor data obtained by the transcutaneous glucose sensor tracking glucose concentration as it rose and fell over time. The time-corresponding blood glucose values show the correlation of the sensor data to the blood glucose data, indicating appropriate tracking of glucose concentration over time.

[0630] The raw data signal obtained from the sensor electronics has a current measurement in the picoAmp range. Namely, for every unit (mg/dL) of glucose, approximately 3.5pA or less to 7.5 pA or more current is measured. Generally, the approximately 3.5 to 7.5 pA/mg/dL sensitivity exhibited by the device can be attributed to a variety of design factors, including resistance of the membrane system to glucose, amount of enzyme in the membrane system, surface area of the working electrode, and electronic circuitry design. Accordingly, a current in the picoAmp range enables operation of an analyte sensor that: 1) requires (or utilizes) less enzyme (*e.g.*, because the membrane system is highly resistive and allows less glucose through for reaction in the enzyme domain); 2) requires less

oxygen (*e.g.*, because less reaction of glucose in the enzyme domain requires less oxygen as a co-reactant) and therefore performs better during transient ischemia of the subcutaneous tissue; and 3) accurately measures glucose even in hypoglycemic ranges (*e.g.*, because the electronic circuitry is able to measure very small amounts of glucose (hydrogen peroxide at the working electrode)). Advantageously, the analyte sensors of the preferred embodiments exhibit improved performance over convention analyte sensors at least in part because a current in the picoAmp range enables operation in conditions of less enzyme, and less oxygen, better resolution, lower power usage, and therefore better performance in the hypoglycemic range wherein lower mg/dL values conventionally have yielded lower accuracy.

[0631] Fig. 22B is a graphical representation showing transcutaneous glucose sensor data and corresponding blood glucose values over time in a human. The x-axis represents time; the y-axis represents glucose concentration in mg/dL. As depicted on the legend, the small diamond points represent the calibrated glucose data measured from a transcutaneous glucose sensor of a preferred embodiment; while the larger points represent blood glucose values of blood withdrawn from a finger stick and analyzed using an *in vitro* self-monitoring blood glucose meter (SMBG). The calibrated glucose data corresponds to the data of Fig. 22A shown in current, except it has been calibrated using algorithms of the preferred embodiments. Accordingly, accurate subcutaneous measurement of glucose concentration has been measured and processed using the systems and methods of the preferred embodiments.

[0632] Fig. 23A is a graphical representation showing transcutaneous glucose sensor data and corresponding blood glucose values obtained over approximately seven days in a human. The x-axis represents time; the y-axis represents glucose concentration in mg/dL. As depicted on the legend, the small diamond points represent the calibrated glucose data measured from a transcutaneous glucose sensor of a preferred embodiment; while the larger points represent blood glucose values of blood withdrawn from a finger stick and analyzed using an *in vitro* self-monitoring blood glucose meter (SMBG). The calibrated glucose data corresponds to a sensor that was implanted in a human for approximately seven days, showing an extended functional life, as compare to three days, for example.

Differentiation of Sensor Systems

[0633] Some embodiments provide sensor systems suitable for implantation for 1, 3, 5, 7,10, 15, 20, 25, or 30 days or more. Alternatively, sensors designed for shorter or longer durations can have one or more specific design features (*e.g.*, membrane systems, bioactive agent(s), architecture, electronic design, power source, software, or the like) customized for the intended sensor life. Similarly, some embodiments provide sensor systems suitable for a variety of uses such as pediatrics, adults, geriatrics, persons with type-1 diabetes, persons with type-2 diabetes, intensive care (ICU), hospital use, home use, rugged wear, everyday wear, exercise, and the like, wherein the sensor systems include particular design features (*e.g.*, membrane systems, bioactive agent(s), architecture, electronic design, power source, software, or the like) customized for an intended use. Accordingly, it can be advantageous to differentiate sensor systems that are substantially similar, for example, sensors wherein the electronics unit of a sensor system can releasably mate with different mounting units, or sensors wherein different electronics units designed for different functionality can mate with a specific mounting unit.

[0634] In some embodiments, the mechanical, electrical, and/or software design enables the differentiation (*e.g.*, non-interchangeability) of these different sensor systems. In other words, the sensor systems can be "keyed" to ensure a proper match between an electronics unit and a mounting unit (housing including sensor) as described herein. The terms "key" and "keyed" as used herein are broad terms and are used in their ordinary sense, including, without limitation, to refer to systems and methods that control the operable connection or operable communication between the sensor, its associated electronics, the receiver, and/or its associated electronics. The terms are broad enough to include mechanical, electrical, and software "keys." For example, a mechanically designed key can include a mechanical design that allows an operable connection between two parts, for example, a mating between the electronics unit and the mounting unit wherein the contacts are keyed to mutually engage contacts of complementary parts. As another example, an electronically designed key can be embedded in a radio frequency identification chip (RFID chip) on the mounting unit, wherein the electronics unit is programmed to identify a predetermined identification number (e.g., key) from the RFID chip prior to operable

connection or communication between the sensor and/or sensor electronics. Alternatively, the sensor's packaging can include an RFID chip with the key embedded therein and configured to provide key information to the electronics unit and/or receiver. As yet another example, a software key can include a code or serial number that identifies a sensor and/or electronics unit.

[0635] Accordingly, systems and methods are provided for measuring an analyte in a host, including: a sensor configured for transcutaneous insertion into a host's tissue; a housing adapted for placement external to the host's tissue and for supporting the sensor; and an electronics unit releasably attachable to said housing, wherein at least one of the housing and the electronics unit are keyed to provide a match between the sensor and the electronics unit.

[0636] In some embodiments, the housing (including a sensor) and its matching electronics unit(s) are keyed by a configuration of the one or more contacts thereon. Figs. 4A to 4C illustrate three unique contact configurations, wherein the configurations are differentiated by a distance between the first and second contacts located within the housing. In this embodiment, a properly keyed electronics unit is configured with contacts that mate with the contacts on a mating housing (Figs. 4A to 4C), for example a narrow contact configuration on a housing mates only with a narrow contact configuration on an electronics unit. Accordingly, in practice, only an electronics unit comprising a contact configuration that is designed for mutual engagement with a similarly "keyed" housing can be operably connected thereto.

[0637] In some embodiments, the electronics unit is programmed with an ID, hereinafter referred to as a "transmitter ID," that uniquely identifies a sensor system. In one exemplary embodiment, wherein a first sensor system is designed for 3 day use and a second sensor system is designed for 7 day use, the transmitter ID can be programmed to begin with a "3" or a "7" in order to differentiate the sensor systems. In practice, a 3 day sensor system is programmed for 3 day use (see enforcement of sensor expiration described in more detail below), and thus upon operable connection of a 3 day sensor system, the receiver can function for the appropriate duration according to the transmitter ID.

[0638] In some embodiments, each sensor system is associated with a unique or near-unique serial number, which is associated with one or a set of sensor systems. This serial number can include information such as intended duration, calibration information, and the like, so that upon sensor insertion, and operable connection of the sensor electronics, the serial number can be manually entered into the receiver (from the packaging, for example) or can be automatically transmitted from the sensor's electronics unit. In this way, the serial number can provide the necessary information to enable the sensor system to function for the intended duration.

[0639] Additionally or alternatively, the electronics unit and/or mounting unit can be labeled or coded, for example, alpha-numerically, pictorially, or colorfully, to differentiate unique sensor systems. In this way, a user is less likely to confuse different sensor systems.

Enforcement of Sensor Expiration (Duration of Sensor Life)

[0640] In some embodiments, sensor systems are packaged as starter sets, which include at least one reusable (durable) receiver, at least one reusable (durable) electronics unit and one or more single-use sensors, each including an applicator and a mounting unit with the sensor. In some alternative embodiments, the electronics unit is designed for single-use and can optionally be integrally formed with the sensor and/or mounting unit. Preferably, a single receiver, and in some embodiments a single electronics unit, is configured for use (e.g., reusable) with a plurality of sensors. Additionally, single-use sensors can be packaged individually or as sets (e.g., 5-, 10-, or 15 sensor systems per package (e.g., sensor refill packs)). Preferably, each sensor is configured for a predetermined duration (e.g., 3-, 5-, 7-, 10-, 15-, 20-, 25-, or 30 days or more of operation). In alternative embodiments, the electronics unit can be configured for single-use; for example, the electronics unit may be integral with the sensor (e.g., mounting unit with sensor) described with this embodiment. Additionally, the applicator can be coupled to the mounting unit prior to packaging or configured to be coupled by the user prior to insertion.

