



- (51) International Patent Classification:  
A61B 5/04 (2006.01) A61B 5/0488 (2006.01)
- (21) International Application Number:  
PCT/US2015/040543
- (22) International Filing Date:  
15 July 2015 (15.07.2015)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
62/058,729 2 October 2014 (02.10.2014) US
- (71) Applicant: LIFEQ GLOBAL LIMITED [IE/IE]; Arthur Cox Building, Earlsfort Terrace, Dublin 2 (IE).
- (72) Inventor; and
- (71) Applicant : OLIVIER, Laurence, Richard [US/US]; 145 Staghound Court, Alpharetta, GA 30005 (US).
- (74) Agents: KIRSCH, Gregory J. et al.; Smith Gambrell & Russell LLP, 1230 Peachtree Street, N.E., Suite 3100, Promenade, Atlanta, GA 30309 (US).

- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:  
— with international search report (Art. 21(3))

(54) Title: SYSTEM AND METHOD FOR MOTION ARTIFACT REDUCTION USING SURFACE ELECTROMYOGRAPHY

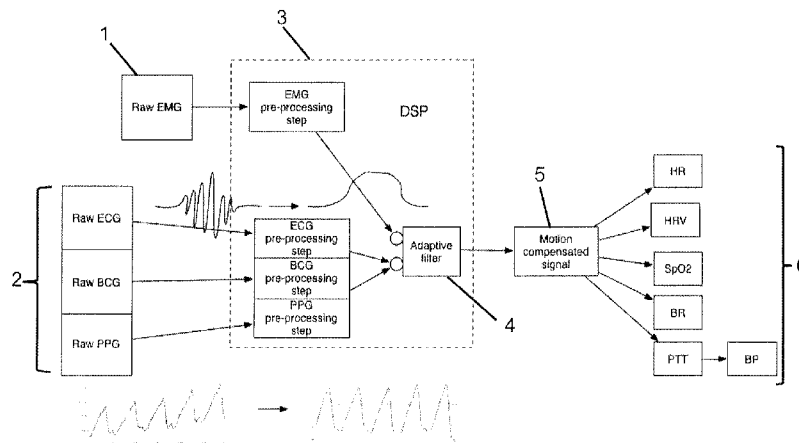


Figure 1

(57) Abstract: A system and method for motion artifact reduction using surface EMG are provided. The method of the invention is to be applied to physiological signal analysis. The system and method of the invention can compensate for motion artifacts which corrupt physiological signals, measured by wearable devices, during movement.

WO 2016/053444 A1

## SYSTEM AND METHOD FOR MOTION ARTIFACT REDUCTION USING SURFACE ELECTROMYOGRAPHY

### FIELD OF THE INVENTION

[0001] The present invention relates to the field of non-invasive digital health monitoring and signal processing. In particular, a system and method for motion artifact reduction in measured human physiological signals is introduced. The invention comprises a wearable device which may be placed on an area of the body including, but not limited to, the wrist, the forearm or the upper arm and is composed of a plurality of surface electromyography (sEMG) electrodes. In addition, the wearable device comprises a sensor(s) for measuring physiological signals such as photoplethysmography (PPG), electrocardiography (ECG) and balistocardiography (BCG). Motion compensation is achieved in the time and/or frequency domain by using a derivative of the raw sEMG signal and through adaptive filtering. This method is particularly useful in situations when physiological signals recorded by, but not limited to, PPG, ECG and BCG sensors are distorted by movement during everyday activities such as typing on a keyboard or operating a mobile device.

### BACKGROUND OF THE INVENTION

[0002] Optical- and ECG-based solutions for heart rate measurement, as well as other physiological metrics, have become central to the field of portable health, fitness and wellness monitoring. Traditionally, measurements such as heart rate were

only applicable in a fixed medical/hospital setting, however, there is an increasing demand for wearable devices which can provide continuous monitoring in almost any environment. This includes, but is not limited to, sports, quantified-self and medical applications in which the subject and/or healthcare practitioner is provided with real-time data gathered over a sustained period of time. Importantly, this data can be used to motivate and guide subjects to achieve or maintain personal health, wellness and fitness goals and/or to guide healthcare practitioners in their medical decisions. Optionally, this data may also be useful in a scientific and clinical research setting.

