the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHU CHUAN (JJ) LIU whose telephone number is (571)270-5507. The examiner can normally be reached on M-TH 8:00am~4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tse Chen can be reached on (571)272-3672. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CHU CHUAN (JJ) LIU/
Examiner, Art Unit 3777

/TSE CHEN/
Supervisory Patent Examiner, Art Unit 3777

Notice of References Cited	Application/Control No. 13/354,941	Applicant(s)/Patent Under Reexamination CHON ET AL.	
	Examiner CHU CHUAN (JJ) LIU	Art Unit 3777	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-6,067,462	05-2000	Diab et al.	600/310
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13354941	CHON ET AL.
	Examiner	Art Unit
	CHU CHUAN (JJ) LIU	3777

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/24/2013	03/12/2014							
	1	✓	✓							
	2	✓	✓							
	3	✓	✓							
	4	✓	✓							
	5	✓	✓							
	6	✓	✓							
	7	✓	✓							
	8	✓	✓							
	9	✓	✓							
	10	N	N							
	11	N	N							
	12	N	N							
	13	N	N							
	14	N	N							
	15	N	N							
	16	N	N							
	17	N	N							
	18	✓	✓							
	19	✓	✓							
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	30	✓	✓							
	31	✓	✓							
	32	✓	✓							
	33	✓	✓							
	34	✓	✓							
	35	N	N							
	36	N	N							

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13354941	CHON ET AL.
	Examiner	Art Unit
	CHU CHUAN (JJ) LIU	3777

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/24/2013	03/12/2014							
	37	N	N							
	38	N	N							
	39	✓	✓							
	40	✓	✓							
	41	✓	✓							
	42	✓	✓							
	43	✓	✓							
	44	✓	✓							
	45	N	N							
	46	N	N							
	47	N	N							
	48	N	N							
	49	✓	✓							
	50	✓	✓							
	51	✓	✓							
	52	✓	✓							
	53	✓	✓							

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13354941	CHON ET AL.
	Examiner	Art Unit
	CHU CHUAN (JJ) LIU	3777

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
600	300, 301, 309, 310, 322, 323, 324, 326, 330, 336, 473, 476, 500, 501, 502, 508, 509,518	10/24/2013	CCL
600	300, 301, 309, 310, 322, 323, 324, 326, 330, 336, 473, 476, 500, 501, 502, 508, 509,518	03/12/2014	CCL

SEARCH NOTES		
Search Notes	Date	Examiner
Inventor Name Search (PALM and EAST)	10/23/2013	CCL
EAST Search (TEXT, USPGPUB, USPAT) See Search History	10/24/2013	CCL
Google NPL Search	10/24/2013	CCL
Updated EAST Search (TEXT, USPGPUB, USPAT) See Search History	03/12/2014	CCL
Google NPL Search	03/12/2014	CCL

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

/CHU CHUAN (JJ) LIU/ Examiner.Art Unit 3777	

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EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S57	1	kurtosis and Shannon with entropy same (motion noise)	US-PGPUB; USPAT	OR	ON	2014/03/11 14:56
S56	1	kurtosis and shannon adj entropy same (noise motion)	US-PGPUB; USPAT	OR	ON	2014/03/11 13:03
S55	19	kurtosis and entropy same motion	US-PGPUB; USPAT	OR	ON	2014/03/11 12:59
S54	33	600/336.ccls. and motion with threshold	US-PGPUB; USPAT	OR	ON	2014/03/11 12:09
S53	208	600/336.ccls. and motion	US-PGPUB; USPAT	OR	ON	2014/03/11 11:59

EAST Search History (Interference)

<This search history is empty>

3/ 12/ 2014 11:11:41 AM
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Ki H. Chon et al.
Application Number: 13/354,941
Filed: January 20, 2012
Title: PHYSIOLOGICAL PARAMETER MONITORING WITH A MOBILE COMMUNICATION DEVICE

Examiner: LIU, CHU CHUAN
Group Art Unit: 3777
Confirmation No. 9133

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Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE AFTER FINAL

Sir:

In reply to the final Office Action dated March 21, 2014, Applicants submit the following amendments and remarks that place the application in condition for allowance or, in the alternative, in better form for appeal. An After Final Consideration Request form is also attached hereto.

Amendments to the claims begin on page 2 of this paper.

Remarks begin on page 17 of this paper.

Attachments to this paper also include a copy of Form PTO/SB/434 (1 sheet).

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of the claims.

1. (Currently amended) A method for physiological parameter monitoring, the method comprising:
providing a physiological indicator signal to a handheld mobile communication device;

analyzing, using the handheld mobile communication device, the physiological indicator signal to obtain measurements of one or more physiological parameters; and

detecting, using the handheld mobile communication device and using only the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters and deciding whether to retain the measurements;
wherein detecting effects of motion artifacts in the measurements comprises:

a. preprocessing a segment from the measurement of one physiological parameter;
b. obtaining a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment;
c. including the segment in analyses of physiological measurements, if comparison of the value of the at least one indicator of volatility with a predetermined threshold indicates noise/motion artifacts are not present; and
d. selecting another segment of the signal from the physiological measurement and proceeding to step (a), if the value of the at least one indicator of volatility is less than a predetermined threshold and another segment is available.

2. (Canceled)

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3. (Currently amended) The method of claim ~~2~~1 wherein said at least one indicator of volatility comprises kurtosis.

4. (Currently amended) The method of claim ~~2~~1 wherein said at least one indicator of volatility comprises Shannon entropy.

5. (Currently amended) The method of claim ~~2~~1 wherein said at least one measure of volatility comprises kurtosis and Shannon entropy.

6. (Currently amended) The method of claim ~~2~~1 wherein the predetermined threshold is determined using receiver operator characteristic (ROC) analysis.

7. (Currently amended) The method of claim 1 wherein providing a physiological indicator signal comprises:
placing a portion of a subject's body over an objective lens of a camera in a handheld mobile communication device; and

obtaining video images of the portion of the subject's body.

8. (Previously presented) The method of claim 1 wherein providing a physiological indicator signal comprises obtaining a signal from a physiological monitoring sensor.

9. (Previously presented) The method of claim 8 wherein the physiological monitoring sensor is a photoplethysmographic (PPG) sensor or an electrocardiogram sensor.

10. (Withdrawn) The method of claim 1 wherein the one or more physiological measurements comprise heart rate and heart rate variability.

11. (Withdrawn) The method of claim 10 wherein obtaining measurements of heart rate and heart rate variability comprise:

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determining beats for the physiological indicator signal;

determining beat to beat intervals; and

applying a cubic spline algorithm to obtain a substantially continuous beat to beat interval signal indicative of heart rate.

12. (Withdrawn) The method of claim 1 wherein the one or more physiological measurements comprise respiratory rate.

13. (Withdrawn) The method of claim 12 wherein measurement of respiratory rate comprises:
obtaining time–frequency spectrum of the physiological indicator signal utilizing variable frequency complex demodulation (VFCDM); and

obtaining respiratory rates by extracting a frequency component that has a largest amplitude for each time point at a heart rate frequency band.

14. (Withdrawn) The method of claim 1 wherein the one or more physiological measurements comprise a measure of oxygen saturation.

15. (Withdrawn) The method of claim 14 wherein providing a physiological indicator signal comprises:
placing a portion of a subject's body over an objective lens of a camera in a mobile communication device; and

obtaining video images of the portion of the subject's body, and

wherein obtaining the measure of oxygen saturation comprises:

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obtaining an average intensity of a red component and a blue component of the video images of the portion of the subject's body; the average intensity of the red component and the average intensity of the blue component constituting DC_{RED} and DC_{BLUE} respectively;

obtaining a standard deviation of the red component and the blue component; the standard deviation of the red component and the blue component constituting AC_{RED} and AC_{BLUE} respectively; and

obtaining the measure of oxygen saturation (SpO2) by

$$SpO2 = A - B\frac{AC_{RED}/DC_{RED}}{AC_{BLUE}/DC_{BLUE}}.$$

16. (Withdrawn) The method of claim 1 wherein the one or more physiological measurements comprise a measure of blood loss.

17. (Withdrawn) The method of claim 16 wherein obtaining the measure of blood loss comprises:
obtaining time–frequency spectrum of the physiological indicator signal utilizing variable frequency complex demodulation (VFCDM);

obtaining the amplitude modulation (AM) series from a set of the largest instantaneous amplitude at each time sample within the heart rate frequency band of the time–frequency spectrum; and

determining whether the amplitude modulation decreases; a decrease in the amplitude modulation indicating blood volume loss in subject.

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18. (Previously presented) The method of claim 1 wherein the one or more physiological measurements comprise a measure of atrial fibrillation.

19. (Currently amended) ~~The method of claim 18~~ A method for physiological parameter monitoring, the method comprising:

providing a physiological indicator signal to a handheld mobile communication device;

analyzing, using the handheld mobile communication device, the physiological indicator signal to obtain measurements of one or more physiological parameters; and

detecting, using the handheld mobile communication device and using only the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters and deciding whether to retain the measurements;

wherein the one or more physiological measurements comprise a measure of atrial fibrillation;

wherein obtaining the measure of atrial fibrillation comprises:

obtaining a time-varying coherence function by multiplying two time-varying transfer functions (TVFTs), the two time-varying transfer functions obtained using two adjacent data segments, from the physiological indicator signal, with one data segment as input signal and the other data segment as output to produce the first TVTF; the second TVTF is produced by reversing the input and output signals; and

determining whether the time-varying coherence function is less than a predetermined quantity.

20. (Previously presented) The method of claim 19 wherein determining whether the time-varying coherence function is less than the predetermined quantity comprises:

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obtaining one or more indicators of atrial fibrillation; and

determining whether the one or more indicators of atrial fibrillation exceed predetermined thresholds.

21. (Previously presented) The method of claim 20 wherein the one or more indicators of atrial fibrillation comprise a variance of the time-varying coherence function.

22. (Previously presented) The method of claim 21 wherein the one or more indicators of atrial fibrillation also comprise Shannon entropy.

23. (Previously presented) The method of claim 20 wherein the predetermined thresholds are determined using receiver operator characteristic (ROC) analysis.

24. (Currently amended) A system for physiological parameter monitoring, the system comprising:
a physiological indicator signal sensing component; and a handheld mobile communication device comprising:

at least one processor; and

at least one computer usable medium, the computer usable medium having computer readable code embodied therein, the computer readable code causing the at least one processor to:

analyze the physiological indicator signal to obtain measurements of one or more physiological parameters; and

detect effects of motion artifacts in the measurements of the one or more physiological parameters;

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wherein the computer readable code, in causing the at least one processor to detect effects of motion artifacts, causes the at least one processor to:

a. preprocess a segment from the measurement of one physiological parameter;

b. obtain a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment;

c. include the segment in analyses of physiological measurements, if comparison of the value of the at least one indicator of volatility with a predetermined threshold indicates noise/motion artifacts are not present;

d. select another segment of the signal from the physiological measurement and proceeding to step (a), if the value of the at least one indicator of volatility is less than a predetermined threshold and another segment is available

~~an analysis component analyzing the physiological indicator signal to obtain measurements of one or more physiological parameters; and~~

~~a motion artifact detection component detecting, using only the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters.~~

25-26. (Canceled)

27. (Currently amended) The system of claim ~~26~~24 wherein said at least one indicator of volatility comprises kurtosis.

28. (Currently amended) The system of claim ~~26~~24 wherein said at least one indicator of volatility comprises Shannon entropy.

29. (Currently amended) The system of claim ~~26~~24 wherein said at least one measure of volatility comprises kurtosis and Shannon entropy.

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30. (Currently amended) The system of claim ~~26~~24 wherein the predetermined threshold is determined using receiver operator characteristic (ROC) analysis.

31. (Original) The system of claim 24 wherein the physiological indicator signal sensing component comprises an image acquisition component, said acquisition component capable of acquiring a number of frames, each frame acquired at a predetermined time.

32. (Currently amended) The system of claim 31 wherein the handheld mobile communications device comprises said image acquisition component.

33. (Previously presented) The system of claim 24 wherein the physiological indicator signal sensing component comprises a physiological monitoring sensor.

34. (Previously presented) The system of claim 33 wherein the physiological monitoring sensor is a photoplethysmographic (PPG) sensor or an electrocardiogram sensor.

35. (Withdrawn) The system of claim 25 wherein the physiological indicator signal sensing component comprises an image acquisition component, said acquisition component capable of acquiring a number of frames, each frame acquired at a predetermined time; wherein said image acquisition component acquires a color image having red, green and blue components; wherein one or more physiological measurements comprise a measure of oxygen saturation; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain an average intensity of a red component and a blue component of the images of a portion of a subject's body; the average intensity of the red component and the average intensity of the blue component constituting DC_{RED} and DC_{BLUE} respectively;

obtain a standard deviation of the red component and the blue component; the standard deviation of the red component and the blue component constituting AC_{RED} and AC_{BLUE} respectively; and

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obtain the measure of oxygen saturation by

$$SpO2 = A - B\frac{AC_{RED}/DC_{RED}}{AC_{BLUE}/DC_{BLUE}}.$$

36. (Withdrawn) The system of claim 25 wherein the one or more physiological measurements comprise heart rate and heart rate variability; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

determine beats for the physiological indicator signal;

determine beat to beat intervals; and

apply a cubic spline algorithm to obtain a substantially continuous beat to beat interval signal indicative of heart rate.

37. (Withdrawn) The system of claim 25 wherein the one or more physiological measurements comprise respiratory rate; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain time–frequency spectrum of the physiological indicator signal utilizing variable frequency complex demodulation (VFCDM); and

obtain respiratory rates by extracting a frequency component that has a largest amplitude for each time point at a heart rate frequency band.

38. (Withdrawn) The system of claim 25 wherein the one or more physiological measurements comprise a measure of blood loss; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

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obtain time–frequency spectrum of the physiological indicator signal utilizing variable frequency complex demodulation (VFCDM);

obtain the amplitude modulation (AM) series from set of the largest instantaneous amplitude at each time sample within the heart rate frequency band of the time–frequency spectrum; and

determine whether the amplitude modulation decreases; a decrease in the amplitude modulation indicating blood volume loss in subject.

39. (Currently amended) A system for physiological parameter monitoring, the system comprising:

a physiological indicator signal sensing component; and a handheld mobile communication device comprising:

at least one processor; and

at least one computer usable medium, the computer usable medium having computer readable code embodied therein, the computer readable code causing the at least one processor to:

analyze the physiological indicator signal to obtain measurements of one or more physiological parameters; and

detect effects of motion artifacts in the measurements of the one or more physiological parameters; ~~The system of claim 25~~

wherein the one or more physiological measurements comprise a measure of atrial fibrillation; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain a time-varying coherence function by multiplying two time-varying transfer functions (TVFTs), the two time-varying transfer functions obtained using two adjacent data segments , from the physiological indicator signal, with one data segment as input

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signal and the other data segment as output to produce the first TVTF; the second TVTF is produced by reversing the input and output signals; and

determine whether the time-varying coherence function is less than a predetermined quantity.

40. (Previously presented) The system of claim 39 wherein the computer readable code, in causing the at least one processor to determine whether the time-varying coherence function is less than the predetermined quantity, causes the at least one processor to:

obtain one or more indicators of atrial fibrillation; and

determine whether the one or more indicators of atrial fibrillation exceed predetermined thresholds.

41. (Previously presented) The system of claim 40 wherein the one or more indicators of atrial fibrillation comprise a variance of the time-varying coherence function.

42. (Previously presented) The system of claim 41 wherein the one or more indicators of atrial fibrillation also comprise Shannon entropy.

43. (Previously presented) The system of claim 41 wherein the predetermined thresholds are determined using receiver operator characteristic (ROC) analysis.

44. (Currently amended) A non-transitory computer usable medium having computer readable code embodied therein, the computer readable code causing at least one processor to:

analyze a physiological indicator signal to obtain measurements of one or more physiological parameters; and

detect, using only the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters;

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wherein the computer readable code, in causing the at least one processor to detect effects of motion artifacts, causes the at least one processor to:

e. preprocess a segment from the measurement of one physiological parameter;

f. obtain a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment;

g. include the segment in analyses of physiological measurements, if comparison of the value of the at least one indicator of volatility with a predetermined threshold indicates noise/motion artifacts are not present;

h. select another segment of the signal from the physiological measurement and proceeding to step (a), if the value of the at least one indicator of volatility is less than a predetermined threshold and another segment is available.

45. (Withdrawn) The computer usable medium of claim 44 wherein the physiological indicator signal comprises a video color image having red, green and blue components, the video color image being an image obtained from of a portion of a subject's body; wherein the measurements of one or more physiological parameters comprise a measure of oxygen saturation; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain an average intensity of the red component and a blue component of the video color image of a portion of a subject's body; the average intensity of the red component and the average intensity of the blue component constituting DC_{RED} and DC_{BLUE} respectively;

obtain a standard deviation of the red component and the blue component; the standard deviation of the red component and the blue component constituting AC_{RED} and AC_{BLUE} respectively; and

obtain the measure of oxygen saturation by

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$$SpO2 = A - B\frac{AC_{RED}/DC_{RED}}{AC_{BLUE}/DC_{BLUE}}.$$

46. (Withdrawn) The computer usable medium of claim 44 wherein the one or more physiological measurements comprise heart rate and heart rate variability; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

determine beats for the physiological indicator signal;

determine beat to beat intervals; and

apply a cubic spline algorithm to obtain a substantially continuous beat to beat interval signal indicative of heart rate.

47. (Withdrawn) The computer usable medium of claim 44 wherein the one or more physiological measurements comprise respiratory rate; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain time–frequency spectrum of the physiological indicator signal utilizing variable frequency complex demodulation (VFCDM); and

obtain respiratory rates by extracting a frequency component that has a largest amplitude for each time point at a heart rate frequency band.

48. (Withdrawn) The computer usable medium of claim 44 wherein the one or more physiological measurements comprise a measure of blood loss; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain time–frequency spectrum of the physiological indicator signal utilizing variable frequency complex demodulation (VFCDM);

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obtain the amplitude modulation (AM) series from set of the largest instantaneous amplitude at each time sample within the heart rate frequency band of the time–frequency spectrum; and

determine whether the amplitude modulation decreases; a decrease in the amplitude modulation indicating blood volume loss in subject.

49. (Currently amended) A non-transitory computer usable medium having computer readable code embodied therein, the computer readable code causing at least one processor to:

analyze a physiological indicator signal to obtain measurements of one or more physiological parameters; and

detect, using only the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters;

~~The non-transitory computer usable medium of claim 44~~ wherein the one or more physiological measurements comprise a measure of atrial fibrillation; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain a time-varying coherence function by multiplying two time-varying transfer functions (TVFTs), the two time-varying transfer functions obtained using two adjacent data segments, from the physiological indicator signal, with one data segment as input signal and the other data segment as output to produce the first TVTF; the second TVTF is produced by reversing the input and output signals; and

determine whether the time-varying coherence function is less than a predetermined quantity.

50. (Currently amended) The non-transitory computer usable medium of claim 44 wherein the computer readable code, in causing the at least one processor to determine whether the time-

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varying coherence function is less than the predetermined quantity, causes the at least one processor to:

obtain one or more indicators of atrial fibrillation; and

determine whether the one or more indicators of atrial fibrillation exceed predetermined thresholds.

51. (Previously presented) The non-transitory computer usable medium of claim 50 wherein the one or more indicators of atrial fibrillation comprise a variance of the time-varying coherence function.

52. (Previously presented) The non-transitory computer usable medium of claim 51 wherein the one or more indicators of atrial fibrillation also comprise Shannon entropy.

53. (Previously presented) The computer usable medium of claim 50 wherein the predetermined thresholds are determined using receiver operator characteristic (ROC) analysis.

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REMARKS

Applicants have carefully reviewed the final Office Action dated March 21, 2014, and this response addresses the Examiner's concerns. Entry of this amendment into the application is respectfully requested.

I. STATUS OF THE CLAIMS

Claims 1-53 are pending in the application.

Claims 10-17, 35-38 and 45-48 are withdrawn from consideration.

Claims 1-9, 18-34, 39-44 and 49-53 are rejected.

Claims 1, 3-7, 19, 24, 27-30, 32, 39, 44 and 49-50 are amended.

Claims 2, 25 and 26 are canceled.

Support in the specification for the claim amendments

Amendments to claims 1, 7, 19, 24, 39 stating that the mobile computer system is handheld finds support in paragraph 28, 74, 76, 87, 90 and 91. Other amendments resulted from introducing limitations from claims afterward canceled into independent claims 1, 24, 44, from making claims 19 and 39 independent by including the original claims on which claims 19 and 39 were dependent, and from adjusting the dependency of claims formerly dependent on canceled claims.

II. THE 35 U.S.C. 102/103 REJECTIONS

Claims 1-2, 8-9, 24-26, 33-34 and 44 are rejected under pre-AIA 35 U.S.C. 102(b) as anticipated by Diab et al. (USPN 6,067,462) or, in the alternative, under pre-AIA 35 U.S.C. 103(a) as obvious over Lichter et al. (USPN 6,159,147 — cited in previous action).

Claim 1 has been amended to include claim 2 and also to recite that "the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment." Claim 24 has been amended to include the limitations of claims 25 and 26 and to recite that "the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment." Claim 44 has been amended to include the functions of claim 2 and to recite that "the at least one indicator of volatility being at least one of kurtosis or

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Shannon entropy for the preprocessed segment." Claims 1 and 24 have been amended to recite that the mobile communication device is a handheld mobile communication device.

Applicants respectfully state that neither Diab nor Lichter teach or suggest all the limitations of claims 1, 24 or 44.

Claims *2,* 8-9 are dependent on claim 1 and claims 25-26, 33-34 are dependent on claim 24.

Applicants with likely state that claims 1-2, 8-9, 24-26, 33-34 and 44, as amended, are not anticipated by Diab and a *prima facie* case of obviousness has not been established for claims 1-2, 8-9, 24-26, 33-34 and 44 as amended.

III. THE 35 U.S.C. 103 REJECTIONS

Claims 3-5 and 27-29 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Diab as applied to claims 1, 24 and 44 above, and further in view of Addison et al. (USPGPUB 2005/0070774 — cited in previous action). In regard to claims 3-5 and 27-29, Diab discloses all the claimed limitations except said at least one measure of volatility comprises kurtosis and Shannon entropy.

Claim 1 has been amended to include claim 2 and also to recite that "the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment." Claim 24 has been amended to include the limitations of claims 25 and 26 and to recite that "the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment." Claim 44 has been amended to include the functions of claim 2 and to recite that " the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment." Applicants respectfully state that, based on the arguments below, a prima facie case of obviousness has not been established for claims 1-5, 24, 27-29 and 44.

Addison et al. suggest the calculation of kurtosis and entropy for the wavelet transformed signal. The kurtosis is defined as:

$$k = \frac{E(x-\mu)^4}{\sigma^4} \quad (1)$$

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where μ is the mean of x, σ is the standard deviation of x, and $E(t)$ represents the expected value of the quantity t (specification, page 9, lines 25-30)
and the Shannon entropy SE can be calculated as

$$SE = -\sum_{i=1}^{k} \frac{p(i)*\log[p(i)]}{\log(\frac{1}{k})} \qquad (2)$$

where i represents the bin number, and $p(i)$ is the probability distribution of the signal amplitude (specification, page10, lines 4-8).

Applicants respectfully state that none of the properties of the continuous wavelet transform, linearity, shift property, scaling property energy conservation or localization properties (see, for example Vetterli, Kovacevic, Wavelets and Subband Coding, ISBN 0-13-097080-8, 1995, pp. 304-308) indicate that the inverse transform of the kurtosis of the wavelet transforms signal is the same as the kurtosis of the preprocessed segment of the measurement of one physiological parameter, which is recited in claim 3. By a similar argument, Sarkela (cited by the Examiner) calculate the entropy in terms of the coefficients of the wavelet transform. Applicants respectfully state that none of the properties of the continuous wavelet transform indicate that the inverse transform of the entropy calculated by Sarkela is the same as the Shannon entropy calculated from the preprocessed segment of the measurement of one physiological parameter.

This quandary can be easily understood in terms of the infinite support cousin of the wavelet transform, the Fourier transform. Applicants respectfully challenge the Examiner to show that the kurtosis of a Fourier transform can be inverted to provide the kurtosis of the signal. That is, if f(t) is the signal and F(ω) is the Fourier transform, is the kurtosis of F(ω) invertible into the kurtosis of f(t)? The Examiner may be able to find out pathological cases in which this is true but in general it cannot be shown to be true. The same argument applies to the Shannon entropy of the Fourier transform.

Applicants respectfully refer the Examiner to MPEP 2144.03C and respectfully request, as suggested by MPEP 2144.03C and the cases cited therein, that the Examiner

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provide adequate evidence for the Examiner's conclusions. Applicants respectfully state that the Examiner's present argument is not supported by substantial evidence.

The Office Action states that "the limitation of "at least one indicator of volatility" does not exclude other indicators suitable for other analyses." Applicants respectfully disagree. The claim recites "an indicator of volatility for the preprocessed segment." The Examiner has not provided any evidence that the supporting the fact that the kurtosis and Shannon entropy of the wavelet signal are "indicators of volatility for the preprocessed segment." Applicants respectfully state that the Examiner's present argument is not supported by substantial evidence.

"'[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" *KSR*, 550 U.S. at 418, 82 USPQ2d at 1396 (quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)). MPEP 2143.01 IV

Applicants respectfully state that neither Diab nor Addison teach or suggest "obtaining a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy," a limitation of amended claims 1, 24 and 44, since the Examiner has not shown and can not show that the kurtosis and Shannon entropy in their wavelet domain can be inverted to provide kurtosis and Shannon entropy in the time domain where the preprocessed segments are found.

Applicants respectfully state that there is no likelihood of success in this combination. Applicants also respectfully state that the combination is not enabling for the limitation cited.

Applicants respectfully state that the combination does not enable the practice of the claimed invention.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

In order to render a claimed apparatus or method obvious, the cited prior art as a whole must enable one skilled in the art to make and use the apparatus or method. Beckman Instruments, Inc. v. LKB Produkter AB, 892 F.2d 1547, 1551 (Fed. Cir. 1989).

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OBVIOUSNESS REQUIRES A REASONABLE EXPECTATION OF SUCCESS (MPEP 2143.02).

Applicants respectfully state that a *prima facie* case of obviousness has not been established for amended claims 1, 24 and 44. Claims 3-5 are dependent on claim 1 and claims 27-29 are dependent on claim 24.

Applicants respectfully state that a *prima facie* case of obviousness has not been established for claims 1,3-5, 24, 27-29 and 44.

Claims 6, 30, and 53 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over the combination of Diab and Addison as applied to claims 1, 24 and 44 above, and further in view of Echauz et al. (USPN 6,678,548 — cited in previous action).

Claim 6 is dependent on claim 1, claim 30 is dependent on claim 24 and claim 53 is dependent on claim 44.

As stated above, Applicants respectfully state that neither Diab nor Addison teach or suggest "obtaining a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment," a limitation of amended claims 1, 24 and 44, since the Examiner has not shown and can not show that the kurtosis and Shannon entropy in their wavelet domain can be inverted to provide kurtosis and Shannon entropy in the time domain where the preprocessed segments are found.

Applicants respectfully state that there is no likelihood of success in this combination. Applicants also respectfully state that the combination is not enabling for the limitation cited.

Furthermore, the Examiner, in the Office Action, states that "Echauz teaches a threshold value can be determined using receiver operator characteristic (ROC) analysis for changing the sensitivity of feature classifications which includes wavelet coefficients and entropy analysis (Col 4 lines 26-51; Col 21 line 56 - Col 22 line 7)." Echauz, in Col 4 lines 26-51, teaches that:

> The feature extraction portion 40 contains selectable algorithms and mathematical formulas that distill relevant seizure-predictive and seizure-indicative attributes from the high-dimensional preprocessed signals. Multichannel data within the sliding observation window (typically 400 to hundreds of thousands of numbers) are converted into a low dimensional vector [X.sub.1 X.sub.2 . . . X.sub.n] containing 10 or less features for each time scale (usually 40 or less numbers in

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> the complete vector). Features can be any linear or nonlinear projection of raw data into another space, including the same raw data without compression as a special case. Features can be updated as fast as the raw data sampling rate (e.g., 200 Hz), but typically the fastest feature sampling is set as one every 0.45 seconds. Longer-horizon features can be updated less frequently according to a no-less-than-50% sliding window overlap criterion. Distinctly from all the prior art contemplating features, the feature vector is made patient-specific and optimized from a rich feature library of instantaneous, historical, spatial, and artificial features. An exemplary feature library is disclosed in co-pending Application Serial No. 09/735,364. Examples of useful features include accumulated energy profiles, quick fractal dimension (curvelength), absolute values of wavelet coefficients, nonlinear energy, spectral entropy, prodrome templates, the statistical moments of any feature, and custom-made genetically found, neurally computed features.

Applicants respectfully state that Echauz, in Col 4 lines 26-51, teaches extracting attributes of the preprocessed signal. Echauz, in Col 21 line 56 - Col 22 line 7, teaches that:

> Increasing the risk of FPs raises the probability threshold, reducing the system's propensity to declare S.sub.T. Similarly, increasing the risk of FNs lowers the threshold, making the system more sensitive. If **instead of the above thresholds on the likelihood ratio or the probability, some other constant is used, the classifier's operating point moves along the "receiver operating characteristic" (ROC; P_{CP} vs. P_{FP}) curve, trading off the ability to detect preseizures for the ability to detect nonpreseizures (and losing optimality as initially defined by the performance metrics, of course). Changing these simple thresholds on the likelihood ratio or the probability implies that the classifier's complex decision boundaries also change in the n-dimensional space of features. Except for academic special cases, separately thresholding one-dimensional features, as commonly found in prior art systems, creates suboptimal decision rules.** For two or more features, the resulting suboptimal decision regions are piecewise rectangular, with boundaries parallel to the feature axes.

Applicants respectfully state that Echauz teaches that the classifier operating point moves along the ROC when something other than the optimal decision rule based on likelihood ratio or probability is used. According to Echauz moving along the ROC changes the classifier's complex decision boundaries and creates suboptimal decision rules. For the case that Echauz describes, Echauz teaches that moving along the ROC is discouraged. One skilled in the art would be discouraged from moving along the ROC away from the optimal decision rule based on likelihood ratio or probability.

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The Examiner has not provided any evidence that the ROC used by Echauz can be used for determining the threshold for comparing the value of the indicator of volatility. Applicants respectfully state that the Examiner's present argument is not supported by substantial evidence.

"'[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" *KSR*, 550 U.S. at 418, 82 USPQ2d at 1396 (quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)). MPEP 2143.01 IV

Applicants respectfully state that neither Diab nor Addison nor Echauz teach or suggest using the ROC for determining the threshold for comparing the value of the indicator(s) of volatility, a limitation of claims 6, 30 and 53.

Furthermore, Echauz teaches away from the combination.

One skilled in the art would be discouraged from following the path set out in the reference, therefore the reference teaches away. *In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994).

In *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (2007), the Court identified "teaching away" as a strong indicator of nonobviousness.

Even furthermore, Applicants respectfully state that the combination of Diab and Addison and Echauz does not enable the claimed invention of claims 6, 30 and 53.

Applicants respectfully state that a *prima facie* case of obviousness has not been established for claims 6, 30 and 53.

Claims 7 and 31-32 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Diab as applied to claims 1, 24-25 and 44 above, and further in view of Jacobsen et al. (USPN 6,198,394 — cited in previous action).

Applicants respectfully state that neither Diab nor Jacobsen teach or suggest placing a portion of the subject's body over an objective lens of a camera in a handheld mobile communication device, a limitation of claims 7 and 31-32.

The Office Action states that "Jacobsen teaches placing a portion of a subject's body over an objective lens of a camera in a mobile communication device (element 376, Fig. 5A; Fig. 8; Col 13 lines 55-67); and obtaining video images of the portion of the subject's body (element

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376, Fig. 5A; Fig. 8; Col 13 lines 55-67)." Col. 11, lines 51-52 of Jacobsen state that "Referring now to FIGS. 5 and 5A there is shown the components of a leader/medic unit 320." Col 13 lines 55-67 of Jacobsen are reproduced below:

> Referring now specifically to FIG. 5A, the micro-computer 330 can also operate several other devices. As electronics continue to be reduced in size and require less energy, the additional sensors 372, such as chemical and biological warfare sensors 374 can be added to the leader/medic unit 320. Additionally, other types of information gathering equipment, such as a video camera, may also be included. Such a feature will be especially beneficial to medics who will be able to transmit images of wounds, etc., for additional input from medical personnel at a central command center. To facilitate transmission of the information, the micro-computer 330 includes circuitry for image compression.