[0641] Because in some embodiments, the receiver is intended to be reused with a plurality of sensor systems, which sensor systems are configured for a predetermined duration, systems and methods for enforcing the prescribed use of each sensor system can be advantageous to ensure that the user removes and reinserts the sensor systems within

prescribed time periods. Accordingly, systems and methods are provided for limiting the use of each sensor system to its predetermined duration.

[0642] In general, transcutaneous sensor systems can be designed for a predetermined (prescribed) amount of time (*e.g.*, a few hours to 30 days or more). Some embodiments provide sensors suitable for 1-, 3-, 5-, 7-, 10-, 15-, 20-, 25-, or 30 days or more of operation. One potential problem that can occur in practice is the continued use of the sensor beyond its intended life; for example, a host may not remove the sensor after its intended life and/or the host can detach and reattach the electronics unit into the mounting unit (which may cause a refresh of the sensor system and/or use beyond its intended life in some circumstances). Accordingly, systems and methods are needed for ensuring the sensor system is used for its proper duration and that accidental or intentional efforts to improperly extend or reuse the sensor system are avoided.

[0643] The preferred embodiments provide systems and methods for measuring an analyte in a host, the system including: a sensor adapted for transcutaneous insertion through the skin of a host; a housing adapted for placement adjacent to the host's skin and for supporting the sensor upon insertion through the skin; and an electronics unit operably connected to the housing, wherein the sensor system is configured to prevent use of the sensor (*e.g.*, to render the sensor inoperative or disable display of sensor data) beyond a predetermined time period.

[0644] In some embodiments, the sensor system is configured to destroy the sensor when the electronics unit is removed and/or after a predetermined time period has expired. In one exemplary embodiment, a loop of material surrounds a portion of the sensor and is configured to retract the sensor (from the host) when the electronics unit is removed from the housing. In another embodiment, the sensor system is configured to cut, crimp, or otherwise destroy the sensor when the electronics unit is removed from the housing.

[0645] In some embodiments, the sensor system is programmed to determine whether to allow an initialization of a new sensor. For example, the receiver can be programmed to require the sensor be disconnected prior to initiation of the receiver for an additional sensor system. In one such exemplary embodiment, the receiver can be programmed to look for a zero from the electronics unit, indicating the sensor has been

disconnected, prior to allowing a new sensor to be initiated. This can help to ensure that a user actually removes the electronics unit (and/or sensor) prior to initialization of a new sensor. In another such embodiment, sensor insertion information can be programmed into the sensor electronics, such that the sensor insertion information is transmitted to the receiver to allow initialization of a new sensor.

[0646] In some embodiments, the receiver software receives information from the electronics unit (*e.g.*, intended duration, transmitter ID, expiration date, serial code, manufacture date, or the like) and is programmed to automatically shut down after a predetermined time period (intended duration) or sensor expiration, for example.

[0647] In some embodiments, the receiver is programmed to algorithmically identify a new sensor insertion by looking for change in signal characteristic (*e.g.*, a spike indicating break-in period, no change in sensor count values during the first hour, or the like). If a user has not inserted a new sensor, then the continued use of an expired sensor can be detected and can be used to trigger a shut down of the sensor and/or receiver.

[0648] In some embodiments, each sensor system is associated with a unique or near-unique serial number, which is associated with one or a set of sensor systems as described in more detail above. In general, the serial number can include information such as calibration information, intended duration, manufacture date, expiration date, and the like. For example, the serial number can provide sensor life (intended duration) information, which can be used to shut down the sensor and/or receiver (e.g., display of sensor data and/or use of the sensor) after the intended sensor life.

[0649] In some embodiments, one or a set of sensors are packaged such that a serial number, which is associated with the one sensor and/or the set of sensors, also referred to as a key or license code, is provided to enable the use of the sensor system. In preferred embodiments, the license code includes one or more of the following: a unique number, a receiver ID, a sensor duration, and a number of sensors for which the license code is enabled. The unique number preferably includes an auto-generated number that increments each time a license is issued. However, one skilled in the art will appreciate that a variety of unique numbering techniques can be utilized; the unique number is designed to reduce or eliminate fraud, such as reuse of a license code. The receiver ID (receiver identification) preferably

includes a unique number associated with an individual receiver, which ensures that the license code is used with a particular receiver. The sensor duration preferably includes a predetermined time period for which the sensor use is prescribed (e.g., sensor life such as 1-, 3-, 5-, 7-, 10-, 15-, 20-, 25-, or 30 days or more) after which the sensor is disabled. The number of sensor systems for which the license code is enabled preferably includes a number that represents how many sensor insertions (e.g., number of sensor initializations or how many iterations of the sensor duration) are allowed using the unique license code; in some embodiments, this is the number of sensors provided in a packaged set of sensors.

[0650] The license code is designed to be input, either manually or automatically, into the sensor system (e.g., receiver or on-skin device), after which the sensor system (e.g., receiver or on-skin device) controls the display of sensor data. In one embodiment, a user is instructed to obtain a license code and manually enter the code into the receiver. In one alternative embodiment, a sensor system (e.g., packaging, single-use portion of the sensor, mounting unit and/or electronics unit) includes an embedded license code, for example, within an embedded RFID chip. In one exemplary embodiment, the RFID chip is configured to transmit the license code information to the receiver (e.g., when requested by the receiver).

[0651] Preferably, the license code is configured control the amount of time over which information is obtained from the sensor. The phrase "information ... obtained from the sensor" can refer without limitation to any sensor information obtained, including measured, processed, transmitted and/or displayed in any manner including: measurement of the analyte information (e.g., glucose concentration) by the sensor, digitalizing of the sensor information (e.g., raw or filtered data) by the electronics unit, transmission of the sensor information (e.g., sensor data) from the electronics unit, receiving of the sensor information by the receiver, storing or processing of the sensor information by the receiver, and/or displaying of the sensor information by the receiver or other device. Accordingly, when the licensed (or prescribed) sensor duration and/or number of sensor insertions has been met, the receiver is configured to disable the "obtaining of information" (e.g., disabling display of the sensor data and/or any other method such as described above). In some embodiments, the sensor can continue to collect and store data after the sensor system has disabled "obtaining of information." Additionally or alternatively, the prescribed sensor duration can be enforced

using any of the mechanical (e.g., destruction of the sensor), electrical, or software techniques described elsewhere herein and as will be appreciated by one skilled in the art.

[0652] The above described systems and methods for differentiating sensor systems and enforcing sensor lifetimes can be used alone or in combination, and can be combined with any of the preferred embodiments.

Distributing and controlling use of sensor systems including single-use (disposable) and reusable (durable) parts

[0653] Fig. 23B is a flow diagram that illustrates a method for distributing and controlling use of sensor systems including disposable and reusable parts **300** in one embodiment.

[0654] At block **302**, a user (doctor, patient, or other care provider) obtains reusable sensor system parts. Preferably sensor system is distributed with a starter pack including at least one of each reusable part. In general, the reusable sensor parts include at least the receiver, whereby a plurality of single-use sensors can be used with the receiver. In some embodiments the electronics unit is also reusable as shown and described in the illustrated embodiments; however, the sensor electronics can be integral with the single-use mounting unit/sensor in some embodiments as described elsewhere herein.

[0655] At block **304**, the user obtains single-use sensor system parts. In some embodiments, the starter pack described above further includes one or more single-use sensors. Additionally or alternatively, one or a plurality of single-use sensors are packaged together.

[0656] At block **306**, the user obtains a key, also referred to as a license code, configured to enable predefined (prescribed) use of the sensor system as described in more detail elsewhere herein. In some embodiments, the key is provided on or in the packaging. In some embodiments, the key is obtained by contacting the distributor electronically (e.g., via the Internet or e-mail), via telephone, written communication, or other communications protocol. In some embodiments, the key is embedded in a chip (e.g., RFID) on the single-use device or packaging. Although a few methods for obtaining a license key are described herein, numerous other methods for providing a key are possible as is appreciated by one skilled in the art.