[0003] While wearable ECG-based monitors are proven to provide an accurate measure of heart rate, they are limited by their chest strap property and by the discomfort that may arise from wearing the strap for extended periods of time. ECG-based monitors therefore do not provide a seamless user experience. A wristwatch form factor is generally a more favorable option, however, with this requirement comes the challenge of measuring heart rate under conditions which may cause distortion to the signal. Measuring heart rate on the extremities includes correcting for the motion of the extremities, a problem which does not affect chest strap recordings. Since the PPG technique is traditionally applied to measurements which are taken from a motionless subject, situations in which the subject is no longer stationary are not accounted for. In addition to broad motion patterns, such as swinging the arms during running, a wrist-worn device can provide a number of challenges with regard to fine hand and finger movements that distort the optical signal and which are part of everyday activities such as typing. There are a number of ways to go about compensating for motion artifacts in a physiological signal and therefore some of the most relevant prior art items focused on such techniques are reviewed below.

[0004] Inertial motion sensors, such as accelerometers, are a popular tool for mea-

asuring motion and/or activity. They therefore form part of a number of inventions aiming to compensate for the motion artifacts known to corrupt physiological signals. In a patent to Texas Instruments Inc., US 20110098583, a chest-worn heart rate monitor which includes an accelerometer is disclosed. The accelerometer signal is processed to generate a body motion signal which is then used for motion artifact cancellation to generate an acceleration-based heart rate measurement. Similarly, in patent US 8483788 a motion compensated pulse oximeter is described which also incorporates an accelerometer to measure the changes induced by motion between the light emitter and detector. An attenuation factor is then calculated using a combination of the accelerometer data, an equation related to a model distance between light emitter and detector and a model based on the expected behavior of light. A look-up table is then used to find a motion measurement that corresponds to the attenuation factor. This measure is then used to better calculate the physiological parameter of interest. In addition to inertial motion sensors, optical techniques have also been utilized to achieve the same end. In patent US 20140213863 to Texas Instruments Inc. a motion compensation method for a wearable PPG device which employs an optical motion signal is described. In addition to the main light emitting diode (LED) that is used to gather the PPG signal, the light detected from a second LED, which either has a lower driving current or a different wavelength to the primary LED, acts as a reference motion signal. This reference signal is used to reduce noise and motion artifact by subtracting it from the desired heart rate signal. Accelerometer data is further used to determine if the signal does indeed contain noise and whether processing should occur to compensate for this. The patent focuses specifically on sensor displacement or changes in position of the sensor in the context of a wrist-worn device. A similar method is also employed by US 20120150052A1 to Schoshe Industries Inc.. Another approach described by US 7020507 explains how

specific digital signal processing steps can be used for motion artifact removal. This method comprises transforming the data into the frequency domain and selecting candidate spectral cardiac peaks, along with their harmonics. These peaks are then reconstructed in the time domain and the second order derivative is computed to separate unwanted artifacts that are generated by motion. Importantly, this method does not use a separate noise channel in addition to the PPG signal. In addition to the above mentioned techniques for motion compensation, digital filters can also be used to achieve a motion-corrected signal. For example, US 5853364 describes a method which employs model-based adaptive filtering, more specifically a Kalman filter, to estimate what the output signal should be under noisy conditions. The method employs mathematical models to describe how the measured physiological signal changes in time and how it is related to measurements affected by motion artifact. Lastly, US 8655436 describes a heart rate meter and a signal processor which, using a bandpass filter, passes a frequency component in a pre-determined narrow band to remove noise and motion artifact.