Applicants respectfully state that there is no teaching or suggestion in Jacobsen (or in Diab) of placing a leader/medic unit on the soldier or of placing a portion of the soldier's body over an objective lens of the video camera in the leader/medic unit. Applicants also respectfully state that, if a portion of the soldier's body having a wound is placed over the objective lens of the video camera in the leader/medic unit, such a procedure would be counter to the known art since it would expose the wound to infection, would coat the objective lens or the objective lens cover with blood and would not produce an image of the entire wound (by optical considerations of where an objective lens should be relative to a scene in order to produce an image). The combination would render Jacobsen not workable for the purpose it was intended for.

One skilled in the art would be discouraged from following the path set out in the combination, therefore the reference teaches away. *In re Gurley,* 27 F.3d 551, 553 (Fed. Cir. 1994).

"If when combined, the references "would produce a seemingly inoperative device," then they teach away from their combination. In re Sponnoble, 56 C.C.P.A. 823, 405 F.2d 578, 587, 160 U.S.P.Q. (BNA) 237, 244 (CCPA 1969); see also In re Gordon, 733 F.2d 900, 902, 221 U.S.P.Q. (BNA) 1125, 1127 (Fed. Cir. 1984) (finding no suggestion to modify a prior art device where the modification would render the device inoperable for its intended purpose)" (as cited in *Tec-Air Inc. v. Denso Manufacturing*, 192 F.3d 1353, 1360 (Fed. Cir. 1999).) MPEP 2143

In *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (2007), the Court identified "teaching away" as a strong indicator of nonobviousness.

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Since neither Jacobsen nor Diab, either separately or in combination, teach or suggest all the limitations of claims 7 and 31-32 and since the combination would render Jacobsen not workable for the purpose it was intended for, applicants respectfully state that prima facie case of obviousness has not been established for claims 7 and 31-32.

Claims 18-22, 39-42, and 49-52 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Diab as applied to claims 1, 24-25 and 44 above, and further in view of Zhang (USPGPUB 2009/0112110 — cited in previous action).

Claim 18 is dependent on an amended claim 1. As stated above, Applicants respectfully state that neither Diab nor Addison teach or suggest "obtaining a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy," a limitation of amended claims 1, 24 and 44. Applicants effectively state that Zhang does not teach or suggest the missing limitations.

Applicants respectfully state that a *prima facie* case of obviousness has not been established for claim 18.

Claims 19, 39 and 49 have been rewritten in independent form by including the limitations of the intervening original claims. Applicants respectfully state that, for the reasons given below, a *prima facie* case of obviousness has not been established for claims 19-22, 39-42 and 49-52.

The Office Action states that:

> Diab discloses the measurement of ECG signals (Col 23 lines 51-57) but does not specifically discloses a measure of atrial fibrillation. Zhang teaches a measure of atrial fibrillation based on ECG signal analysis (abstract and Figs. 1-9). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the method (Diab) to incorporate the ECG-based atrial fibrillation analysis (Zhang) in order to obtain more health information of the user.
>
> In regard to claims 19-22, 39-42, and 49-52, Diab as modified by Zhang discloses comparing the ECG signals in two adjacent data segments (Figs. 5-9 and associated descriptions of Zhang), Shannon entropy analysis ([0042] of Zhang), adaptive thresholds ([0036] of Zhang), detecting threshold ([0041-0042] of Zhang) but does not specifically disclose the recited limitations. However, time-varying coherence function(s) for analyzing two signals are known in the art as evidenced by Buck et al. (USPN 201 0/01 50375 — cited in previous action).

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> Therefore, it would have obvious to one with ordinary skill in the art at the time of the invention was made to modify the method to incorporate time-varying coherence function analysis through investigations or researches in order to obtain optimal atrial fibrillation information.

Zhang, in the abstract, teaches detecting P wave characteristics, where the detected characteristics include entropy of the cardiac signal within the T/Q window, amplitude of the P wave and latency of the P wave, and at least one of max-min analysis, multi-beat averaging, heart rate variability and RAR interval analysis. The detected characteristics compared to a threshold value in order to determine whether the patient is in atrial fibrillation (abstract, figure 9, paragraphs 61-66, Zhang).

Applicants respectfully state that neither Diab nor Zhang, either separately or in combination, teach or suggest the use of a time varying coherence function of the physiological indicators signal in order to determine whether the patient is in atrial fibrillation.

The Office Action states that "Zhang….. does not specifically disclose the recited limitations. However, time-varying coherence function(s) for analyzing two signals are known in the art as evidenced by Buck et al. (USPN 201 0/01 50375 — cited in previous action). Therefore, it would have obvious to one with ordinary skill in the art at the time of the invention was made to modify the method to incorporate time-varying coherence function analysis through investigations or researches in order to obtain optimal atrial fibrillation information."

Applicants respectfully state that coherence, a statistical operation in signal processing, is a mathematical operation that has been known, in the open literature, since about 1950. However, coherence typically relates to stationary signals and the concept of time-varying coherence requires an extension to non-stationary (non-ergodic) signals requires an extension of the concept. There is no indication in Buck of extending to nonstationary signals. In fact to the contrary, Buck starts by actively filtering the signals, by creating a short time coherence using power density spectra that is smoothed in time, and then further smoothing the short time coherence (paragraphs 32, 36, 37, Buck). Applicants respectfully state that Buck does not teach or suggest "obtaining a time-varying coherence function by multiplying two time-varying transfer functions (TVFTs), the two time-varying transfer functions obtained using two adjacent data segments, from the with one data segment as input signal and the other data segment as

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output to produce the first TVTF; the second TVTF is produced by reversing the input and output signals," a limitation of claims 19-22, 39-42 and 49-52, and neither does Diab or Zhang. Neither Diab or Zhang nor Buck teach or suggest each or suggest determining the presence of atrial fibrillation by determining whether the time varying coherence function is less than a predetermined quantity, a limitation of claims 19-22, 39-42 and 49-52.

The Examiner has presented no evidence that either Zhang or Buck teach or suggest determining the presence of atrial fibrillation by determining whether the time varying coherence function is less than a predetermined quantity. Applicants respectfully state that the Examiner's present argument is not supported by substantial evidence.

"'[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" *KSR,* 550 U.S. at 418, 82 USPQ2d at 1396 (quoting *In re Kahn,* 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)). MPEP 2143.01 IV.

Applicants respectfully state that a *prima facie* case of obviousness has not been established for claims 19-22, 39-42 and 49-52.

Claims 23 and 43 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over the combination of Diab and Zhang as applied to claims 19-21 and39-41 above, and further in view of Echauz.

Claim 23 is dependent upon claim 19 and claim 43 is dependent on claim 39.

As stated above, Buck does not teach or suggest "obtaining a time-varying coherence function by multiplying two time-varying transfer functions (TVFTs), the two time-varying transfer functions obtained using two adjacent data segments, from the with one data segment as input signal and the other data segment as output to produce the first TVTF; the second TVTF is produced by reversing the input and output signals," a limitation of claims 19-22, 39-42 and 49-52, and neither does Diab or Zhang; and neither Diab or Zhang nor Buck teach or suggest each or suggest determining the presence of atrial fibrillation by determining whether the time varying coherence function is less than a predetermined quantity, a limitation of claims 19-22, 39-42 and 49-52.

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Also, as stated above, Echauz teaches that the classifier operating point moves along the ROC when something other than the optimal decision rule based on likelihood ratio or probability is used. According to Echauz moving along the ROC changes the classifier's complex decision boundaries and creates suboptimal decision rules. For the case that Echauz teaches that moving along the ROC is discouraged. One skilled in the art would be discouraged from moving along the ROC away from the optimal decision rule based on likelihood ratio or probability.

The Examiner has not provided any evidence that the ROC used by Echauz can be used for determining the threshold for comparing the value of one or more indicators of atrial fibrillation. Applicants respectfully state that the Examiner's present argument is not supported by substantial evidence.

"'[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" *KSR,* 550 U.S. at 418, 82 USPQ2d at 1396 (quoting *In re Kahn,* 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)). MPEP 2143.01 IV

Applicants respectfully state that neither Diab nor Zhang nor Echauz teach or suggest using the ROC for determining the threshold for comparing the value of one or more indicators of atrial fibrillation, a limitation of claims 23 and 43.

Furthermore, Echauz teaches away from the combination.

Applicants respectfully state that a *prima facie* case of obviousness has not been established for claims 23 and 43.

VI. CONCLUSION

Any amendments to the claims as set forth herein, including the modification, addition, cancellation, or withdrawal of any claims, have been offered to advance this application to issue. None of the amendments made herein should be construed as an admission that the subject matter of the claims, as originally filed, is anticipated by or made obvious in light of any art of record whether considered singularly or in combinations. Applicants expressly reserve the right to pursue the originally filed claims in another co-pending application without being prejudiced by any amendments, including cancellation of claims, made herein.

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The Director of Patents and Trademarks is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account 03-2410 (Order No. 30210-201).

The following information is presented in the event that a call may be deemed desirable by the Examiner:

ORLANDO LOPEZ (617) 345-3000.

Respectfully submitted,

Dated: May 21, 2014

By: _____

Orlando Lopez
Reg. No. 46,880
Attorney for Patent Application Owners

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Doc Code: A.NE.AFCP
Document Description: After Final Consideration Pilot Program Request

PTO/SB/434 (05-13)

CERTIFICATION AND REQUEST FOR CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0

Practitioner Docket No.:	Application No.:	Filing Date:
30210-201	13/354,941	January 20, 2012
First Named Inventor:	**Title:**	
Ki H. Chon	PHYSIOLOGICAL PARAMETER MONITORING WITH A MOBILE COMMUNICATION DEVICE	

APPLICANT HEREBY CERTIFIES THE FOLLOWING AND REQUESTS CONSIDERATION UNDER THE AFTER FINAL CONSIDERATION PILOT PROGRAM 2.0 (AFCP 2.0) OF THE ACCOMPANYING RESPONSE UNDER 37 CFR 1.116.

1. The above-identified application is (i) an original utility, plant, or design nonprovisional application filed under 35 U.S.C. 111(a) [a continuing application (*e.g.*, a continuation or divisional application) is filed under 35 U.S.C. 111(a) and is eligible under (i)], or (ii) an international application that has entered the national stage in compliance with 35 U.S.C. 371(c).
2. The above-identified application contains an outstanding final rejection.
3. Submitted herewith is a response under 37 CFR 1.116 to the outstanding final rejection. The response includes an amendment to at least one independent claim, and the amendment does not broaden the scope of the independent claim in any aspect.
4. This certification and request for consideration under AFCP 2.0 is the only AFCP 2.0 certification and request filed in response to the outstanding final rejection.
5. Applicant is willing and available to participate in any interview requested by the examiner concerning the present response.
6. This certification and request is being filed electronically using the Office's electronic filing system (EFS-Web).
7. Any fees that would be necessary consistent with current practice concerning responses after final rejection under 37 CFR 1.116, *e.g.*, extension of time fees, are being concurrently filed herewith. [There is no additional fee required to request consideration under AFCP 2.0.]
8. By filing this certification and request, applicant acknowledges the following:
   - Reissue applications and reexamination proceedings are not eligible to participate in AFCP 2.0.
   - The examiner will verify that the AFCP 2.0 submission is compliant, *i.e.*, that the requirements of the program have been met (see items 1 to 7 above). For compliant submissions:
     - The examiner will review the response under 37 CFR 1.116 to determine if additional search and/or consideration (i) is necessitated by the amendment and (ii) could be completed within the time allotted under AFCP 2.0. If additional search and/or consideration is required but cannot be completed within the allotted time, the examiner will process the submission consistent with current practice concerning responses after final rejection under 37 CFR 1.116, *e.g.*, by mailing an advisory action.
     - If the examiner determines that the amendment does not necessitate additional search and/or consideration, or if the examiner determines that additional search and/or consideration is required and could be completed within the allotted time, then the examiner will consider whether the amendment places the application in condition for allowance (after completing the additional search and/or consideration, if required). If the examiner determines that the amendment does not place the application in condition for allowance, then the examiner will contact the applicant and request an interview.
       - The interview will be conducted by the examiner, and if the examiner does not have negotiation authority, a primary examiner and/or supervisory patent examiner will also participate.
       - If the applicant declines the interview, or if the interview cannot be scheduled within ten (10) calendar days from the date that the examiner first contacts the applicant, then the examiner will proceed consistent with current practice concerning responses after final rejection under 37 CFR 1.116.

Signature	Date
	May 21, 2014
Name (Print/Typed) Orlando Lopez	**Practitioner Registration No.** 46,880

Note: *This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4(d) for signature requirements and certifications. Submit multiple forms if more than one signature is required, see below*.*

☐ * Total of _____ forms are submitted.

Electronic Acknowledgement Receipt

EFS ID:	19089292
Application Number:	13354941
International Application Number:	
Confirmation Number:	9133
Title of Invention:	PHYSIOLOGICAL PARAMETER MONITORING WITH A MOBILE COMMUNICATION DEVICE
First Named Inventor/Applicant Name:	Ki H. Chon
Customer Number:	26486
Filer:	Marlo Schepper Grolnic
Filer Authorized By:	
Attorney Docket Number:	30210-201
Receipt Date:	21-MAY-2014
Filing Date:	20-JAN-2012
Time Stamp:	12:34:42
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1		201RFOA.pdf	1876807 601fedced38b95a765c14cc427d052a3da5bc463	yes	30

	Multipart Description/PDF files in .zip description		
	Document Description	**Start**	**End**
	Response After Final Action	1	1
	Claims	2	16
	Applicant Arguments/Remarks Made in an Amendment	17	29
	After Final Consideration Program Request	30	30
Warnings:			
Information:			
	Total Files Size (in bytes):	1876807	

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number	Filing Date	☐ To be Mailed
13/354,941	01/20/2012	

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	minus 20 =	*	X $ =	
INDEPENDENT CLAIMS (37 CFR 1.16(h))	minus 3 =	*	X $ =	
☐ APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is $310 ($155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			
☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT **05/21/2014**

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 50	Minus	** 53	= 0	X $40 =	0
Independent (37 CFR 1.16(h))	* 6	Minus	***3	= 3	X $210 =	630
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	**630**

AMENDMENT

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/DEBORAH POLLARD/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Document code: WFEE

United States Patent and Trademark Office
Sales Receipt for Accounting Date: 06/10/2014

DPOLLARD	SALE	#00000001	Mailroom Dt: 05/21/2014	032410	13354941	
		01 FC : 2201	630.00 DA			

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/354,941	01/20/2012	Ki H. Chon	30210-201	9133

26486 7590 06/20/2014

BURNS & LEVINSON, LLP
125 SUMMER STREET
BOSTON, MA 02110

EXAMINER	
LIU, CHU CHUAN	

ART UNIT	PAPER NUMBER
3777	

NOTIFICATION DATE	DELIVERY MODE
06/20/2014	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@burnslev.com

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 13/354,941	**Applicant(s)** CHON ET AL.	
	Examiner CHU CHUAN (JJ) LIU	**Art Unit** 3777	**AIA (First Inventor to File) Status** No

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 21 May 2014 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

NO NOTICE OF APPEAL FILED

1. ☒ The reply was filed after a final rejection. No Notice of Appeal has been filed. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114 if this is a utility or plant application. Note that RCEs are not permitted in design applications. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action; or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   c) ☐ A prior Advisory Action was mailed more than 3 months after the mailing date of the final rejection in response to a first after-final reply filed within 2 months of the mailing date of the final rejection. The current period for reply expires months from the mailing date of *the prior Advisory Action* or SIX MONTHS from the mailing date of the final rejection, whichever is earlier.
   Examiner Note: If box 1 is checked, check either box (a), (b) or (c). ONLY CHECK BOX (b) WHEN THIS ADVISORY ACTION IS THE FIRST RESPONSE TO APPLICANT'S FIRST AFTER-FINAL REPLY WHICH WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. ONLY CHECK BOX (c) IN THE LIMITED SITUATION SET FORTH UNDER BOX (c). See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) or (c) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendments filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   b) ☐ They raise the issue of new matter (see NOTE below);
   c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): (a) ☒ will not be entered, or (b) ☐ will be entered, and an explanation of how the new or amended claims would be rejected is provided below or appended.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.
9. ☐ The affidavit or other evidence filed after final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
10. ☐ The affidavit or other evidence filed after the date of filing the Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
11. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

12. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
13. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
14. ☒ Other: See Continuation Sheet.

STATUS OF CLAIMS

15. The status of the claim(s) is (or will be) as follows:
    Claim(s) allowed: .
    Claim(s) objected to: .
    Claim(s) rejected: 1-9,18-34,39-44 and 49-53.
    Claim(s) withdrawn from consideration: 10-17, 35-38 and 45-48.

/TSE CHEN/ Supervisory Patent Examiner, Art Unit 3777	/CHU CHUAN (JJ) LIU/ Examiner, Art Unit 3777

Petitioner Ex-1004, 0240

Continuation of 3. NOTE: The amendments change the scopes of the claims and therefore require further consideration and/ or search.

Continuation of 11. does NOT place the application in condition for allowance because: The amendments change the scopes of the claims and therefore require further consideration and/ or search.

Continuation of 14. Other: Applicant's request for entry into AFCP 2.0 is acknowledged, but is denied because the response cannot be reviewed and a search conducted in the limited amount of time authorized for this pilot program. Therefore, the response is being reviewed under pre-pilot practice.

DO NOT ENTER: /CCL/

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Ki H. Chon et al.
Application Number: 13/354,941
Filed: January 20, 2012
Title: PHYSIOLOGICAL PARAMETER MONITORING WITH A MOBILE COMMUNICATION DEVICE

Examiner: LIU, CHU CHUAN
Group Art Unit: 3777
Confirmation No. 9133

BURNS & LEVINSON, LLP
125 Summer St.
Boston, MA 02110
(617) 345-3243

TO: Mail Stop AF
Commissioner for Patents
P.O. Box 1450,
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE AFTER FINAL

Sir:

In reply to the final Office Action dated March 21, 2014, Applicants submit the following amendments and remarks that place the application in condition for allowance or, in the alternative, in better form for appeal. An After Final Consideration Request form is also attached hereto.

Amendments to the claims begin on page 2 of this paper.

Remarks begin on page 17 of this paper.

Attachments to this paper also include a copy of Form PTO/SB/434 (1 sheet).

Doc code: RCEX
Doc description: Request for Continued Examination (RCE)

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

REQUEST FOR CONTINUED EXAMINATION(RCE)TRANSMITTAL
(Submitted Only via EFS-Web)

Application Number	13354941	Filing Date	2012-01-20	Docket Number (if applicable)	30210-201	Art Unit	3777
First Named Inventor	Ki H. Chon			Examiner Name	Chu Chuan Liu		

This is a Request for Continued Examination (RCE) under 37 CFR 1.114 of the above-identified application.
Request for Continued Examination (RCE) practice under 37 CFR 1.114 does not apply to any utility or plant application filed prior to June 8, 1995, or to any design application. The Instruction Sheet for this form is located at WWW.USPTO.GOV

SUBMISSION REQUIRED UNDER 37 CFR 1.114

Note: If the RCE is proper, any previously filed unentered amendments and amendments enclosed with the RCE will be entered in the order in which they were filed unless applicant instructs otherwise. If applicant does not wish to have any previously filed unentered amendment(s) entered, applicant must request non-entry of such amendment(s).

☒ Previously submitted. If a final Office action is outstanding, any amendments filed after the final Office action may be considered as a submission even if this box is not checked.

- ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
- ☐ Other _____

☐ Enclosed

- ☐ Amendment/Reply
- ☐ Information Disclosure Statement (IDS)
- ☐ Affidavit(s)/ Declaration(s)
- ☐ Other _____

MISCELLANEOUS

☐ Suspension of action on the above-identified application is requested under 37 CFR 1.103(c) for a period of months _____ (Period of suspension shall not exceed 3 months; Fee under 37 CFR 1.17(i) required)

☐ Other _____

FEES

The RCE fee under 37 CFR 1.17(e) is required by 37 CFR 1.114 when the RCE is filed.

☒ The Director is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account No 032410

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

☒ Patent Practitioner Signature

☐ Applicant Signature

PTO/SB/30EFS (07-09)
Approved for use through 07/31/2012. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Signature of Registered U.S. Patent Practitioner			
Signature	/Orlando Lopez/	Date (YYYY-MM-DD)	2014-06-23
Name	Orlando Lopez, Ph.D.	Registration Number	46880

This collection of information is required by 37 CFR 1.114. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.

2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.

3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.

4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).

5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.

6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).

7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.

8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.

9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Electronic Patent Application Fee Transmittal

Application Number:	13354941
Filing Date:	20-Jan-2012
Title of Invention:	PHYSIOLOGICAL PARAMETER MONITORING WITH A MOBILE COMMUNICATION DEVICE
First Named Inventor/Applicant Name:	Ki H. Chon
Filer:	Marlo Schepper Grolnic
Attorney Docket Number:	30210-201

Filed as Small Entity

Utility under 35 USC 111(a) Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Miscellaneous:				
Request for Continued Examination	2801	1	600	600
		Total in USD ($)		**600**

Electronic Acknowledgement Receipt

EFS ID:	19375107
Application Number:	13354941
International Application Number:	
Confirmation Number:	9133
Title of Invention:	PHYSIOLOGICAL PARAMETER MONITORING WITH A MOBILE COMMUNICATION DEVICE
First Named Inventor/Applicant Name:	Ki H. Chon
Customer Number:	26486
Filer:	Marlo Schepper Grolnic
Filer Authorized By:	
Attorney Docket Number:	30210-201
Receipt Date:	23-JUN-2014
Filing Date:	20-JAN-2012
Time Stamp:	10:01:36
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	yes
Payment Type	Deposit Account
Payment was successfully received in RAM	$600
RAM confirmation Number	8229
Deposit Account	032410
Authorized User	

The Director of the USPTO is hereby authorized to charge indicated fees and credit any overpayment as follows:

Charge any Additional Fees required under 37 C.F.R. Section 1.16 (National application filing, search, and examination fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.17 (Patent application and reexamination processing fees)

Petitioner Ex-1004, 0248

Charge any Additional Fees required under 37 C.F.R. Section 1.19 (Document supply fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.20 (Post Issuance fees)

Charge any Additional Fees required under 37 C.F.R. Section 1.21 (Miscellaneous fees and charges)

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Request for Continued Examination (RCE)	201RCETransmittal.pdf	841525 e3594faaee5593a375ea36cff2af224c62183740	no	3
Warnings:					
Information:					
2	Fee Worksheet (SB06)	fee-info.pdf	30674 21f6cbe9e6f13ea530549809aebabc760e252568	no	2
Warnings:					
Information:					
		Total Files Size (in bytes):	872199		

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111
If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371
If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office
If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

PTO/SB/06 (09-11)
Approved for use through 1/31/2014. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PATENT APPLICATION FEE DETERMINATION RECORD Substitute for Form PTO-875	Application or Docket Number 13/354,941	Filing Date 01/20/2012	☐ To be Mailed

ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
☐ BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	
☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
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☐ MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				
* If the difference in column 1 is less than zero, enter "0" in column 2.			TOTAL	

APPLICATION AS AMENDED – PART II

AMENDMENT 06/23/2014

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	* 50	Minus	** 53	= 0	X $40 =	0
Independent (37 CFR 1.16(h))	* 6	Minus	***6	= 0	X $210 =	0
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	0

AMENDMENT

	(Column 1) CLAIMS REMAINING AFTER AMENDMENT		(Column 2) HIGHEST NUMBER PREVIOUSLY PAID FOR	(Column 3) PRESENT EXTRA	RATE ($)	ADDITIONAL FEE ($)
Total (37 CFR 1.16(i))	*	Minus	**	=	X $ =	
Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
☐ Application Size Fee (37 CFR 1.16(s))						
☐ FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))						
					TOTAL ADD'L FEE	

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.
** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".
*** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 3, enter "3".
The "Highest Number Previously Paid For" (Total or Independent) is the highest number found in the appropriate box in column 1.

LIE
/LINDA A. WASHINGTON/

This collection of information is required by 37 CFR 1.16. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**
If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/354,941	01/20/2012	Ki H. Chon	30210-201	9133

26486 7590 09/24/2014

BURNS & LEVINSON, LLP
125 SUMMER STREET
BOSTON, MA 02110

EXAMINER
LIU, CHU CHUAN

ART UNIT	PAPER NUMBER
3777	

NOTIFICATION DATE	DELIVERY MODE
09/24/2014	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@burnslev.com

Office Action Summary	Application No. 13/354,941	Applicant(s) CHON ET AL.	
	Examiner CHU CHUAN (JJ) LIU	Art Unit 3777	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06/23/2014*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *1,3-24 and 27-53* is/are pending in the application.

5a) Of the above claim(s) *10-17,35-38 and 45-48* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,3-9,18-24,27-34,39-44 and 49-53* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

2) ☐ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

4) ☐ Other: _____.

Petitioner Ex-1004, 0252

DETAILED ACTION

1. The present application is being examined under the pre-AIA first to invent provisions.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/21/2014 has been entered.

3. Claims 1, 3-24, and 27-53 are pending for examination. Claims 2, 25 and 26 are cancelled. Claims 10-17, 35-38 and 45-48 are withdrawn from consideration.

Claim Rejections - 35 USC § 112

4. The following is a quotation of 35 U.S.C. 112(b):

> (b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 3-9, 18, 24, 27-34, and 44 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention. Claims that depend directly or indirectly from claim(s) 1, 24 and 44 is/are also rejected due to said dependency.

6. Claims 1, 24 and 44 recites "detecting… effects of motion artifacts in the measurements… and deciding whether to retain the measurements…". It is not clear if the decision is made according to the "detected effects of motion artifacts" or based on other information. Examiner interprets the decision is made based on other information for the purpose of examination.

In addition, claims 1, 24 and 44 "…deciding **whether to** retain the measurements …(c or g) including the segment in analyses of physiological measurements, **if** comparison of the value…(d or h) selecting another segment…**if** the value…". The limitations appear to be conditional/optional languages which are not positive limitations ("Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation", see MPEP 2103 C and 2111.04). Therefore, claim limitations recited after "whether to" and the steps (c or g) and (d or h) are not given sufficient patentable weights. It is suggested that the term of "whether to", the limitation should be set forth "deciding to retain the measurement when/ based on (certain condition is met) or not to retain the measure when/ based on (certain condition is met); the terms "if" should be set forth "when" to more positively claim the limitations.

7. Claims 19, 39, 49 recites "the two time-varying transfer functions obtained using **two adjacent data segments**, from the physiological indicator signal, with **one data segment** as **input** signal and **the other segment** as **output** to produce the first TVTF; the second TVTF is produced by reversing **the input and output signals**". Although the limitation recites one data segment and the other segment, it is unclear if the data

segments are part of the "two adjacent data segments" or other possible data segments. Furthermore, the limitation recites input signal, output, the input and output signals. The relationships between them are not clearly recited in the claims. It is suggested that the limitation should be set forth "the two time-varying transfer functions obtained using two adjacent data segments, from the physiological indicator signal, with one of the two adjacent data segment as an input signal and the other one of the two adjacent segment as an output signal to produce the first TVTF; the second TVTF is produced by reversing the input signal and the output signal[s]".

Claim Rejections - 35 USC § 103

8. The following is a quotation of pre-AIA 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 3, 8-9, 24, 27, 33-34, and 44 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Addison et al. (USPGPUB 2005/0070774 – cited in previous action) in view of Lichter et al. (USPN 6,159,147 – cited in previous action). In regard to claims 1, 3, 24, 27, and 44, Addison discloses a method and an apparatus for physiological parameter monitoring (abstract; Figs. 1-17 and associated descriptions), the method comprising: providing a physiological indicator signal (PPG, abstract; Figs. 1-2 and associated descriptions; [0008]; [0072]) to a device (computer 14, Fig. 17 and

[0124]); analyzing, using the device, the physiological indicator signal to obtain measurements of one or more physiological parameters ([0005-0006]; [0021]; Figs. 8b, 9b and 10b and associated descriptions); and detecting, using the device and using only the measurements of the one or more physiological parameters ([0023]), effects of motion artifacts in the measurements of the one or more physiological parameters ([0023]) and deciding whether to retain the measurements ([0023]; Figs. 5 and 6d and associated descriptions), wherein the step of detecting effects of motion artifacts in the measurements comprises: a. preprocessing a segment from the measurement of one physiological parameter (Figs. 2 and associated descriptions); b. obtaining a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment (kurtosis and entropy, [0110]). It is noted that steps (c or g) and (d or h) are not given sufficient patentable weights referring to the 35 USC 112 2nd rejection above. Addison does not specifically disclose the computer is a handheld mobile communication device. Lichter teaches a handheld mobile communication device (personal computer 27, Figs. 2-3) which can be connected to various sensors to measure and analyze the collected data (Figs. 16) including pulse oximetry signals and ECG signals (Fig. 15). Addison additionally discloses that PPG signals and ECG are obtained ([0009]). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the computer (Addison) with the handheld mobile communications device (Lichter) to yield predictable results. It is noted that the rejection is made as best understood.

In regard to claims 8-9, 33-34, Addison as modified by Lichter discloses providing a physiological indicator signal comprises obtaining a signal from a PPG sensor and an ECG sensor (Figs. 2 and 17 and associated descriptions of Addison; Fig. 15 and associated descriptions of Lichter).

10. Claims 4-5 and 28-29 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over the combination of Addison and Lichter as applied to claims 1 and 24 above, and further in view of Sarkela (USPGPUB 2007/0197930 – cited in previous action). In regard to claims 4-5 and 28-29, Addison as modified by Lichter disclose the use of kurtosis and entropy ([0110] of Addison) but does not specifically disclose the entropy is Shannon entropy. Sarkela teaches the use of kurtosis and Shannon entropy to analyze physiological signals in wavelet domain ([0043-0052]) and many types of entropies can be utilized in the analysis of wavelet coefficient ([0048]. Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the entropy analysis (Addison as modified by Lichter) with the Shannon entropy analysis (Sarkela) to yield predictable results.

11. Claims 6 and 30 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over the combination of Addison and Lichter as applied to claims 1 and 24 above, and further in view of Echauz et al. (USPN 6,678,548 – cited in previous action). In regard to claims 6 and 30, Addison as modified by Lichter discloses all the claimed limitation except the predetermined threshold is determined using receiver operator

characteristic (ROC) analysis. Echauz teaches a threshold value can be determined using receiver operator characteristic (ROC) analysis for changing the sensitivity of feature classifications which includes wavelet coefficients and entropy analysis (Col 4 lines 26-51; Col 21 line 56 – Col 22 line 7). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the method and the apparatus (Addison as modified by Lichter) to incorporate the ROC determined threshold (Echauz) in order to better removing/ reducing the noise content of the detected signals.

12. Claims 7 and 31-32 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over the combination of Addison and Lichter as applied to claims 1 and 24 above, and further in view of Jacobsen et al. (USPN 6,198,394 – cited in previous action). In regard to claims 7 and 31-32, Addison as modified by Lichter discloses all the claim limitation except placing a portion of a subject's body over an objective lens of a camera in a mobile communication device; and obtaining video images of the portion of the subject's body. Jacobsen teaches placing a portion of a subject's body over an objective lens of a camera in a mobile communication device (element 376, Fig. 5A; Fig. 8; Col 13 lines 55-67); and obtaining video images of the portion of the subject's body (element 376, Fig. 5A; Fig. 8; Col 13 lines 55-67). The portable communication device taught by Jacobsen can be connected to various sensors applied to a user (Figs. 1-3, 5-7, and 8 and associated description) and provide video images associated with specific location of the user to the command center (Col 13 lines 55-67). Therefore, it would

have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the method and the apparatus (Addison as modified by Lichter) to incorporate the camera of the portable communication device (Jacobsen) in order to obtain video images associated with specific location of the user and transferring to a central monitoring system/ unit.