[0657] At block **308**, the key is input into the sensor system, for example, into the receiver. In some embodiments, the key is provided to the user via paper or other communication from the distributor, the key is input manually using buttons on the receiver, for example. In some alternative embodiments, the key is transmitted from a chip, for example, an RFID chip embedded in the single-use sensor and/or packaging associated with the single use device. Other methods for inputting the key are possible as is appreciated by one skilled in the art.

[0658] At block **310**, the sensor is inserted into the user, as described in more detail elsewhere herein and/or as is known in the art. See also U.S. Patent No. 6,974,437; U.S. Patent No. 6,892,085; U.S. Patent No. 6,809,507; U.S. Patent No. 6,689,056; U.S. Patent No. 6,666,821; U.S. Patent No. 6,520,326; U.S. Patent No. 6,512,939; U.S. Patent No. 6,261,280; U.S. Patent No. 6,572,542; U.S. Patent No. 6,284,478; U.S. Patent No. 6,565,509; U.S. Patent No. 6,175,752; U.S. Patent No. 6,329,161; U.S. Patent No. 6,695,860; and U.S. Patent No. 6,613,379. In some embodiments, the sensor is inserted into the host prior to inputting the license code into the receiver. Generally, it is preferred that the user be required to input the license code into the sensor system prior to obtaining information (i.e., sensor data) from the sensor.

[0659] At block **312**, the sensor measures and displays the host's analyte values for the predetermined time period. As described in more detail elsewhere herein, the sensor is generally designed for a particular duration of use, for example a 3 day sensor is designed for a duration of 3 days. Some sensors may be designed for longer or shorter durations.

[0660] At block **314**, the sensor system is disabled. Preferably, the disabling of the sensor includes at least discontinuing the display of sensor data. By discontinuing the display of sensor data, a host will be encouraged to remove the sensor at the appropriate time. However, further mechanical and software designs to disable the use of the device, such as destroying the sensor and shutting down all electronics can also be employed, as are described in more detail elsewhere herein. By utilizing the method of distributing and controlling use of sensor systems including disposable and reusable parts described herein, patients are more likely to use the sensor systems in a manner consistent with physician and/or prescriptive use.

Examples

[0661] The following examples serve to illustrate certain preferred embodiments and aspects and are not to be construed as limiting the scope thereof.

Transcutaneous glucose sensor with cellulose acetate interference domain

[0662] A short term (transcutaneous) sensor was built by providing a platinum wire, vapor-depositing the platinum with Parylene to form an insulating coating, helically winding a silver wire around the insulated platinum wire (to form a "twisted pair"), masking sections of electroactive surface of the silver wire, vapor-depositing Parylene on the twisted pair, chloridizing the silver electrode to form silver chloride reference electrode, and removing a radial window on the insulated platinum wire to expose a circumferential electroactive working electrode surface area thereon, this assembly also referred to as a "parylene-coated twisted pair assembly."

[0663] An interference domain was formed on the parylene-coated twisted pair assembly by dip coating in an interference domain solution comprising 7 weight percent, 50,000 molecular weight cellulose acetate (Sigma-Aldrich, St. Louis, MO) in a 2:1 acetone/ethanol solvent solution, followed by drying at room temperature for three minutes. This interference domain solution dip coating step was repeated three more times to form an interference domain comprised of four layers of cellulose acetate on the assembly. The dip length (insertion depth) was adjusted to ensure that the cellulose acetate covered from the tip of the working electrode, over the exposed electroactive working electrode window, to cover a distal portion of the exposed electroactive reference electrode.

[0664] An enzyme domain was formed over the interference domain by subsequently dip coating the assembly in an enzyme domain solution and drying in a vacuum oven for 20 minutes at 50°C. This dip coating process was repeated once more to form an enzyme domain comprised of two layers. A resistance domain was formed over the enzyme domain by subsequently spray coating the assembly with a resistance domain solution and dried in a vacuum oven for 60 minutes at 50°C. Both the enzyme domain and the resistance domain were formed as described in more detail in U.S. Publication No. US-2006-0020187-A1.

[0665] Additionally, selected sensors (test sensors) were exposed to electron beam radiation at a dose of 25 kGy, while others (control sensors) were not exposed to electron beam radiation.

Transcutaneous glucose sensor with cellulose acetate/Nafion® interference domain

[0666] Transcutaneous glucose sensors with a cellulose acetate/Nafion® interference domain (CA/Naf sensors) were constructed as described with reference to the transcutaneous glucose sensors with a cellulose acetate interference domain above; however, after dip coating the parylene-coated twisted pair assembly in the cellulose acetate solution, the cellulose acetate coated assembly was further dip coated in a 5 weight percent Nafion® solution in low aliphatic alcohols (Sigma-Aldrich, St. Louis, MO) and allowed to dry at room temperature for 10 minutes. This Nafion® solution dip coating step was repeated twice to form three layers of Nafion® over the cellulose acetate layers. Enzyme and resistance domains were subsequently coated onto the cellulose acetate/Nafion® interference domain coated assembly, and selected test sensors were exposed to electron beam radiation, as described in more detail above.

In vitro Testing

[0667] *In vitro* tests were run to evaluate the ability of the above-described sensors to resist uric acid, ascorbic acid, and acetaminophen. Namely, four CA sensors (two before and two after electron beam exposure) were immersed in 40, 200, and 400 mg/dL glucose while their electrical signal was monitored. Subsequently, the sensors were immersed into a solution containing 400 mg/dL glucose plus one of either 0.5 mM uric acid (Fig. 24A), 0.23 mM ascorbic acid (Fig. 24B), or 0.22 mM acetaminophen (Fig. 24C).

[0668] Fig. 24A is a bar graph that illustrates the ability of the CA sensors to resist uric acid pre- and post-electron beam exposure. The x-axis represents the sensors involved in the *in vitro* testing. Namely, 3CA represents an interference domain formed on sensors comprised of four dip coated layers of cellulose acetate as described above. Half of the CA sensors were tested pre-electron beam exposure and half of the sensors were tested post-electron beam exposure as indicated on the legend. The y-axis represents the percentage amount of signal due to the interferant (uric acid) as compared to a control sensor (*i.e.*, sensor(s) without an interference domain).

[0669] The bar graph shows that in a first set CA sensors (E3), 3% of the control signal was produced by the electron beam treated sensor upon immersion into the uric acid containing solution (as compared to the control sensor); in contrast, the sensor that was not treated with electron beam produced an 18% signal increase when immersed in the uric acid containing solution. In a second set of CA sensors (E4), 0.5% of the control signal was produced by the electron beam treated sensor upon immersion into the uric acid containing solution (as compared to the control sensor); in contrast, the sensor that was not treated with electron beam produced 3% of the control signal when immersed in the uric acid containing solution. Accordingly, it is believed that electron beam exposure provides improved ability to block uric acid in sensors *in vitro* as compared with sensors that have not been electron beam sterilized.

[0670] Fig. 24B is a bar graph that illustrates the ability of the CA sensors to resist ascorbic acid pre- and post-electron beam exposure. The x-axis represents the sensors involved in the *in vitro* testing. Namely, 3CA represents an interference domain formed on sensors comprised of four dip coated layers of cellulose acetate, as described above. Half of the sensors were tested pre-electron beam exposure and half of the sensors were tested post-electron beam exposure as indicated on the legend. The y-axis represents the amount of signal due to the interferant (ascorbic acid) as compared to a control sensor (*i.e.*, sensor(s) without an interference domain).

[0671] The bar graph shows that in a first set CA sensors (E3), 11% of the control signal was produced by the electron beam treated sensor upon immersion into the ascorbic acid containing solution (as compared to the control sensor); in contrast, the sensor that was not treated with electron beam produced 39% of the control signal when immersed in the ascorbic acid containing solution. In a second set of CA sensors (E4), 7% of the control signal was produced by the electron beam treated sensor upon immersion into the ascorbic acid containing solution (as compared to the control sensor); in contrast, the sensor that was not treated with electron beam produced 35% of the control signal when immersed in the ascorbic acid containing solution.