[0005] While the above mentioned approaches all provide methods for achieving motion compensation, none of these provide a solution which incorporates what is known about the physiology of human movement. sEMG represents a good candidate for capturing a physiologically relevant human motion signal and therefore forms the basis of the current invention. sEMG is a non-invasive method for measuring the electrical activity of the muscles. While the forearm contains numerous muscles which are responsible for flexion, extension and pronation of the hand and fingers, only the superficial muscle activity can be measured with sEMG and therefore electrodes must be placed strategically. Furthermore, sEMG has many applications comprising physical rehabilitation, the detection of neuromuscular disease, analysis of signals for

prosthetic devices and the analysis of the mechanics of human movement i.e. kinesiology and biomechanics. It therefore follows that sEMG may provide a solution for compensating for the motion artifacts that are observed when particular muscles are neurologically activated. A search of the prior art has shown that sEMG has not been used specifically for the reduction of motion artifacts in optical physiological signals. This is however not the case with regard to ECG-based measurements. Since both EMG and ECG use the same recording modality, unwanted sEMG signals are often picked up in addition to heart rate. Methods have therefore been described for canceling noise generated by sEMG from the ECG signal (US5337753 and CA 2236877). US5337753 applies specifically to a hollow cylindrical bar containing electrodes for use in exercise apparatus whereby the subject grips the cylinder with their hands for a heart rate measurement. An sEMG recording is also taken from each electrode pad to account for noise due to muscular movement and the recordings are subtracted from one another to generate a zero output reading from the sEMG. CA2236877 applies specifically to an ECG-based heart rate monitor which removes unwanted EMG signals by a learning adaptive threshold detection system. This method further removes EMG peaks and enhance ECG peak since ECG peaks have steeper slopes and sharper tips than typical EMG waves.

[0006] Since sEMG electrodes can track muscle activity quite efficiently it is not surprising that EMG technology has also been exploited for gesture control and hands-free applications. In patent US 0327171 to Microsoft Inc., a system for inferring hand and finger movement by sensing muscle activity in the forearm is disclosed. Electrodes are placed within a wearable device that sits on the upper forearm and a machine learning model is then trained to recognize specific gestures from the sampled EMG recordings. In addition, this technology also features in US 8170656 where its appli-

cation is extended to gesture control of other parts of the body. A similar system is described in US 20130317648 which describes a system consisting of multiple surface electrodes incorporated into a “biosleeve”. This system is intended for use in manipulating objects in space, factories as well as in the military. While these methods focus on muscle activity elicited from the upper forearm, patent CN103654774 describes a system which includes at least two EMG electrodes placed around the wrist. In addition to gesture control the system is able to relay information concerning muscular strength and fatigue.

[0007] The information that can be extracted from EMG surface electrodes has also been used to provide additional functionality to health monitoring devices. An example includes US 20140135631 to Fitbit Inc., which discloses a method for activating a wearable heart rate monitor on demand by a user interaction such as moving the hand-wearing device in a defined motion pattern. In addition, US 20140142437 discloses a method which uses EMG recordings taken from the footpad electrodes of a weighing-scale ballistocardiograph (BCG) device to detect the motion of the user while he/she stands on the device. This method does not directly use the EMG signal to improve the heart rate measurement, but rather uses the information to assess whether the subject’s movement is excessive and if it would be of interest to take the reading again.

[0008] These prior art applications show that EMG technology captures a physiologically relevant ‘motion signal’ which is used by the method of the current invention to provide a sensitive motion artifact reduction solution.

### SUMMARY OF THE INVENTION

[0009] The present invention overcomes problems and obstacles associated with motion artifacts present in physiological signals measured using techniques including, but not limited to, PPG, ECG and BCG. In the current invention, motion compensation is achieved by exploiting a simultaneously measured sEMG signal. EMG is defined as a measure of the electrical activity of skeletal muscle and can be measured non-invasively using surface electrodes. Muscular contraction and/or relaxation, from which certain motion artifacts originates, can be efficiently captured by EMG equipment and provides a physiologically relevant signal for use in motion compensation. The process of muscular contraction is initiated by the motor neurons of the anterior horn of the spinal cord which carry nerve impulses to the muscles. Action potentials are transmitted across the neuromuscular junction and are propagated throughout the muscle. Due to the T-tubule system of muscle, the signal is carried deep into the muscle fibers and allows for the release of calcium, which is necessary for the process of excitation-contraction coupling, the formation of actin-myosin cross-bridges and ultimately muscle contraction. EMG action potentials have a conduction velocity of 2-6m/sec and the signal captured by sEMG electrodes and equipment can be described as as a burst of activity centered around a resting voltage. Using a derivative of the raw sEMG signal in the time and/or frequency domain, this signal can be transformed into a continuous signal which is easily subtracted from a physiological signal in a similar manner in which accelerometer data can be subtracted to achieve motion compensation. In some cases the current invention has shown to provide a more accurate prediction than an accelerometer and in addition, the current inven-



