



TRANSLATION CERTIFICATION

Date: July 1, 2025

To whom it may concern:

I, Frank McGee, a translator fluent in the Japanese and English languages, on behalf of Morningside, do solemnly and sincerely declare that the following is, to the best of my knowledge and belief, a true and correct translation of the document(s) listed below in a form that best reflects the intention and meaning of the original text.

The document is designated as:

- JP 2000-074829 A

All statements made in this declaration of my own knowledge are true and all statements made on information and belief are believed to be true. I make these statements with the understanding that willful false statements and the like are punishable by fine or imprisonment, or both (18 U.S.C. 1001).

I declare under penalty of perjury that the forgoing is true and correct.

A handwritten signature in blue ink, appearing to read "Frank McGee", is written over a horizontal line.

Frank McGee

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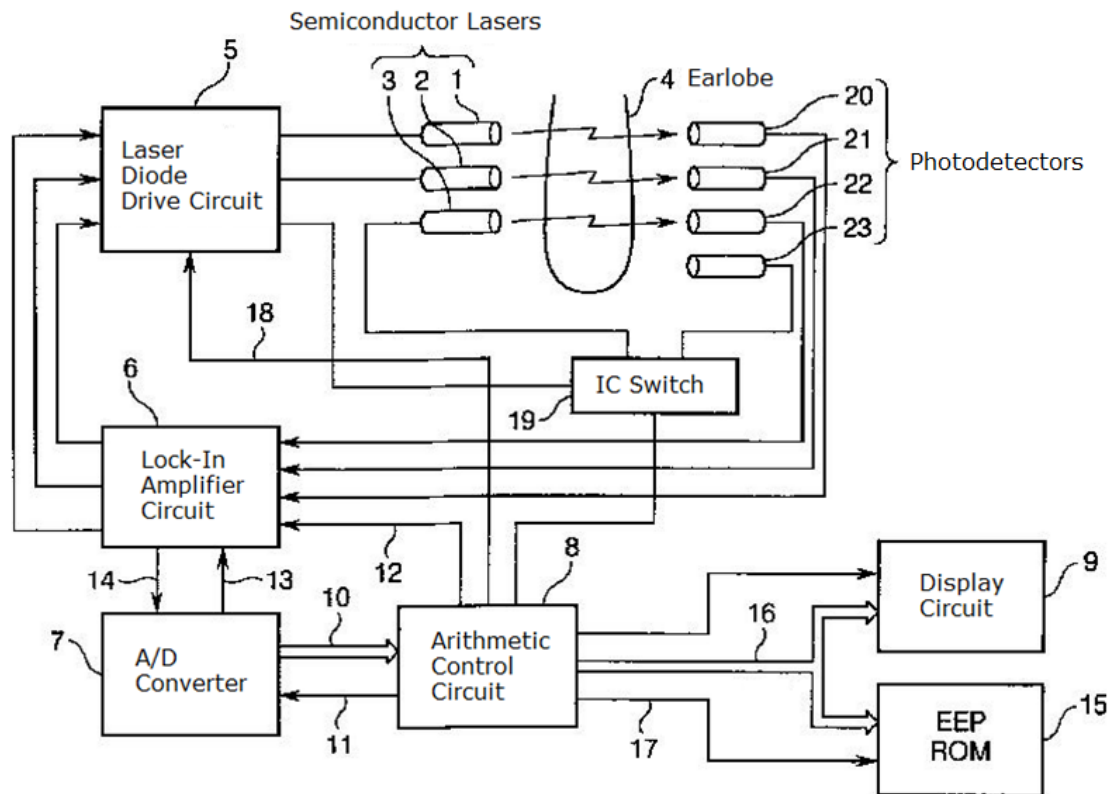
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(54) [Title of the Invention] Glucose Sensor



[Claims]

[Claim 1]

A glucose sensor comprising: a light emitting means for irradiating light having wavelength λ_1 in the glucose absorption wavelength band, light having wavelength λ_2 outside of the glucose absorption wavelength band, and light having wavelength λ_3 in the infrared wavelength band for measuring volume of blood flow at the light irradiation site; a detecting means for detecting the intensity of the light having the three wavelengths transmitted or reflected by a living body; a calculating means for determining the light intensity ratio of λ_1 and λ_2 , and determining the amount of glucose from this ratio; a detecting means for measuring body temperature; a calculating means for performing temperature correction on the amount of glucose based on body temperature; a calculating means for calculating the volume of blood flow at the light irradiation site from the light having wavelength λ_3 ; and a calculating means for calculating the blood glucose concentration at the light irradiation site from the temperature-corrected amount of glucose and the volume of blood flow.

[Claim 2]

The glucose sensor according to claim 1, wherein the wavelengths of the light emitting means are set within the ranges of $\lambda_1 = 1.5$ to $1.6 \mu\text{m}$, $\lambda_2 = 1.3$ to $1.4 \mu\text{m}$, and $\lambda_3 = 0.80$ to $0.85 \mu\text{m}$.