[0672] Fig. 24C is a bar graph that illustrates the ability of the CA sensors to resist acetaminophen pre- and post-electron beam exposure. The x-axis represents the

sensors involved in the *in vitro* testing. Namely, 3CA represents an interference domain formed on sensors comprised of four dip coated layers of cellulose acetate, as described above. Half of the sensors were tested pre-electron beam exposure and half of the sensors were tested post-electron beam exposure as indicated on the legend. The y-axis represents the amount of signal due to the interferant (acetaminophen) as compared to a control sensor (*i.e.*, sensor(s) without an interference domain).

[0673] The bar graph shows that in a first set CA sensors (E3), 6% of the control signal was produced by the electron beam treated sensor upon immersion into the acetaminophen containing solution (as compared to the control sensor); in contrast, the sensor that was not treated with electron beam produced 25% of the control signal when immersed in the acetaminophen containing solution. In a second set of CA sensors (E4), 4% of the control signal was produced by the electron beam treated sensor upon immersion into the acetaminophen containing solution (as compared to the control sensor); in contrast, the sensor that was not treated with electron beam produced 20% of the control signal when immersed in the acetaminophen containing solution.

[0674] While not wishing to be bound by theory, it is believed that treatment of an interference domain comprising a cellulosic polymer, such as cellulose acetate, by ionizing radiation, such as electron beam radiation, crosslinks the domain and thereby improves the structure of the domain and its ability to block interfering species.

In vivo Testing

[0675] Figs. 25A is a graphical representation that shows the results of an experiment wherein a glucose sensor was implanted in a streptozocin-induced diabetic rat. Particularly, the glucose sensor was constructed with a cellulose acetate interference domain and was treated with electron beam exposure as described above. The x-axis represents time; the first y-axis represents counts from a raw data stream obtained from the glucose sensor (sensor with CA interference domain); and the second y-axis represents blood glucose in mg/dL obtained from tail sticks and measured on a reference self-monitoring blood glucose meter (smbg).

[0676] The rat was implanted with the CA sensor and was taken through a glucose excursion study on day 1 (see approximately 1 PM to 2 PM). On day 2 of the study,

the rat was injected in the gut with 75%, 150%, and 225% of the maximum therapeutic dose of acetaminophen 0.22 mM (equal to approximately 0.165, 0.33 and 0.495 mM acetaminophen, respectively) at approximately 9 AM, 9:30 AM, and 10 AM, respectively as indicated by the arrows on the graph.

[0677] The graph illustrates the results of the glucose sensor as compared with a reference blood glucose meter during the glucose and acetaminophen tracking studies. During the glucose excursion study on day 1, one can see that the glucose sensor is indeed tracking glucose as shown by the sensor's increase and subsequent decrease in counts and corresponding smbg values. Furthermore, during the acetaminophen tracking study, the relative minimal change in sensor value (with corresponding reference blood glucose meter) indicates the sensor's ability to block signal due to acetaminophen similar to that of the reference blood glucose meter. Namely, if the sensor had been constructed without an interference domain, one would expect to see three step increases in the sensor's signal corresponding to the three bolus injections described above. Thus, it is believed that the incorporation of the CA interference domain that has been exposed to ionizing beam radiation as described above enables the glucose sensor to substantially resist acetaminophen *in vivo*.

[0678] Figs. 25B is a graphical representation that shows the results of an experiment the wherein a glucose sensor was implanted in a streptozocin-induced diabetic rat. Particularly, the glucose sensor was constructed with a cellulose acetate/Nafion® interference domain and was treated with electron beam exposure as described above. The x-axis represents time; the first y-axis represents counts from a raw data stream obtained from the glucose sensor (sensor with CA/Nafion® interference domain); and the second y-axis represents blood glucose in mg/dL obtained from tail sticks and measured on a reference self-monitoring blood glucose meter (smbg).

[0679] The rat was implanted with the CA/Nafion® sensor and was taken through a glucose excursion study on day 1 (see approximately 3 PM to 4 PM). On day 2 of the study, the rat was injected in the gut with 75%, 150%, and 225% of the maximum therapeutic dose of acetaminophen 0.22 mM (equal to approximately 0.165, 0.33 and 0.495 mM

acetaminophen, respectively) at approximately 11 AM, 11:30 AM, and 12 PM, respectively as indicated by the arrows on the graph.

[0680] The graph illustrates the results of the glucose sensor as compared with a reference blood glucose meter during the glucose and acetaminophen tracking studies. During the glucose excursion study on day 1, one can see that the glucose sensor is indeed tracking glucose as shown by the sensor's increase and subsequent decrease in counts and corresponding smbg values. Furthermore, during the acetaminophen tracking study, the relatively minimal change in sensor value (with corresponding reference blood glucose meter) indicates the sensor's ability to block signal due to acetaminophen similar to that of the reference blood glucose meter. Namely, if the sensor had been constructed without an interference domain, one would expect to see three step increases in the sensor's signal corresponding to the three bolus injections as shown in Fig. 24C. Thus, it is believed that incorporation of the CA/Nafion® interference domain that has been exposed to ionizing radiation as described above enables the glucose sensor to substantially resist acetaminophen *in vivo*.

[0681] Fig. 25C is a graphical representation that illustrates the lack of acetaminophen blocking ability of a control glucose sensor without an interference domain in the study of Fig. 25B. Particularly, the glucose sensor was constructed without an interference domain The x-axis represents time; the first y-axis represents counts from a raw data stream obtained from the glucose sensor (without an interference domain); and the second y-axis represents blood glucose in mg/dL obtained from tail sticks and measured on a reference self-monitoring blood glucose meter (smbg).

[0682] The rat was implanted with the interference domain-free sensor and was taken through a glucose excursion study on day 1 (see approximately 3 PM to 4 PM). On day 2 of the study, the rat was injected in the gut with 75%, 150%, and 225% of the maximum therapeutic dose of acetaminophen 0.22 mM (equal to approximately 0.165, 0.33 and 0.495 mM acetaminophen, respectively) at approximately 11 AM, 11:30 AM, and 12 PM, respectively as indicated by the arrows on the graph.

[0683] The graph illustrates the results of the control glucose sensor as compared with a reference blood glucose meter during the glucose and acetaminophen tracking studies.

During the glucose excursion study on day 1, one can see that the glucose sensor is indeed tracking glucose as shown by the sensor's increase and subsequent decrease in counts and corresponding smbg values. Furthermore, during the acetaminophen tracking study on day 2, three step increases in the sensor's signal can be seen, which correspond to the three bolus acetaminophen injections described above. These three signal increases indicate the affect of acetaminophen on the sensor signal as compared with corresponding reference blood glucose meter values (smbg) indicates the sensor's lack of ability to block signal due to acetaminophen as compared with that of the reference blood glucose meter, for example. Thus, it is believed that the incorporation of the CA and/or CA/Nafion® interference domain that has been exposed to ionizing radiation as described above enables the glucose sensor to substantially resist acetaminophen *in vivo* as compared to a glucose sensor without the interference domain of the preferred embodiments.

Transcutaneous Glucose Sensor with Cellulose Acetate Interference Domain and PVP Electrode Domain

[0684] Transcutaneous glucose sensors with a cellulose acetate (CA) interference domain with and without a PVP electrode domain were each built as described with reference to the transcutaneous glucose sensors above. Namely, a first (control) set of parylene-coated twisted pair assemblies were dip-coated with a CA interference domain and subsequent enzyme and resistance domains as described in more detail. Additionally, a second (test) set of parylene-coated twisted pair assemblies were dip-coated one time with a 10 wt. % PVP (International Specialty Products PVP K-90) solution in DI water, prior to the application of a CA interference domain and subsequent enzyme and resistance domains.