tion may provide a more power efficient and compact measure of signal distortion compared to other methods. This motion compensation method can be applied to the measurement of metric comprising, but not limited to, heart rate, heart rate variability, oxygen saturation, breathing rate and pulse transit time.

### BRIEF DESCRIPTION OF THE DRAWINGS

[0010] The preferred embodiments of the invention will be described by way of example only, with reference to the accompanying drawings:

[0011] Figure 1: A schematic representation of an exemplary embodiment of the overall process of the current invention illustrated by a flow diagram.

[0012] Figure 2: A schematic representation of an exemplary embodiment of a wearable device comprising sEMG electrodes (8) and a PPG sensor (9).

[0013] Figure 3: A basic embodiment of the invention in the context of mobile and internet technologies.

[0014] Figure 4: (A) Measured signals from a heart rate sensor, accelerometer, sEMG electrodes and an optical near infrared (NIR) light and sensor. (B) A plot showing the correlation between the noise in the heart rate monitor signal and the measured accelerometer, sEMG and NIR signals over time.

[0015] Figure 5: Two different graphs showing heart rate output, where either the accelerometer or sEMG signal is used as a noise reference signal in an adaptive filter.

## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0016] The following detailed description and drawings describe different aspects of the current invention. The description and drawings serve to enable one skilled in the art to fully understand the current invention and are not intended to limit the scope of the invention in any manner. Before the present methods and systems are disclosed and described, it is to be understood that the methods and systems are not limited to special methods, special components, or to particular implementations. It is also to be understood that the terminology used herein is for the purpose of describing particular aspects only and is not intended to be limiting. As used in the specification and the appended claims, the word “comprise” and variations of the word, such as “comprising” and “comprises,” means “including but not limited to,” and is not intended to exclude, for example, other components or steps. “Exemplary” means “an example of” and is not intended to convey an indication of a preferred or ideal embodiment. “Such as” is not used in a restrictive sense, but for explanatory purposes. The singular forms “a,” “an,” and “the” also include plural elements unless the context clearly dictates otherwise. “Optional” or “optionally” means that the subsequently described event or circumstance may or may not occur and that the description includes instances where said event or circumstance occurs and instances where it does not.

[0017] Figure 1 depicts an exemplary embodiment of the current invention which shows a flow diagram of the process of the current invention. Both the raw sEMG signal (1) and physiological signal (2), measured by techniques including, but not limited to, PPG, BCG and ECG may be subjected to a pre-processing step (3).

This step may comprise taking the derivative of the raw signals in the time and/or frequency domain. Following this the processed sEMG signal may be subtracted from the physiological signal in order to compensate for signal distortion due to motion. This process may make use of an adaptive filter (4) to produce a motion compensated signal (5). The method of the current invention may be applied to the measurement of metrics comprising heart rate (HR), heart rate variability (HRV), oxygen saturation (SpO<sub>2</sub>), breathing rate (BR) and pulse transit time (PTT) (6).

[0018] Figure 2 depicts an exemplary embodiment of a wearable device (7) which shows how sEMG electrodes (8) can be placed in a band configuration around the wrist. Finger flexion and extension motions can be easily identified in the sEMG signal, with index finger movement providing a particularly distinct sEMG signal. The sEMG electrodes may be incorporated into one or more devices which uses a sensor (9) to measures physiological signals such as heart rate. These physiological signals may be measured based on techniques including, but not limited to, photoplethysmography, balistocardiography and/or electrocardiography. Furthermore, the electrodes may be incorporated into a band with the physiological sensor which contacts the skin and may be worn on parts of the body including, but not limited to, the wrist, forearm and upper arm.