13. Claim 18 is rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over the combination of Addison and Lichter as applied to claim 1 above, and further in view of Zhang (USPGPUB 2009/0112110 – cited in previous action). In regard to claim 18, Addison as modified by Lichter discloses the measurement of ECG signals (Fig. 2 and associated descriptions of Addison; Fig. 5 and associated descriptions of Lichter) but does not specifically discloses a measure of atrial fibrillation. Zhang teaches a measure of atrial fibrillation based on ECG signal analysis (abstract and Figs. 1-9). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to modify the method (Addison as modified by Lichter) to incorporate the ECG-based atrial fibrillation analysis (Zhang) in order to obtain more health information of the user.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the claims at issue are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the reference application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO internet Web site contains terminal disclaimer forms which may be used. Please visit http://www.uspto.gov/forms/. The filing date of the application will determine what form should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to http://www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

15. Claims 19-23, 39-43, 49-53 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 8,755,876 in view of Addison and Lichter. In regard to claims 19-23, 39-43, 49-53 of present application, claims 1-16 of '876 recite all the limitations except a system and a method comprises providing a physiological indicator signal to a handheld mobile communication device; analyzing, using the device, the physiological indicator signal to obtain measurements of one or more physiological parameters; and detecting, using the a handheld mobile communication device and using only the measurements of the one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters and deciding whether to retain the measurements. Addison teaches a system and a method comprises providing a physiological indicator signal (PPG, abstract; PPG and ECG, Figs. 1-2 and associated descriptions; [0008]; [0072]) to a device (computer 14, Fig. 17 and [0124]); analyzing, using the device, the physiological indicator signal to obtain measurements of one or more physiological parameters ([0005-0006]; [0021]; Figs. 8b, 9b and 10b and associated descriptions); and detecting, using the device and using only the measurements of the one or more physiological parameters ([0023]), effects of motion artifacts in the measurements of the one or more physiological parameters ([0023]) and deciding whether to retain the measurements ([0023]; Figs. 5 and 6d and associated descriptions). Claims 1-16 of '876 recite a processor to process data related to R-R intervals (claims 1, 2, 6, 7, 12 and 13) but do not recite the processor is in part of a computing device. Addison teaches the measurements of PPG and ECG signals. Therefore, it would have been obvious to one

with ordinary skill in the art at the time of the invention was made to modify the method and the apparatus (claims 1-16 of '876) to incorporate the device (Addison) in order to obtain more information from the user. Claims 1-16 of '876 as modified by Addison does not specifically recite the device is a handheld mobile communication device. Lichter teaches a handheld mobile communication device (personal computer 27, Figs. 2-3) which can be connected to various sensors to measure and analyze the collected data (Figs. 16) including pulse oximetry signals obtained from the oximeter and ECG signals obtained from ECG sensor (Fig. 15). Therefore, it would have been obvious to one with ordinary skill in the art at the time of the invention was made to substitute the computer (Claims 1-16 of '876 as modified by Addison) with the handheld mobile communications device (Lichter) to yield predictable results.

Response to Arguments

16. Applicant's amendment and argument with respect to claims 1-9, 18-34, 39-44, 49-53 filed on 05/21/2014 have been fully considered but they are deemed to be moot in views of the new grounds of rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHU CHUAN (JJ) LIU whose telephone number is (571)270-5507. The examiner can normally be reached on M-TH 8:00am~4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tse Chen can be reached on (571)272-3672. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TSE CHEN/
Supervisory Patent Examiner, Art Unit 3777

/CHU CHUAN (JJ) LIU/
Examiner, Art Unit 3777

EAST Search History

EAST Search History (Prior Art)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S77	2	(13/684979).APP.	US-PGPUB; USPAT	OR	OFF	2014/09/15 09:47
S76	0	("136894979").PN.	US-PGPUB; USPAT	OR	OFF	2014/09/15 09:47
S75	32	coherence with function and 600/508-518.ccls.	US-PGPUB; USPAT	OR	ON	2014/09/15 09:32
S74	0	coherence with function with input with output with switch$3	US-PGPUB; USPAT	OR	ON	2014/09/15 09:27
S73	119	coherence with function with input with output	US-PGPUB; USPAT	OR	ON	2014/09/15 09:27
S72	25	coherence with function with revers$3	US-PGPUB; USPAT	OR	ON	2014/09/15 09:25
S71	0	coherence same input same ouput same revers$3	US-PGPUB; USPAT	OR	ON	2014/09/15 09:25
S70	0	corherence same input same ouput same revers$3	US-PGPUB; USPAT	OR	ON	2014/09/15 09:25
S69	175	fibrillation and 600/310-344.ccls.	US-PGPUB; USPAT	OR	ON	2014/09/03 14:59
S68	8	coherence and arterial with fibrillation and "600".clas.	US-PGPUB; USPAT	OR	ON	2014/09/03 14:52
S67	153	arterial with fibrillation and "600".clas.	US-PGPUB; USPAT	OR	ON	2014/09/03 14:51
S66	81	atrial with fibrillation and "600".clas. and (EEG ECG) and coherence	US-PGPUB; USPAT	OR	ON	2014/09/03 13:36
S65	54	(kurtosis entropy) same motion and ECG	US-PGPUB; USPAT	OR	ON	2014/09/03 11:56
S64	225	(kurtosis entropy) same (noise motion) and ECG	US-PGPUB; USPAT	OR	ON	2014/09/03 11:56
S63	93	(kurtosis shannon adj entropy) same (noise motion) and ECG	US-PGPUB; USPAT	OR	ON	2014/09/03 11:53
S62	24	S61 and "600".clas.	US-PGPUB; USPAT	OR	ON	2014/09/03 10:38
S61	211	(kurtosis Shannon with entropy) with (noise artifact)	US-PGPUB; USPAT	OR	ON	2014/09/03 10:37
S60	1	(kurtosis and Shannon with entropy) with (noise artifact)	US-PGPUB; USPAT	OR	ON	2014/09/03 10:37
S59	5	(kurtosis and Shannon with entropy) and noise with level	US-PGPUB; USPAT	OR	ON	2014/09/03 10:33
S58	632	(kurtosis Shannon with entropy) and noise with level	US-PGPUB; USPAT	OR	ON	2014/09/03 10:33

EAST Search History (Interference)

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Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13354941	CHON ET AL.
	Examiner	Art Unit
	CHU CHUAN (JJ) LIU	3777

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/24/2013	03/12/2014	09/16/2014						
	1	✓	✓	✓						
	2	✓	✓	-						
	3	✓	✓	✓						
	4	✓	✓	✓						
	5	✓	✓	✓						
	6	✓	✓	✓						
	7	✓	✓	✓						
	8	✓	✓	✓						
	9	✓	✓	✓						
	10	N	N	N						
	11	N	N	N						
	12	N	N	N						
	13	N	N	N						
	14	N	N	N						
	15	N	N	N						
	16	N	N	N						
	17	N	N	N						
	18	✓	✓	✓						
	19	✓	✓	✓						
	20	✓	✓	✓						
	21	✓	✓	✓						
	22	✓	✓	✓						
	23	✓	✓	✓						
	24	✓	✓	✓						
	25	✓	✓	-						
	26	✓	✓	-						
	27	✓	✓	✓						
	28	✓	✓	✓						
	29	✓	✓	✓						
	30	✓	✓	✓						
	31	✓	✓	✓						
	32	✓	✓	✓						
	33	✓	✓	✓						
	34	✓	✓	✓						
	35	N	N	N						
	36	N	N	N						

Index of Claims	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13354941	CHON ET AL.
	Examiner	**Art Unit**
	CHU CHUAN (JJ) LIU	3777

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

☐ Claims renumbered in the same order as presented by applicant ☐ CPA ☐ T.D. ☐ R.1.47

CLAIM		DATE								
Final	Original	10/24/2013	03/12/2014	09/16/2014						
	37	N	N	N						
	38	N	N	N						
	39	✓	✓	✓						
	40	✓	✓	✓						
	41	✓	✓	✓						
	42	✓	✓	✓						
	43	✓	✓	✓						
	44	✓	✓	✓						
	45	N	N	N						
	46	N	N	N						
	47	N	N	N						
	48	N	N	N						
	49	✓	✓	✓						
	50	✓	✓	✓						
	51	✓	✓	✓						
	52	✓	✓	✓						
	53	✓	✓	✓						

Search Notes	Application/Control No.	Applicant(s)/Patent Under Reexamination
	13354941	CHON ET AL.
	Examiner	Art Unit
	CHU CHUAN (JJ) LIU	3777

CPC- SEARCHED		
Symbol	Date	Examiner

CPC COMBINATION SETS - SEARCHED		
Symbol	Date	Examiner

US CLASSIFICATION SEARCHED			
Class	Subclass	Date	Examiner
600	300, 301, 309, 310, 322, 323, 324, 326, 330, 336, 473, 476, 500, 501, 502, 508, 509,518	10/24/2013	CCL
600	300, 301, 309, 310, 322, 323, 324, 326, 330, 336, 473, 476, 500, 501, 502, 508, 509,518	03/12/2014	CCL
600	300, 301, 309, 310, 322, 323, 324, 326, 330, 336, 473, 476, 500, 501, 502, 508, 509,518	09/16/2014	CCL

SEARCH NOTES		
Search Notes	Date	Examiner
Inventor Name Search (PALM and EAST)	10/23/2013	CCL
EAST Search (TEXT, USPGPUB, USPAT) See Search History	10/24/2013	CCL
Google NPL Search	10/24/2013	CCL
Updated EAST Search (TEXT, USPGPUB, USPAT) See Search History	03/12/2014	CCL
Google NPL Search	03/12/2014	CCL
Updated EAST Search (TEXT, USPGPUB, USPAT) See Search History	09/16/2014	CCL

INTERFERENCE SEARCH			
US Class/ CPC Symbol	US Subclass / CPC Group	Date	Examiner

/CHU CHUAN (JJ) LIU/ Examiner.Art Unit 3777	

Petitioner Ex-1004, 0268

Petitioner Ex-1004, 0268

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Ki H. Chon et al.
Application Number: 13/354,941
Filed: January 20, 2012
Title: PHYSIOLOGICAL PARAMETER MONITORING WITH A MOBILE COMMUNICATION DEVICE

Examiner: LIU, CHU CHUAN
Group Art Unit: 3777
Confirmation No. 9133

BURNS & LEVINSON, LLP
125 Summer St.
Boston, MA 02110
(617) 345-3243

TO: Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450,
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE TO OFFICE ACTION

Madam:

In reply to the non-final Office Action dated September 24, 2014, Applicants submit the following amendments and remarks that place the application in condition for allowance or, in the alternative, in better form for appeal.

Amendments to the claims begin on page 2 of this paper.

Remarks begin on page 17 of this paper.

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of the claims.

1. (Currently amended) A method for physiological parameter monitoring, the method comprising:
providing a physiological indicator signal to a handheld mobile communication device;

analyzing, using the handheld mobile communication device, the physiological indicator signal to obtain measurements of one or more physiological parameters; and

detecting, using the handheld mobile communication device and using only the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters and deciding whether to retain the measurements based on detected effects of motion artifacts;
wherein detecting effects of motion artifacts in the measurements comprises:
   a. preprocessing a segment from the measurement of one physiological parameter;
   b. obtaining a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment;
   c. including the segment in analyses of physiological measurements, ~~if~~ when comparison of the value of the at least one indicator of volatility with a predetermined threshold indicates noise/motion artifacts are not present; and
   d. selecting another segment of the signal from the physiological measurement and proceeding to step (a)[[,]] when ~~if~~ the value of the at least one indicator of volatility is less than a predetermined threshold and when another segment is available.

2. (Canceled)

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3. (Previously presented) The method of claim 1 wherein said at least one indicator of volatility comprises kurtosis.

4. (Previously presented) The method of claim 1 wherein said at least one indicator of volatility comprises Shannon entropy.

5. (Previously presented) The method of claim 1 wherein said at least one measure of volatility comprises kurtosis and Shannon entropy.

6. (Previously presented) The method of claim 1 wherein the predetermined threshold is determined using receiver operator characteristic (ROC) analysis.

7. (Previously presented) The method of claim 1 wherein providing a physiological indicator signal comprises:
placing a portion of a subject's body over an objective lens of a camera in a handheld mobile communication device; and

obtaining video images of the portion of the subject's body.

8. (Previously presented) The method of claim 1 wherein providing a physiological indicator signal comprises obtaining a signal from a physiological monitoring sensor.

9. (Previously presented) The method of claim 8 wherein the physiological monitoring sensor is a photoplethysmographic (PPG) sensor or an electrocardiogram sensor.

10. (Withdrawn) The method of claim 1 wherein the one or more physiological measurements comprise heart rate and heart rate variability.

11. (Withdrawn) The method of claim 10 wherein obtaining measurements of heart rate and heart rate variability comprise:

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determining beats for the physiological indicator signal;

determining beat to beat intervals; and

applying a cubic spline algorithm to obtain a substantially continuous beat to beat interval signal indicative of heart rate.

12. (Withdrawn) The method of claim 1 wherein the one or more physiological measurements comprise respiratory rate.

13. (Withdrawn) The method of claim 12 wherein measurement of respiratory rate comprises:
obtaining time–frequency spectrum of the physiological indicator signal utilizing variable frequency complex demodulation (VFCDM); and

obtaining respiratory rates by extracting a frequency component that has a largest amplitude for each time point at a heart rate frequency band.

14. (Withdrawn) The method of claim 1 wherein the one or more physiological measurements comprise a measure of oxygen saturation.

15. (Withdrawn) The method of claim 14 wherein providing a physiological indicator signal comprises:
placing a portion of a subject's body over an objective lens of a camera in a mobile communication device; and

obtaining video images of the portion of the subject's body, and

wherein obtaining the measure of oxygen saturation comprises:

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obtaining an average intensity of a red component and a blue component of the video images of the portion of the subject's body; the average intensity of the red component and the average intensity of the blue component constituting DC_{RED} and DC_{BLUE} respectively;

obtaining a standard deviation of the red component and the blue component; the standard deviation of the red component and the blue component constituting AC_{RED} and AC_{BLUE} respectively; and

obtaining the measure of oxygen saturation (SpO2) by

$$SpO2 = A - B\frac{AC_{RED}/DC_{RED}}{AC_{BLUE}/DC_{BLUE}}.$$

16. (Withdrawn) The method of claim 1 wherein the one or more physiological measurements comprise a measure of blood loss.

17. (Withdrawn) The method of claim 16 wherein obtaining the measure of blood loss comprises:
obtaining time–frequency spectrum of the physiological indicator signal utilizing variable frequency complex demodulation (VFCDM);

obtaining the amplitude modulation (AM) series from a set of the largest instantaneous amplitude at each time sample within the heart rate frequency band of the time–frequency spectrum; and

determining whether the amplitude modulation decreases; a decrease in the amplitude modulation indicating blood volume loss in subject.

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18. (Previously presented) The method of claim 1 wherein the one or more physiological measurements comprise a measure of atrial fibrillation.

19. (Currently amended) A method for physiological parameter monitoring, the method comprising:

providing a physiological indicator signal to a handheld mobile communication device;

analyzing, using the handheld mobile communication device, the physiological indicator signal to obtain measurements of one or more physiological parameters; and

detecting, using the handheld mobile communication device and using only the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters and deciding whether to retain the measurements based on effects of motion artifacts in the measurements;

wherein the one or more physiological measurements comprise a measure of atrial fibrillation;

wherein obtaining the measure of atrial fibrillation comprises:

obtaining a time-varying coherence function by multiplying two time-varying transfer functions (TVFTs), the two time-varying transfer functions obtained using two adjacent data segments, from the physiological indicator signal, ~~with one data segment as input signal and the other data segment as output to produce the first TVTF; the second TVTF is produced by reversing the input and output signals~~ one of the two adjacent data segment as an input signal and another of the two adjacent data segment as an output signal to produce a first TVTF; a second TVTF is produced by reversing the input and the output signals, using said another of the two adjacent data segment as the input signal and said one of the two adjacent data segment as the output signal; and

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determining whether the time-varying coherence function is less than a predetermined quantity.

20. (Previously presented) The method of claim 19 wherein determining whether the time-varying coherence function is less than the predetermined quantity comprises:
obtaining one or more indicators of atrial fibrillation; and

determining whether the one or more indicators of atrial fibrillation exceed predetermined thresholds.

21. (Previously presented) The method of claim 20 wherein the one or more indicators of atrial fibrillation comprise a variance of the time-varying coherence function.

22. (Previously presented) The method of claim 21 wherein the one or more indicators of atrial fibrillation also comprise Shannon entropy.

23. (Previously presented) The method of claim 20 wherein the predetermined thresholds are determined using receiver operator characteristic (ROC) analysis.

24. (Currently amended) A system for physiological parameter monitoring, the system comprising:
a physiological indicator signal sensing component; and a handheld mobile communication device comprising:

at least one processor; and

at least one computer usable medium, the computer usable medium having computer readable code embodied therein, the computer readable code causing the at least one processor to:

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analyze the physiological indicator signal to obtain measurements of one or more physiological parameters; and

detect effects of motion artifacts in the measurements of the one or more physiological parameters;

wherein the computer readable code, in causing the at least one processor to detect effects of motion artifacts, causes the at least one processor to:

a. preprocess a segment from the measurement of one physiological parameter;

b. obtain a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment;

c. include the segment in analyses of physiological measurements[[,]] ~~if~~ when comparison of the value of the at least one indicator of volatility with a predetermined threshold indicates noise/motion artifacts are not present;

d. select another segment of the signal from the physiological measurement and proceeding to step (a)[[,]] ~~if~~ when the value of the at least one indicator of volatility is less than a predetermined threshold and another segment is available.

25-26. (Canceled)

27. (Previously presented) The system of claim 24 wherein said at least one indicator of volatility comprises kurtosis.

28. (Previously presented) The system of claim 24 wherein said at least one indicator of volatility comprises Shannon entropy.

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29. (Previously presented) The system of claim 24 wherein said at least one measure of volatility comprises kurtosis and Shannon entropy.

30. (Previously presented) The system of claim 24 wherein the predetermined threshold is determined using receiver operator characteristic (ROC) analysis.

31. (Previously presented) The system of claim 24 wherein the physiological indicator signal sensing component comprises an image acquisition component, said acquisition component capable of acquiring a number of frames, each frame acquired at a predetermined time.

32. (Previously presented) The system of claim 31 wherein the handheld mobile communications device comprises said image acquisition component.

33. (Previously presented) The system of claim 24 wherein the physiological indicator signal sensing component comprises a physiological monitoring sensor.

34. (Previously presented) The system of claim 33 wherein the physiological monitoring sensor is a photoplethysmographic (PPG) sensor or an electrocardiogram sensor.

35. (Withdrawn) The system of claim 25 wherein the physiological indicator signal sensing component comprises an image acquisition component, said acquisition component capable of acquiring a number of frames, each frame acquired at a predetermined time; wherein said image acquisition component acquires a color image having red, green and blue components; wherein one or more physiological measurements comprise a measure of oxygen saturation; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain an average intensity of a red component and a blue component of the images of a portion of a subject's body; the average intensity of the red component and the average intensity of the blue component constituting DC_{RED} and DC_{BLUE} respectively;

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obtain a standard deviation of the red component and the blue component; the standard deviation of the red component and the blue component constituting AC_{RED} and AC_{BLUE} respectively; and

obtain the measure of oxygen saturation by

$$SpO2 = A - B\frac{AC_{RED}/DC_{RED}}{AC_{BLUE}/DC_{BLUE}}.$$

36. (Withdrawn) The system of claim 25 wherein the one or more physiological measurements comprise heart rate and heart rate variability; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

determine beats for the physiological indicator signal;

determine beat to beat intervals; and

apply a cubic spline algorithm to obtain a substantially continuous beat to beat interval signal indicative of heart rate.

37. (Withdrawn) The system of claim 25 wherein the one or more physiological measurements comprise respiratory rate; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain time–frequency spectrum of the physiological indicator signal utilizing variable frequency complex demodulation (VFCDM); and

obtain respiratory rates by extracting a frequency component that has a largest amplitude for each time point at a heart rate frequency band.

38. (Withdrawn) The system of claim 25 wherein the one or more physiological measurements comprise a measure of blood loss; and wherein the computer readable code, in

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causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain time–frequency spectrum of the physiological indicator signal utilizing variable frequency complex demodulation (VFCDM);

obtain the amplitude modulation (AM) series from set of the largest instantaneous amplitude at each time sample within the heart rate frequency band of the time–frequency spectrum; and

determine whether the amplitude modulation decreases; a decrease in the amplitude modulation indicating blood volume loss in subject.

39. (Currently amended) A system for physiological parameter monitoring, the system comprising:

a physiological indicator signal sensing component; and a handheld mobile communication device comprising:

at least one processor; and

at least one computer usable medium, the computer usable medium having computer readable code embodied therein, the computer readable code causing the at least one processor to:

analyze the physiological indicator signal to obtain measurements of one or more physiological parameters; and

detect effects of motion artifacts, using only the measurements of one or more physiological parameters, in the measurements of the one or more physiological parameters;

wherein the one or more physiological measurements comprise a measure of atrial fibrillation; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

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obtain a time-varying coherence function by multiplying two time-varying transfer functions (TVFTs), the two time-varying transfer functions obtained using two adjacent data segments , from the physiological indicator signal, ~~with one data segment as input signal and the other data segment as output to produce the first TVTF; the second TVTF is produced by reversing the input and output signalswith one data segment as input signal and the other data segment as output to produce the first TVTF; the second TVTF is produced by reversing the input and output signals~~ one of the two adjacent data segment as an input signal and another of the two adjacent data segment as an output signal to produce a first TVTF; a second TVTF is produced by reversing the input and the output signals, using said another of the two adjacent data segment as the input signal and said one of the two adjacent data segment as the output signal; and

determine whether the time-varying coherence function is less than a predetermined quantity.

40. (Previously presented) The system of claim 39 wherein the computer readable code, in causing the at least one processor to determine whether the time-varying coherence function is less than the predetermined quantity, causes the at least one processor to:

obtain one or more indicators of atrial fibrillation; and

determine whether the one or more indicators of atrial fibrillation exceed predetermined thresholds.

41. (Previously presented) The system of claim 40 wherein the one or more indicators of atrial fibrillation comprise a variance of the time-varying coherence function.

42. (Previously presented) The system of claim 41 wherein the one or more indicators of atrial fibrillation also comprise Shannon entropy.

43. (Previously presented) The system of claim 41 wherein the predetermined thresholds are determined using receiver operator characteristic (ROC) analysis.

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44. (Currently amended) A non-transitory computer usable medium having computer readable code embodied therein, the computer readable code causing at least one processor to:

analyze a physiological indicator signal to obtain measurements of one or more physiological parameters; and

detect, using only the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters;

wherein the computer readable code, in causing the at least one processor to detect effects of motion artifacts, causes the at least one processor to:

e. preprocess a segment from the measurement of one physiological parameter;

f. obtain a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment;

g. include the segment in analyses of physiological measurements[[,]]~~if~~ when comparison of the value of the at least one indicator of volatility with a predetermined threshold indicates noise/motion artifacts are not present;

h. select another segment of the signal from the physiological measurement and proceeding to step (a)[[,[[~~if~~ when the value of the at least one indicator of volatility is less than a predetermined threshold and another segment is available.

45. (Withdrawn) The computer usable medium of claim 44 wherein the physiological indicator signal comprises a video color image having red, green and blue components, the video color image being an image obtained from of a portion of a subject's body; wherein the measurements of one or more physiological parameters comprise a measure of oxygen saturation; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

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obtain an average intensity of the red component and a blue component of the video color image of a portion of a subject's body; the average intensity of the red component and the average intensity of the blue component constituting DC_{RED} and DC_{BLUE} respectively;

obtain a standard deviation of the red component and the blue component; the standard deviation of the red component and the blue component constituting AC_{RED} and AC_{BLUE} respectively; and

obtain the measure of oxygen saturation by

$$SpO2 = A - B\frac{AC_{RED}/DC_{RED}}{AC_{BLUE}/DC_{BLUE}}.$$

46. (Withdrawn) The computer usable medium of claim 44 wherein the one or more physiological measurements comprise heart rate and heart rate variability; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

determine beats for the physiological indicator signal;

determine beat to beat intervals; and

apply a cubic spline algorithm to obtain a substantially continuous beat to beat interval signal indicative of heart rate.

47. (Withdrawn) The computer usable medium of claim 44 wherein the one or more physiological measurements comprise respiratory rate; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain time–frequency spectrum of the physiological indicator signal utilizing variable frequency complex demodulation (VFCDM); and

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obtain respiratory rates by extracting a frequency component that has a largest amplitude for each time point at a heart rate frequency band.

48. (Withdrawn) The computer usable medium of claim 44 wherein the one or more physiological measurements comprise a measure of blood loss; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain time–frequency spectrum of the physiological indicator signal utilizing variable frequency complex demodulation (VFCDM);

obtain the amplitude modulation (AM) series from set of the largest instantaneous amplitude at each time sample within the heart rate frequency band of the time–frequency spectrum; and

determine whether the amplitude modulation decreases; a decrease in the amplitude modulation indicating blood volume loss in subject.

49. (Currently amended) A non-transitory computer usable medium having computer readable code embodied therein, the computer readable code causing at least one processor to:

analyze a physiological indicator signal to obtain measurements of one or more physiological parameters; and

detect, using only the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters; wherein the one or more physiological measurements comprise a measure of atrial fibrillation; and wherein the computer readable code, in causing the at least one processor to analyze the physiological indicator signal, causes the at least one processor to:

obtain a time-varying coherence function by multiplying two time-varying transfer functions (TVFTs), the two time-varying transfer functions obtained using two adjacent

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data segments, from the physiological indicator signal, ~~with one data segment as input signal and the other data segment as output to produce the first TVTF; the second TVTF is produced by reversing the input and output signalswith one data segment as input signal and the other data segment as output to produce the first TVTF; the second TVTF is produced by reversing the input and output signals~~ one of the two adjacent data segment as an input signal and another of the two adjacent data segment as an output signal to produce a first TVTF; a second TVTF is produced by reversing the input and the output signals, using said another of the two adjacent data segment as the input signal and said one of the two adjacent data segment as the output signal; and

determine whether the time-varying coherence function is less than a predetermined quantity.

50. (Previously presented) The non-transitory computer usable medium of claim 44 wherein the computer readable code, in causing the at least one processor to determine whether the time-varying coherence function is less than the predetermined quantity, causes the at least one processor to:

obtain one or more indicators of atrial fibrillation; and

determine whether the one or more indicators of atrial fibrillation exceed predetermined thresholds.

51. (Previously presented) The non-transitory computer usable medium of claim 50 wherein the one or more indicators of atrial fibrillation comprise a variance of the time-varying coherence function.

52. (Previously presented) The non-transitory computer usable medium of claim 51 wherein the one or more indicators of atrial fibrillation also comprise Shannon entropy.

53. (Previously presented) The computer usable medium of claim 50 wherein the predetermined thresholds are determined using receiver operator characteristic (ROC) analysis.

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REMARKS

Applicants have carefully reviewed the non-final Office Action dated September 24, 2014, and this response addresses the Examiner's concerns. Entry of this amendment into the application is respectfully requested.

I. STATUS OF THE CLAIMS

Claims 1, 3-24 and 27-53 are pending in the application.

Claims 10-17, 35-38 and 45-48 are withdrawn from consideration.

Claims 1, 3-9, 18-24, 27-34, 39-44 and 49-53 are rejected.

Claims 1, 19, 24, 39, 44 and 49 are amended.

II. THE 35 U.S.C. 112 REJECTIONS

Claims 1, 3-9, 18, 24, 27-34, and 44 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

Claims 1, 19, 24, 39, 44 and 49 have been amended following the Examiner's suggestions. Applicants respectfully state that the 35 USC 112 rejections have been traversed.

III. THE 35 U.S.C. 103 REJECTIONS

Claims 1, 3, 8-9, 24, 27, 33-34, and 44 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over Addison et al. (USPGPUB 2005/0070774 — cited in previous action) in view of Lichter et al. (USPN 6,159,147 — cited in previous action).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim Construction

The first step in determining whether a claim is anticipated, or is obvious in view of prior art, is to interpret the claim. ("It is elementary in patent law that, in determining whether a patent is valid ……., the first step is to determine the meaning and scope of each claim in suit." *Lemelson v. Gen. Mills, Inc.*, 968 F.2d 1202, 1206, 23 U.S.P.Q.2D (BNA) 1284, 1287 (Fed. Cir. 1992).) When not defined by applicant in the specification, the words of a claim must be read as they would be interpreted by those of ordinary skill in the art. (MPEP 2111.01) (*Rexnord Corp. v. Laitram Corp.*, 274 F.3d 1336, 1342, 60 USPQ2d 1851, 1854 (Fed. Cir. 2001) ("explaining the court's analytical process for determining the meaning of disputed claim terms")). The US Patent and Trademark Office ("USPTO") determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction "in light of the specification as it would be interpreted by one of ordinary skill in the art." *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364[, 70 USPQ2d 1827, 1830] (Fed. Cir. 2004). MPEP 2111.

One skilled in the art, upon reading the specification, would interpret kurtosis for the preprocessed segment and Shannon entropy for the preprocessed segment has been computed using the segment and equations (1) and (2) in paragraphs 48 and 49 of the specification.

the level of ordinary skill in the pertinent art

One skilled in the art has knowledge of signal processing, at an equivalent graduate-level, and knowledge of biomedical applications.

scope and contents of the prior art

Addison teaches decomposing a pulse oximetry signal, suitably a photoplethysmogram (PPG), by wavelet transform techniques, and analyzing the decomposed signal to provide selected physiological data. The signal may be processed to remove noise, artefacts, or transient features. Addison teaches using a modulus maxima technique for separating artifacts from the signal (paragraph 23). Addison teaches analyzing features, such as wavelet entropy, of the

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wavelet transform signal and provides an example of wavelet entropy in figure 13 (paragraphs 109-112).

Lichter teaches a real-time biological data processing PC card that is lightweight, cost effective, and portable. The real-time biological data processing PC card is capable of converting a host personal computer system into a powerful diagnostic instrument. Each real-time biological data processing PC card is adapted to input and process biological data from one or more biological data sensors, and is interchangeable with other real-time biological data processing PC cards.

the differences between the prior art and the claims at issue

Applicants respectfully state that neither Addison nor Lichter teach or suggest detecting, using the handheld mobile communication device and using **only** the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters and deciding whether to retain the measurements based on detected effects of motion artifacts;

wherein detecting effects of motion artifacts in the measurements comprises:

a. preprocessing a segment from the measurement of one physiological parameter;
b. obtaining a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment.

Addison teaches decomposing a pulse oximetry signal, suitably a photoplethysmogram (PPG), by wavelet transform techniques.

A wavelet transform

$$\gamma(s,\tau) = \int f(t)\psi^*_{s,\tau}(t)dt$$

is the transformation from the time space to a space characterized by the two variables s and τ. The wavelet function is a function with finite support. Wavelet have found use in signal analysis. One quantity that has been found useful is the so-called wavelet entropy introduced by Blanco et al., Time-frequency analysis of electroencephalogram series. III. Wavelet packets

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and information cost function, PHYSICAL REVIEW E VOLUME 57, NUMBER 1 JANUARY 1998 (a copy of which is attached). As stated by Blanco, the Wavelet Entropy, shows a correlation between oscillating structures corresponding to different scales while the Shannon entropy shows how redundant the time series is. The probabilities used in computing the Wavelet Entropy are based on the energy in each resolution level while the probabilities used in the Shannon entropy are computed based on the signal amplitude (see paragraph 49 of the specification).

One skilled in the art would recognize that the Wavelet Entropy is different from the Shannon entropy.

Furthermore, since the Wavelet Entropy is a function of the two variables s and τ, taking the inverse transform to express the equivalent time function, where the inverse transform is given by

$$f(t) = \int\int \gamma(s,\tau)\psi_{s,\tau}(t)d\tau ds$$

does not produce the Shannon entropy.