[0685] Fig. 26A is a bar graph that represents the break-in time of the test sensors vs. the control sensors. Five test sensors and five control sensors were built as described above and inserted bi-laterally into a rat (each rat receiving one test sensor and one control sensor). After insertion, the sensors measured glucose for a time period at least beyond the electrochemical break-in time of each sensor. The data was analyzed to determine the electrochemical break-in of each sensor. Electrochemical break-in is well documented and is appreciated by one skilled in the art, however it can be stated that the time at which reference glucose data (e.g., from an SMBG meter) substantially correlates with sensor glucose data is

an indicator of electrochemical break-in of the sensor. The y-axis represents the amount of time required for electrochemical break-in in minutes. The x-axis represents the 5 rats in this experiment showing the test and control sensors for each rat. It can be seen from the bar graph that the break-in time of the test sensors (with the PVP electrode domain) had faster break-in times than the control sensors (without PVP electrode domain). Namely, the control sensors had break-in time periods in the range of about 50 to about 130 minutes, while the test sensors had break-in time periods in the range of about 10 to about 40 minutes. Thus, a membrane system comprising a cellulosic derivative (e.g., cellulose acetate butyrate) and an electrode domain comprising a hydrophilic polymer (e.g., PVP) enables fast break-in times for a sensor, including not more than about 40 minutes, not more than about 30 minutes, preferably not more than about 20 minutes, and more preferably not more than about 10 minutes.

Transcutaneous Glucose Sensor with Cellulose Acetate Butyrate Interference Domain

[0686] Transcutaneous glucose sensors with a cellulose acetate butyrate (CAB) interference domain were each constructed as described with reference to the transcutaneous glucose sensors above, namely, by dip-coating a parylene-coated twisted pair assembly with three coats of 17.7 wt. % cellulose acetate butyrate CAB (Eastman Chemical 553-0.4) solution in 2:1 acetone:ethanol. Enzyme and resistance domains were subsequently coated onto the cellulose acetate butyrate interference domain coated assembly as described in more detail above. Subsequent testing showed effective blocking of acetaminophen, a known interferant, at therapeutic levels. Additionally, at least some sensors (test sensors) were exposed to electron beam radiation at a dose of 25 kGy, while others (control sensors) were not exposed to electron beam radiation after electron beam sterilization at a dose of 25 kGy, all of which showed equivalent blocking ability of acetaminophen.

Transcutaneous Glucose Sensors with Cellulose Acetate Butyrate Interference Domain and PVP Electrode Domain

[0687] In some circumstances, a cellulose acetate butyrate interference domain may alter or reduce the sensitivity of some glucose oxidase-based sensor assemblies. Accordingly, in some circumstances, it can be useful to apply an electrode domain (e.g., more proximal to the electroactive surface) of polyvinylpyrrolidone (PVP), or the like, on the

electroactive surface(s) (e.g., working and/or reference electrodes) prior to application of the CAB interference domain. Accordingly, in addition the above described CAB interference-based sensors, some sensors were coated with 20 wt. % PVP (International Specialty Products PVP K-90) solution in DI water prior to the application of CAB and the subsequent coatings described above. These sensors showed that the addition of a PVP electrode domain beneath the CAB interference domain results in an increase in glucose sensitivity (e.g., slope) of the sensor and a reduction of slope variability (e.g., from sensor to sensor).

[0688] Fig. 26B is a graph that represents the response of glucose sensors to a variety of interferents. Five sensors were built including a PVP electrode domain and CAB interference domain as described above and immersed for at least three minutes in a variety of heated (37°C) PBS solutions each containing an interferent as shown in Table 1, below.

Table 1.

Interferent	Solution Concentration Tested, mg/dL	Therapeutic Concentration, mg/dL
acetaminophen	6.5	1-2
ascorbic acid	3.8	0.8-1.2
dopamine	3.1	0.03-0.104
ibuprofen	40	0.5-2.04
salicylic acid	50	15-30
tolbutamide	70	5.3-10
creatinine	30	1.5
uric acid	9.5	7
ephedrine	0.94	0.005-0.01
L-dopa	1.82	0.02-0.3
methyl dopa	1.735	0.1-0.5
tetracycline	0.44	0.4

[0689] The graph of Fig. 26B represents data as an average of the five sensors tested in each of the interferent solutions at high concentrations (see column entitled, "Solution Concentration Tested" in Table 1). The y-axis represents signal strength in picoAmps after a three-minute immersion time in each solution. The x-axis represents the interferents tested. It is noted that at least three interferents showed substantially no response (Ascorbic acid, Ibuprofen and Tetracycline). Other interferents (Acetaminophen, Creatinine, Ephedrine, Salicylic acid, Tolazamide, Tolbutamide and Uric Acid) showed minimal response, which is believed to provide sufficient interferent blocking to enable functional

(useful) sensor data even in the presence of these interferents at the tested concentrations (see Fig. 26C).

[0690] Fig. 26C is a graph that represents an apparent glucose concentration or "equivalent glucose signal" caused by each of the interferent solutions at high concentrations (see column entitled, "Solution Concentration Tested" in Table 1). For the purposes of calculating the equivalent glucose signal, a sensitivity of 3.5 pA/mg/dL is assumed and the signal strength converted to an "equivalent glucose signal" (or apparent glucose concentration) in mg/dL. The y-axis represents the equivalent glucose signal in mg/dL. The x-axis represents the interferents tested. As discussed above, at least three interferents showed zero "equivalent glucose signal" (Ascorbic acid, Ibuprofen and Tetracycline). Other interferents (Acetaminophen, Creatinine, Salicylic acid, and Tolazamide, showed very minimal signal (or "equivalent glucose signal"); namely, less than about 10 mg/dL "equivalent glucose signal." An additional three of the interferants, (ephedrine, tolbutamide and uric acid) showed minimal signal; namely, less than 20 mg/dl equivalent) which is believed to provide sufficient interferent blocking (resistance) to enable functional (useful) sensor data even in the presence of these interferents at the tested concentrations. Although three of the interferents tested showed more response than other of the interferents, these three interferents were re-tested at their therapeutic concentrations (see column entitled, "Therapeutic Concentration" it Table 1.) After a three-minute immersion time in the therapeutic concentration, the "equivalent glucose signal" for Dopamine, L-dopa, and Methyldopa, respectively, was measured as 10, 14, and 52 mg/dL. Accordingly, the glucose sensors of the preferred embodiments effectively block a plurality of interfering species selected with an "equivalent glucose signal" of less than about 30 mg/dL, preferably less than about 20 mg/dL, and more preferably less than about 10 mg/dL or less at therapeutic doses of interfering species of the glucose sensor.

[0691] The glucose sensors of the preferred embodiments, constructed with a cellulose acetate butyrate interference domain, and including embodiments with a PVP electrode domain, have been shown to block a broad spectrum of exogeneous and endogeneous interferents in therapeutic concentrations, including, but not limited to, Acetaminophen, Ascorbic acid, Dopamine, Ibuprofen, Salicylic acid, Tolbutamide,

Creatinine, Uric acid, Ephedrine, L-dopa, methyl dopa and Tetracycline. Additionally, while some prior art interference domains have been known to create altered sensitivity of the sensor to glucose (e.g., variability and/or unreliability of sensors in manufacture), the preferred glucose sensors built with a cellulose acetate butyrate interference domain, and including embodiments with a PVP electrode domain, provide excellent glucose sensitivity consistency for sensor manufacture. Furthermore, it was observed that the preferred embodiments described herein provide glucose sensors that reduce or eliminate break-through upon prolonged exposure to a solution containing an interferant.

Deposition of Resistance Domain using Physical Vapor Deposition

[0692] Twenty nine (29) transcutaneous sensors were fabricated by providing a platinum wire, vapor-depositing the platinum with Parylene to form an insulating coating, helically winding a silver wire around the insulated platinum wire (to form a "twisted pair"), masking sections of electroactive surface of the silver wire, vapor depositing Parylene on the twisted pair, chloridizing the silver electrode to form a silver chloride reference electrode, and removing a radial window on the insulated platinum wire to expose a circumferential electroactive working electrode surface area thereon, this assembly also referred to as a "parylene-coated twisted pair assembly." The electroactive surface of the radial window of each Parylene-coated twisted pair was then cleaned by surface treatment.