[0019] Figure 3 depicts a basic embodiment of the invention where (7) is the wearable electronic device containing the necessary sensor means to measure a physiological and sEMG signal. The wearable device optionally contains a display (10) and is capable of transmitting data to a mobile device (11) and or directly to an internet based platform (12). The data can be stored and further processed on a server (13) for future retrieval and to be viewed on a computing platform exemplified by the personal computer (14), the mobile phone (11) and or wearable device (7).

[0020] Figure 4A is an exemplary embodiment of the invention which depicts the measured signals from a PPG-based heart rate sensor (15), accelerometer (16), sEMG electrodes (17) and an optical near infrared (NIR) light and sensor (18). In this exemplary embodiment a device with the above mentioned sensors was placed around the wrist of a subject. The bursts of activity seen between baseline readings are generated from specific hand gestures such as typing and were interspersed with rest periods.

[0021] Figure 4B depicts a correlation plot (19), generated from said second embodiment, between the noise in the heart rate sensor signal and the measured accelerometer, sEMG and NIR signals over time. It is ideal for a reference signal to have a very low correlation during resting periods and a high correlation during movement, which then makes it a good contender for use in a noise canceling adaptive filter. The IR reference has a very high correlation with the heart rate sensor during rest because the HR is picked up in both sensors. During movement, the correlation decreases but still remains high, partly since the nature of the corruption in the heart rate sensor and IR signals are similar. This makes it difficult to compare the IR reference with regards to correlations, but it was still included for comparison. Both the accelerometer and sEMG signal provide a similar level of correlation with the noise signal from the heart rate sensor. In some places sEMG leads to higher correlations, while in other places the accelerometer does better.

[0022] Figure 5 depicts an exemplary embodiment which shows two different heart rate output graphs based on PPG heart rate sensor data. These graphs compare heart rate predications which use either an accelerometer or an sEMG signal as the noise reference in an adaptive filter to provide a motion compensated heart rate. The signals are compared to each other and to a set of heart rate data collected

simultaneously with an ECG chest strap. The above graph (20) shows that with this particular dataset using the sEMG signal as a reference outperforms using the accelerometer. The opposite is found in the graph below (21).

What is claimed:

1. A method for augmenting the determination of at least one physiological parameter by way of using a measured surface electromyography (sEMG) signal for motion artifact reduction, the method comprising;
  - (a) measuring a raw sEMG signal from a subject;
  - (b) measuring a raw physiological signal, other than the raw sEMG, from a subject;
  - (c) processing the raw physiological signal and the raw sEMG signal;
  - (d) transforming the raw physiological signal with the raw sEMG signal, or the raw physiological signal with the processed sEMG signal, or the processed physiological signal with the raw sEMG signal, or the processed physiological signal with the processed sEMG signal, so as to generate a motion compensated physiological signal;
  - (e) determining at least one physiological parameter from the motion compensated physiological signal;
  - (f) transmitting the motion compensated physiological signal or at least one physiological parameter.
2. The method of claim 1 wherein the processing step for the raw sEMG and raw physiological signal may include using the derivative of the signals in the time or frequency domain.
3. The method of claim 1 wherein the raw or processed sEMG signal is subtracted from the raw or processed physiological signal in the time domain to generate a motion compensated physiological signal.

4. The process of claim 1 wherein the raw or processed sEMG signal is subtracted from the raw or processed physiological signal in the frequency domain to generate a motion compensated physiological signal.
5. The method of claim 1 wherein the process of generating a motion compensated physiological signal may include the use of an adaptive filter.
6. The at least one physiological parameters of claim 1 which may include, but are not limited to, heart rate, heart rate variability, oxygen saturation, breathing rate and pulse transit time.
7. The method of claim 1, which includes a means to transmit the motion compensated physiological signal(s) or physiological parameter(s) to mobile electronic devices, such as a mobile phone or personal computer.
8. The method of claim 1, which includes the means to transmit the motion compensated physiological signal(s) or physiological parameter(s) wirelessly to a platform where said data can be stored, analyzed and viewed by client computing platforms including, but not limited to, mobile computing devices, home computers or wearable devices.
9. A system for augmenting the determination of at least one physiological parameter by way of using a measured surface electromyography (sEMG) signal for motion artifact reduction, the system comprising;
  - (a) a wearable device for measuring a raw sEMG signal and a raw physiological signal, other than a raw sEMG, from a subject; and
  - (b) a processor for:
    - (i) processing the raw physiological signal and raw sEMG signal;