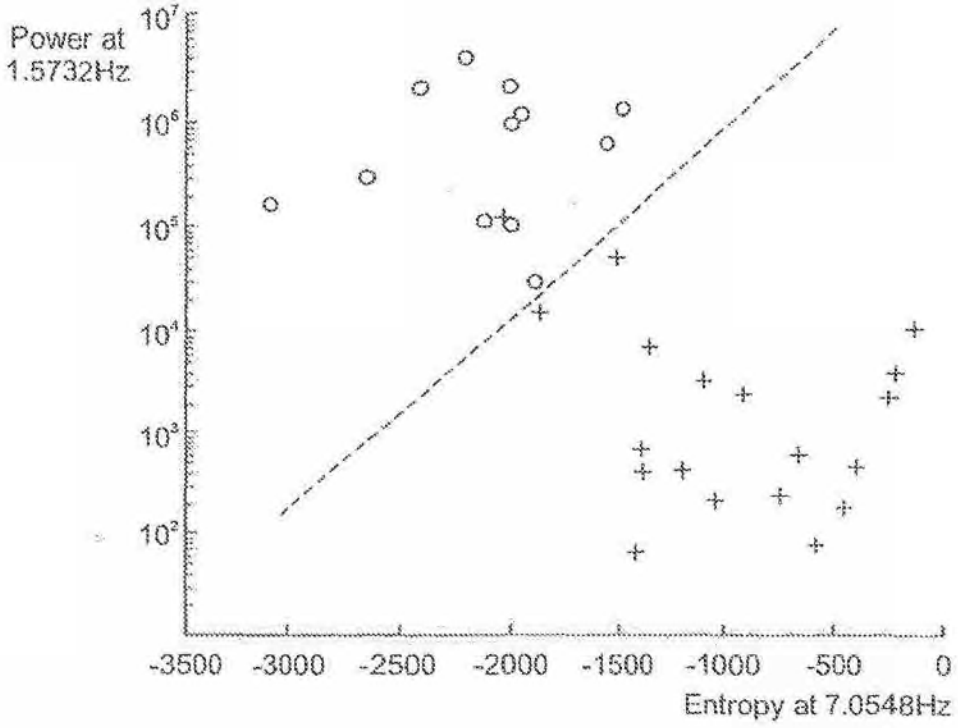
The Examiner, in the office action, states that Addison teaches "obtaining a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment (kurtosis and entropy) in paragraph 110.

Applicants respectfully state that paragraphs 109-110 and Fig. 13 of Addison, reproduced below:

> [0109] Wavelet Feature Analysis
>
> [0110] A scheme is described for the analysis of features derived from statistical measures of the wavelet transformed signal at a given frequency level or by following a time-frequency feature in wavelet space--where the transform can be

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represented as the actual transform values, the modulus of transform values, the squared transform values (the scalogram) or some other simple transformation of the wavelet transform values. **In the preferred embodiment these features derived from the wavelet transform at a selected frequency level may include the power, mean, skew, kurtosis and entropy.** In addition, these may be found for the peak frequency for each individual scalogram rather than a constant predefined frequency level, where peak frequency is defined as the frequency level containing the most power when integrated across the scalogram to produce a wavelet power spectrum. FIG. 12 shows a schematic of the wavelet transform scalogram and the wavelet power spectrum obtained from integration along the time domain at each frequency level. The selected frequency level across which the statistical measures are obtained is shown dashed in the scalogram plot.



teach the calculation of wavelet entropy, such as the entropy at a frequency used in Figure 13. Addison only teaches the obtaining of wavelet entropy.

Furthermore, Addison does not teach the use of entropy for detecting motion artifacts. Instead, in paragraph 23, Addison teaches the use of a modulus maxima technique for separating artifacts from the signal.

Applicants respectfully state that Addison does not teach or suggest detecting, using the handheld mobile communication device and using **only** the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters and deciding whether to retain the measurements based on detected effects of motion artifacts;
wherein detecting effects of motion artifacts in the measurements comprises:

a. preprocessing a segment from the measurement of one physiological parameter;
b. obtaining a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment, a limitation of claims 1, 24 and 44.

Lichter also does not does not teach or suggest detecting, using the handheld mobile communication device and using **only** the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters and deciding whether to retain the measurements based on detected effects of motion artifacts;
wherein detecting effects of motion artifacts in the measurements comprises:

a. preprocessing a segment from the measurement of one physiological parameter;
b. obtaining a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment, a limitation of claims 1, 24 and 44.

Applicants respectfully state that neither Addison nor Lichter teach or suggest all the limitations of claim 1 or claim 24 or claim 44.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

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Applicants respectfully state that a prima facie case of obviousness has not been established for claims 1, 24 or 44.

Claims 3, 8-9 are dependent on claim 1. Claims 27, 33-34 are dependent on claim 24.

Applicants respectfully state that a prima facie case of obviousness has not been established for claims 1, 3, 8-9, 24, 27, 33-34 and 44.

Claims 4-5 and 28-29 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over the combination of Addison and Lichter as applied to claims 1 and 24 above, and further in view of Sarkela (USPGPUB 2007/0197930 — cited in previous action).

Applicants respectfully state that, for the reasons given below, a prima facie case of obviousness has not been established for claims 4-5 and 28-29.

Claims 4-5 at dependent on claim 1 and claims 28-29 are dependent on claim 24. As stated above, neither Addison nor Lichter teach or suggest all the limitations of claim 1 or claim 24

Sarkela teaches the detection of epileptiform activity. In order to accomplish a mechanism with improved specificity to epileptiform activity and with the capability to detect specific type of epileptic patterns, brain wave signal data obtained from a subject is decomposed into at least one predetermined subband, each subband being indicative of a specific type of epileptiform activity (abstract). The subbands are obtained by the use of wavelet transforms (paragraph 44, Sarkela). Sarkela teaches the calculation of entropy in the subbands (paragraph 48) which is calculation of entropy of the wavelet coefficients, that is wavelet entropy. Sarkela teaches the calculation of kurtosis of the wavelet coefficients (paragraph 50).

The same reasoning as presented above applies for wavelet kurtosis. Sarkela uses kurtosis as a sub band specific indicator while kurtosis for a time series, such as the segment of a signal, is an indicator of how outlier prone that signal is. One skilled in the art would recognize that Sarkela teaches the use of wavelet kurtosis and not kurtosis of a time series. Again, taking the inverse transform to obtain a time series related function, the inverse transform of wavelet kurtosis is not kurtosis for a time series.

Applicants respectfully state that Sarkela also does not teach or suggest detecting, using the handheld mobile communication device and using **only** the measurements of one or more

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physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters and deciding whether to retain the measurements based on detected effects of motion artifacts;

wherein detecting effects of motion artifacts in the measurements comprises:

a. preprocessing a segment from the measurement of one physiological parameter;
b. obtaining a value of at least one indicator of volatility for the preprocessed segment; the at least one indicator of volatility being at least one of kurtosis or Shannon entropy for the preprocessed segment, a limitation of claims 1, 24 and 44.

Applicants respectfully state that neither Addison nor Lichter nor Sarkela teach or suggest all the limitations of claims 4-5 or 28-29.

Applicants respectfully state that a prima facie case of obviousness has not been established for claims 4-5 or 28-29.

Claims 6 and 30 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over the combination of Addison and Lichter as applied to claims 1 and 24 above, and further in view of Echauz et al. (USPN 6,678,548 — cited in previous action).

Claims 7 and 31-32 are rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over the combination of Addison and Lichter as applied to claims 1 and 24 above, and further in view of Jacobsen et al. (USPN 6,198,394 — cited in previous action).

Claim 18 is rejected under pre-AIA 35 U.S.C. 103(a) as being unpatentable over the combination of Addison and Lichter as applied to claim 1 above, and further in view of Zhang (USPGPUB 2009/0112110 — cited in previous action).

Claims 6, 7 and 18 are dependent on claim 1 and claims 30, 31-32 are dependent on claim 24. As stated above, neither Addison nor Lichter teach or suggest all the limitations of claim 1 or claim 24. Applicants respectfully state that neither Echauz nor Jacobsen nor Zhang teach or suggest the limitations that are not taught or suggested by Addison or Lichter.

Applicants respectfully state that a prima facie case of obviousness has not been established for claims 6, 7, 18, 30, 31-32.

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VI. DOUBLE PATENTING

Claims 19-23, 39-43, 49-53 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 8,755,876 in view of Addison and Lichter.

While Applicants are not opposed to filing a terminal disclaimer, Applicants respectfully state that nonstatutory obviousness double patenting requires a prima facie case of obviousness. U.S. Patent No. 8,755,876 only claims the detection of atrial fibrillation while claim 19 recites "detecting, using the handheld mobile communication device and using **only** the measurements of one or more physiological parameters, effects of motion artifacts in the measurements of the one or more physiological parameters and deciding whether to retain the measurements based on effects of motion artifacts in the measurements. " Claims 39 and 49 also recite detecting, using the handheld mobile communication device and using **only** the measurements of one or more physiological parameters, effects of motion artifacts. Addison teaches constructing a wavelet representation of the signal and using the wavelet decomposition to separate artifacts from the signal components. Applicants respectfully state that Addison does not teach or suggest using **only** the measurements of one or more physiological parameters to detect the effect of motion artifacts. Applicants respectfully state that Lichter also does not teach or suggest using **only** the measurements of one or more physiological parameters to detect the effect of motion artifacts. As stated above the claims of U.S. Patent No. 8,755,876 also do not teach or suggest using **only** the measurements of one or more physiological parameters to detect the effect of motion artifacts. Applicants respectfully state that a prima facie case of obviousness has not been established for 19-23, 39-43, 49-53 and nonstatutory obviousness double patenting is not proper.

V. CONCLUSION

Any amendments to the claims as set forth herein, including the modification, addition, cancellation, or withdrawal of any claims, have been offered to advance this application to issue. None of the amendments made herein should be construed as an admission that the subject matter of the claims, as originally filed, is anticipated by or made obvious in light of any art of

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record whether considered singularly or in combinations. Applicants expressly reserve the right to pursue the originally filed claims in another co-pending application without being prejudiced by any amendments, including cancellation of claims, made herein.

The Director of Patents and Trademarks is hereby authorized to charge any underpayment of fees, or credit any overpayments, to Deposit Account 03-2410 (Order No. 30210-201).

The following information is presented in the event that a call may be deemed desirable by the Examiner:

ORLANDO LOPEZ (617) 345-3000.

Respectfully submitted,

Dated: December 24, 2014

By: /Orlando Lopez/

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Attorney for Patent Application Owners

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APPENDIX

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Time-frequency analysis of electroencephalogram series. III. Wavelet packets and information cost function

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Signals obtained during tonic-clonic epileptic seizures are usually neglected for analysis by the physicians due to the presence of noise caused by muscle contractions. Although noise obscures completely the recording, some information about the underlying brain activity can be obtained with wavelet transform by filtering those frequencies associated with muscle activity. One great advantage of this method over traditional filtering is that the filtered frequencies do not modify the pattern of the remanent ones. An accurate analysis of the different seizure stages was achieved using the wavelet packet method, and through the information cost function the brain dynamical behavior can be accessed. [S1063-651X(97)09712-2]

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I. INTRODUCTION

The electroencephalogram (EEG) can be raftly defined as the mean electrical activity of the brain in different sites of the head. EEG patterns are correlated with functions, dysfunctions, and diseases of the central nervous system based on an empirical basis. Then clinical interpretation of EEG records are achieved by associating pathology characteristics (clinical symptomatology) with the visual inspection and pattern recognition of the EEG. Although this traditional analysis is quite useful, the visual inspection of the EEG is subjective, and hardly allows any systematization [1–4]. In order to overcome this, quantitative EEG analysis introduces objective measures reflecting the characteristics of the brain activity as well as the associated dynamics. However, we must remark that these methods are not developed for replacing traditional EEG visual analysis, but rather they complement them as additional tools.

Quantitative EEG analysis as a field includes a wide variety of techniques. These are frequency decomposition (spectral analysis), topographic mapping, compressed spectral arrays, significance probability mapping, and other complex analytical techniques [1–4]. A new approach to the problem of the quantification of the EEG series was achieved with nonlinear dynamics [5–11].

EEG's are complex signals whose statistical properties depends on both space and time. Regarding temporal characteristics, EEG signals are chaotic [5–11] and highly nonstationary (nevertheless, they can be analytically subdivided into short representative epochs where stationarity hypothesis is accomplished [9–11]).

Recently, we introduced two different techniques that allowed an analysis of an EEG time series in the time-frequency domain. The first was based on the Gabor transform [10,12–14], and the second one on the wavelet transform [15]. In the present work we present two significant improvements to the time-frequency analysis of the EEG series using wavelet transform. The first improvement is the introduction of the wavelet packet analysis [16]. The second improvement is the introduction of the information cost function (ICF), defined in terms of the wavelet coefficients, and essentially representing a Shannon entropy function [17,18]. We would like to remark that the applicability of these methods are not restricted only to EEG recordings.

Until the introduction of long term monitoring, spontaneous seizure EEG's were obtained only in those lucky situations in which the patient had a seizure during the few minutes of the recording. Normally, interictal EEG's (EEG's without seizure activity) were analyzed looking for pathological characteristics such as spikes, paroxysms, low frequency activity, etc. During those interictal EEG's, seizures were activated with photoestimulation, hyperventilation, and other clinical methods. However, provoked seizures do not necessarily have the same behavior as spontaneous ones. In order to overcome this limitation, long term video-EEG monitoring systems were developed. With video-EEG, after days of recording, clinical and electroencephalographic information can be correlated for obtaining an accurate evaluation of the seizures. Seizure starting, duration, post-seizure recovering, classification of the seizure, and different stages are some of the characteristics usually analyzed. However, in the case of tonic clonic seizures, muscle activity provoked by violent movements completely obscures the EEG recordings, limiting the analysis only to the starting and the post-seizure stages. Visual inspection of the EEG, and traditional mathematical methods such as Fourier transform are no longer applicable in these cases, owing to the great amount of noise involved. In consequence, brain activity during this kind of

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seizure has been observed only in special cases, for example in patients treated with "curare" (a drug that inhibits muscle responses) [19], or by filtering the signal in the frequency range of the muscle activity with standard methods [20]. However, filtering has several disadvantages, because it is impossible to separate brain and muscle activity and, further, it is well known that filtering high frequencies also affects the morphology of the low ones.

The aims of this work are to study a tonic clonic seizure, avoiding noise related limitations, by using wavelet transform and derived magnitudes in order to help physicians to identify and characterize the dynamical stage of the seizure as a complement of the video-EEG. The paper is organized in the following way. In Sec. II the clinical data and the experimental setup are presented. In Sec. III the time-frequency method based on wavelet transform is reviewed. The wavelet packets, as well as the information cost function, are introduced. In Sec. IV the analysis of a scalp EEG time series corresponding to an epileptic seizure is performed. Finally, in Sec. V a summary is given.

II. EXPERIMENTAL SETUP AND CLINICAL DATA

A scalp EEG signal is a nonstationary time series that usually presents artifacts due to an electrooculogram, an electromyogram, an electrocardiogram (ECG), and others [1–4]. Artifacts make a mathematical analysis of scalp EEG signals difficult. Sometimes, artifacts are presented for a few seconds, and can be obviated because they obscure only a small portion of the total EEG. In other cases, almost the total signal appears noisy and obscured by them, and very little information about the underlying brain activity can be extracted. An example of this kind of scalp EEG signal is the one corresponding to a tonic-clonic seizure [3].

A tonic-clonic "grand mal" seizure normally lasts around 40–90 s, and is characterized by violent muscle contractions. Initial massive tonic spasms are supplanted some seconds later by a clonic phase, with violent flexor movements and characteristic rhythmic spasms that last until the ending of the seizure.

Samples of EEG time series corresponding to generalized tonic-clonic seizures of epileptic patients were analyzed. Scalp and sphenoidal electrodes were applied following the 10-20 international system [1,2]. Each signal was digitized at 409.6 Hz through a 12 bit analog to digital converter, and filtered with an antialiasing eight pole low-pass Bessel filter with a cutoff frequency of 50 Hz. Then signals were digitally filtered with a 1–50-Hz bandwidth Butterworth filter and stored, after decimation, at 102.4 Hz in a personal computer hard drive. Recordings were done under video control in order to have an accurate determination of the different stages of the seizure. Analysis of each event included 1 min of EEG preseizure activity, and 2 min of the seizure and post-seizure phases. The different stages of EEG signals were determined by the physician team.

As an example, in Fig. 1 we present a scalp EEG signal, corresponding to a tonic-clonic epileptic seizure recorded in a central right location (C4 channel). In this record, the seizure starts at second 10, with a "discharge" of high frequencies. The tonic phase starts around second 35 with increasing amplitudes of the EEG, and the clonic phase begins around second 50 when the spasms dominates the EEG. The seizure clearly ends at second 85.

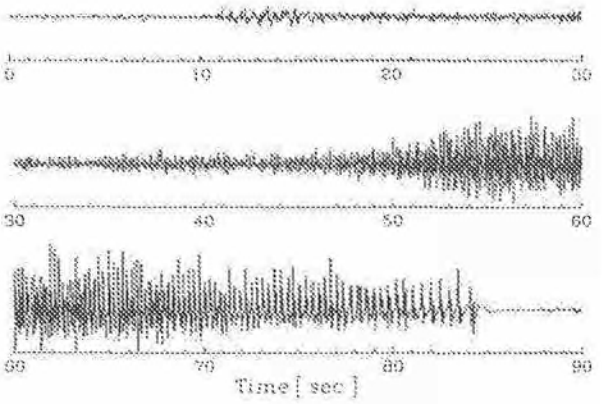


FIG. 1. Scalp EEG signal. Seizure starts at second 10, tonic phase at second 35, clonic phase at second 50. The seizure ends at second 85.

III. TIME-FREQUENCY ANALYSIS

A. Wavelet transform

Wavelet analysis gives us a powerful tool to confront very diverse problems in applied sciences or pure mathematics [21–27]. The wavelet is a smooth and quickly vanishing oscillating function with good localization both in frequency and time. It can be interpreted as single signals, or atoms, of short times with oscillating structures.

A wavelet family $\psi_{a,b}$ is the set of elemental functions generated by dilations and translations of a unique admissible mother wavelet $\psi(t)$,

$$\psi_{a,b}(t)=|a|^{-1/2}\psi\left(\frac{t-b}{a}\right), \tag{1}$$

where $a,b\in\Re, a\neq 0$ are the scale and translation parameters respectively, and t is the time. As a increases, the wavelet became more narrow. Thus we have a unique analystic pattern and its replicas at different scales and with variable localization in time.

Given a finite energy signal $S(t)$, the different correlations $\langle S,\psi_{a,b}\rangle$ indicate how precisely the wavelet function locally fits the signal at every scale a. This correlation operation defines the transformation that synthesizes the numerical information obtained in this way. From a different viewpoint, the wavelets of a family play the roles of elemental functions, representing the functions as a superpositions of wavelets correlated with the function for different scales (different a's). This makes it possible to organize the information in some particular structure to distinguish, for example, trends, or the shape associated with long scales of the local details from corresponding short scales.

The continuous wavelet transform of a signal $S(t)\in L^2(\Re)$ is defined as the correlation between the function $S(t)$ with the family wavelet $\psi_{a,b}$ for each a [23],

$$(W_\psi S)(a,b)=|a|^{-1/2}\int_{-\infty}^{\infty}S(t)\psi^*\left(\frac{t-b}{a}\right)dt=\langle S,\psi_{a,b}\rangle; \tag{2}$$

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the asterisk denotes complex conjugation.

For special selections of the function, ψ and a discrete net of parameters $a_j=2^{-j}$ and $b_{j,k}=2^{-j}k$, with $j,k\in\mathbb{Z}$ and the scale 2^{-j}, give us the shift parameter. The subfamily

$$\psi_{j,k}(t)=2^{j/2}\psi(2^j t-k) \quad j,k\in\mathbb{Z}, \tag{3}$$

constitutes an orthonormal basis of the Hilbert space $L^2(\mathbb{R})$ [21,22]. In this way, we can obtain discrete transformations, and it is possible to expand the signal in a series of wavelets. Then we can join the advantages of the wavelet transform with the atomic decomposition of $S(t)$.

The discrete wavelet transform associated with ψ is simply seen as a restriction of the continuous wavelet transform at the parameter set $\{a_j,b_{j,k}\}$. In this case, as it is well known, the information given by the discrete wavelet transform can be organized according a hierarchical scheme of nested subspaces called the multiresolution analysis in $L^2(\mathbb{R})$ [23–24].

In the present analysis we used a multiresolution scheme based on cubic orthogonal spline functions as the mother wavelet, with a discretized version of the integral wavelet transform given by Eq. (2) [25]. We selected this wavelet due to the fact that it forms a base in $L^2(\mathbb{R})$ with a very convenient characteristic of symmetry and simplicity. Moreover, the smoothness of its derivatives are very suitable for representing natural phenomena.

In the following we will assume that the EEG signal is given by sampled values $\{s_0(n)\}$, $n=1,\ldots,M$, which correspond to a uniform time grid with sampling time Δt. Without loss of generality, we can suppose that the sampling rate is $\Delta t=1$. We define the representation of the signal by interpolating the sampled data in the form

$$S(t)=\sum_k s_0(k)\phi(t-k), \tag{4}$$

where $\phi(t)$ is the cubic cardinal spline, verifying $\phi(n)=\delta_{n0}$ [22].

For any resolution level $N<0$, we can write the decomposition of the signal as

$$S(t)=\sum_k s_N(k)\phi(2^N t-k)+\sum_{j=-N}^{-1}\sum_k C_j(k)\psi_{j,k}(t), \tag{5}$$

where $C_j(k)$ are the wavelet coefficients, and the sequence $\{s_N(k)\}$ represents the coarser signal data at resolution level N, where $N=Ln_2(M)$. The second term is the wavelet expansion. The wavelet coefficients $C_j(k)$ can be interpreted as the local residual errors between successive signal approximations at scales j and $j+1$, and

$$r_j(t)=\sum_k C_j(k)\psi_{j,k}(t) \tag{6}$$

is the *detail signal* at scale j. It contains the information of the signal $S(t)$ corresponding to the frequencies $2^j\pi\leq|\omega|\leq 2^{j+1}\pi$. If the decomposition is carried out over all resolution levels, then the wavelet expansion will be

$$S(t)=\sum_{j=-N}^{-1}\sum_k C_j(k)\psi_{j,k}(t)=\sum_{j=-N}^{-1} r_j(t). \tag{7}$$

Since the family $\{\psi_{j,k}(t)\}$ is an *orthonormal* basis for $L^2(\mathbb{R})$, the concept of energy is linked with the usual notions derived from the Fourier theory. Then the wavelet coefficients are given by $C_j(k)=(S,\psi_{j,k})$, and the total energy by $\|S\|^2=\Sigma_{j<0}\Sigma_k|C_j(k)|^2$.

In the wavelet multiresolution framework (described above) it is possible to evaluate the energy corresponding to each level, and they can be used for the detection of the characteristic epileptic events [15]. Since we are using dyadic decomposition of the range of frequencies, from a signal of M samples, we have $M/2^{-j}$ coefficients at level j. In order to obtain an accurate event detection, we distribute the "atoms" of energy in each level j uniformly along 2^{-j} points. The energy in each resolution level $j=-1,\ldots,-N$, will be $E_j=\Sigma_k|C_j(k)|^2$, and the energy at each sampled time k will be $E(k)=\Sigma_{j=-1}^{-N}|C_j(k)|^2$.

Natural time series are usually combination of stochastic (noisy) and chaotic behaviors. Many applications, like nonlinear dynamics, require the separation of signal and noise [28,29]. Otherwise, when nonlinear invariants are evaluated (i.e., characteristic dimensions or Lyapunov exponents) the contaminating noise can give spurious results, and the obtained values will underestimate (if noise has strong periodic or almost periodic components) or overestimate (if noise is representative of a deterministic high dimensional or stochastic process) the real complexity of the system under study. When noise is present only in specific frequency bands, a filtering process can be implemented. However, from the point of view of nonlinear dynamics, filtering could be suitable only in some cases depending on the system under study. It is important to emphasize that a poorly designed filtering of the signal can give spurious results (i.e., filtering frequencies that determine the real dynamics of the signal).

Thus in these cases a filtering based on wavelet transform can be implemented in order to obtain a more accurate signal of the process under interest. Supposing, as in the case of tonic-clonic seizures, that we are interested in eliminating high frequency noise, using Eq. (7) at level j, the residual will be a smoothed version of the original signal, having fewer high frequencies in comparison to level $j+1$. This new signal will have half the data of the previous level; therefore, an interpolation with spline functions is applied in order to obtain the remaining data. On the other hand, interpolation by the cubic spline gives an efficient and very good approximation of the underlying physical signal given by samples [30]. Then this method can be accurately used for separation of noise, and the cleaned signal can be obtained as a sum of the interpolated residual components corresponding to the interesting frequency bands.

In summary, this method allows the elimination of nondesired frequency bands that hide other more interesting or unknown effects. Due to the orthogonality of the wavelet functions employed, we can be assured that only the unwanted and previously selected frequency bands were extracted, without needing to assume that linearity is necessary for making the traditional Fourier-based digital filtering.

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B. Wavelet packets

As it is well known, wavelet analysis provides a *time-scale* description of any finite energy signal. Essentially, it is a successive decomposition of the signal in different scales. At each step, the corresponding details are separated, providing useful information for detecting and characterizing short time phenomena or abrupt changes of energy.

However, since wavelets do not possess a well defined average in frequency, they are not well suited to describe and characterize stationary phenomena or to detect time-frequency structures. This is an important limitation, because significant events often involve joint variations of time and frequency [24]. To overcome this problem, wavelet packet analysis appears as a natural extension of wavelet analysis. Moreover, this technique allows a time-scale-frequency description of the signals.

A family of wavelet packets is a collection of elemental signals obtained from appropriate linear combination of wavelets. They look like locally oscillating wave forms resembling modulated sines or cosines. Moreover, they can be organized on an orthonormal basis of the space of finite energy signals. The main advantage of using wavelet packets is that standard wavelet analysis can be extended with a flexible strategy. Thus, the description of the given signal can be well adapted according to the significant structures. Several families of wavelet packets have been proposed in the literature [16,24,27]. Here we will apply trigonometric spline wavelet packets [16]. First let us briefly review the proposed technique.

Given a finite energy signal $s_0(t)$, using spline wavelet analysis we can successively decompose them with the recursive scheme

$$s_{j+1}(t)=s_j(t)\oplus r_j(t) \tag{8}$$

for each scale $j=0,-1,\ldots,-N$. As already mentioned, the components $s_{j+1}(t)$ and $s_j(t)$ add to the information of the signal corresponding to the frequency bands $-2^{j+1}\pi\leqslant\omega\leqslant 2^{j+1}\pi$ and $-2^{j}\pi\leqslant\omega\leqslant 2^{j}\pi$, respectively. This means that the decomposition at level j consists of filtering the components $s_{j+1}(t)$, giving the details corresponding to the remaining frequencies $2^{j}\pi\leqslant|\omega|\leqslant 2^{j+1}\pi$. The component $r_j(t)$ adds to this information, and we can describe the signal $S(t)$ in term of detail signals as

$$S(t)=\sum_{j<0} r_j(t). \tag{9}$$

On the other hand, the detail components can be described in terms of wavelet atoms

$$r_j(t)\sum_k C_j(k)\psi_{j,k}(t). \tag{10}$$

Since each wavelet $\psi_{j,k}(t)=2^{j/2}\psi(2^j t-k)$ is well localized in the interval $2^{-j}k\leqslant t\leqslant 2^{-j}(k+1)$, the corresponding coefficient $C_j(k)$ adds to the local information of the detail. However, as we mentioned above, these coefficients average all the involved frequencies $2^{j}\pi\leqslant|\omega|\leqslant 2^{j+1}\pi$, and we will not gain explicit information about stationary structures.

Now we are interested in how to improve the frequency precision. The main idea is to decompose the components $r_j(t)$ in portions, each one covering a longer interval. Then we will locally implement an appropriate frequency technique.

We define any portion or local signal as

$$r_j^{(m,l)}(t)=\sum_{k=l}^{l+2^m-1} C_j(k)\psi_{j,k}(t), \tag{11}$$

where the parameters m and l are chosen in order that $r_j^{(m,l)}(t)$ covers the full time interval $2^{-j}l\leqslant t\leqslant 2^{-j}(l+2^m)$, which is a relatively long interval of length 2^{m-j}. Note that we defined the local wavelet packet with of 2^m basic functions $\psi_{j,k}(t)$ for $k=l,\ldots,l+2^m-1$.

Now, we define the set of fundamental frequencies

$$\omega_{mh}=\pi+2h\pi/2^m, \tag{12}$$

with $0\leqslant h\leqslant 2^{m-1}$, and associated the Fourier matrix $\mathbf{M}^{(m)}$ given by

$$M_{nk}^{(m)}=2^{-m/2}\begin{cases}\sin\left[\pi(k+1/2)\right] & \text{if } n=1\\ 2^{1/2}\cos\left[\omega_{mh}(k+1/2)\right] & \text{if } n \text{ is even}\\ 2^{1/2}\sin\left[\omega_{mh}(k+1/2)\right] & \text{if } n \text{ is odd}\\ \cos\left[2\pi(k+1/2)\right] & \text{if } n=2^m,\end{cases} \tag{13}$$

with $1\leqslant n\leqslant 2^m$, $0\leqslant k<2^m$ and $h=[[n/2]]$, where $[[\,]]$ denotes the integer part. It can be demonstrated that $\mathbf{M}^{(m)}$ is a $2^m\times 2^m$ dimensional orthogonal matrix [16].

Then we can define the new set of elemental functions in order to expand $r_j^{(m,l)}(t)$ as a 2^m dimensional vector obtained from

$$\theta_{j,n}^{(m,l)}(t)=\sum_{k=l}^{l+2^m-1} M_{nk}^{(m)}\psi_{j,k}(t) \tag{14}$$

for $1\leqslant n\leqslant 2^m$.

Clearly, these functions constitute a new local orthonormal basis covering the interval under analysis, $2^{-j}l\leqslant t\leqslant 2^{-j}(l+2^m)$. Therefore we can give a second description of the local signal as

$$r_j^{(m,l)}(t)=\sum_{n=1}^{2^m} D_j^{(m,l)}(n)\theta_{j,n}^{(m,l)}(t). \tag{15}$$

The corresponding coefficients are easily computed as

$$D_j^{(m,l)}(n)=\sum_{k=l}^{l+2^m-1} M_{nk}^{(m)}C_j(k), \tag{16}$$

where $1\leqslant n\leqslant 2^m$.

The trigonometric wavelet packets $\theta_{j,n}^{(m,l)}(t)$ have zero mean, oscillate on the interval $2^{-j}l\leqslant t\leqslant 2^{-j}(l+2^m)$, and decay with exponential ratio. Moreover, their wave forms resemble modulate sines or cosines. In fact, it can be demonstrated that each Fourier transform $\hat{\theta}_{j,n}^{(m,l)}(\omega)$ is centered at the fundamental frequency ω_{mh}, when $n=2h$ or $n=2h$

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$+1$. Moreover, $\hat{\theta}_{j,n}^{(m,l)}(\omega)=0$ on the other fundamental frequencies, and it has a fast decay outside the range $2^j\pi \leq|\omega|\leq 2^{j+1}\pi$.

In other words, the coefficients $\{D_j^{(m,l)}(n)\}$ can be considered as the discrete Fourier spectrum for the local signal $r_j^{(m,l)}(t)$. Summing up, in the double set of coefficients $\{C_j(k),D_j^{(m,l)}(n)\}$ we add to the time-scale-frequency information of the local signal $r_j^{(m,l)}(t)$.

Finally, to analyze the complete function $r_j(t)$, that is, the details at level j, we choose some partition in local components $r_j^{(m_i,l_i)}(t)$, according the structure of the signal,

$$r_j(t)=\sum_{m_i} r_j^{(m_i,l_i)}(t), \tag{17}$$

where the sequence of index l_i verifies $l_{i+1}=l_i+2^{m_i}$. Then we implement the time-scale-frequency technique for each local signal, referred to above.

C. Information cost function

Assuming that the given data series $S=\{s_0(n)\}$ has a finite energy, i.e.,

$$\sum_k |s_0(k)|<\infty \tag{18}$$

and $\Delta t=1$, we can approximate the energy of its spline representation in the form

$$\|S\|^2=\sum_k |s_0(k)|^2, \tag{19}$$

then the values

$$p_0(n)=|s_0(n)|^2 \Big/ \sum_n |s_0(n)|^2, \tag{20}$$

give the probability distribution of the signal's energy in the time domain.