[0693] An electrode domain was formed over the electroactive surface areas of the working and reference electrodes by dip coating the assembly in an electrode solution (comprising BAYHYDROL® 123, an aliphatic polycarbonate urethane resin) and drying. An enzyme domain was formed over the electrode domain by subsequently dip coating the assembly in an enzyme solution (comprising BAYHYDROL® 140AQ, an aliphatic polyester urethane resin, and glucose oxidase) and drying. A resistance domain was formed over the enzyme domain using a physical vapor deposition process as described above; namely, by placing twenty nine of the assemblies coated with the electrode and enzyme domains into a vacuum chamber and using an ultrasonic nozzle to produce a mist of micro-droplets of the resistance domain solution (comprising a blend of CHRONOTHANE®-1020 (a polyetherurethaneurea based on polytetramethylene glycol, methylene diisocyanate and organic amines) and CHRONOTHANE®-H (a polyetherurethaneurea based on

polytetramethylene glycol, polyethylene glycol, methylene diisocyanate, and organic amines)) within the vacuum chamber (solution feed rate 1.5 ml/minute; nozzle power 1.5 watts; solution temperature ambient room temp.; chamber temperature 30°C; nozzle frequency 120 kHz; chamber gas argon; purge gas pressure 3 psi; solvent physical properties: tetrahydrofuran (boiling point 65-67°C, vapor pressure 143 mm Hg @ 20°C) and dimethylacetamide (boiling point 164.5°C, vapor pressure 2 mm Hg @ 25°C)). The contact time with the mist within the vacuum chamber was about 36 minutes in duration and included 12 spray cycles lasting three minutes each. The resistance domain was then dried for 1 hr at 50°C, 26" vacuum. After drying, the twenty nine sensors were tested *in vitro* to determine their slope (i.e., glucose sensitivity). The twenty nine sensors had an average slope of 4.97 pA/mg/dL, with a standard deviation of 0.55 pA/mg/dL, showing the use of vapor deposition methods, as described herein, to produce functional sensors with good consistency and uniformity. Specifically, the manufacturing lot consisted of sensors having *in vitro* sensitivities with a standard deviation of about 11%. Methods for producing manufacturing lots of sensors can be employed to produce sensors typically with a standard deviation of less than about 20%, preferably less than about 18%, more preferably a standard deviation of less than about 16%, more preferably still a standard deviation of less than about 12%, and most preferably a standard deviation of less than about 8%.

[0694] In the above-described method, the morphology of the resistance domain was controlled by adjusting the solvent evaporation rate of the coating liquid through chamber temperature and chamber vacuum control to yield a surface with the preferred morphology (e.g., non-smoothness). Namely, in contrast to prior art devices which are fabricated using methods specifically adapted to depositing a smooth surface (see, for example, WO/2003-072269-A1 to Leiby et al.), devices of the preferred embodiment fabricated using the above-described method have a resistance domain including a substantially non-smooth surface (e.g., a roughness on the surface that varies in appearance under magnification from a super-positioning of disc shaped objects, such as coins, to a beadlike surface) A variety of parameters of the vapor deposition apparatus/process can be adjusted to produce the desired non-smooth membrane surface; namely, parameters including: feed rate, nozzle power, chamber vacuum, liquid solution temperature (to be

sprayed), chamber temperature, purge gas pressure or flow rate, identity of the purge gas, total cycle time, number of cycles, and solvent physical properties can be altered, and are dependent on one another, to produce desired membrane surface properties.

[0695] Fig. 27 is a photomicrograph obtained by Scanning Electron Microscopy (SEM) at 350× magnification of a sensor formed as described in the example above, including vapor depositing the resistance domain onto the sensor. Fig. 27 shows the substantially non-smooth surface of the sensor after deposition of the resistance domain; namely, Fig. 27 shows a plurality of super-positioned disc-shaped objects, wherein the disc-shaped objects are a result of the deposition of the resistance domain. Preferably, the disc-shaped objects are rounded, for example, circular, oval or tear drop-shaped. In this example, the average diameter of the disc-shaped objects (by either the shortest or longest dimension) is preferably from about 5 to about 250 microns, more preferably from about 10 to about 100 microns, and more preferably still from about 30 to about 80 microns; however, larger or smaller average diameters can be desirable in certain embodiments. For example, in one alternative embodiment, certain parameters of the vapor deposition process were modified (e.g., temperature), which resulted in smaller diameter beads (e.g., a speckled appearance) than shown in Fig. 27.

[0696] Methods and devices that are suitable for use in conjunction with aspects of the preferred embodiments are disclosed in U.S. Patent No. 4,994,167; U.S. Patent No. 4,757,022; U.S. Patent No. 6,001,067; U.S. Patent No. 6,741,877; U.S. Patent No. 6,702,857; U.S. Patent No. 6,558,321; U.S. Patent No. 6,931,327; and U.S. Patent No. 6,862,465.

[0697] Methods and devices that are suitable for use in conjunction with aspects of the preferred embodiments are disclosed in U.S. Publication No. US-2005-0176136-A1; U.S. Publication No. US-2005-0251083-A1; U.S. Publication No. US-2005-0143635-A1; U.S. Publication No. US-2005-0181012-A1; U.S. Publication No. US-2005-0177036-A1; U.S. Publication No. US-2005-0124873-A1; U.S. Publication No. US-2005-0051440-A1; U.S. Publication No. US-2005-0115832-A1; U.S. Publication No. US-2005-0245799-A1; U.S. Publication No. US-2005-0245795-A1; U.S. Publication No. US-2005-0242479-A1; U.S. Publication No. US-2005-0182451-A1; U.S. Publication No. US-2005-0056552-A1; U.S. Publication No. US-2005-0192557-A1; U.S. Publication No. US-2005-0154271-A1;

U.S. Publication No. US-2004-0199059-A1; U.S. Publication No. US-2005-0054909-A1; U.S. Publication No. US-2005-0112169-A1; U.S. Publication No. US-2005-0051427-A1; U.S. Publication No. US-2003-0032874; U.S. Publication No. US-2005-0103625-A1; U.S. Publication No. US-2005-0203360-A1; U.S. Publication No. US-2005-0090607-A1; U.S. Publication No. US-2005-0187720-A1; U.S. Publication No. US-2005-0161346-A1; U.S. Publication No. US-2006-0015020-A1; U.S. Publication No. US-2005-0043598-A1; U.S. Publication No. US-2003-0217966-A1; U.S. Publication No. US-2005-0033132-A1; U.S. Publication No. US-2005-0031689-A1; U.S. Publication No. US-2004-0045879-A1; U.S. Publication No. US-2004-0186362-A1; U.S. Publication No. US-2005-0027463-A1; U.S. Publication No. US-2005-0027181-A1; U.S. Publication No. US-2005-0027180-A1; U.S. Publication No. US-2006-0020187-A1; U.S. Publication No. US-2006-0036142-A1; U.S. Publication No. US-2006-0020192-A1; U.S. Publication No. US-2006-0036143-A1; U.S. Publication No. US-2006-0036140-A1; U.S. Publication No. US-2006-0019327-A1; U.S. Publication No. US-2006-0020186-A1; U.S. Publication No. US-2006-0020189-A1; U.S. Publication No. US-2006-0036139-A1; U.S. Publication No. US-2006-0020191-A1; U.S. Publication No. US-2006-0020188-A1; U.S. Publication No. US-2006-0036141-A1; U.S. Publication No. US-2006-0020190-A1; U.S. Publication No. US-2006-0036145-A1; U.S. Publication No. US-2006-0036144-A1; and U.S. Publication No. US-2006-0016700A1.

[0698] Methods and devices that are suitable for use in conjunction with aspects of the preferred embodiments are disclosed in U.S. Application No. 09/447,227 filed November 22, 1999 and entitled "DEVICE AND METHOD FOR DETERMINING ANALYTE LEVELS"; U.S. Application No. 11/280,672 filed November 16, 2005, and entitled "TECHNIQUES TO IMPROVE POLYURETHANE MEMBRANES FOR IMPLANTABLE GLUCOSE SENSORS"; U.S. Application No. 11/280,102 filed November 16, 2005, and entitled "TECHNIQUES TO IMPROVE POLYURETHANE MEMBRANES FOR IMPLANTABLE GLUCOSE SENSORS"; U.S. Application No. 11/201445 filed August 10, 2005 and entitled "SYSTEM AND METHODS FOR PROCESSING ANALYTE SENSOR DATA"; U.S. Application No. 11/335879 filed January 18, 2006 and entitled "CELLULOSIC-BASED INTERFERENCE DOMAIN FOR AN ANALYTE SENSOR"; U.S. Application No. 11/334876 filed January 18, 2006 and entitled "TRANSCUTANEOUS

ANALYTE SENSOR"; U.S. Application No. 11/333837 filed January 17, 2006 and entitled "LOW OXYGEN IN VIVO ANALYTE SENSOR".