[Detailed Description of the Invention]

[0001]

[Technical Field of the Invention]

The present invention relates to a sensor device for detecting the glucose concentration in the blood of a living body such as the human body.

[0002]

[Prior Art]

Until now, it has been necessary to prick the skin and draw blood each time glucose concentrations are measured. Blood obtained by pricking the skin is brought into contact with the tip of a sensor, and approximately 3 to 5 μ l of blood is drawn into the sensor by capillary action to obtain a measurement. The sensor contains glucose oxidase, an enzyme that catalyzes the oxidation reaction of glucose, and ferricyanide ions, which act as electron carriers between the oxygen reaction system and the electrodes. Glucose in the blood is oxidized by glucose oxidase, producing ferrocyanide ions in proportion to the amount of glucose, as shown in Formula 1. Next, the ferrocyanide ions generated are oxidized at the electrodes as depicted in Formula 2, and the glucose concentration is calculated from the oxidation current value.

[0003]

Glucose + ferricyanide ions $\rightarrow$
gluconic acid + ferrocyanide ions (1)
Ferrocyanide ions $\rightarrow$
ferricyanide ions + electrons (2)

The sensor part is disposed after each use, but this type of glucose sensor is widely used.

[0004]

Glucose concentration measurements using a laser are described in Fresenius J. Anal. Chem. (1996) 354: 306-310. Specifically, laser light emitted from two high-powered lasers is incident on a glucose solution sample, and the two rays of transmitted light are converted into voltages by separate photodetectors. The amount of glucose is calculated by adding the values obtained by changing the phase of these two voltages. In addition, a third laser is used to irradiate the glucose solution sample with laser light emitted from the laser, and the transmitted light is converted into voltage by the third photodetector. The paper states that a sample temperature can be estimated from this voltage value.

[0005]

[Problem to Be Solved by the Invention]

However, when these glucose sensors are used, a part of the human body has to be injured in order to obtain blood. Therefore, frequent measurements caused significant physical and mental distress to patients. It was also necessary to pay attention to the risk of infection from the wound. Also, while laser-based glucose meters have been proposed in the past, they have not been widely adopted as blood glucose meters due to their low measurement accuracy and high cost.

[0006]

It is an object of the present invention to solve this problem by allowing for non-invasive measurement of glucose concentrations. More specifically, it is an object of the present invention to provide a glucose sensor that can accurately measure changing glucose concentrations over time, and that is simple, gives real-time results, and is reusable.

[0007]

[Means for Solving the Problem]

The present invention is a glucose sensor comprising: a light emitting means for irradiating light having wavelength λ_1 in the glucose absorption wavelength band, light having wavelength λ_2 outside of the glucose absorption wavelength band, and light having wavelength λ_3 in the infrared wavelength band for measuring volume of blood flow at the light irradiation site; a detecting means for detecting the intensity of the light having the three wavelengths transmitted or reflected by a living body; a calculating means for determining the light intensity ratio of λ_1 and λ_2 , and determining the amount of glucose from this ratio; a detecting means for measuring body temperature; a calculating means for performing temperature correction on the amount of glucose based on body temperature; a calculating means for

calculating the volume of blood flow at the light irradiation site from the light having wavelength λ_3 ; and a calculating means for calculating the blood glucose concentration at the light irradiation site from the temperature-corrected amount of glucose and the volume of blood flow. Using the present invention, the blood glucose concentration can be measured without collecting blood, thereby reducing the burden placed on the subject and enabling real-time measurement, which also allows for the measurement of the glucose concentration as it changes over time. Also, by calculating the amount of glucose from the ratio of the intensity of light having wavelength λ_1 , which is within the glucose absorption wavelength band, to the intensity of light having wavelength λ_2 , which is outside of the glucose absorption wavelength band, and then performing temperature correction, the measurement becomes less susceptible to variations in the measurement device and environmental conditions, enabling accurate measurements.

[0008]

Preferably, the wavelengths of the light emitting means are set within the ranges of $\lambda_1 = 1.5$ to $1.6 \mu\text{m}$, $\lambda_2 = 1.3$ to $1.4 \mu\text{m}$, and $\lambda_3 = 0.80$ to $0.85 \mu\text{m}$. Highly accurate measurements can be performed when these wavelengths are used.