- (ii) transforming the raw physiological signal with the raw sEMG signal, or the raw physiological signal with the processed sEMG signal, or the processed physiological signal with the raw sEMG signal, or the processed physiological signal with the processed sEMG signal, so as to generate a motion compensated physiological signal;
  - (iii) determining at least one physiological parameter from the motion compensated physiological signal; and
  - (iv) transmitting the motion compensated physiological signal or at least one physiological parameter.
10. The system of claim 9 wherein the processing step for the raw sEMG and raw physiological signal may include using the derivative of the signals in the time or frequency domain.
11. The system of claim 9 wherein the raw or processed sEMG signal is subtracted from the raw or processed physiological signal in the time domain to generate a motion compensated physiological signal.
12. The system of claim 9 wherein the raw or processed sEMG signal is subtracted from the raw or processed physiological signal in the frequency domain to generate a motion compensated physiological signal.
13. The system of claim 9 wherein the process of generating a motion compensated physiological signal may include the use of an adaptive filter.
14. The system of claim 9, wherein the at least one physiological parameter may include, but are not limited to, heart rate, heart rate variability, oxygen saturation, breathing rate and pulse transit time.



15. The system of claim 9, wherein the wearable device comprises at least one surface EMG electrode which contacts the user's skin and at least one sensor for measurement of a physiological signal, other than sEMG.
16. The system of claim 15, wherein the at least one surface sEMG electrode may comprise dry or wet electrodes.
17. The system of claim 15, wherein the sensor includes, but is not limited to, a photoplethysmography (PPG) sensor, an electrocardiography (ECG) sensor or a balistocardiography (BCG) sensor.
18. The system of claim 9, further comprising a display for displaying the motion compensated physiological signal(s) or physiological parameter(s).
19. The system of claim 9, further including a means to transmit the motion compensated physiological signal(s) or the at least one physiological parameter to a mobile electronic device.
20. The system of claim 19, wherein the mobile electronic device is configured to display the motion compensated physiological signal(s) or the at least one physiological parameter.
21. The system of claim 9, further including a means to transmit the motion compensated physiological signal(s) or the at least one physiological parameter wirelessly to a platform where said data can be stored, analyzed and viewed on a client computing platform, including but not limited to mobile computing devices, home computers or wearable electronic devices.