[0699] All references cited herein, including but not limited to published and unpublished applications, patents, and literature references, and also including but not limited to the references listed in the Appendix, are incorporated herein by reference in their entirety and are hereby made a part of this specification. To the extent publications and patents or patent applications incorporated by reference contradict the disclosure contained in the specification, the specification is intended to supersede and/or take precedence over any such contradictory material.

[0700] The term "comprising" as used herein is synonymous with "including," "containing," or "characterized by," and is inclusive or open-ended and does not exclude additional, unrecited elements or method steps.

[0701] All numbers expressing quantities of ingredients, reaction conditions, and so forth used in the specification are to be understood as being modified in all instances by the term "about." Accordingly, unless indicated to the contrary, the numerical parameters set forth herein are approximations that may vary depending upon the desired properties sought to be obtained. At the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of any claims in any application claiming priority to the present application, each numerical parameter should be construed in light of the number of significant digits and ordinary rounding approaches.

[0702] The above description discloses several methods and materials of the present invention. This invention is susceptible to modifications in the methods and materials, as well as alterations in the fabrication methods and equipment. Such modifications will become apparent to those skilled in the art from a consideration of this disclosure or practice of the invention disclosed herein. Consequently, it is not intended that this invention be limited to the specific embodiments disclosed herein, but that it cover all modifications and alternatives coming within the true scope and spirit of the invention.

WHAT IS CLAIMED IS:

1. A sensor for transcutaneous measurement of an analyte in a host, the sensor comprising:

at least one electrode formed from a conductive material; and

a membrane disposed on an electroactive portion of the electrode, wherein the membrane is configured to control an influx of the analyte therethrough, and wherein the membrane comprises a substantially non-smooth outer surface.

2. The sensor of claim 1, wherein the substantially non-smooth surface appears under magnification to resemble a super-positioning of disc shaped objects.

3. The sensor of claim 1, wherein the disc shaped objects comprise a rounded shape.

4. The sensor of claim 1, wherein the disc shaped objects have an average diameter of from about 5 microns to about 250 microns.

5. The sensor of claim 1, wherein the membrane further comprises an enzyme domain.

6. The sensor of claim 5, wherein the membrane further comprises an interference domain.

7. The sensor of claim 5, wherein the membrane further comprises an electrode domain.

8. The sensor of claim 1, wherein the membrane is at least partially formed by a vapor deposition coating process.

9. The sensor of claim 8, wherein the vapor deposition coating process comprises a physical vapor deposition coating process.

10. The sensor of claim 9, wherein the physical vapor deposition coating process comprises ultrasonic vapor deposition.

11. The sensor of claim 1, wherein the membrane substantially resists ascorbate flux therethrough.

12. The sensor of claim 1, wherein the electrode comprises a wire comprising a conductive material, and wherein the sensor is configured for substantially continuous measurement of glucose in a host.

13. A method for manufacturing a transcutaneous analyte sensor, the method comprising the steps of:

providing at least one electrode comprising an electroactive portion; and

applying a membrane to the electroactive portion, wherein at least one layer of the membrane is applied by vapor deposition.

14. The method of claim 13, wherein the vapor deposition comprises physical vapor deposition.

15. The method of claim 14, wherein the physical vapor deposition comprises ultrasonic vapor deposition.

16. The method of claim 13, wherein the layer of the membrane is deposited in a vacuum chamber.

17. The method of claim 16, wherein the layer is configured to resist flow of the analyte therethrough.

18. The method of claim 13, wherein at least one layer of the membrane is applied using an ultrasonic nozzle.

19. The method of claim 18, wherein the layer is configured to resist flow of the analyte therethrough.

20. The method of claim 13, wherein the step of applying a membrane comprises applying an enzyme domain.

21. The method of claim 20, wherein the step of applying an enzyme domain comprises applying an enzyme domain by dip coating.

22. The method of claim 13, wherein the step of applying a membrane comprises applying an electrode domain.

23. The method of claim 22, wherein the step of applying the electrode domain comprises applying the electrode domain by dip coating.

24. The method of claim 13, wherein the electrode comprises a wire comprising a conductive material, and wherein the sensor is configured for substantially continuous measurement of glucose in a host.

25. A method for manufacturing a plurality of transcutaneous analyte sensors, the method comprising:

providing a plurality of electrodes, each electrode comprising an electroactive portion;

placing the plurality of electrodes into a vacuum chamber; and

vapor depositing at least one membrane layer thereon.

26. The method of claim 25, where the membrane layer is configured to control influx of an analyte therethrough.

27. The method of claim 25, wherein an *in vitro* sensitivity of the plurality of sensors deviates from a median *in vitro* sensitivity by less about 20%.

28. The method of claim 25, wherein an *in vitro* sensitivity of the plurality of sensors deviates from a median *in vitro* sensitivity by less about 16%.

29. The method of claim 25, wherein an *in vitro* sensitivity of the plurality of sensors deviates from a median *in vitro* sensitivity by less about 12%.

30. The method of claim 25, further comprising:

curing the membrane layer.

31. The method of claim 30, wherein the curing step comprises placing a plurality of electrodes, each comprising the membrane layer, into a vacuum oven.

32. The method of claim 30, wherein the curing step comprises placing a plurality of electrodes, each comprising the membrane layer, into a convection oven.

33. The method of claim 30, wherein the curing step comprises placing a plurality of electrodes, each comprising the membrane layer, into a variable frequency microwave oven.

34. The method of claim 25, wherein each electrode comprises a wire comprising a conductive material, and wherein each sensor is configured for substantially continuous measurement of glucose in a host.

35. A method for limiting use of an analyte sensor to a predetermined time period, the method comprising:

providing a key associated with an analyte sensor, wherein the key is configured to control an amount of time over which information is obtained from the analyte sensor.

36. The method of claim 35, wherein the analyte sensor is a transcutaneous glucose sensor.

37. The method of claim 35, wherein the sensor is operatively connected to a receiver, wherein the receiver is configured to display sensor data.

38. The method of claim 37, wherein the receiver is configured to receive the key.

39. The method of claim 38, wherein the receiver is configured to control an amount of time over which information is displayed on the receiver from the sensor in response to the key.

40. The method of claim 35, wherein the key is a software key.

41. The method of claim 35, wherein the key is a unique code.

42. The method of claim 35, wherein the key is selected from the group consisting of a unique number, a receiver ID, a sensor duration, a number of sensor systems, and combinations thereof.

43. The method of claim 35, wherein the key is configured for use with a plurality of sensors.

44. The method of claim 35, wherein the key is provided by an information tag.

45. A method for distributing and controlling use of implantable sensor systems comprising reusable and disposable parts, the method comprising:

providing a single-use device associated with the sensor system, wherein the single-use device is configured to be inserted into a host's tissue;

providing a key associated with the single-use device; and

providing a reusable device associated with a sensor system, wherein the reusable device is configured to provide sensor information responsive to receipt of the key.

46. The method of claim 45, wherein the reusable device comprises a receiver configured to receive sensor information.

47. The method of claim 46, wherein the reusable device further comprises an electronics unit configured to releasably mate with the single-use device.

48. The method of claim 45, further comprising:

obtaining a package containing a plurality of single-use devices.

49. The method of claim 45, wherein the single-use device is a transcutaneous analyte sensor configured for insertion into a subcutaneous tissue of a host.

50. The method of claim 45, wherein the key comprises a written license code packaged with the single-use device.

51. The method of claim 45, wherein the step of providing the key comprises:

providing a license code via at least one communication selected from the group consisting of written communication, voice communication, and electronic communication.