Furthermore, in the wavelet multiresolution analysis of the time series $\{s_0(n)\}$, the energy in each resolution level j ($j<0$) is the energy of the detail signal

$$E_j=\|r_j\|^2=\sum_k |C_j(k)|^2; \tag{21}$$

as a consequence, the total energy can be obtained by

$$E_{\text{tot}}=\|S\|^2=\sum_{j<0} E_j. \tag{22}$$

Then the normalized values

$$p_j=E_j/E_{\text{tot}}, \tag{23}$$

for $j=-1,-2,\ldots,-N$, define by scales the probability distribution of the energy. Clearly,

$$\sum_{j<0} p_j=\sum_n p_0(n)=1 \tag{24}$$

and the pair of distributions $(\{p_0(n)\},\{p_j\})$ can be considered as a time-scale density. They give a suitable tool for detecting and characterizing specific phenomena. The Shannon entropy gives a useful criteria for analyzing and comparing these distributions, since as is well known, it provides a measure of the information of any distribution.

We define the information cost function [17,18] as

$$C_t=-\sum_n p_0(n)Ln_2[p_0(n)] \tag{25}$$

and

$$C_\omega=-\sum_{j<0} p_j Ln_2[p_j]. \tag{26}$$

The first function shows how redundant the time series is. In other words, it leads us to inquire whether the patterns are periodic phenomena. On the other hand, the second function shows the correlation between oscillating structures corresponding to different scales. In particular with this function self-similar processes can be detected.

It has become quite common in analyses of experimental time series with nonlinear systems to make a time delay reconstruction of the phase space in which the dynamic can be observed. The phase space portrait can be analyzed mathematically to demonstrate the existence of an attractor (the region of the phase space of lower dimension where the signal is confined in its future evolution) and its dimension [28,29]. A useful way to describe the dynamic behavior is to use Lyapunov exponents. These exponents measure the rate at which nearby points on an attractor diverge or converge along nearby trajectories [28,29]. We must emphasize that these metric parameters (dimensions, Lyapunov exponent, etc.) are defined only for stationary systems. In previous works, we confirmed, from a nonlinear dynamical analysis of epileptic EEG time series [10–12], the validity of the basic assumption that, at the seizure onset, a transition takes place in the dynamical behavior of the neural network from a complex behavior to a simpler one [6,8]. That means that, during an epileptic seizure the dimension of the attractor and the larger Lyapunov exponent present lower values compared with those evaluated at preseizure and post-seizure stages. Also the reconstructed attractor in phase space looks more simple and ordered.

The information cost function gives a measure of the order or disorder of the system in time. Thus, the ICF is a good parameter in order to detect dynamical changes in the system behavior, as well as a form of quantifying it [17,18]. The analysis of the ICF as a function of the different frequency bands and time shows in which bands the system has a tendency to order, or to a less chaotic behavior, during an epileptic seizure. In addition, the ICF has the following advantages over the following parameters: (i) over the entropy, because it is capable of detecting changes in a nonstationary signal due to the localization characteristics of the wavelet transform; (ii) over dimensions and Lyapunov exponents (which are only defined for stationary behaviors), because the computational time is significantly lower, since the algorithm involves the use of fast wavelet transforms in a multiresolution framework.

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TABLE I. Frequency boundaries (in Hz) associated with the different resolution wavelet levels according with sample frequency $\omega_s = 102.4$ Hz. The traditional EEG frequency bands correspond to the following frequencies: δ (0.5–3.5 Hz), θ (3.5–7.5 Hz); α (7.5–12.5 Hz); β (12.5–30 Hz); γ (greater than 30 Hz).

Notation	ω_{min}	ω_{max}	Resolution level	EEG band
B_1	25.6	51.2	-1	γ, β
B_2	12.8	25.6	-2	β
B_3	6.4	12.8	-3	α, θ
B_4	3.2	6.4	-4	θ
B_5	1.6	3.2	-5	δ
B_6	0.8	1.6	-6	δ
B_7	0.4	0.8	-7	δ

IV. RESULT AND DISCUSSION

Orthogonal wavelet transform was used to analyze the scalp EEG signal corresponding to a tonic-clonic (TC) epileptic seizure. In Fig. 1 we show the signal. The seizure starts at second 10 with a discharge of slow waves superimposed by fast ones with lower amplitude. The tonic phase starts around second 35 with increasing amplitudes, and the clonic phase starts around second 50. The seizure finishes at second 85.

EEG spectral analysis is traditionally performed by studying different frequency bands, whose boundaries are well defined but could have some small variations according to the particular experiment being considered [1–3]. Absolute and relative intensities of these bands are analyzed and correlated with different pathologies. In this work, we chose seven frequency bands associated with resolution levels appropriate to the wavelet analysis in the scheme of multiresolution proposed. We denoted these band-resolution levels by B_j ($|j| = 1, \ldots, 7$), and their frequency limits, as well as their correspondence to traditional EEG frequency bands, are given in Table I.

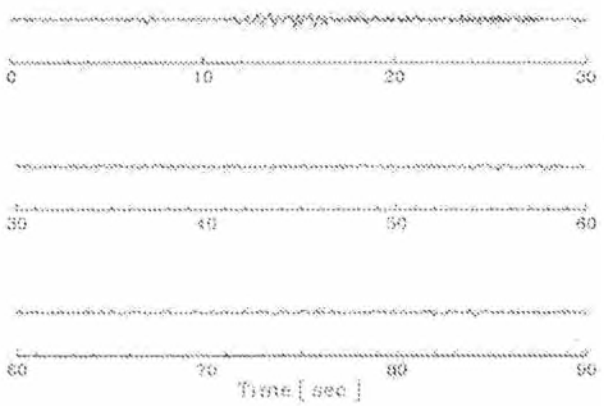


FIG. 2. Noise-free EEG signal. Same as Fig. 1, but without the fast frequencies (B_1 and B_2 bands).

Applying wavelet transform, we can filter the signal by subtracting the different bands. Figure 2 shows the smoothed time series corresponding to the signal of Fig. 1, where oscillations associated with the frequencies corresponding to B_1 and B_2 bands, with wavelet resolution level $j = -1$ and -2 respectively, were subtracted. For recovering the original sampling rate, this residual smoothed signal was interpolated with cubic splines. Owing to the fact that one of the goals of this work is to analyze middle and low frequency brain activity during an epileptic seizure, we eliminated B_1 and B_2 bands, both containing high frequency artifacts that obscure the EEG. Although high frequency brain activity will also be eliminated, it is well accepted that the components are not important in the study of an epileptic seizure [14,19,20].

We chose the frequency bands B_3 and B_4 for performing an analysis with wavelets packets, as was described in Sec. III. We selected these frequency bands because they carry the brain activity that is traditionally analyzed during an epileptic seizure. The series of $C_j(k)$ for $j = -3$ was segmented with a sliding windows of $l = 32$ samples corresponding to

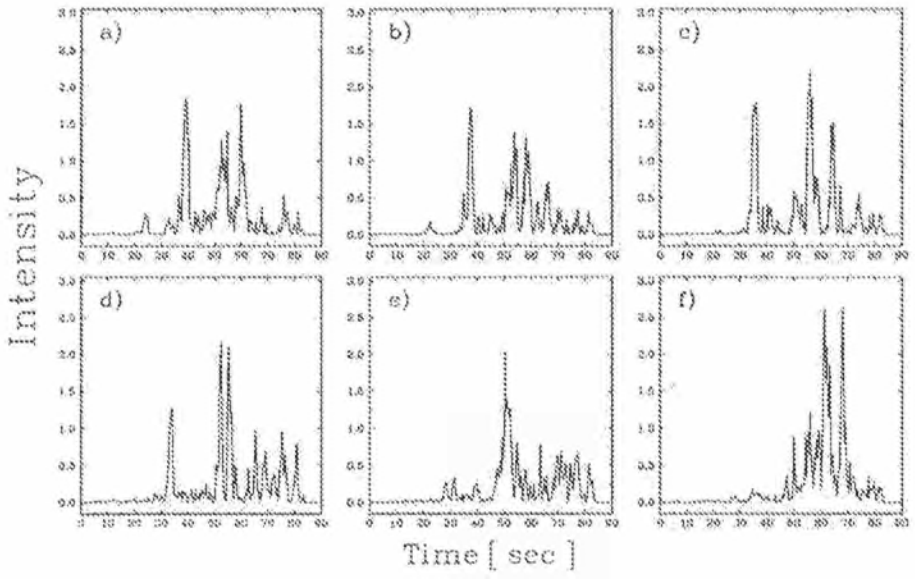


FIG. 3. Relevant wave packet intensities for the frequency band B_3 corresponding to the EEG signal displayed in Fig. 1. The wave packets are centered at the following frequencies: (a) 7.2 Hz, (b) 7.6 Hz, (c) 8.0 Hz, (d), 8.4 Hz, (e) 9.2 Hz, and (f) 10.8 Hz.

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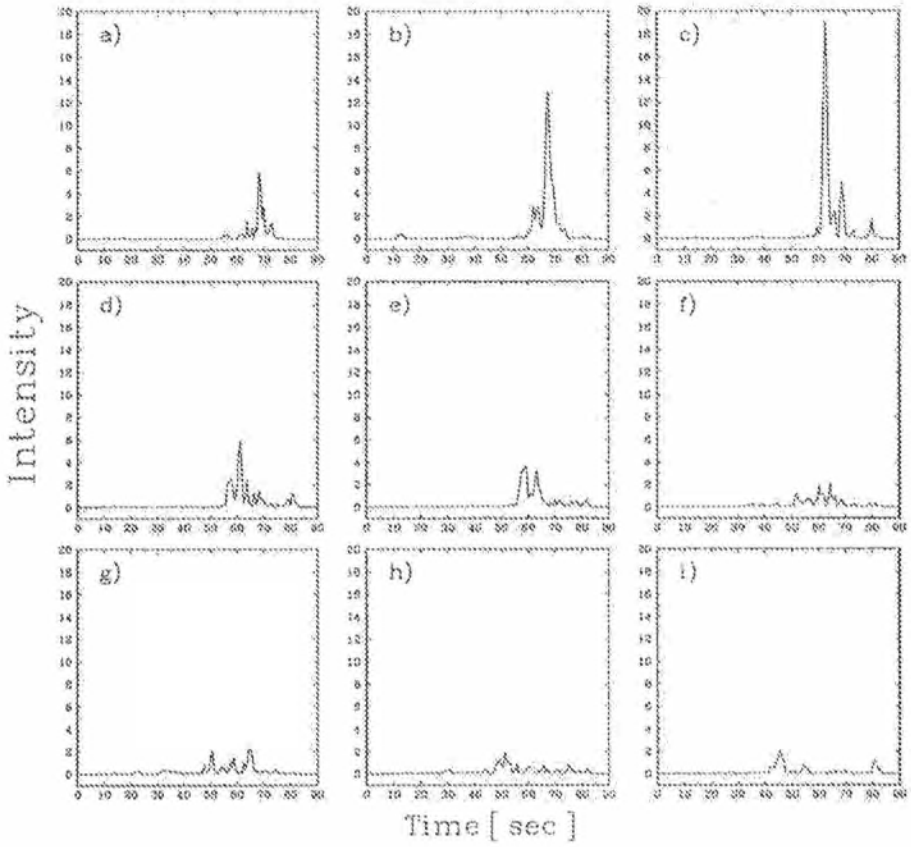


FIG. 4. Wave packet intensities for the frequency band B_4 corresponding to the EEG signal displayed in Fig. 1. The wave packets are centered at the following frequencies: (a) 3.2 Hz, (b) 3.6 Hz, (c) 4.0 Hz, (d) 4.4 Hz, (e) 4.8 Hz, and (f) 5.2 Hz, (g) 5.6 Hz, (h) 6.0 Hz, and (i) 6.4 Hz.

time intervals of $\Delta t = 2.5$ s. Discrete sets of $1 + l/2$ different frequencies between 6.4 and 12.8 Hz, with intervals of 0.4 Hz, were obtained.

Figure 3 shows wave packets of relevant amplitudes. They are centered at the frequencies (a) 7.2, (b) 7.6, (c) 8.0, (d) 8.4, (e) 9.2, and (f) 10.8 Hz. An important peak at second 35 can be identified in agreement with the starting of the tonic phase of the seizure, as was established by the physician team. It can be observed, mainly in the wave packets (b), (c), and (d), which means that its frequency structure can be decomposed mostly in these ranges. At 50 another peak indicates the starting of the clonic phase. It involves wave packets (d), (e), and (f). We can observe that the higher amplitudes in this band correspond to frequencies around 10 Hz, in agreement with previous works [14,19,20].

The same analysis for the B_4 band was achieved using $l = 16$ samples corresponding to time intervals of $\Delta t = 2.5$ s and discrete sets of frequencies between 3.2 and 6.4 Hz with intervals of 0.4 Hz. Note that the $j = -4$ level has half the dispersion in frequency compared with the $j = -3$ level (see Table I), and for this reason we used a window of 16 samples in order to obtain the same definition. These packets have a dispersion of ± 0.2 Hz. Figure 4 shows the amplitudes of wave packets centered in (a) 3.2, (b) 3.6, (c) 4.0, (d) 4.4, (e) 4.8, (f) 5.2, (g) 5.6, (h) 6, and (i) 6.4 Hz. The amplitudes of the corresponding wave packets show a peak around second 70, mainly in frequencies (b) and (c). This peak corresponds to a significant change in the morphology of the signal toward the end of the clonic phase of the seizure. This fact is in agreement with the low frequencies observed at the end of the seizure, and also mentioned in previous works [14,19,20].

The normalized energy as a function of time for the frequency bands B_1–B_7 is shown in Fig. 5. An increase of the energy can be observed at the start of the seizure (10 s), and at the beginning of the tonic phase (35 s), and largest increase appears around second 50 with the start of the clonic stage. The largest increase of energy corresponds to the high frequencies concentrated in the B_1 and B_2 bands. The energy

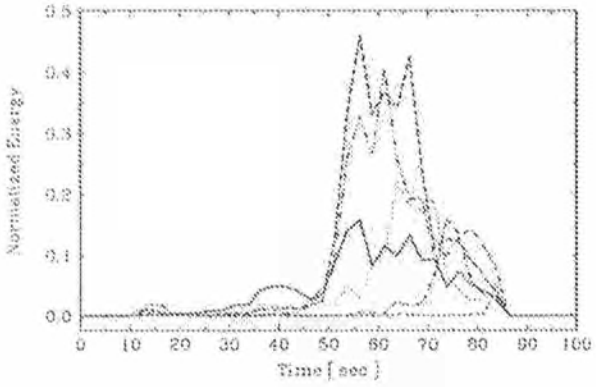


FIG. 5. Energy per band normalized to the total energy corresponding to the EEG signal displayed in Fig. 1, as a function of time. B_1 band (triple dot-dashed line), B_2 band (long dashed line), B_3 band (solid line), B_4 band (dotted line), B_5 band (dot-dashed line), and B_6 band (short dashed line). The B_7 band is not displayed because its values are almost zero for the considered interval.

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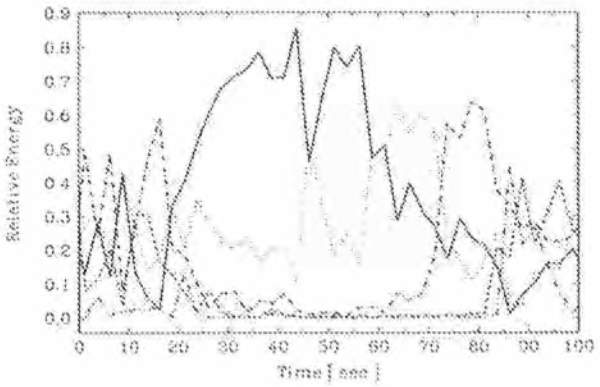


FIG. 6. Relative frequency band energy respect to the total energy, without the contribution of B_1 and B_2 bands. B_3 band (solid line), B_4 band (dotted line), B_5 band (dot-dashed line), B_6 band (short-dashed line), and B_7 band (triple-dot-dashed line).

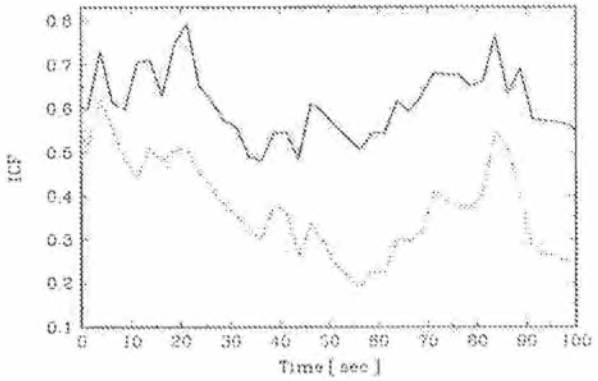


FIG. 7. Information cost function ICF (Shannon entropy) for the signal displayed in Fig. 1. The solid line represents the total ICF, and the dotted line is the same without the contribution of B_1 and B_2 bands.

of the B_3 band presents increasing values starting around seconds 35 and 50, in agreement with the beginning of the tonic and clonic phases, respectively. The energy of the B_4 band presents an increase in its values around second 65 (clonic phase). At this time a morphological change can be observed in the signal (see Fig. 1). The energy in the other frequency bands is low except in B_5, which presents an increment at the end of the seizure. In Fig. 6 we show the relative energy distribution among the frequency bands $B_3 \cdots B_7$, where the contribution of the frequency band B_1 and B_2 were removed from the total energy. We can observe in this figure that during an epileptic tonic-clonic seizure the dominant brain activity is concentrated in the B_3 and B_4 bands.

In summary, the above analysis shows that the energy is accumulated mainly in the fast frequencies during the tonic phase, and, when the seizure is ending, the slow and medium frequencies are the ones that become more relevant in the other stages. In conclusion, wavelet packets allow an identification of the dominant frequencies in each phase of the seizure, as well as a determination of the starting of each phase.

In Fig. 7 we display the total information cost function, and the ICF without the contributions of frequency bands B_1 and B_2, as a function of time. It is interesting to note that there is a remarkable decrease of the values at around second 35, corresponding to the beginning of the tonic phase, and then an increase around second 70, when the clonic phase of the seizure reaches its end. The observed decreasing values in the total ICF during the seizure could be associated with a more rhythmic behavior induced by the muscle activity, but, looking at the ICF without this kind of activity (B_1 and B_2 bands), we confirmed that the medium and low frequencies are also responsible for the signal order. This result confirms that the brain dynamical behavior during an epileptic seizure is more ordered than the preseizure and post-seizure stages.

V. CONCLUSIONS

With wavelet transform and derived methods, it is possible to clean an EEG signal in order to obtain dynamical parameters and hidden frequency information. These noisy EEG signals are usually neglected by physicians.

The analysis carried out in a tonic-clonic epileptic seizure using wavelet transform and wave packets has shown that, during an epileptic seizure, the relevant brain activity presents frequencies around 10 Hz, and when the seizure nears completely the brain activity become slower, with frequencies around 4 Hz. High frequency muscle activity obscures the signal. These high frequencies are the ones that accumulate energy during the tonic phase of the seizure.

The peaks observed while performing wave packet analyses in B_3 and B_4 bands establish with accurate precision the starting and the ending of the different phases of the TC seizure. They also mark changes in the signal morphology that could be correlated with the clinical symptomatology. The analysis of the total energy, relative energy, and ICF as functions of time shed light on the dynamical process or tendency to order during the seizure. These changes only can be actually observed through the video-EEG.

Several numerical methods were developed for describing the EEG signal in the time-frequency domain. Orthogonal wavelet transform appears to be very convenient, due to its capability for separating different frequency bands without modifying the remanent ones. It is specially straightforward for analyzing brain activity information. Moreover, this method is suitable for studying the energy accumulation and its exchange among the different frequency bands at different stages of the seizure. The dynamic of the seizure can also be accessed by performing an analysis based on the information cost function, showing at which stage and in which frequency band a less chaotic behavior is involved.

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Petitioner Ex-1004, 0304

Electronic Acknowledgement Receipt

EFS ID:	21059560
Application Number:	13354941
International Application Number:	
Confirmation Number:	9133
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First Named Inventor/Applicant Name:	Ki H. Chon
Customer Number:	26486
Filer:	David William Gomes
Filer Authorized By:	
Attorney Docket Number:	
Receipt Date:	24-DEC-2014
Filing Date:	20-JAN-2012
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Application Type:	Utility under 35 USC 111(a)

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ENTITY: ☐ LARGE ☒ SMALL ☐ MICRO

APPLICATION AS FILED – PART I

FOR	(Column 1) NUMBER FILED	(Column 2) NUMBER EXTRA	RATE ($)	FEE ($)
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☐ SEARCH FEE (37 CFR 1.16(k), (i), or (m))	N/A	N/A	N/A	
☐ EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	
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Independent (37 CFR 1.16(h))	* 6	Minus	***6	= 0	X $210 =	0
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AMENDMENT

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Independent (37 CFR 1.16(h))	*	Minus	***	=	X $ =	
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Application Number	13354941
Filing Date	2012-01-20
First Named Inventor	Ki H. Chon
Art Unit	3777
Examiner Name	Chu Chuan Liu
Attorney Docket Number	30210-201

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	Application Number	13354941
	Filing Date	2012-01-20
	First Named Inventor	Ki H. Chon
	Art Unit	3777
	Examiner Name	Chu Chuan Liu
	Attorney Docket Number	30210-201

	1	CHON, K.H. Estimation of Respiratory Rate from Photoplethysmogram Data Using Time-Frequency Spectral Estimation. IEEE Transactions of Biomedical Engineering, 56(8), August 2009: 2054-2063.	☐
	2	MIDDLETON, P.M. et al. Spectral Analysis of Finger Photoplethysmogram Waveform Variability in a Model of Mild to Moderate Haemorrhage. Journal of Clinical Monitoring and Computing (2008) 22:343-353.	☐
	3	PELEGRIS, P. et al. A Novel Method to Detect Heart Beat Rate Using a Mobile Phone. Proceeding of the IEEE 32nd Annual International Conference, August 2010: 5488-5491.	☐

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	13354941
	Filing Date	2012-01-20
	First Named Inventor	Ki H. Chon
	Art Unit	3777
	Examiner Name	Chu Chuan Liu
	Attorney Docket Number	30210-201

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☐ The fee set forth in 37 CFR 1.17 (p) has been submitted herewith.

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Signature	/Marlo Schepper Grolnic/	Date (YYYY-MM-DD)	2015-01-08
Name/Print	Marlo Schepper Grolnic	Registration Number	57194

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International Application Number:	
Confirmation Number:	9133
Title of Invention:	PHYSIOLOGICAL PARAMETER MONITORING WITH A MOBILE COMMUNICATION DEVICE
First Named Inventor/Applicant Name:	Ki H. Chon
Customer Number:	26486
Filer:	Marlo Schepper Grolnic
Filer Authorized By:	
Attorney Docket Number:	
Receipt Date:	08-JAN-2015
Filing Date:	20-JAN-2012
Time Stamp:	12:21:09
Application Type:	Utility under 35 USC 111(a)

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	2	20060211930	A1	2006-09-21	Scharf et al.	
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	1	KRISHNAN, R. et al. Analysis and detection of motion artifact in photoplethysmographic data using higher order statistics. IEEE International Conference on Acoustics, Speech and Signal Processing, March 2008: 613-616.	☐
	2	KRISHNAN, R. et al. Two-Stage Approach for Detection and Reduction of Motion Artifacts in Photoplethysmographic Data. IEEE Transactions on Biomedical Engineering 57(8), August 2010: 1867-1876.	☐
	3	GRECO, A. et al. Kurtosis, Renyi's Entropy and Independent Component Scalp Maps for the Automatic Artifact Rejection from EEG data. International Journal of Computer, Information, Systems and Control Engineering 2(9), January 2008: 180-184.	☐
	4	DELORME, A. et al. Enhanced detection of artifacts in EEG data using higher-order statistics and independent component analysis. Neuroimage 34(4), February 2007: 1443-1449.	☐
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Name/Print	Marlo Schepper Grolnic	Registration Number	57194

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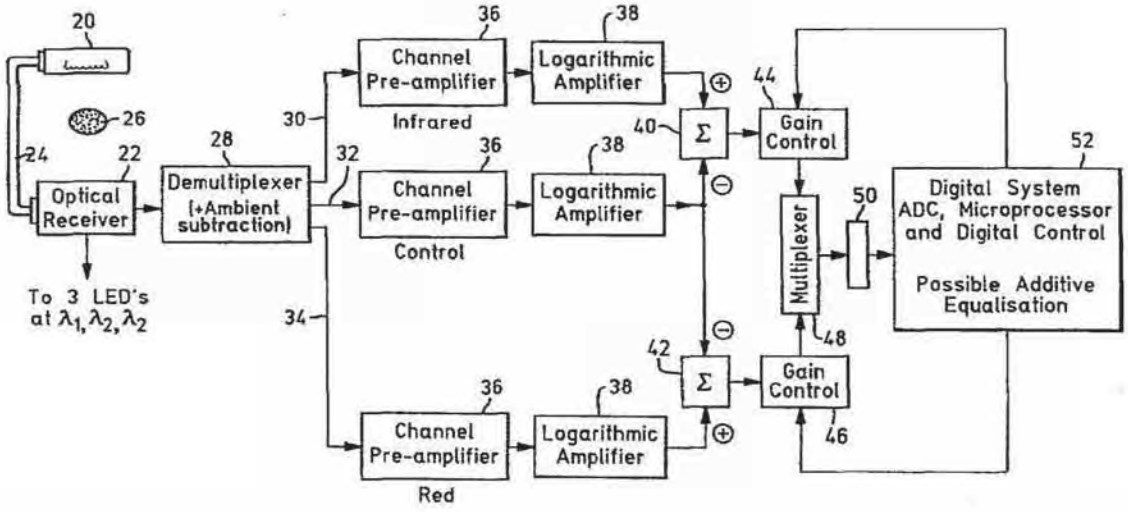
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(71) Applicant *(for all designated States except US)*: BTG INTERNATIONAL LIMITED [GB/GB]; 10 Fleet Place, Limeburner Lane, London EC4M 7SB (GB).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: SMITH, Peter, Richard [GB/GB]; 10 Fairmount Drive, Loughborough, Leicestershire LE11 3JR (GB). HAYES, Matthew, James [GB/GB]; 50 Oldershaw Road, East Leake, Loughborough, Leicestershire LE11 6NG (GB).

(74) Agent: BUTTRICK, Richard; BTG International Limited, Patents Dept., 10 Fleet Place, Limeburner Lane, London EC4M 7SB (GB).

(54) Title: ARTEFACT REDUCTION IN PHOTOPLETHYSMOGRAPHY



(57) Abstract

In order to remove motion artefact prior to digital processing, the invention provides a method of monitoring living tissue comprising the steps of emitting electromagnetic radiation at said tissue at at least first and second different wavelengths, receiving the radiation at the different wavelengths after it has been transmitted through or reflected within said tissue, providing at least first and second signals which are a logarithmic measure of the received first and second radiation wavelengths and subtracting the second signal from the first signal, removing a DC component of the result of the subtraction and providing an AC component to digital sampling means, and processing the digital samples in order to provide a desired value representing a property of the tissue.

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ARTEFACT REDUCTION IN PHOTOPLETHYSMOGRAPHY

The present invention concerns the reduction of artefact in photoplethysmography, in particular the reduction of movement artefact. It is particularly significant in the context of remote (i.e. non-contact) photoplethysmography and pulse oximetry.

Photoplethysmography (PPG) is a well known technique for monitoring non-invasively variations in the light absorption by a component being monitored (e.g. oxygen in the blood stream). The major application for PPG at the present time is in pulse oximetry, used for non-invasive oxygen saturation measurement. The majority of pulse oximeters utilise PPG signals obtained by light transmission through tissue, rather than by reflection. The measurement of arterial oxygen saturation is made by obtaining and quantitatively comparing at least two PPG signals at different optical wavelengths (usually visible red and infra-red) from which an indication of blood colour (and hence oxygenation) is made. The technique requires the measurement of arterial pulsations, since these are used in a calibration process. Corruption of the PPG signal arises from inadvertent measurement of ambient light (ambient artefact) and from voluntary and involuntary subject movement (movement artefact).

Ambient artefact can, in theory, be removed in the recovery of photoplethysmographic signals, provided that the instrumentation correctly subtracts the ambient signal and that appropriate sensor packaging is utilised. Recent clinical publications however suggest that ambient light is a problem in practical systems, mainly due to the severity of artefact experienced in the operating theatre. It is not uncommon practice for clinicians to cover the finger and pulse oximeter with a black bag to eliminate problems caused by particularly strong ambient lighting.

Movement artefact is by far the most important problem with current technology. An ability to significantly reduce or even remove the effect of such artefact would be of great importance in patient monitoring, particularly in the case of patients who have been difficult to monitor in the past. Movement artefact is manifested by mechanical forces giving rise to changes in:

1. probe coupling
2. physiology

Petitioner Ex-1004, 0320

3. optical properties of tissue due to geometric realignment
4. combinations of the above.

All PPG systems respond to changes in venous blood volume as well as arterial blood volume changes, indeed this is used clinically in the study of venous insufficiency, for example. However changes in venous blood volume may be caused variously by:

1. physiology (e.g. exercise or temperature)
2. gravity (e.g. raising limb or bending down)
3. pressure (e.g. pressure on the probe or pressure on the body)
4. other mechanical forces (e.g. stress, strain)

As long as these changes take place on time scales greater than a few heart cycles, the conventional implementation of pulse oximetry will (in theory) be unaffected, as the method is insensitive to quasi-static changes in the non-pulsatile tissue characteristics. PPG studies in contexts other than oximetry relate to both arterial and venous blood changes, and there is therefore a clear distinction to be drawn between the nature of artefact in the context of pulse oximetry (i.e. all dynamic components which do not originate from the arterial blood pulsations) and that of PPG (i.e. all dynamic components which do not originate from changes in blood volume).

If the consequences of a typical mechanical movement which might give rise to severe artefact are considered, such as a subject attached to a finger clip raising their arm to take hold of an object, then it is likely that all the above mentioned types of artefact will be generated. The physical contact of the probe to the skin is a major factor in generating secondary artefacts. In taking note of these effects, pulse oximeter designers have made more significant progress in improving the mechanical design of finger clips, ear clips and more recently semi-disposable adhesive probes. This progress has proceeded in parallel with other efforts to eliminate the undesirable effects of artefact, most notably by signal processing methods.

There have been a number of attempts at tackling the problem of artefact in the context of pulse oximetry, for example:

1. Correlation cancellation (for example, as described in International Patent Application WO 96/12435)

Petitioner Ex-1004, 0321

2. Feature-based recognition of corrupt pulses (for example, as described in International Patent Application WO 94/22360)
3. Cancellation via control of light source (for example, as described in International Patent Application WO 94/03102)
4. Inversion of non-linear artefact model (for example, as described in International Patent Application WO 97/00041)
5. Identifying periods of artefact and subsequently suppressing the oximeter output – see US-A-4,714,341.

Both 1 and 3 ideally use an independent measurement of artefact supplied by another transducer (e.g. piezo or optical). Both 1 and 3 assume that artefact is a linear addition to the pulsatile signal. Basic observation of the PPG signal under typical artefact-producing conditions casts doubt on this hypothesis. 2 provides a method of output suppression in the presence of artefact, established by a simple feature recognition analysis. However this approach is not a solution to artefact equalisation.

In 4, the processing of the PPG signals is carried out following digital conversion. There is no attempt to eliminate the motion signal in any way, by measuring the motion signal, cancelling it by feedback, or mathematical manipulation. Rather the digital processing uses assumptions based on characteristics of the motion signal. 4 assumes a non-linear (multiplicative) model for the motion artefact and a Beer-Lambert law for the light transmission through tissue. The artefact becomes additive following a logarithmic transformation of the PPG signals, an expression for the oxygen saturation is derived by means of a linear solution of the three equations derived from observations of PPG signals at three source wavelengths. The calculation of oxygen saturation is unnecessarily complex, and any practical implementation would require an unnecessarily complex calibration involving the determination of at least six coefficients (page 11 of the published patent application).