[0009]

[Embodiment of the Invention]

FIG. 1 shows the glucose sensor in the present invention. This device measures the blood glucose concentration of blood flowing through the microvessels in the earlobe 4 of the human body. The wavelength of the light outputted from the first semiconductor laser 1 is $1.55 \mu\text{m}$, which is within the glucose absorption wavelength band. It passes through the earlobe 4 and is received by the first photodetector 20. The wavelength of the light outputted from the second semiconductor laser 2 is $1.33 \mu\text{m}$, which is outside of the glucose absorption wavelength band. It passes through the earlobe 4 and is received by the second photodetector 21. The third semiconductor laser 22 is used to measure the volume of blood flow, and the wavelength of the light that it emits has a wavelength of $0.83 \mu\text{m}$. It passes through the earlobe 4 and is detected by the third photodetector 22. The volume of blood flow is measured using the Doppler effect, so infrared light, which has good transmissibility through biological tissue, is used to minimize the attenuation of light reflected by hemoglobin.

[0010]

The body temperature at the laser irradiation is measured by receiving the heat radiation from the irradiation site with a fourth photodetector 23, which is an infrared radiation thermometer. The IC switch 19 switches between measuring the temperature at the irradiation site and measuring the volume of blood flow at the irradiation site. In the present embodiment of the invention, each signal from the photodetectors that detects each light intensity is directed to a lock-in amplifier 6. The circuit 5 used to drive the semiconductor lasers and the lock-in amplifier 6 reduce the noise caused by external disturbances that the light emitted from each semiconductor laser encounters before reaching the photodetectors. Here, modulation occurs at 10 kHz. The analog voltages 14 from the photodetectors, which has been converted to direct current by the lock-in amplifier 6, are sent to the A/D converter 7 in synchronization with the control signal 13 and converted to digital signals. The digital signals 10 are sent to an arithmetic control circuit 8 in synchronization with an A/D converter start signal 11. In the arithmetic control circuit, calculations are performed based on the absolute values of the signals outputted from the first photodetector 20, the second photodetector 21, the third photodetector 22, and the fourth photodetector 23.

[0011]

In order to start the measurement, a calibration operation must be performed first to maintain a predetermined level with nothing coming between the semiconductor lasers and the photodetectors. Specifically, the voltage values outputted from the photodetectors is compared with the initial setting values for the photodetectors written to the EEPROM 15. If there is a difference, the semiconductor drive current for the semiconductor laser diode drive circuit 5 is changed using control signals 18 so that the voltage values of the photodetectors and the initial values of the settings in the EEPROM 15 are kept at constant values before a measurement is performed.

[0012]

A measurement is performed by placing an earlobe 4 between the semiconductor laser unit and the photodetector unit, and calculating the glucose concentration in the earlobe 4 by calculating the photodetector output values at that time. In the arithmetic control circuit 8, calculations are performed to calculate the amount of glucose using the relationship between glucose concentration values previously written to the EEPROM and the photodetector output values, and the relationship between glucose solution temperatures and the photodetector output values. FIG. 2 shows an example of the relationship between glucose concentrations and outputs from the first photodetector 20 measured with glucose solutions placed in a container. FIG. 3 shows an example of the relationship between glucose solution temperatures and outputs from the first photodetector 20. In FIG. 3, as the temperature of the glucose solution increases, molecular expansion and contraction become more active, resulting in less light absorption. Therefore, as the temperature of the glucose solution increases, the output of the photodetector increases. Temperature compensation is performed using the temperature obtained from the fourth photodetector 23, and the amount of glucose is divided by the volume of blood flow calculated from the third photodetector 22. The result is displayed on a display circuit 9 via digital signals 16.

[0013]

The calculation procedure is shown below. The intensity of heat radiation from the body is obtained as a voltage value from the fourth photodiode 23. This is compared with the data in EEPROM 15, the temperature at the body measurement site is measured, and a correction coefficient k for the temperature and the first photodiode output is determined from FIG. 3. The light emitted from the third semiconductor laser 3 passes through the earlobe 4 and is received by the third photodetector 22, and an output value is acquired. The data in the EEPROM 15 is compared with the output value to calculate the volume of blood flow V. The light emitted from the first semiconductor laser 1 passes through the earlobe 4 and is received by the first photodetector 20. The output value from this photodetector is used as V1. The light emitted from the second semiconductor laser 2 passes through the earlobe 4 and is received by the [second] photodetector 2[1]. The output value from this photodetector is used as V2. The amount of glucose X after temperature correction of the semiconductor irradiation site is calculated using the following equation.

[0014]

$$X = k \cdot (1 - V1/V2)$$

The blood glucose concentration is obtained by dividing the amount of glucose X at the irradiation site by the volume of blood flow V. This glucose concentration value is displayed on the display circuit 9. In the present embodiment, light transmitted through the body site is measured, but reflected light can also be measured.

[0015]

[Effects of the Invention]

As explained above, the glucose sensor of the present invention allows for accurate measurement of blood glucose concentrations in a non-invasive manner, without extracting blood from the body, using a relatively inexpensive device. This makes it possible to reduce pain compared to the previous method of extracting blood from the body for each measurement. Also, continuous monitoring becomes possible, allowing for precise diabetes management.