52. The method of claim 45, wherein the reusable device is configured to receive the key via manual entry.

53. The method of claim 45, wherein the reusable device is configured to wirelessly receive the key.

54. The method of claim 45, wherein the key comprises sensor duration information configured to enable the sensor system to control an amount of time over which information is obtained from the single-use device or is displayed by the reusable device.

55. The method of claim 45, wherein the single-use device comprises a transcutaneous analyte sensor configured for insertion in a subcutaneous tissue of a host, and wherein the key comprises sensor insertion information configured to enable the sensor system to control a number of sensor insertions.

56. The method of claim 45, wherein the single-use device comprises a transcutaneous analyte sensor configured for insertion in a subcutaneous tissue of a host, and wherein the step of inserting the single-use device into a host comprises using an applicator to insert the sensor into the host.

57. The method of claim 45, wherein the step of obtaining sensor information from the sensor system comprises at least one step selected from the group consisting of measurement of analyte information, digitalizing of sensor information, transmission of sensor information, receiving of sensor information, storing of sensor information, processing of sensor information, and displaying of sensor information.

58. A method for limiting use of a glucose sensor system to a predetermined time period, the method comprising:

inputting a key into a receiver, wherein the key is configured to control an amount of time over which information is obtained from a sensor system, after which time the sensor system is disabled such that glucose information cannot be obtained, wherein the sensor system is a transcutaneous glucose sensor system comprising a sensor configured for insertion into a tissue of a host and an electronics unit operatively connected to the sensor and configured to provide a signal representative of a glucose concentration in the host, and wherein the receiver is configured to receive the signal representative of a glucose concentration in the host and to display corresponding glucose information; and

obtaining glucose information from the sensor.

59. The method of claim 58, wherein the step of inputting the key into the receiver is performed before the step of obtaining glucose information from the sensor.

60. A device for measuring an analyte in a host, the device comprising:

a sensor operably connected to sensor electronics, the sensor electronics configured for measuring an analyte in a host;

at least one electrical contact configured to connect the sensor to the sensor electronics; and

a sealing member, wherein the sealing member at least partially surrounds at least one of the sensor and the electrical contact, wherein the sealing member comprises a material having a durometer hardness of from about 5 Shore A to about 80 Shore A.

61. The device of claim 60, wherein the durometer hardness is from about 10 Shore A to about 50 Shore A.

62. The device of claim 61, wherein the durometer hardness is about 20 Shore A.

63. The device of claim 61, wherein the durometer hardness is about 50 Shore A

64. The device of claim 60, wherein the sensor comprises a wire.

65. The device of claim 60, wherein the sensor comprises a planar substrate.

66. The device of claim 60, wherein the sealing material comprises a silicone.

67. The device of claim 60, further comprising a sealant adjacent to the sealing member.

68. The device of claim 60, wherein the sensor electronics are housed within an electronics unit configured to mate with the electrical contact.

69. The device of claim 68, wherein the electronics unit and the sealing member are configured to mate to provide a compression force therebetween.

70. The device of claim 60, further comprising at least one raised portion configured to provide a compression force to the sealing member when the electrical contact is connected to the sensor electronics.

71. A device for use in measuring an analyte in a host, the device comprising:

a sensor operably connected to sensor electronics, the sensor electronics configured for measuring an analyte in a host;

at least one electrical contact configured to operably connect the sensor to the sensor electronics; and

a sealing member at least partially surrounding at least one of the sensor and the electrical contact, wherein the sealing member is configured to seal the electrical contact from moisture when the sensor is operably connected to the sensor electronics.

72. The device of claim 71, wherein the sealing member comprises a material having a durometer hardness of from about 5 Shore A to about 80 Shore A.

73. The device of claim 71, further comprising a sealant adjacent to the sealing member.

74. The device of claim 71, further comprising a housing on which the sealing member is disposed, wherein the housing is configured to mechanically or chemically hold the sealing member thereon.

75. The device of claim 74, further comprising an adhesive configured to hold the sealing member on the housing.

76. The device of claim 74, further comprising at least one protrusion configured to substantially mate with at least one depression, whereby the sealing member is held on the housing.

77. The device of claim 71, wherein the sealing member comprises at least one gap that is maintained when the electrical contact is operably connected to the sensor electronics.

78. The device of claim 77, wherein the sensor at least partially extends through the gap.

79. The device of claim 77, wherein the gap is filled with a sealant.

80. The device of claim 71, further comprising at least one channel communicating between a first side of the sealing member and a second side of the sealing member.

81. The device of claim 80, wherein the channel is filled with a sealant.

82. The device of claim 71, wherein substantially no air gaps are adjacent to the electrical contact when the electrical contact is operably connected to the sensor electronics.

83. The device of claim 71, wherein the sealing member comprises a material selected from the group consisting of silicone, silicone/polyurethane hybrid, polyurethane, polysulfide, and mixtures thereof.

84. The device of claim 83, wherein the sealing member is self-lubricating.

85. The device of claim 71, wherein the sealing member comprises a sealant sandwiched between an upper portion of the sealing member and a lower portion of the sealing member.

86. The device of claim 71, further comprising a guide tube configured to maintain an opening in the sealing member prior to sensor insertion into the host.

87. The device of claim 86, further comprising a lubricant between the sealing member and the guide tube.

88. A device for use in measuring an analyte in a host, the device comprising:

a sensor operably connected to sensor electronics, the sensor electronics configured for measuring an analyte in a host;

at least one electrical contact configured to connect the sensor to the sensor electronics, wherein the electrical contact comprises a material having a durometer hardness of from about 5 Shore A to about 80 Shore A; and

a sealing member at least partially surrounding at least one of the sensor and the electrical contact, wherein the sealing member comprises a material having a durometer hardness of from about 5 Shore A to about 80 Shore A.

89. The device of claim 88, wherein the durometer hardness of the electrical contact is higher than the durometer hardness of the sealing member.

90. The device of claim 89, wherein the durometer hardness of the electrical contact is about 50 Shore A.

91. The device of claim 88, wherein the durometer hardness of the sealing member is higher than the durometer hardness of the contact.

92. The device of claim 91, wherein the durometer hardness of the sealing member is about 50 Shore A.

93. The device of claim 88, wherein the sealing member comprises a filler material.

94. The device of claim 93, wherein the filler material is configured to stiffen the sealing member.

95. A sensor system for measuring an analyte concentration in a host, the system comprising:

at least one electrode configured for implantation in a host and configured to measure an analyte concentration in a tissue of the host;

sensor electronics operably connected to the electrode and configured to provide analyte data representative of an analyte concentration in the host; and

an information tag comprising sensor information.

96. The sensor system of claim 95, wherein the information tag comprises a memory.

97. The sensor system of claim 96, wherein the information tag transmits information using at least one connection selected from the group consisting of a serial connection, a radio frequency connection, an acoustic frequency connection, an infrared frequency connection, and a magnetic induction connection.

98. The sensor system of claim 95, further comprising:

a mounting unit configured to maintain the sensor positioned transcutaneously within the tissue of the host.

99. The sensor system of claim 98, wherein the information tag is embedded within the mounting unit.

100. The sensor system of claim 95, further comprising a receiver configured to receive the analyte data from the sensor electronics.

101. The sensor system of claim 100, wherein the receiver is configured to read sensor information from the information tag.

102. The sensor system of claim 95, further comprising packaging configured to contain at least a portion of a sensor system during transport.

103. The sensor system of claim 102, wherein the information tag is in or on the packaging.

104. The sensor system of claim 95, wherein the sensor information comprises at least one item selected from the group consisting of manufacturing information, calibration information, identification information, expiration information, sensor duration information, and archived data.

105. The sensor system of claim 95, wherein the sensor information comprises a license code.

106. A transcutaneous analyte sensor assembly, the assembly comprising:

a mounting unit adapted for mounting on a skin of a host;

an electronics unit configured to releasably mate with the mounting unit;

a sensor configured to measure a concentration of an analyte in the host, wherein the sensor is operably connected to the electronics unit when the electronics unit is mated to the mounting unit; and

an information tag comprising sensor information.

107. The sensor assembly of claim 106, wherein the sensor information is embedded in an information tag within the mounting unit.

108. The sensor assembly of claim 107, further comprising a receiver, wherein the receiver is configured to read sensor information from the information tag.