In 5, US-A-4,714,341, periods of artefact, are identified and the oximeter output is subsequently suppressed, rather than remaining the artefact from the PPG signals. A third light source with a different wavelength is included, so that the oxygen saturation may be calculated simultaneously with the red and third wavelength, and the infrared and third wavelength. Assuming that artefact affects the signals in a similar manner,

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the two values for the calculated saturation will be different during periods of artefact and the result can be disregarded.

The present invention seeks to approach the problem of artefact from a new direction based on observations made by the inventors of the nature of typical artefact and on a physical model for the light/tissue interaction in the presence of artefact. A key element of the model is the optical receiver, which has a non-linear response characteristic. This property of the receiver is important in providing calibration of the signals and leads to a very effective method for artefact equalisation. The method may be implemented by analogue electronics and is suitable for electronic miniaturisation.

In the present invention, the optical receiver is modelled, employing the following assumptions:

1. The received light has additive components due to direct coupling with the light source, coupling through non-pulsatile tissue and pulsatile tissue.
2. The light travelling through non-pulsatile tissue and pulsatile tissue is modulated by movement artefact and this artefact is represented by a multiplicative coefficient.
3. The light receiver provides a logarithmic response, either in the light receiving diode itself, or in a subsequent logarithmic amplifier, and two such light signals at different wavelengths are subtracted from one another. This it will be shown provides a large DC signal which is of no interest and can be filtered out and a smaller AC component which represents the light signal component due to pulsatile tissue, but with the motion artefact removed.
4. The AC component signal representing light through pulsatile tissue may then be digitised and subjected to DSP operations in order to derive values representing oxygen saturation.

Accordingly, in a first aspect the present invention provides a method of monitoring living tissue comprising the steps of emitting electromagnetic radiation at said tissue at at least first and second different wavelengths, receiving the radiation at the different wavelengths after it has been transmitted through or reflected within said tissue, providing at least first and second signals which are a logarithmic measure of the received first and second radiation wavelengths and subtracting the second signal from

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the first signal, removing a DC component of the result of the subtraction and providing an AC component to digital sampling means, and processing the digital samples in order to provide a desired value representing a property of the tissue.

In a preferred application of the invention to pulse oximetry a third wavelength of electromagnetic radiation is employed and the second wavelength signal is subtracted from a logarithmic form of the signal produced in response to the third wavelength in order to provide a further AC component resulting from this subtraction which is applied to the digital sampling needs, thereby oxygen saturation may be calculated.

In a further aspect, there is provided apparatus for measuring or monitoring living tissue, comprising means for irradiating tissue with electromagnetic radiation at at least first and second different wavelengths, means for receiving the radiation at the different wavelengths after it has been transmitted through or reflected within said tissue for providing respective first and second wavelength signals which are a logarithmic measure of the received radiation signals, means for subtracting the second wavelength signal from the first wavelength signal, means for removing a DC component from the output of the subtracting means, digital sampling means for digitising said AC component, and processing means for processing the digital samples in order to derive a value representing a property of said tissue.

In a still further aspect, there is provided apparatus for measuring or monitoring living tissue, comprising means for irradiating tissue with electromagnetic radiation at at least first and second different wavelengths, means for receiving the radiation at the different wavelengths after it has been transmitted through or reflected within said tissue, logarithmic amplifier means coupled to the receiving means for providing respective first and second wavelength signals which are a logarithmic measure of the received radiation signals, means for subtracting the second wavelength signal from the first wavelength signal, means for removing a DC component from the output of the subtracting means, and processing means for processing the digital samples in order to derive a value representing a property of said tissue.

In accordance with the invention, motion artefact can be completely or at least very substantially eliminated prior to any digital processing of the signal in order to derive desired characteristics.

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A particular advantage of the invention arises in that since it is possible dramatically to remove motion artefact, the invention may be applied in situations where the light emitting means is not directly coupled to the living tissue by means of a clip or other attachment means, as in the prior art. In the prior art it was necessary to couple the light source or other radiation emitting means to a subject in order to reduce as far as possible motion artefact. However in the present invention, in appropriate circumstances, the light source and light receiving means may be mounted in a fixed installation with the patient or living tissue disposed adjacent for receiving radiation but not mechanically coupled to the installation. This introduces an important simplification in that it is not necessary to employ carefully designed clip-type arrangements, and permits use where contact probes fail, such as foetal monitoring, abulatory studies, neonatal monitoring and patient trauma conditions.

Whilst many light receiving diodes have logarithmic responses and will therefore naturally provide an output signal providing a logarithmic measure of input radiation, since such logarithmic responses are not strictly accurate in many cases, it is preferred to provide a light responsive diode with a linear response, and subsequently to provide a logarithmic amplifier which provides an accurate logarithmic measure of the input radiation. Naturally, a separate logarithmic amplifier will be provided in the respective channel for each wavelength signal.

In a further aspect, the present invention provides apparatus for measuring or monitoring living tissue comprising emitting means for emitting electromagnetic radiation, means for receiving said radiation at the different wavelengths after it has been transmitted through or reflected within said tissue, the emitting means and receiving means being fixedly mounted with respect to one another, but there be no means provided for attaching the emitting means or receiving means to living tissue, the receiving means being arranged to provide at least first and second signals representing logarithmic measures of the received wavelength signals, and means for removing motion artefact from said signals and digital sampling means for sampling the motion artefact's removed signals, and means for processing the digital samples.

In one embodiment the optical measuring device is a photoplethysmograph. The device may be a pulse oximeter and include means for displaying the oxygen saturation of the patient's blood.

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In this embodiment use may be made of the derived independence of an equalised pulsatile PPG signal from the tissue characteristics at the wavelength of the second (subtracted) signal. One of three optical wavelengths may be chosen as a control signal, such that there is a high contrast between the tissue characteristics at the signal and control wavelengths.

Brief Description of the Drawings

A preferred embodiment of the invention will now be described with reference to the accompanying drawings, on which:-

Figure 1 is a schematic block diagram of a known arrangement for reducing motion artefact;

Figure 2 is a schematic block diagram of the preferred embodiment of the invention; and

Figure 3 and 4 are waveforms for explaining the application of the present invention.

Description of the Preferred Embodiment

The invention uses a general physical model (a more general model than applied in, say, the disclosure of WO 97/00041), which incorporates a means of ordering the dynamic components of the received signals with respect to both physiological and non-physiological dynamics. The ordering of dynamics implies a system which can derive the arterial oxygen saturation without the need to consider the static portions of the received signals, needing only the pulsatile components. In addition, this calculation is also independent of any tissue characteristics, both dynamic and static, at the control wavelength. Moreover, the oxygen saturation calculation contains only one unknown, which has a physical origin which can be bounded and estimated.

We examine the case when a number of light sources can be used in conjunction with a single receiver to generate one or more photoplethysmographic (PPG) signals. A PiN diode receiver is used, having a logarithmic response to the received light level. Although this non-linear response can lead to complexity in certain aspects of

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measurement, however, it limits saturation and will therefore ultimately allow a greater degree of equalisation to be performed than with a linear receiver. A given PPG signal generated by the receiver may be described by

$$v(t,\lambda) = v_0 ln\left[1 + i_{ph}(t,\lambda)Z\right] \quad (1)$$

where the photocurrent i_{ph} is wavelength dependent through the diode responsivity, Z is a constant characteristic of the receiver, and v_o includes any gain being applied. Both Z and v_o should only be affected significantly by temperature. The photocurrent is linearly proportional to light intensity I at the receiver, which is modulated by pulsations and artefact as well as source characteristics and spatially dependent tissue characteristics. The received light intensity is modelled by

$$I(t,\lambda) = \sum_{j=1}^{n} I_j(t)\left[\alpha_j(t) + \beta_j(t,\lambda) + \gamma_j(t,\lambda)\right] \quad (2)$$

where the coupling coefficients depend on all the geometric, temporal and spectral properties of the source/receiver positioning, artefact, tissue dynamics and tissue optical properties. The coefficients α are interpreted as direct coupling between source and receiver and those labelled β, γ correspond to light coupled via non-pulsatile and pulsatile tissue respectively. In many instruments the active light sources emit fixed power levels but here for the sake of generality they are allowed to vary. The ambient light is assumed to have been eliminated by an electronic multiplexing technique. Oximeters tends to use two or three (n=2,3) light sources and it may be assumed that, in the case of transmission mode, no light will be directly coupled to the receiver.

The nature of the coupling coefficients is now examined more closely. The values of α could also in principle depend on movement artefact, but only in the case of inappropriate sensor design. The values of β depend on tissue optical characteristics and movement artefact and include all effects not attributable to pulsatile signals. The

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coupling of pulsatile signals modulated by movement artefact is represented by the γ coefficients which will normally be much smaller than the corresponding values of β. With these observations in mind we now make the following simplifying assumptions

$$\alpha_j = const \tag{3}$$

$$\beta_j(t) = \beta_j(1 + b_j(t))[1 + m(t)] \tag{4}$$

$$\gamma_j(t) = \gamma_j[1 + m(t)]p_j(t) \tag{5}$$

enabling equation (2) to be written in the form

$$I(t,\lambda) = \sum_{j=1}^{n} I_j(t)\left[\alpha_j + \beta_j(\lambda)[1 + m(t)]\left(1 + b_j(t) + \frac{\gamma_j(\lambda)}{\beta_j(\lambda)}p_j(t)\right)\right] \tag{6}$$

The assumption (3) is valid for probes in which the optoelectronics have fixed relative positions or in which there is no direct coupling of light. Clearly this applies to the majority of conventional probes when operated normally. Equation (4) distinguishes movement artefact ($m(t)$) due to changes in probe coupling from artefact arising due to changes in non-pulsatile blood volume ($b(t)$). The constant of proportionality is free to change between given sources. This assumption is supported by our practical experience. Assumption (5) is justified by criteria similar to those for assumption (4) with the addition of independence between the pulsation dynamics and the movement artefact dynamics.

It is worth noting the ideal limit of negligible artefact, namely

$$v(t,\lambda)\big|_{m\to o, b\to o} \approx v_o \ln\left\{1 + R_j(\lambda)Z\,I_j\left(\alpha_j + \beta_j(\lambda) + \gamma_j(\lambda)p_j(t)\right)\right\} \tag{7}$$

for a constant light source, labelled by j, and receiver responsivity R_j. equation (7) can be approximated to first order in the size of the pulsatile signal as

$$v(t,\lambda)\big|_{m\to o, b\to o} \approx v_o \ln\left\{1 + R_j(\lambda)Z\,I_j\left(\alpha_j + \beta_j(\lambda)\right)\right\} + v_o\left(\frac{\gamma_j(\lambda)p_j(t)}{\alpha_j + \beta_j(\lambda)}\right) \tag{8}$$

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and it may be noted that the measured pulsatile component of the signal is linearised and independent of the light source intensity.

Model Analysis

There are a number of distinct elements of this model which can dominate the final signal and it will be important to analyse the detailed ordering of terms. Taking the case when the direct coupling of light is negligible, which should be a very good approximation for all transmission mode devices and suitably constructed reflection mode devices, and then using (1) and (6).

$$v_j(t,\lambda) = v_o \ln\left\{I + (1 + m(t)Z)\left\{R_j I_j \beta_j \left[1 + b_j(t) + \frac{\gamma_j p_j(t)}{\beta_j(\lambda)}\right]\right\}\right\} \tag{9}$$

By further neglecting dark current compared with all the other sources of current we then obtain

$$v_j(t,\lambda) = v_o \ln\left(R_j I_j Z \beta_j\right) + v_o \ln\left(1 + m(t)\right) + v_o \ln\left(1 + b_j(t) + \frac{\gamma_j(\lambda) p_j(t)}{\beta_j(\lambda)}\right) \tag{10}$$

It is interesting to observe that the assumptions (3) to (5) lead to a separation of probe coupling artefact into a single term not dependant on the light source, suggesting that its removal is trivial. It is important to realise that this degree of separation of movement artefact is only achieved because of the non-linear nature of the receiver.

Probe Coupling Artefact Equalisation

The distinctive nature of the present approach is that the effect of movement artefact has been modelled as a linear factor modulating the coupling coefficients of static and pulsatile tissue. This factor is assumed to scale with the unmodulated coupling coefficients but its functionality is unchanged. This assumption may be inaccurate for certain types of movement artefact (e.g. extreme degrees of movement), especially those which produce differential path length changes between sources and

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receiver, mainly due to skewing of the probe geometry. Nevertheless the ensuant simplicity afforded justifies an investigation of this approximation. It is also worth noting that the approximation is more general than assuming additive signal artefact, an assumption which has received very serious attention (for example in WO 96/12435).

Removal of coupling artefact can be achieved by generating two independent measures of equation (10) and performing a subsequent subtraction, whence

$$v_{jk}^{eq}(t,\lambda,b=0) = v_o \ln\left(\frac{R_j I_j}{R_k I_k}\right) + v_o \ln\left\{\frac{\beta_j(\lambda)+\gamma_j(\lambda)p_j(t)}{\beta_k(\lambda)+\gamma_k(\lambda)p_k(t)}\right\} \tag{11}$$

Equation (11) indicates that an approach to equalisation based on the use of two light sources of contrasting tissue coupling characteristics will provide the most effective isolation of the pulsatile signal. Since oxy-, deoxy-haemoglobin and melanin are strong absorbers of blue light, significant contrast will be obtained between red (or infra-red) light and blue light. In that case, a linearisation of equation (11) yields

$$v_{jk}^{eq}(t,\lambda,b=0) = v_o \ln\left(\frac{R_j I_j \beta_j(\lambda)}{R_k I_k \beta_k(\lambda)}\right) + v_o \frac{\gamma_j(\lambda)p_j(t)}{\beta_j(\lambda)} \tag{12}$$

where j labels the red (or infra-red) light and k labels the blue light. It is to be noted that the pulsatile component of the equalised signal is entirely independent of the blue light.

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Consequences for Oximetry

The introduction of non-linearity at the front end amplifier has allowed us to develop a method for artefact equalisation but some rescaling of the pulsatile signals has been performed. It is now useful to explore the consequences on the determination of saturated oxygen. The Beer-Lambert formulation is usually used as a basis for the theoretical understanding of pulse oximetry and also benefits from simplicity. We use it here, mainly for the latter reason. The Beer-Lambert law couples path length r and effective absorbance μ_{eff} together in a single definition of optical density, so that the total signal may be written as

$$s(t) = s_0 \exp(-\mu_{eff} r) \tag{13}$$

where s_o is a constant for given tissue type and probe placement. The effective absorbence may be interpreted as the combined effects of absorption and scattering. We now make an assumption on the separation of optical path into a small pulsatile part and a larger non-pulsatile dependent part

$$\mu_{eff} r = \mu_{blood} d(t) + \mu_{tissue}(r - d) \tag{14}$$

where *(r-d)* may still be dynamic, due for example to venous blood movement. The dynamic part of the equalised signal, from equation (12), together with (13) and (14) can be expressed as

$$v_{AC} = -v_o s_o \mu_{blood}(\lambda) \frac{\gamma(\lambda)}{\beta(\lambda)} d(t) \tag{15}$$

and changes in this component are found to be only dependent on the path through pulsatile issue. In the usual oximetry formulation we employ the wavelength dependency of μ_{blood} to obtain

$$\frac{\mu_{blood}(\lambda_1)}{\mu_{blood}(\lambda_2)} T_{12} = \frac{\varepsilon_{Hb}(\lambda_1) C_{Hb} + \varepsilon_{HbO_2}(\lambda_1) C_{HbO_2}}{\varepsilon_{Hb}(\lambda_2) C_{Hb} + \varepsilon_{HbO_2}(\lambda_2) C_{HbO_2}} T_{12} = \frac{\Delta v_{AC}(\lambda_1)}{\Delta v_{AC}(\lambda_2)} = R_{12} \tag{16}$$

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where

$$T_{12} = \frac{\gamma(\lambda_1)\beta(\lambda_2)}{\beta(\lambda_1)\gamma(\lambda_2)} \tag{17}$$

from which the oxygen saturation is found to be

$$SaO_2 = \frac{C_{HbO_2}}{C_{Hb} + C_{HbO_2}} = \frac{T_{12}\varepsilon_{Hb}(\lambda_1) - R_{12}\varepsilon_{Hb}(\lambda_2)}{T_{12}\left[\varepsilon_{Hb}(\lambda_1) - \varepsilon_{HbO_2}(\lambda_1)\right] + R_{12}\left[\varepsilon_{HbO_2}(\lambda_2) - \varepsilon_{Hb}(\lambda_2)\right]} \tag{18}$$

Equation (18) differs from the conventional pulse oximetry formulation only by the factor T_{12} which is a ratio of ratios and should be independent of any geometric coupling condition or individual tissue type. The difference in implementation between this formulation and conventional oximetry is that only the pulsatile signal is required for analysis (equation (16)).

To clearly illustrate the invention, Figures 1 and 2 show diagrammatic block diagrams of, respectively, a pulse oximeter device of the prior art and a device according to the invention.

In Figure 1 an optical receiver 2 receives two light signals at different wavelengths (e.g. red visible and infrared). A demultiplexer 4 separates the two signals into two channels 6, 8 and passes them through pre-amplifiers 10. Each signal is passed through a parallel low-pass filter 12 and a high-pass/band-pass filter 14 in order to separate the dc and the ac components. Each component signal is then passed through a separate gain control 16, 17 since the dc and ac components are of very different orders of magnitude, before being multiplexed at 18 and passed into the DSP or microcontroller system 19 in which the comparisons can be made to produce an oxygen saturation measurement (SaO_2). Conventional devices may incorporate artefact reduction into the signal processing at this stage.

In Figure 2, three signals are fed instead into logarithmic amplifiers as shown, and the difference signals between each of the outputs of the logarithmic amplifiers and

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the control amplifier feed into a gain control. Note that in this design it is only necessary to sample the AC (pulsatile) signal components, since the static components play no part in the oxygen saturation calibration. This not only simplifies the electronics (note that only two channels are multiplexed to the microprocessor) but also reduces the complexity of the control algorithm.

Referring to Figure 2 in more detail, a light source 20 is fixedly mounted with an optical receiver 22 in a suitable mechanical installation, indicated as at 24. Living tissue schematic shown as at 26 is disposed between the light source and optical receiver 22, but is not mechanically affixed thereto. The light source emits three different wavelengths, normally red, infrared and a control source (e.g. blue) and the optical receiver has three separate light responsive diodes each responsive to their respective wavelength. The response of each diode is strictly linear in that a voltage or current output signal is provided which is linearly related to the intensity of radiation thereon. The output signals from the diodes are output on a single channel to a demultiplexer 28 which separates the three wavelength signals into respective channels 30, 32, 34. Each channel has a preamplifier 36 followed by a logarithmic amplifier 38 in order to give a logarithmic version of the signal. The signal in channel 32, representing the blue signal is used as a control channel and is subtracted from the infrared signal in channel 30 in a subtractor 40, and is subtracted from the red signal in 34 and subtractor 42. The outputs of the two subtractors are signals which represent equations (11) and (12), referred to previously. The outputs of the subtractors 40, 42 are applied to respective gain control units 44, 46, which gain controls units inherently remove dc components in the signal, i.e. the dc component represented in equation (12). Alternatively a high pass filter may be employed, with a cut off frequency of about 0.5 Hertz in order to remove the dc component. The outputs of the gain control unit are applied to a multiplexor 48, the output of the multiplexer being fed to an analogue to digital converter 50 which provides digital samples of the ac components which will be digital samples of the light passing through pulsatile tissue with motion artefact removed as in equation (12), to a digital system 52 for carrying out a required manipulations as set out above.

Artefact reduction may be incorporated into the DSP system, but the simple front-end analogue electronic arrangement automatically provides a signal

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representative of the difference between the logarithms of the received signals, and therefore allows for compensation of the multiplicative element of the artefact. In addition, the logarithmic amplifiers handle the extremely wide dynamic range of the received signals without saturating.

It is to be noted that in the system of Figure 1 it is impossible to recover the multiplicative element of the signal since the ac and dc components have been separated by the time the signal is processed.

Implementation and testing

Artefact minimisation can be shown with the use of the simultaneous removal of ambient artefact and probe coupling motion artefact. Figures 3 illustrates a trace obtained without employing the artefact reduction of the present invention, and including a period of severe artefact. Figure 4 shows the same situation, but employing the artefact reduction of the invention: the artefact has been completely removed.

Because the present approach provides a good solution to the problem of probe coupling artefact, it allows the consideration of remote PPG and therefore remote pulse oximetry. Since a significant fraction of other artefact is actually induced by mechanical forces being coupled to the subject via the physical contact of the probe (secondary artefact) these will all be removed in a remote system. Furthermore the solution to probe coupling artefact will also reduce (but not remove) primary artefact caused by venous blood motions and any residual ambient artefact.

A further attractive property of this method is that the requisite technology is simple. It may be implemented by purely analogue electronics if necessary, and it is a strong candidate for miniaturisation.

Although the present invention has been described and illustrated purely in the context of optical measuring and monitoring devices, it is believed that it might also be implemented in alternative systems such as in the area of ultrasound devices where movement artefact can cause problems.

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CLAIMS

1. A method of monitoring living tissue comprising the steps of emitting electromagnetic radiation at said tissue at at least first and second different wavelengths, receiving the radiation at the different wavelengths after it has been transmitted through or reflected within said tissue, providing at least first and second signals which are a logarithmic measure of the received first and second radiation wavelengths and subtracting the second signal from the first signal, removing a DC component of the result of the subtraction and providing an AC component to digital sampling means, and processing the digital samples in order to provide a desired value representing a property of the tissue.

2. A method according to claim 1, including providing a third signal which is a logarithmic measure of a third radiation wavelength, subtracting the second signal from the third signal, removing a DC component of the result of the subtraction and providing an AC component to digital sampling means, and processing the digital samples in order to provide a desired value representing oxygen saturation of the tissue.

3. Apparatus for measuring or monitoring living tissue, comprising means for irradiating tissue with electromagnetic radiation at at least first and second different wavelengths, means for receiving the radiation at the different wavelengths after it has been transmitted through or reflected within said tissue for providing respective first and second wavelength signals which are a logarithmic measure of the received radiation signals, means for subtracting the second wavelength signal from the first wavelength signal, means for removing a DC component from the output of the subtracting means, digital sampling means for digitising said AC component, and processing means for processing the digital samples in order to derive a value representing a property of said tissue.

4. Apparatus for measuring or monitoring living tissue, comprising means for irradiating tissue with electromagnetic radiation at at least first and second different

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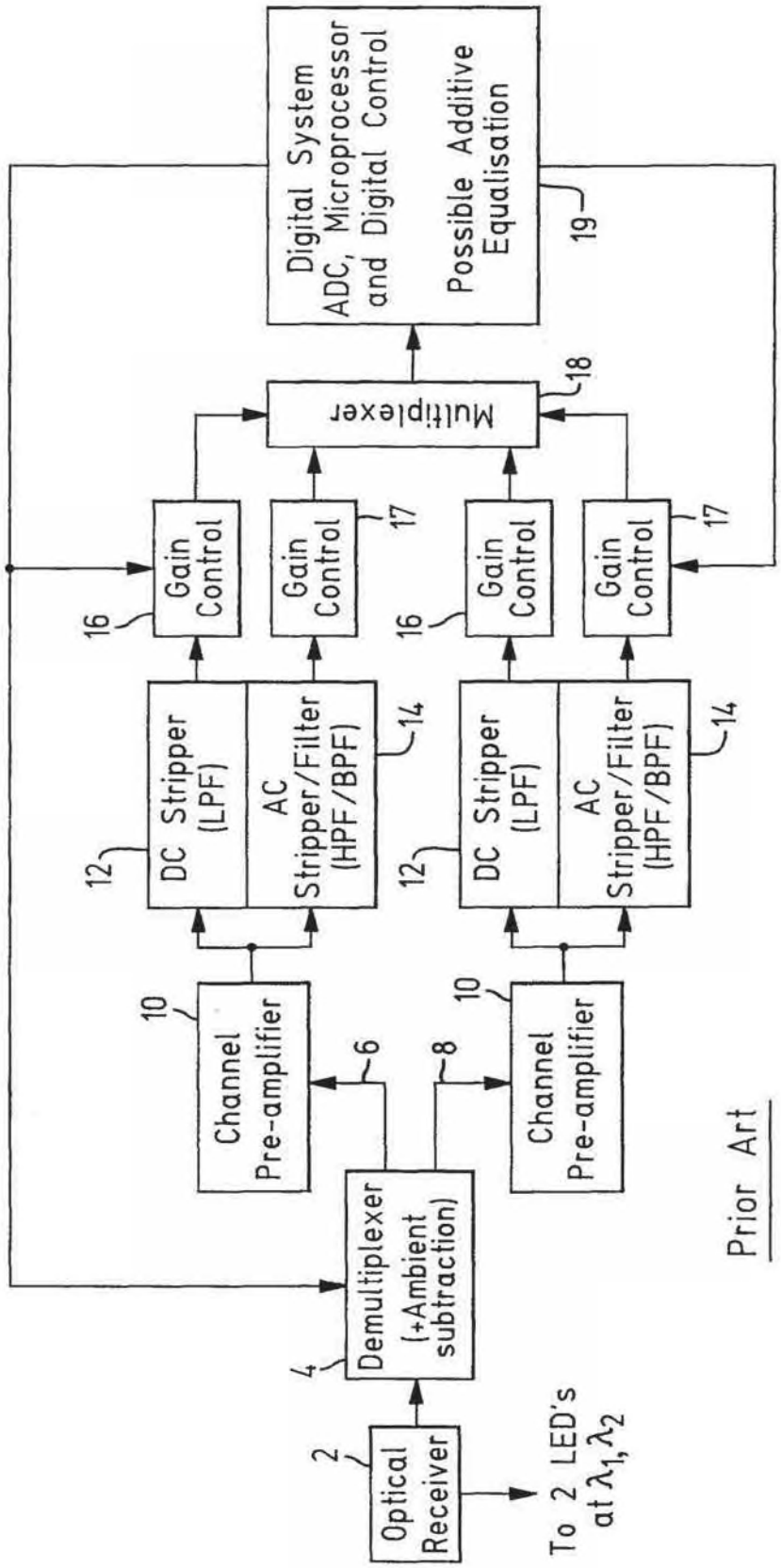
wavelengths, means for receiving the radiation at the different wavelengths after it has been transmitted through or reflected within said tissue, logarithmic amplifier means coupled to the receiving means for providing respective first and second wavelength signals which are a logarithmic measure of the received radiation signals, means for subtracting the second wavelength signal from the first wavelength signal, means for removing a DC component from the output of the subtracting means, and processing means for processing the digital samples in order to derive a value representing a property of said tissue.

5. Apparatus according to claim 3 or 4, wherein the removing means is provided by gain control means.

6. Apparatus according to claim 2 or 3, including means for providing a third wavelength signal which is a logarithmic measure of received radiation at a third wavelength, means for subtracting the second wavelength signal from the third wavelength signal, and means for removing a DC component from the output of the subtracting means

7. Apparatus for measuring or monitoring living tissue comprising emitting means for emitting electromagnetic radiation, means for receiving said radiation at the different wavelengths after it has been transmitted through or reflected within said tissue, the emitting means and receiving means being fixedly mounted with respect to one another, but there be no means provided for attaching the emitting means or receiving means to living tissue, the receiving means being arranged to provide at least first and second signals representing logarithmic measures of the received wavelength signals, and means for removing motion artefact from said signals and digital sampling means for sampling the motion artefact removed signals, and means for processing the digital samples.

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Prior Art

Fig.1

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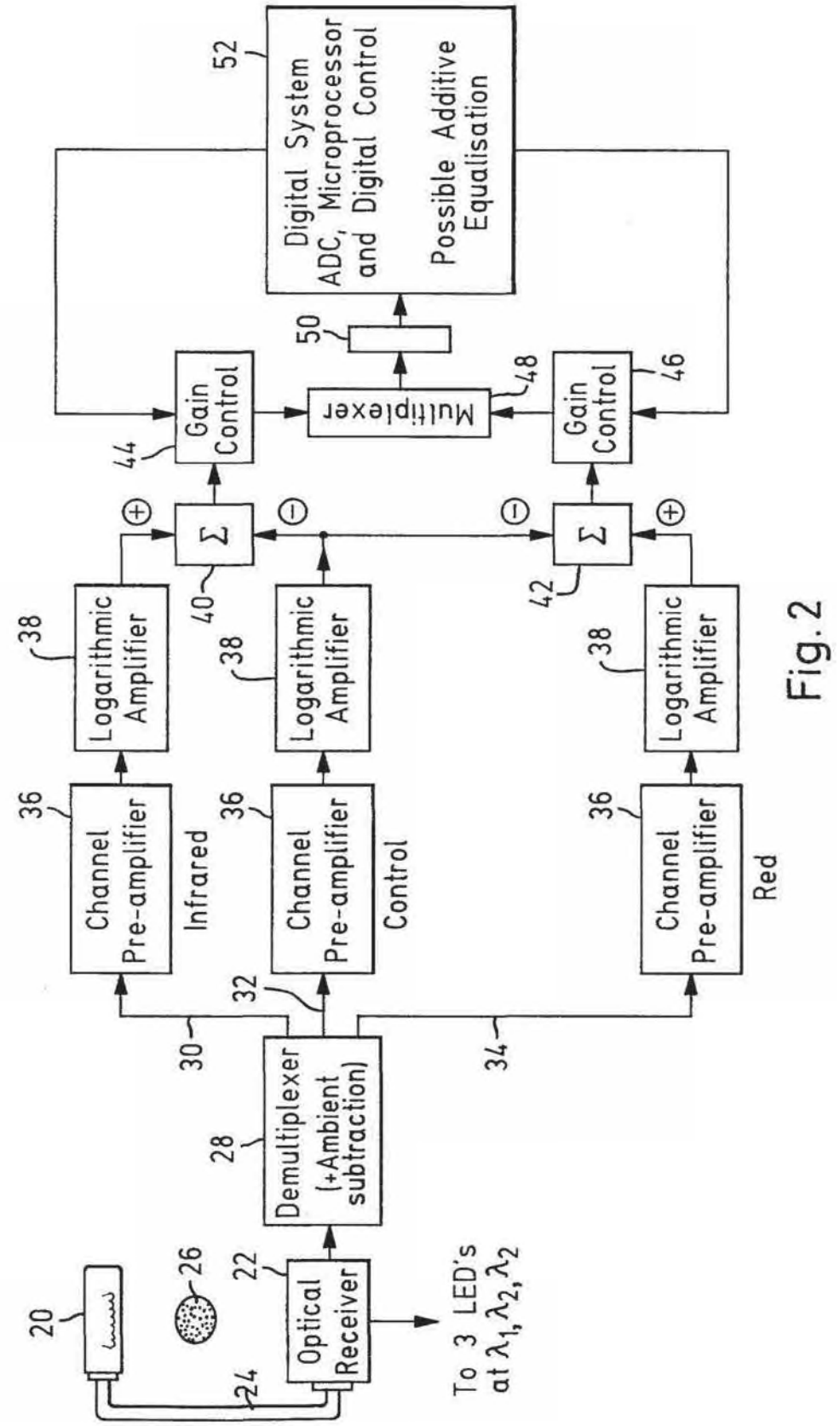


Fig. 2

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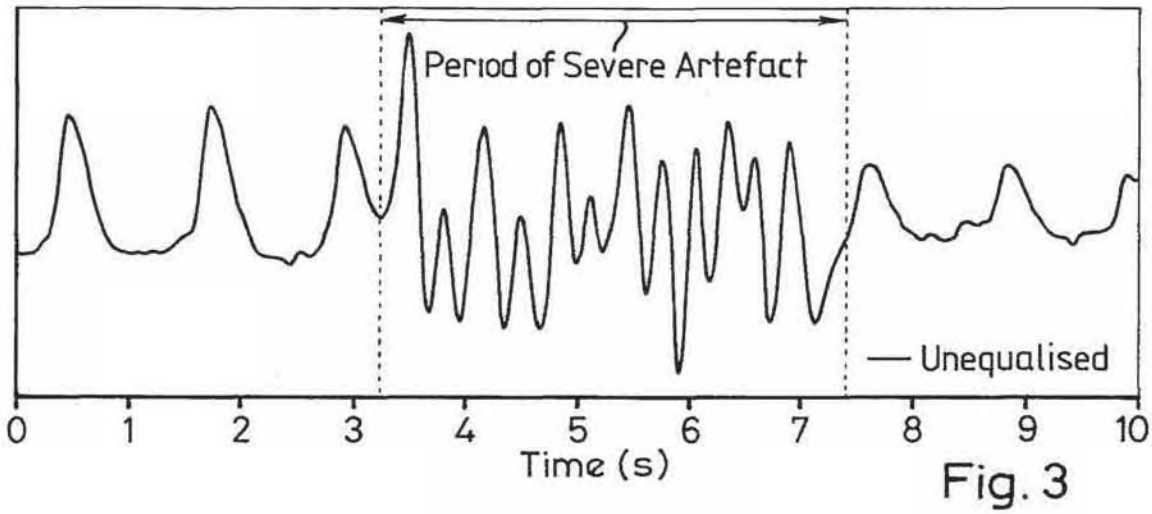

Period of Severe Artefact
— Unequalised
0 1 2 3 4 5 6 7 8 9 10
Time (s)

Fig. 3

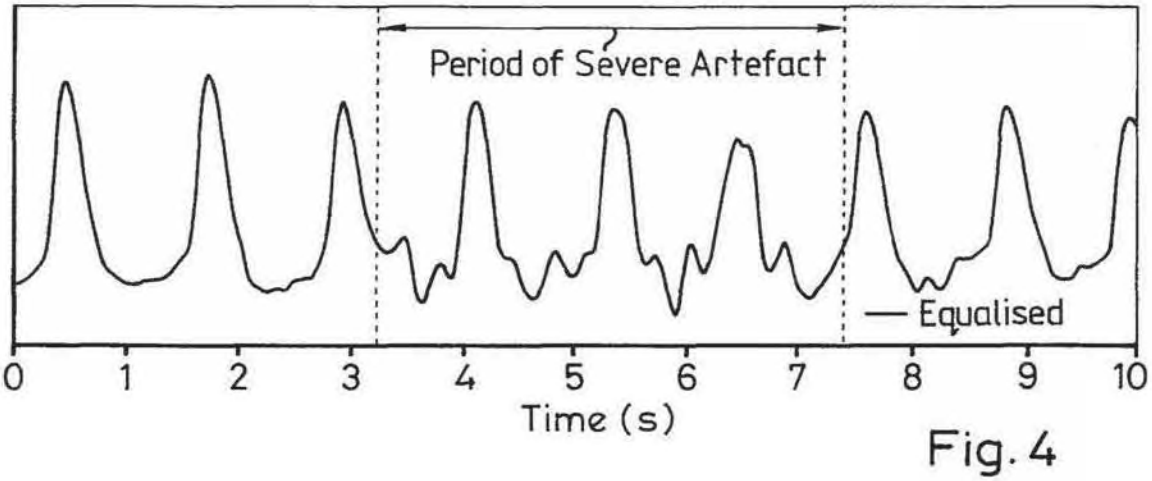

Period of Severe Artefact
— Equalised
0 1 2 3 4 5 6 7 8 9 10
Time (s)

Fig. 4

INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/GB 98/03757

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61B5/00 A61B5/024

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)
IPC 6 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 00041 A (NELLCOR PURITAN BENNETT INC) 3 January 1997 see page 3, line 21 - page 5, line 30 see page 14, line 17 - line 38; figure 1	1-7
A	WO 94 03102 A (UNIV SWANSEA ;PARKER DAWOOD (GB)) 17 February 1994 see page 1, line 24 - page 4, line 10; figures	1-7
A	US 4 714 341 A (HAMAGURI KENJI ET AL) 22 December 1987 cited in the application see the whole document	1-7
A	GB 1 325 039 A (SHAW R F) 1 August 1973 see the whole document	1-7

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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"P" document published prior to the international filing date but later than the priority date claimed

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"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
24 February 1999	02/03/1999

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	Manschot, J

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INTERNATIONAL SEARCH REPORT

Information on patent family members

In tional Application No
PCT/GB 98/03757

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(54) **Title:** METHOD AND SYSTEM FOR MONITORING SLEEP

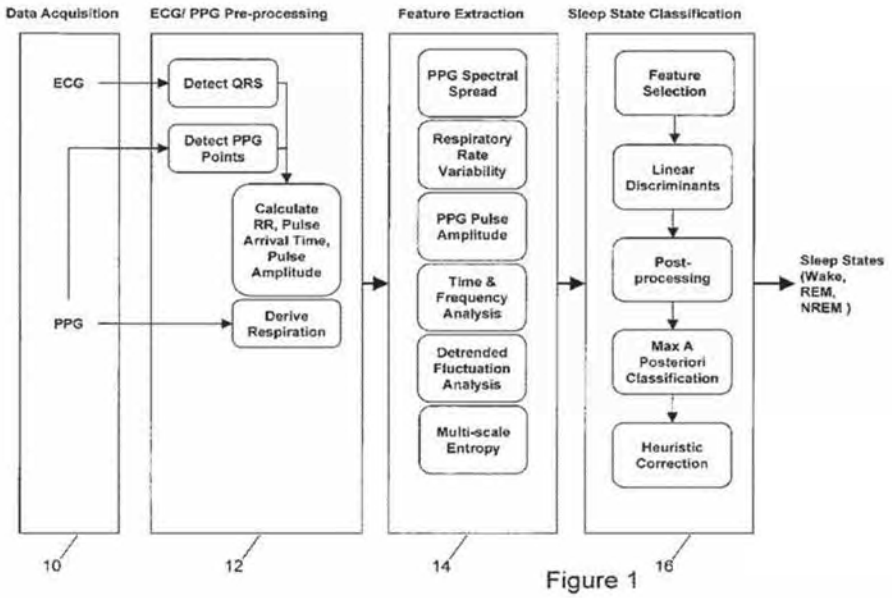


Figure 1

(57) **Abstract:** A method of monitoring sleep comprises simultaneously recording a person's electrocardiogram (ECG) and photoplethysmogram (PPG), deriving a plurality of parameters from the recorded data, and providing an output indicative of a sleep characteristic based upon an analysis of the parameters. The ECG and PPG may be recorded using an apparatus which is a combination of a Holter monitor and a pulse oximeter, which is wearable in ambulatory manner.

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Method and System for Monitoring Sleep

Field of the Invention

The present invention relates to the monitoring of sleep, including sleep state or sleepiness levels of humans in a convenient way, and more specifically to a method and system for acquiring and processing the related information.

Background

Monitoring of sleep state and sleepiness is useful in a clinical context for assessing subjects with suspected obstructive sleep apnoea, and in an industrial context for monitoring sleepiness in vehicle drivers and in actual work environments, particularly where sleepiness-related accidents can have serious consequences.

Obstructive sleep apnoea syndrome (OSAS) is a prevalent but under-diagnosed condition with serious cardiovascular consequences, and is highly treatable. Standard in-laboratory testing for OSAS involves an overnight study to assess severity of apnoea and sleep fragmentation, and may also involve an all-day study to assess daytime sleepiness. Assessment of sleep fragmentation can be achieved by analysing the overnight study to produce a chart of sleep stages, and the assessment of daytime sleepiness can be accomplished by measuring on multiple occasions over a day, the time taken for subjects to fall asleep (the so-called Multiple Sleep Latency Test).

However, due to increasing public awareness of OSAS and resource constraints in healthcare systems, in-laboratory testing for OSAS suffers from low availability in many countries. Therefore there is considerable interest among the professional societies in sleep medicine in the development of reliable low-cost techniques suitable for use in the home environment for identification of subjects with OSAS.

In the general population, the problem of sleepiness is recognised as a contributing factor to occupational and vehicular accidents. In the area of transportation safety, there is a lot of interest in methods to monitor driver fatigue. At the same time, there is interest in techniques that can complement existing in-laboratory clinical tools by assessing sleepiness over prolonged periods in the actual work environment.

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A variety of techniques have been disclosed in the background art for addressing the need for sleep state and sleepiness monitoring outside of the laboratory environment.

For sleep state monitoring, portable systems incorporating the required signals for standard in-laboratory monitoring (2 channels of electro-encephalography, 2 channels of electro-oculography and 1 channel of electro-myography) have been developed. However, these systems require substantial clinical support to operate in the home environment. Subjects usually have to visit the sleep clinic before and after the overnight study to have the equipment set-up and removed. They also require the attachment of electrodes to the head, which can be disruptive and inconvenient.

Another method is to use a subset of the standard signals (such as a single EEG channel) to obtain an approximation. However, EEG monitoring at home requires significant user expertise, and it does not allow concurrent apnoea detection. Methods using other signals to provide estimates have also been proposed. These methods include actimetry, ECG plus respiration, and peripheral arterial tone plus actimetry. However, actimetry alone can only distinguish between wake and sleep but not the different stages of sleep, and also does not allow concurrent apnoea detection. Peripheral arterial tone monitoring requires proprietary and costly hardware and associated software. Respiration monitoring may be prone to sensor displacement in a home environment.

For sleepiness monitoring outside laboratory conditions, methods using eyelid closures, head movements, video surveillance, EEG, and actimetry have been proposed. However, methods using eyelid closures, head movements, video surveillance are not portable, so while it is feasible for applications such as driver sleepiness monitoring, it is not suitable for applications requiring ambulatory monitoring. EEG is ambulatory, but technical difficulties for long-term monitoring exist, and again it is inconvenient to have electrodes attached to the scalp. Sleepiness can be more objectively assessed with measurements such as the Psychomotor Vigilance Test (PVT) which measures a subject's reaction times. It has been shown that in a given subject, the reaction times will decrease as the person becomes sleepier – therefore PVT scores are used as a surrogate for sleepiness. However, PVT scoring takes approximately 10 minutes to carry out, and requires the subject's active attention so cannot be used for in-task monitoring of sleepiness.

Summary

In its broadest aspect the present invention provides a method of monitoring sleep, comprising recording a person's electrocardiogram (ECG), deriving a parameter from the recorded data, and providing an output indicative of a sleep characteristic based upon an analysis of the parameter.

In preferred embodiments the present invention provides a method of monitoring sleep, comprising simultaneously recording a person's electrocardiogram (ECG) and photoplethysmogram (PPG), deriving a plurality of parameters from the recorded data, and providing an output indicative of a sleep characteristic based upon an analysis of the parameters.

Preferably the ECG and PPG are recorded using a recording apparatus wearable in ambulatory manner, most preferably a combination of a Holter monitor and a pulse oximeter.

In a preferred embodiment the parameters include RR interval, pulse amplitude, pulse arrival time and respiratory rate.

In one embodiment the sleep characteristic is sleepiness; in another it is the state of sleep.

The invention also provides a system for monitoring sleep, comprising an apparatus for simultaneously recording a subject's electrocardiogram (ECG) and photoplethysmogram (PPG), and a data processor for deriving a plurality of parameters from the recorded data and providing an output indicative of a sleep characteristic based upon an analysis of the parameters.

The invention enables the monitoring of sleep state or sleepiness level of human subjects in a convenient, non-invasive and low-cost fashion. In particular, the present invention provides the advantage that it requires a minimal number of signals (two signals) that are robust in the home environment to perform sleep state monitoring, and these signals can also be used concurrently for apnoea detection, which is another significant aspect of sleep apnoea diagnostics. In addition, these signals can be acquired in a non-invasive and fully ambulatory manner using relatively low-cost hardware.

The invention has applications to clinical assessment of subjects with suspected sleep apnoea or sleep disorders that disrupt sleep state patterns, such as narcolepsy, monitoring of sleep and sleepiness patterns in healthy subjects, fitness-for-duty tests for sleepiness, sleepiness monitoring in actual work environments such as machinery operation, and driver sleepiness monitoring.

Brief Description of the Drawings

Embodiments of the present invention will now be described, by way of example, with reference to the accompanying drawings in which:

Figure 1 is a block schematic diagram of a system for estimating sleep states according to a first embodiment of the present invention.

Figure 2 are waveform diagrams showing parameters derived from the ECG (upper waveform) and PPG (lower waveform) which are used in the first embodiment (as well as the other embodiments).

Figure 3 is a diagram illustrating the output of the system of Figure 1 for estimating sleep states.

Figure 4 is a block schematic diagram of a system for estimating sleepiness according to a second embodiment of the present invention.

Figure 5 is an example of the variation in features derived from RR interval, pulse arrival time, and pulse amplitude for an individual in an alert state (left hand column) and a sleepy state (right hand column).

Figure 6 is a block schematic diagram of a system for estimating sleepiness according to a third embodiment of the present invention.

Figure 7 is a graph illustrating an example of detrended fluctuation analysis.

Figure 8 illustrates a wrapper-based search process.

Detailed Description

Figure 1 is a block schematic diagram of a system for estimating sleep states according to a first embodiment of the present invention. The system comprises a data acquisition apparatus 10 and data processing stages 12, 14 and 16.

The data acquisition apparatus 10 is a combined Holter monitor and pulse oximeter. The Holter monitor is capable of recording three data channels. In this embodiment two of the channels are used to record two ECG waveforms, and the remaining channel to record the PPG waveform.

In particular, two channels of ECG (modified lead V5 and modified lead V1) and one channel of finger PPG (index finger of non-dominant hand) are recorded simultaneously. Only one channel of ECG (modified lead V5) out of the two channels recorded is used for this embodiment, the other being recorded to provide redundancy and to allow for the possibility of calculating an ECG-derived respiration signal. The data is stored in flash memory within a portable storage device carried by the subject in a sling pouch or in a pocket, and is transferred offline to the data processing stages 12 to 16 for further analysis. The data processing stages 12 to 16 can be implemented by a suitably programmed computer. Alternatively, the portable device can have processing capability so that real-time monitoring can be performed.

It will be noted that this arrangement avoids the subject having to be connected to a bulky recording system. This is in contrast to the current technique of monitoring sleep in a hospital which requires multiple cables to be attached to the subject, these cables terminating at the other end in a bulky recording system. In that arrangement the subject is 'tied' to the recording system for the entire night, as to even go to the washroom would require a technician to remove and subsequently reattach all the cables. In the present embodiment the subject is fully ambulatory.

In the pre-processing stage 12, various parameters are derived from the ECG and PPG. In the feature extraction stage 14, various features suitable for classifying sleep states are extracted from the various parameters derived in stage 12. Finally, in the classification stage 16, a subset of features is fed into a classifier model to obtain estimated sleep states.

Figure 2 are waveform diagrams showing parameters derived in the pre-processing stage 12 from the ECG (upper waveform) and PPG (lower waveform). Four parameters, namely RR interval, pulse amplitude, pulse arrival time and respiration are derived from the ECG and PPG signals. The first three are defined based on characteristic points on the waveforms, shown as small circles in Figure 2. RR intervals are the time differences between successive QRS peaks, which can be detected using conventional methods such as Hilbert-transformation with thresholding. To derive pulse amplitude, the PPG is high-pass filtered at 0.05 Hz to remove a very low frequency baseline and then normalised to unit median pulse amplitude as raw PPG values varies considerably between subjects depending on physiological factors such as body position and technical factors such as probe application pressure. Pulse amplitude is then calculated as the beat by beat trough to peak amplitude, and peaks and troughs can be detected using conventional methods such as derivative with thresholding. Pulse arrival time is calculated as the time interval

between the R peak on the ECG and the point with maximum gradient on the systolic edge of the PPG. Respiration is obtained by band-pass filtering the PPG between 0.06 and 0.5 Hz.

In the feature extraction stage 14 the following features are calculated:

(a) PPG spectral spread. This is the Shannon entropy of the power spectral density of the PPG signal, calculated for consecutive thirty-second epochs. This feature is useful for identifying movement associated with wakefulness as the power spectral density of PPG waveforms when subjects are not moving are characterised by a concentration of spectral power around the heart rate and its first few higher harmonics. In contrast, spectral power is more evenly spread out for waveforms contaminated by artefact.

(b) PPG pulse amplitude. This is the mean of the pulse amplitude, calculated for ten-minute epochs sliding at thirty-second intervals. This feature is useful for identifying peripheral vasoconstriction associated with REM sleep, which causes a decrease in pulse amplitude.

(c) Detrended Fluctuation Analysis (DFA). DFA is a technique from statistical physics useful for determining long-term correlation in non-stationary time series. DFA was computed on ten-minute epochs of the RR interval, pulse amplitude and pulse arrival time, sliding at thirty-second intervals. For each epoch, the DFA process is:

i. The time series (of length N) is first demeaned and integrated to get y[k].

ii. It is then divided into segments each of size n (Figure 7).

iii. It is then piece-wise detrended according to the segments (Figure 7) to get $y[k]-y_n[k]$.

iv. F is then computed as the root mean square of $y[k]-y_n[k]$, i.e.

$$F[n] = \sqrt{\frac{1}{N}\sum_{k=1}^{N}(y[k] - y_n[k])^2}$$

v. The above is repeated for different values of n to obtain F[n].

vi. The log transform is then taken to produce the fluctuation function G[n], i.e. $G[n] = \log_{10}(F[n])$.

Another feature that can be obtained is the scaling exponent, which is the slope of the line obtained by regressing G[n] on $\log_{10}$n. In prior art, Penzel et al suggested the scaling exponents obtained from RR intervals are different between sleep stages. Here we found the values G[n] to be a better feature for identifying deep sleep.

(d) Respiratory rate variability. This is the difference between instantaneous respiratory frequency and a baseline respiratory frequency. Instantaneous respiratory frequency is calculated using two-minute, non-overlapping epochs of the PPG-derived respiration signal by taking the frequency with maximum spectral power between 0.15 - 0.4 Hz. Baseline respiratory frequency is calculated in the same way using ten-minute, non-overlapping epochs. This feature is useful for identifying deep sleep as respiratory frequency tend to be highly regular during these periods.

(e) Time and Frequency Analysis. This includes time and frequency domain descriptors of variability in the RR interval, pulse amplitude and pulse arrival time. Examples include standard deviation and spectral power in the low-frequency band.

(f) Multi-Scale Entropy (MSE). MSE is a statistical physics technique useful for revealing changing complexity across different scale factors in complex time series. MSE was computed on ten-minute epochs of the RR interval, pulse amplitude and pulse arrival time, sliding at thirty-second intervals. For each epoch, the MSE process is as follows:

i. The time series (of length N) is first linearly detrended to get x[k].

ii. For a particular scale factor τ, y is then computed by taking the running mean of τ consecutive, non-overlapping values of x[k], i.e.

$$y^{(\tau)}[p] = \frac{1}{\tau} \sum_{k=(p-1)\tau+1}^{p\tau} x[k]$$

where $1 \leq p \leq N/\tau$.

iii. The above is repeated for different values of τ to obtain $y^{(\tau)}[p]$.

iv. Sample entropy is then computed for each $y^{(\tau)}[p]$. For a given time series, its sample entropy is given by:

$$SE = \ln(A / B)$$

where A is the total count of m-point matches, and B is the total count of m+1 point matches. A m-point match occurs when another set of m-points is within a range of ± r of it. For example, m can be 1 and r can be 15 % of the standard deviation of the time series.

In the classification stage 16, sleep state estimates (wakefulness, REM, non-REM) are obtained as follows:

(a) Feature Selection. Preferably, the features described are calculated for the entire recording, with one feature vector (made up of all the features) describing each thirty-second epoch. A subset of the features can then selected using feature selection methods in conjunction of a training data set. The feature subset that optimises a certain performance measure, such as classification accuracy, is selected. For example, a wrapper-based search engine as depicted in Figure 8 can be employed for this purpose. Briefly, this is an iterative procedure that takes in the entire feature set and outputs a subset of it that optimises a certain performance measure, such as classification accuracy. The modules of this engine are:

i. Feature Set Search. All possible feature subset combinations are systematically evaluated if technically feasible. Otherwise, a search algorithm such as best-first search is used to systematically evaluate feature subsets.

ii. Feature Set Evaluation. This module evaluates each feature subset generated by the Feature Set Search module, and returns its performance estimate. Evaluation can be performed by cross-validation methods such as leave one subject out cross validation, where for each subject, data from all other subjects are used for training, and data from that subject in question is used for testing.

iii. Epoch Classification. This module uses training data to train a classification model, such as a linear discriminant model, and uses the trained model to classify testing data. The module then returns the classification results.

The following table presents a list of example features that can be generated by the feature selection process, to be used subsequently for distinguishing sleep states.

No.	Parameter	Feature
1	PPG	PPG spectral spread
2	RR interval	DFA G[181]
3	PPG	Pulse amplitude
4	Pulse arrival time	Percentage of successive values differing by > 50 ms
5	Pulse arrival time	Normalised low-frequency spectral power (0.04 - 0.15 cycles/ interval)
6	Pulse amplitude	DFA scaling exponent
7	Pulse arrival time	MSE (scale: 8 beats)
8	PPG	Respiratory rate variability

(b). Linear Discriminants. The selected feature subset is extracted to form consecutive feature vectors, each describing a thirty-second epoch. The features are then supplied to a linear discriminant classifier model, which produces probabilities of each epoch being associated with wakefulness, REM sleep or non-REM sleep.

(c) Post-processing. The probabilities are then smoothed to reduce epoch to epoch variability and then adjusted using heuristic rules based on normal sleep physiology in the population with suspected sleep apnoea. These adjustments include setting the probability for REM sleep to zero for the first 60 minutes of the recording, multiplying by a window that increases linearly from 0 to 1 from 60 to 100 minutes of the recording. Another adjustment is to set the probability for non-REM sleep to zero for the first ten minutes of the recording.

(d) Maximum A posteriori classification. The epochs are then classified into wakefulness, REM sleep or non-REM sleep epochs by assigning them to the class with the maximum adjusted probabilities.

(e) Heuristic correction. The classifications are then adjusted using heuristic rules, including reclassifying sections of non-REM sleep shorter than three minutes which are preceded and followed by REM sleep to REM sleep. Another adjustment is to reject short, isolated REM blocks of at most two-minute duration, and to reclassify these epochs to the class with next highest probability. Another adjustment is to reclassify as wake, short isolated sleep blocks of at most one-minute duration centred on a ten-minute block consisting entirely of wake.

Figure 3 gives an example of the classification output by comparing it with the output obtained from standard in-laboratory procedures (polysomnography). (a) Top: Polysomnography-scored sleep stages, Bottom: Apnoea events (High = event). (b) Top: Polysomnography-scored sleep stages collapsed to Wake, REM and Sleep states, Bottom: Corresponding estimated sleep states (Dots indicate epochs that were heuristically corrected). Classification accuracy was 72.3 %, and corresponding Cohen's kappa, which considers accuracy after discounting agreement by chance, was 0.47.

Figure 4 is a block schematic diagram of a system for estimating sleepiness according to a second embodiment of the present invention. The system comprises a data acquisition apparatus 10 and data processing stages 12, 14' and 16'. Apparatus 10 and stage 12 are the same as the corresponding components of the first embodiment.

In the feature extraction stage 14', the following features are derived from the ECG and PPG signals: PPG spectral spread, respiratory rate variability, PPG pulse amplitude, time and frequency analysis, detrended fluctuation analysis and multi-scale entropy. The features are calculated in the same way as described in relation to Figure 1, except that in this embodiment these features are calculated on one-minute, non-overlapping epochs of data.

In the classification stage 16', a subset of features associated with each epoch is first selected using feature selection techniques. The process is conducted in the same way as described in relation to Figure 1. This subset of features is then fed into a linear discriminant classification model, which is trained to distinguish between the alert and sleepy states. The classification model produces and outputs the probabilities of each epoch being associated with a sleepiness score. A priori information (such as time of day) may be used in calculating the discriminant values for the one minute epoch. Epochs of different length (e.g., from 10 seconds to hours) could also be used in assessing sleepiness.

Figure 5 provides an example of how the features derived from RR interval, pulse arrival time, and pulse amplitude vary for an individual in an alert state (left hand column) and a sleepy state (right hand column). The general decrease in variability in the RR interval and pulse arrival time and the general increase in variability in pulse amplitude can be observed qualitatively. Differences in mean levels of heart rate and pulse amplitude can also be observed.

Figure 6 is a block schematic diagram of a system for estimating sleepiness according to a third embodiment of the present invention in which an objective estimate of sleepiness is obtained based on agreement with psychomotor vigilance test (PVT) scores. The system comprises a data acquisition apparatus 10 and data processing stages 12, 14" and 16". Apparatus 10 and stage 12 are the same as the corresponding components of the first embodiment.

In the feature extraction stage 14", the following features are derived from the ECG and PPG signals: PPG spectral spread, respiratory rate variability, PPG pulse amplitude, time and frequency analysis, detrended fluctuation analysis and multi-scale entropy. The features are calculated in the same way as described in relation to Figure 1, except that in this embodiment these features are calculated on ten-minute, non-overlapping epochs of data.

In the sleepiness estimation stage 16", a subset of features associated with each epoch is first selected using feature selection techniques such as stepwise regression. Briefly, in stepwise regression, features are systematically evaluated in terms of a performance measure such as partial correlation with PVT scores, and features with statistically significant partial correlation with PVT scores are selected.

The following table presents a list of example features that can be generated by the feature selection process, to be used subsequently for estimating PVT scores.

No	Parameter	Feature
1	RR Interval	Heart rate
2	RR Interval	Spectral power in low-frequency band (0.04 – 0.15 cycles/interval)

The selected feature subset is then fed into a multiple linear regression model, which is trained to provide estimates of PVT scores based on a linear combination of the feature subset. The regression model can also use a priori information (such as time of day) in calculating the estimated PVT score for the ten minute epochs.

Experimental Results

Sleep state monitoring

48 subjects representing the entire range of apnoea severity (Table I) were randomly recruited from patients referred to the Sleep Disorders Unit at St. Vincent's University Hospital, Ireland, for evaluation of suspected sleep apnoea.

Table I: Subject characteristics (mean ± standard deviation, range)	
Male : Female	42 : 6
Age (years)	49 ± 10 (28 - 73)
Body Mass Index (kg/m^2)	31 ± 6 (21 - 49)
Apnea Hypopnea Index (hr^{-1})	25 ± 32 (0 - 171)
Epworth Sleepiness Scale	11 ± 6 (0 – 23)

All subjects underwent standard overnight diagnostic testing for sleep apnoea (polysomnography). ECG and PPG measurements were simultaneously taken using the system described above for sleep state monitoring. Post-polysomnography, experienced sleep technologists performed standard Rechtschaffen and Kales sleep-staging and scoring of respiratory events. Table II summarises the subjects' sleep stage characteristics.

Table II: Sleep stage characteristics obtained from polysomnography	
Sleep State	Proportion of total time in bed (%)
Wake	23 ± 14 (5 - 75)
REM	14 ± 7 (0 - 29)
Non-REM	62 ± 11 (21 - 79)

The available records were sorted by the subjects' Apnoea-Hypopnea Index (obtained from polysomnography) and assigned alternately to either the training or validation set, yielding training and validation sets of 24 subjects each. This method for splitting the data was used to control for the possible influence of apnoea severity on sleep state estimation.

The system described above was trained using the training set and tested on the validation set. Table III summarises the training and validation classification performance. As shown, performances on the training and validation data set were in close agreement, indicating the robustness of the classifier. Overall, a classification accuracy of 73.5 ± 7.7 % (Cohen's kappa = 0.49 ± 0.12) was achieved. To separately quantify the performance contribution of the linear discriminant classifier model and the heuristic corrections, Table III also presents the results

without heuristic corrections. As expected, the heuristic corrections were useful, but the bulk of performance was contributed by the classifier model.

Table III: Sleep state estimation performance		
	Training Set	Validation Set
With Heuristics Correction		
Accuracy (%)	72.8 ± 8.2	74.1 ± 7.3
Kappa	0.48 ± 0.13	0.50 ± 0.12
Without Heuristics Correction		
Accuracy (%)	71.0 ± 8.7	72.4 ± 7.8
Kappa	0.45 ± 0.13	0.47 ± 0.12

There was also no significant correlation between classification performance and apnoea severity ($r = -0.03$, $p = 0.85$), indicating that the performance of the classifier was limited by factors other than apnoea severity.

Table IV presents the overall confusion matrix combining results from the training and validation data set. Based on the confusion matrix, overall positive and negative predictive value pairs for each of the sleep states were as follows: Wake (64.1 ± 12.9 %, 88.7 ± 9.8 %), REM (50.8 ± 23.6 %, 94.5 ± 4.5 %) and Sleep (83.2 ± 11.9 %, 67.6 ± 10.0 %).

Table IV: Confusion matrix for sleep state estimation					
		Reference (Polysomnography)			
		Wake	REM	Sleep	Total
Estimate (Proposed System)	Wake	5601	501	2813	8915
	REM	603	3644	2666	6913
	Sleep	2395	1220	18710	22325
	Total	8599	5365	24189	38153

Sleepiness monitoring

15 young adults (5 M 10 F, aged 22 ± 3 years, BMI 20.2 ± 2.7 kg/m^2) with no known medical conditions were recruited. All subjects reported normal circadian and sleeping habits, and provided informed consent. Subjects identified a period of alertness and sleepiness each with respect to their normal routine and carried out the same experiment twice on the same day. All

subjects chose the morning and afternoon, with a separation of 5.0 ± 1.6 hours in between experiments, and had been awake for about 2.7 and 7.7 hours respectively when the experiments were conducted.

The experiment consists of two main tasks, performed consecutively in the sitting position. The first task was to watch a ten-minute video, and the second task was to perform a ten-minute Psychomotor Vigilance Test (PVT). Physiological measurements (including ECG, PPG, EEG, respiration and galvanic skin response) were taken throughout the video and PVT tasks.

The system described above for sleepiness monitoring was developed and tested on this set of data. Using a subset of features that are derived from the ECG and PPG, the classifier model was able to distinguish between alert and sleepy epochs recorded during both the video and PVT task with an accuracy of 72 % ± 15 % (Cohen's kappa = 0.43 ± 0.31). Performance was only slightly worse for classifying epochs from the PVT task (70 % ± 21 %, Cohen's kappa = 0.40 ± 0.42) compared to the video task (73 % ± 15 %, Cohen's kappa = 0.47 ± 0.30), indicating that the classification algorithm is robust for classifying data recorded during different mental situations. Furthermore, using subject-specific classifiers, classification accuracies of 100 % (Cohen's kappa = 1) could be achieved for every subject. Certain features were consistently useful across subjects; however, to achieve full classification accuracy, different additional feature subsets were required for some subjects.

The invention is not limited to the embodiments described herein which may be modified or varied without departing from the scope of the invention.

Claims

1. A method of monitoring sleep, comprising recording a person's electrocardiogram (ECG), deriving a parameter from the recorded data, and providing an output indicative of a sleep characteristic based upon an analysis of the parameter.

2. The method claimed in claim 1, comprising recording the person's photoplethysmogram (PPG) simultaneously with the recording of the electrocardiogram (ECG), deriving a plurality of parameters from the recorded data, and providing an output indicative of a sleep characteristic based upon an analysis of the parameters.

3. The method claimed in claim 2, wherein the ECG and PPG are recorded using a recording apparatus wearable in ambulatory manner.

4. The method claimed in claim 3, wherein the recording apparatus comprises a combination of a Holter monitor and a pulse oximeter.

5. The method claimed in claim 2, wherein the parameters include at least one of RR interval, pulse amplitude, pulse arrival time and respiratory rate.

6. The method claimed in claim 5, wherein the parameters are analysed by extracting from the parameters a plurality of features suitable for classifying the sleep characteristic of interest, and feeding a subset of the features into a classifier to obtain an estimate of the characteristic.

7. The method claimed in claim 6, wherein the features include at least one of PPG spectral spread, PPG pulse amplitude, respiratory rate variability, detrended fluctuation analysis, time and frequency analysis and multi-scale entropy.

8. The method claimed in claim 2, wherein the sleep characteristic is sleepiness.

9. The method claimed in claim 2, wherein the sleep characteristic is the state of sleep.

10. A system for monitoring sleep, comprising an apparatus for simultaneously recording a subject's electrocardiogram (ECG) and photoplethysmogram (PPG), and a data processor for deriving a plurality of parameters from the recorded data and providing an output indicative of a sleep characteristic based upon an analysis of the parameters.

11. The system claimed in claim 10, wherein the recording apparatus is wearable in ambulatory manner.

12. The system claimed in claim 11, wherein the recording apparatus comprises a combination of a Holter monitor and a pulse oximeter.

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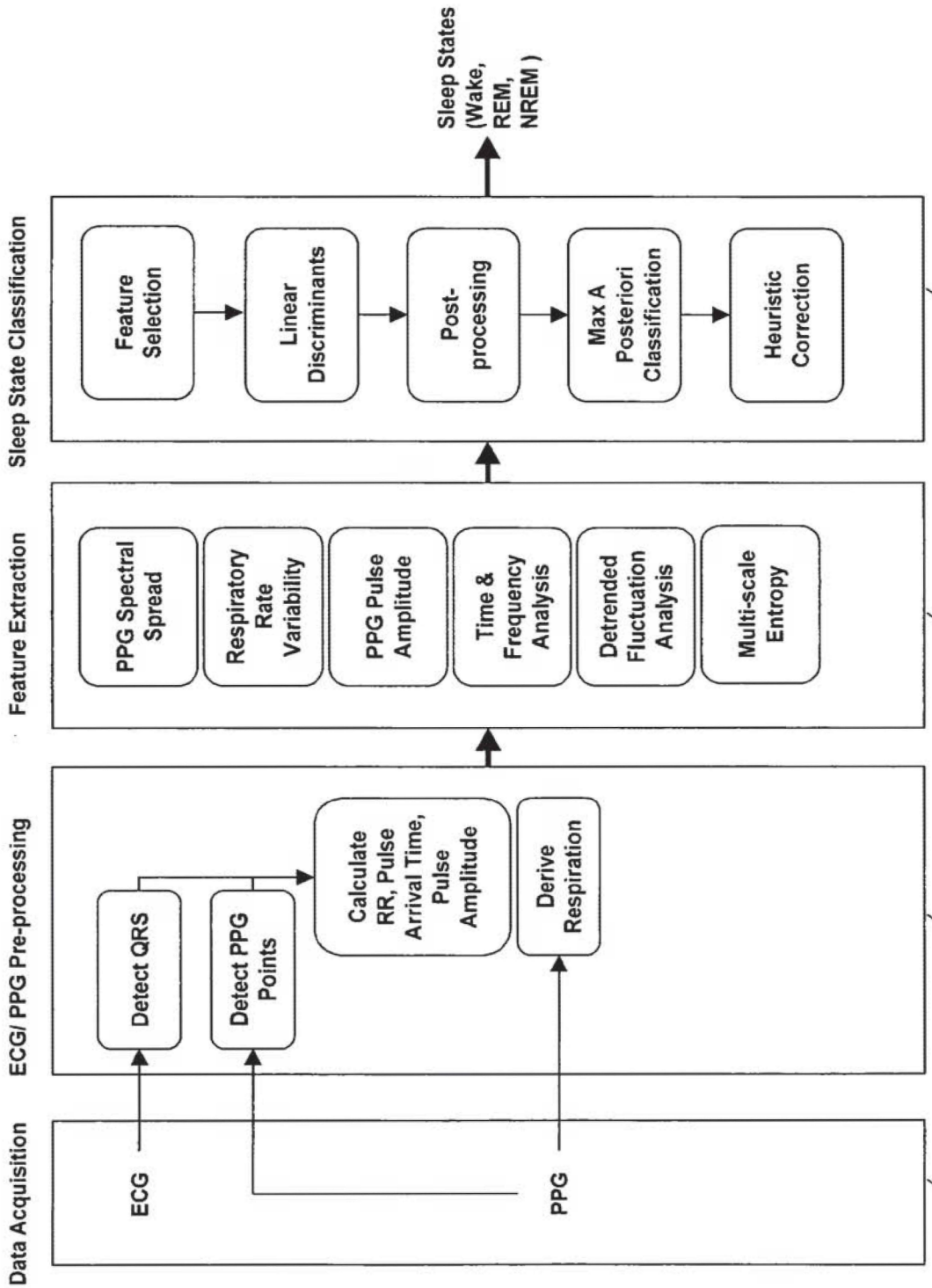


Figure 1

Petitioner Ex-1004, 0359

Petitioner Ex-1004, 0359

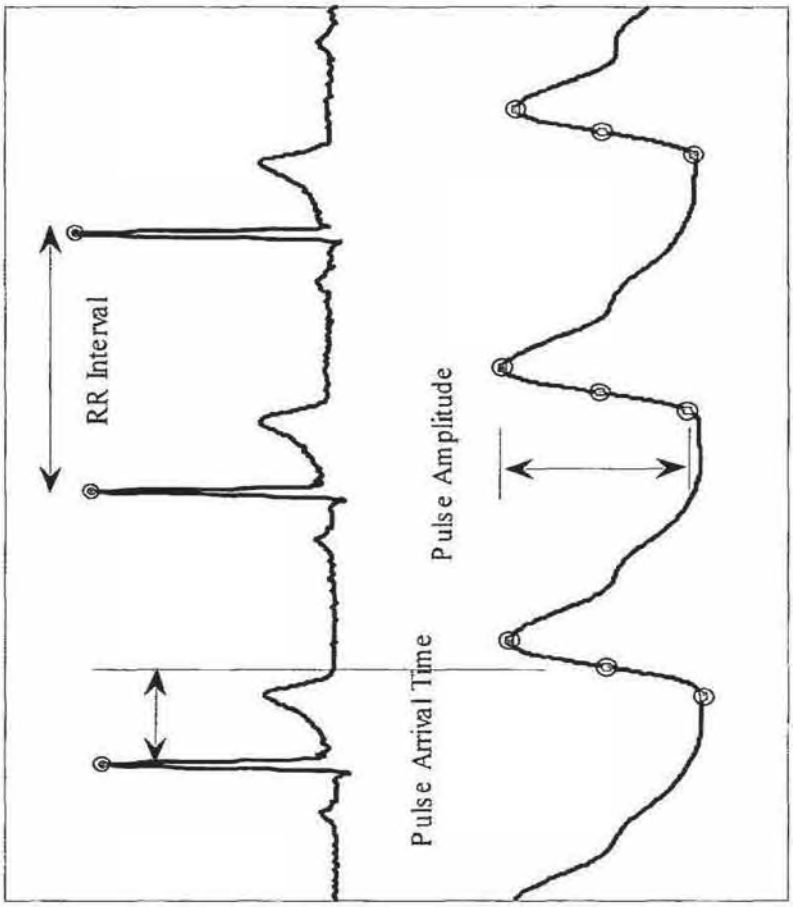


Figure 2

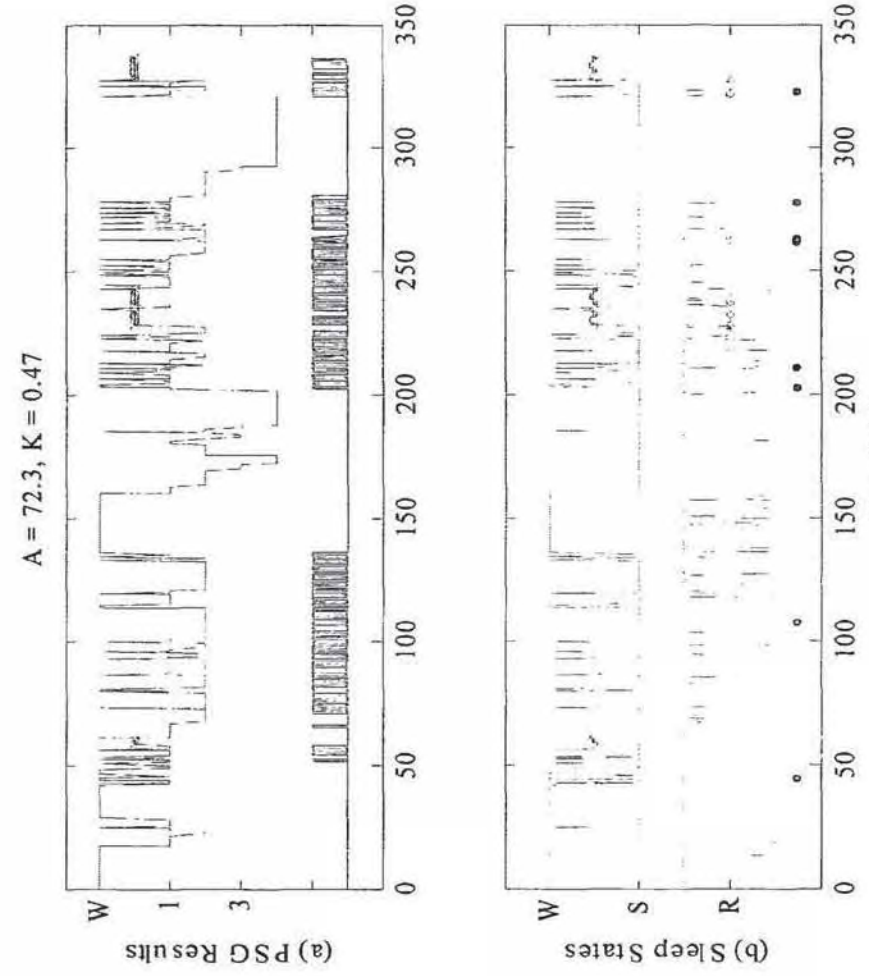

A = 72.3, K = 0.47
(a) PSG Results
W
1
3
0
50
100
150
200
250
300
350
(b) Sleep States
W
S
R
Time (min)

Figure 3

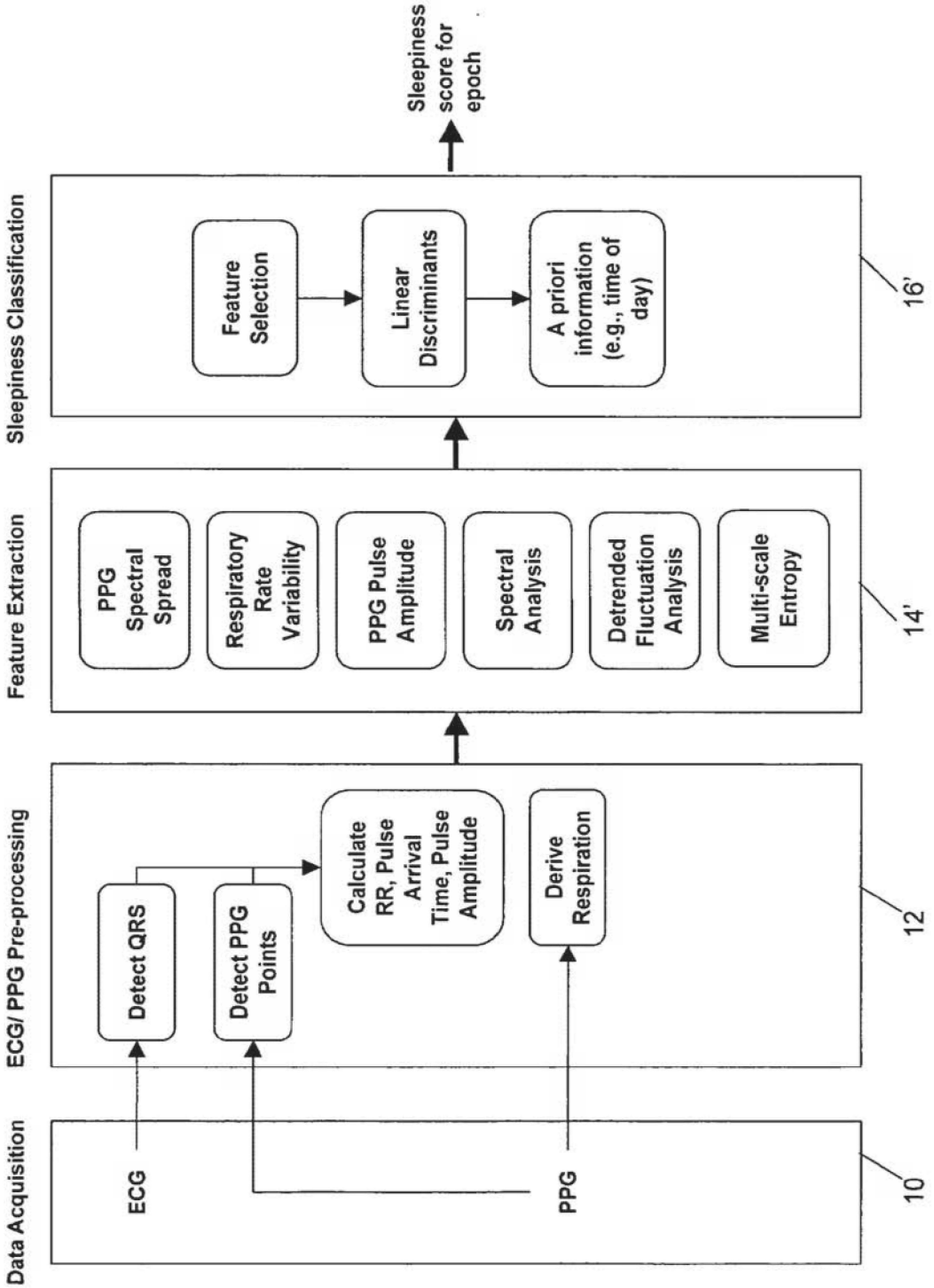


Figure 4

Petitioner Ex-1004, 0362

Petitioner Ex-1004, 0362

Petitioner Ex-1004, 0363

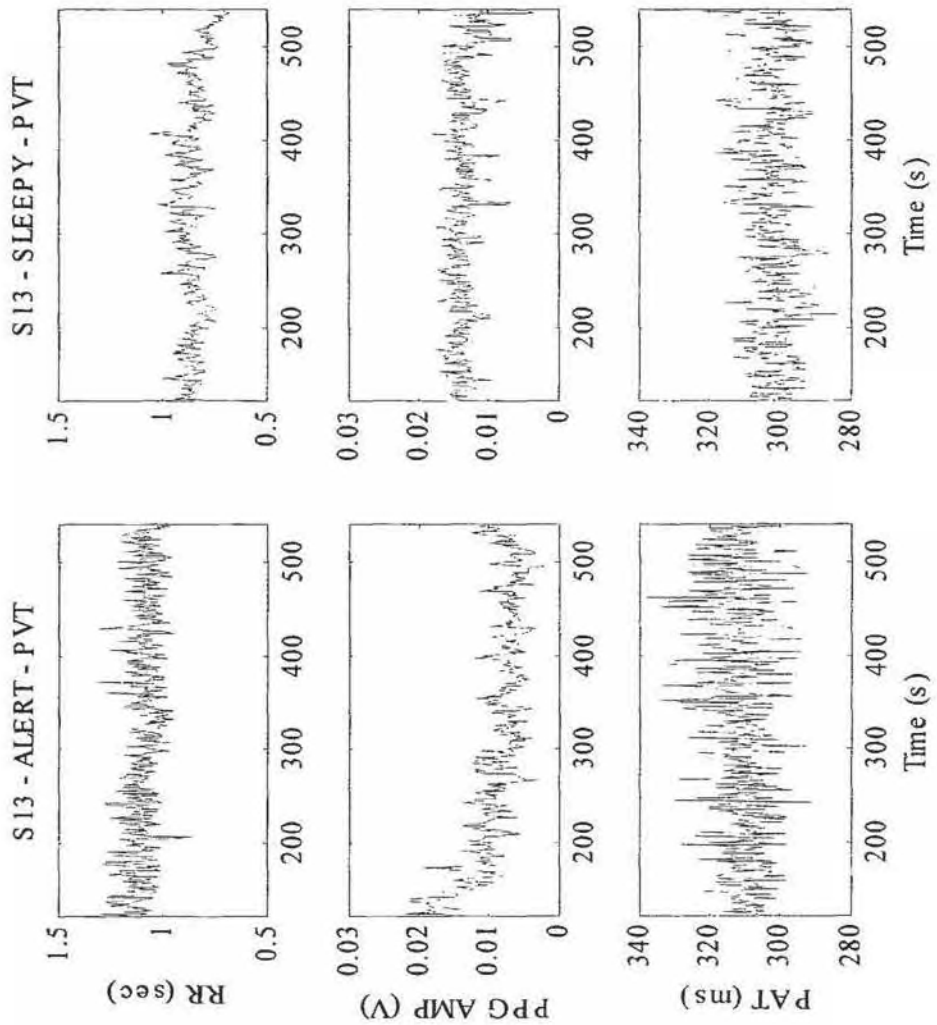


Figure 5

Petitioner Ex-1004, 0363

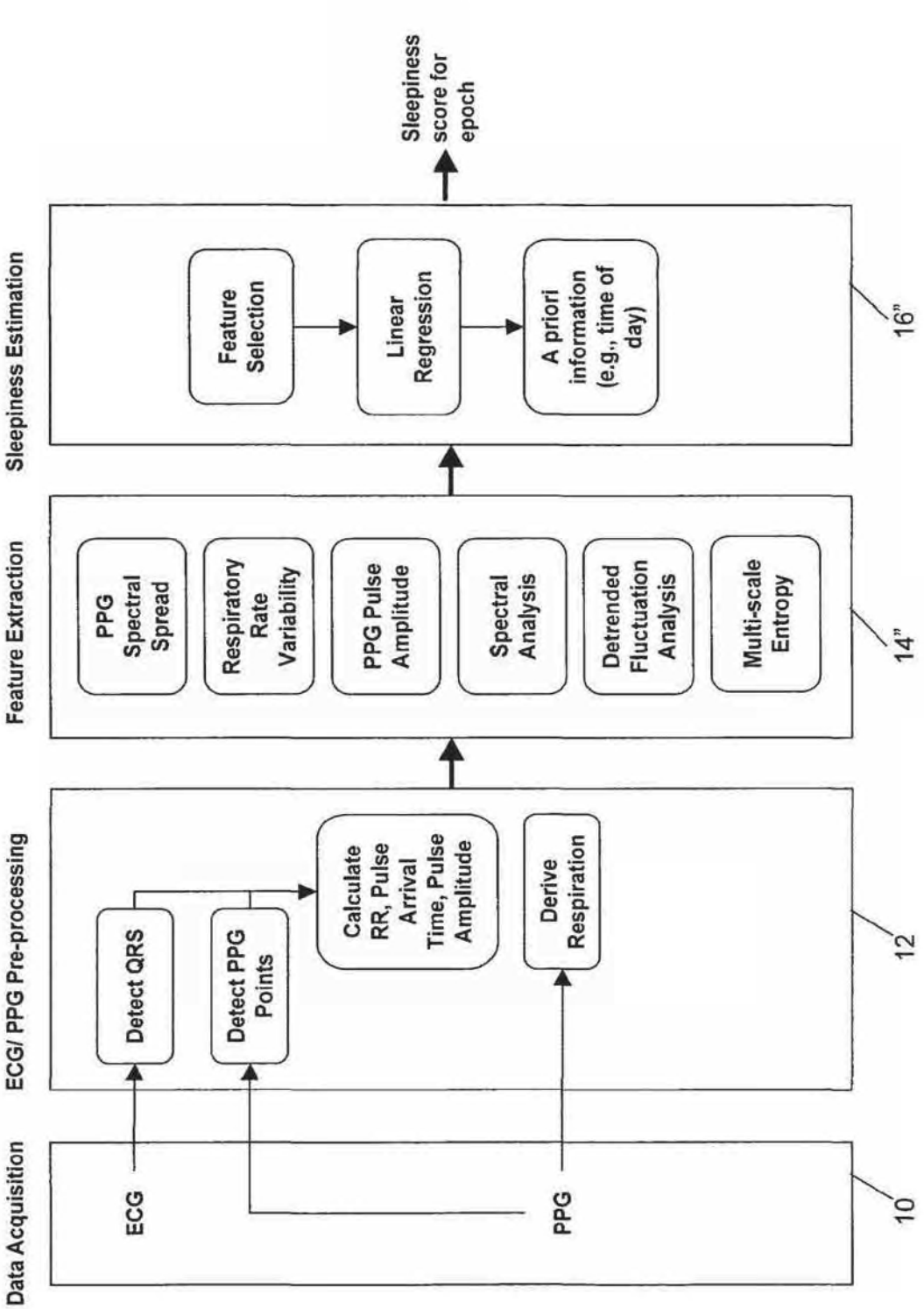
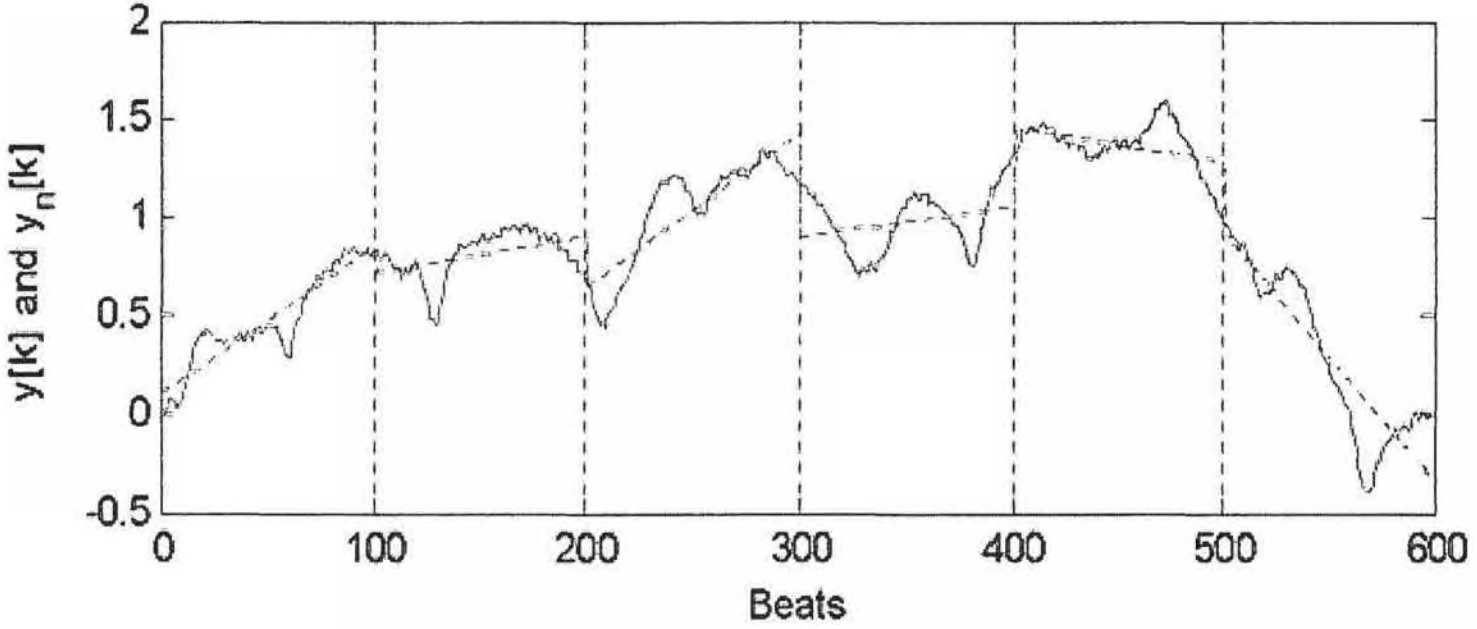


Figure 6

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Petitioner Ex-1004, 0364



Example of DFA for n = 100.

Solid line: y[k], demeaned and integrated RR intervals.
Dotted line: y_n[k], piece-wise least squares fit of y[k].

Figure 7

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Petitioner Ex-1004, 0365

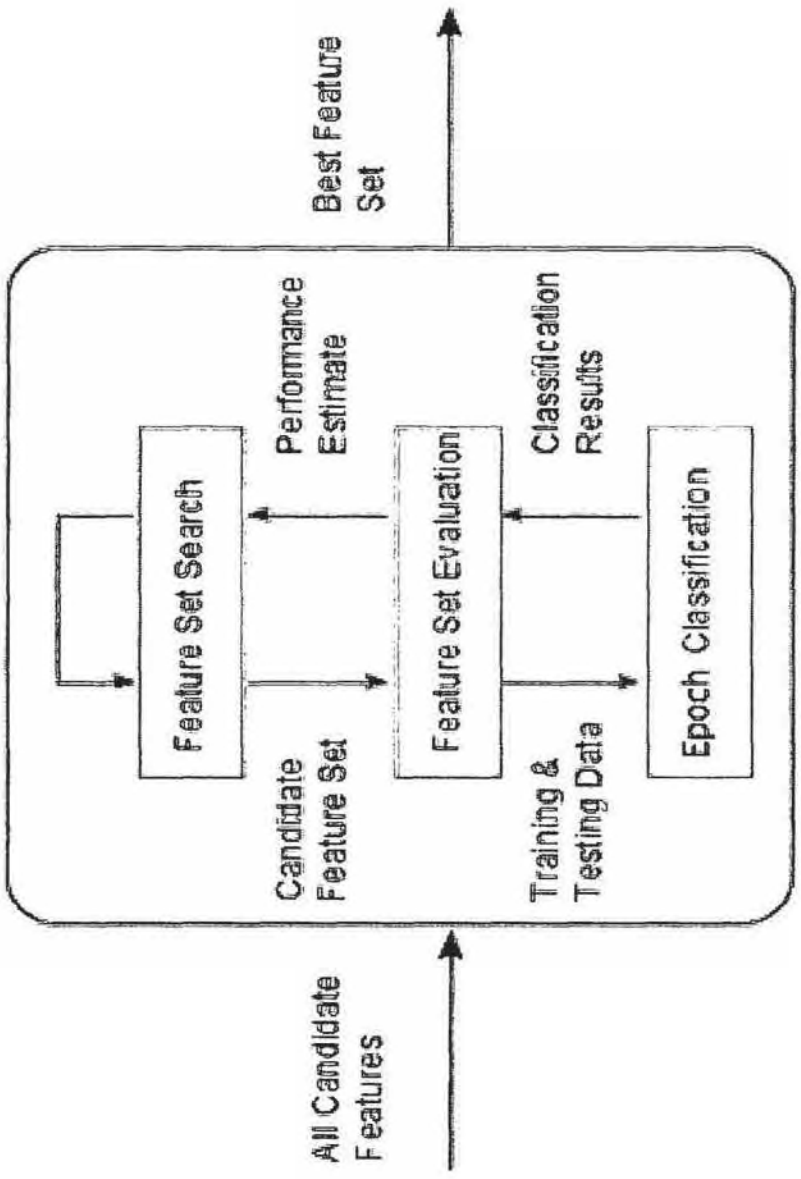


Figure 8

Petitioner Ex-1004, 0366

Petitioner Ex-1004, 0366

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2008/006599

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/00 A61B5/0205 A61B5/0402 A61B5/08

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)
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	WO 2005/067790 A (COMPUMEDICS LTD [AU]; BURTON DAVID [AU]) 28 July 2005 (2005-07-28)	1,3,4, 6-9
Y	abstract page 5, line 23 - line 27 page 6, line 20 - line 28 page 10, line 15 - line 33 page 34, line 23 - line 25 page 36, line 11 - line 17 page 44, line 5 page 48, line 1 - line 2 claim 1 figure 9	11,12

-/--

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

[X] See patent family annex.

* Special categories of cited documents :

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

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"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

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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
13 November 2008	24/11/2008

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, Fax: (+31-70) 340-3016	Tommaseo, Giovanni

Form PCT/ISA/210 (second sheet) (April 2005)

Petitioner Ex-1004, 0367

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2008/006599

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 2006/241708 A1 (BOUTE WILLEM [NL]) 26 October 2006 (2006-10-26) abstract paragraph [0032] - paragraph [0039] figures 1,2	1,2,10 11,12
X	PAGANI J ET AL: "Detection of central and obstructive sleep apnea in children using pulse transit time" COMPUTERS IN CARDIOLOGY 2002. MEMPHIS, TN, SEPT. 22 - 25, 2002; [COMPUTERS IN CARDIOLOGY], NEW YORK, NY : IEEE, US, vol. VOL. 29, 22 September 2002 (2002-09-22), pages 529-532, XP010624206 ISBN: 978-0-7803-7735-6 the whole document	1,10
X	US 2005/148895 A1 (MISCZYNSKI DALE J [US] ET AL) 7 July 2005 (2005-07-07) abstract figure 5 claims 1,6	1,5
X	US 2006/041201 A1 (BEHBEHANI KHOSROW [US] ET AL) 23 February 2006 (2006-02-23) abstract claims 1,2 figure 4	1
X	US 5 769 084 A (KATZ RICHARD A [US] ET AL) 23 June 1998 (1998-06-23) abstract claims 1,5 figures 1,2	1
X	FR 2 859 094 A (UNIV JEAN MONNET [FR]) 4 March 2005 (2005-03-04) abstract page 5, line 1 - page 6, line 19 figure 2	1
A	US 5 105 354 A (NISHIMURA TOSHIHIRO [JP]) 14 April 1992 (1992-04-14) abstract figures 1-3	1-12

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

Petitioner Ex-1004, 0368

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2008/006599

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005067790 A	28-07-2005	AU 2005204433 A1	28-07-2005
		EP 1711104 A1	18-10-2006
		JP 2007517553 T	05-07-2007
		US 2007032733 A1	08-02-2007
US 2006241708 A1	26-10-2006	CA 2605330 A1	02-11-2006
		EP 1876946 A2	16-01-2008
		JP 2008536627 T	11-09-2008
		WO 2006115832 A2	02-11-2006
US 2005148895 A1	07-07-2005	NONE	
US 2006041201 A1	23-02-2006	AU 2005277038 A1	02-03-2006
		CA 2578216 A1	02-03-2006
		EP 1788938 A2	30-05-2007
		WO 2006023940 A2	02-03-2006
US 5769084 A	23-06-1998	NONE	
FR 2859094 A	04-03-2005	WO 2005023106 A1	17-03-2005
US 5105354 A	14-04-1992	NONE	

Electronic Acknowledgement Receipt

EFS ID:	21154772
Application Number:	13354941
International Application Number:	
Confirmation Number:	9133
Title of Invention:	PHYSIOLOGICAL PARAMETER MONITORING WITH A MOBILE COMMUNICATION DEVICE
First Named Inventor/Applicant Name:	Ki H. Chon
Customer Number:	26486
Filer:	Marlo Schepper Grolnic
Filer Authorized By:	
Attorney Docket Number:	
Receipt Date:	08-JAN-2015
Filing Date:	20-JAN-2012
Time Stamp:	13:22:49
Application Type:	Utility under 35 USC 111(a)

Payment information:

Submitted with Payment	no

File Listing:

Document Number	Document Description	File Name	File Size(Bytes)/ Message Digest	Multi Part /.zip	Pages (if appl.)
1	Information Disclosure Statement (IDS) Form (SB08)	2012ndSupplIDSForm.pdf	613212 f066c6e8ef1c8ca328a8913898ab31e1b4499f24	no	4

Warnings:	
Information:	

2	Foreign Reference	WO9932030A1.pdf	1007320 b09f43d6fe09df56c8d6bb1cb6736c7af018b708	no	24
Warnings:					
Information:					
3	Foreign Reference	WO2009024273A1.pdf	982581 9eec7ca819e2943d4e4841f3e225dbacdcd8ba8f	no	28
Warnings:					
Information:					
4	Non Patent Literature	XP5866903A.pdf	763751 b1938ec0e7f650da719eab482fe4be1c4b91d5f6	no	7
Warnings:					
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5	Non Patent Literature	XP11343300A.pdf	1300762 49fc1342607e34dec5c1f219ad5cb01db4817e6c	no	10
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6	Non Patent Literature	XP55129131A.pdf	561599 33c9f0b128e2d378c159ea8b52f08a87e716afd4	no	6
Warnings:					
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7	Non Patent Literature	XP55129125A.pdf	513385 2983a385950069c35050ce7c3fde0003866ee349	no	5
Warnings:					
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8	Non Patent Literature	XP31250626A.pdf	366475 44fb7c445ed378a40fa5760f6dc08a4090bf8490	no	4
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If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/354,941	01/20/2012	Ki H. Chon		9133

26486 7590 03/11/2015

BURNS & LEVINSON, LLP
125 SUMMER STREET
BOSTON, MA 02110

EXAMINER
LIU, CHU CHUAN

ART UNIT	PAPER NUMBER
3777	

NOTIFICATION DATE	DELIVERY MODE
03/11/2015	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@burnslev.com

Office Action Summary	Application No. 13/354,941	Applicant(s) CHON ET AL.	
	Examiner CHU CHUAN (JJ) LIU	Art Unit 3777	AIA (First Inventor to File) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/24/2014*.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5)☒ Claim(s) *1,3-24 and 27-53* is/are pending in the application.

5a) Of the above claim(s) *10-17,35-38 and 45-48* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,3-9,18-24,27-34,39-44 and 49-53* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date *01/08/2015*.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

4) ☐ Other: _____.