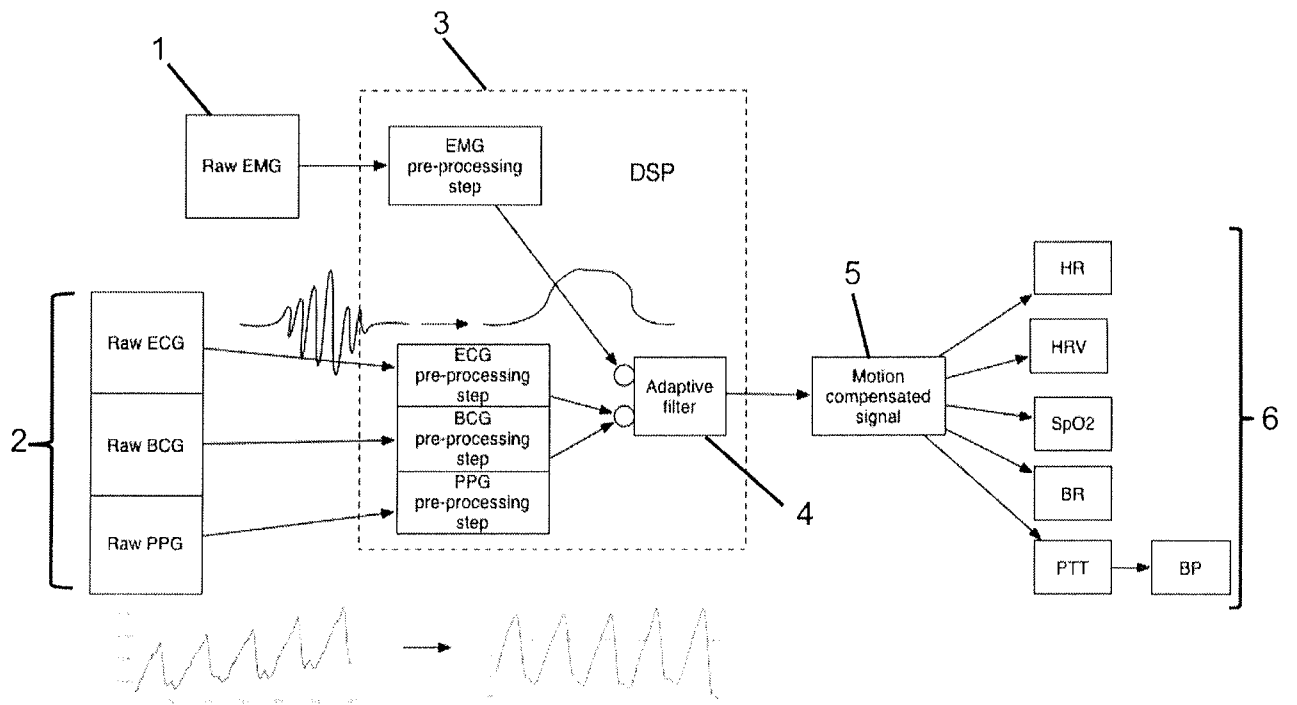


Figure 1

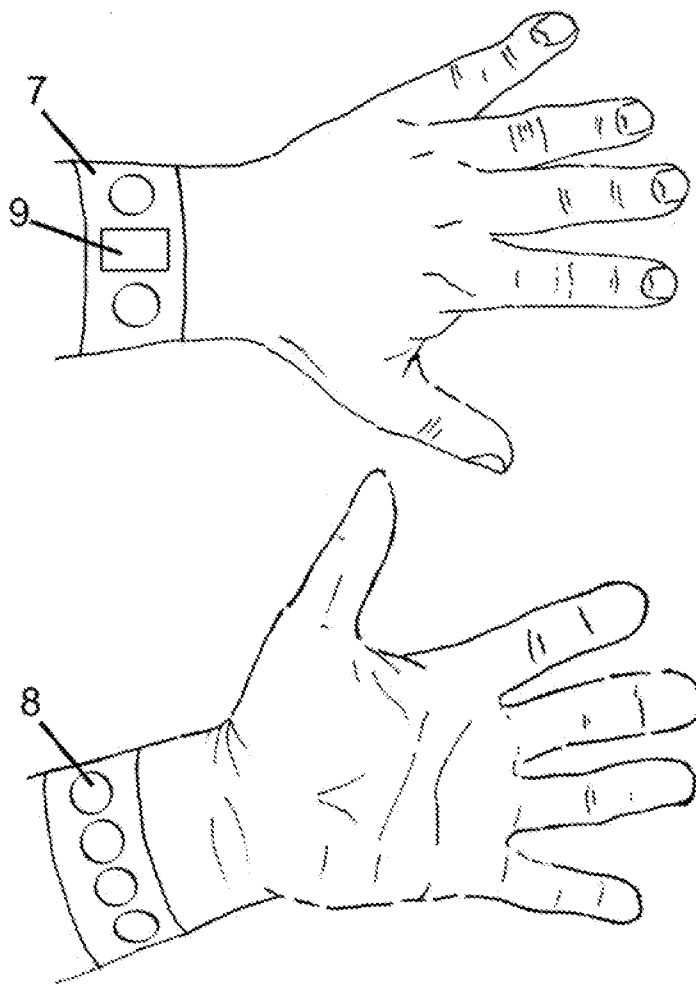


FIG. 2

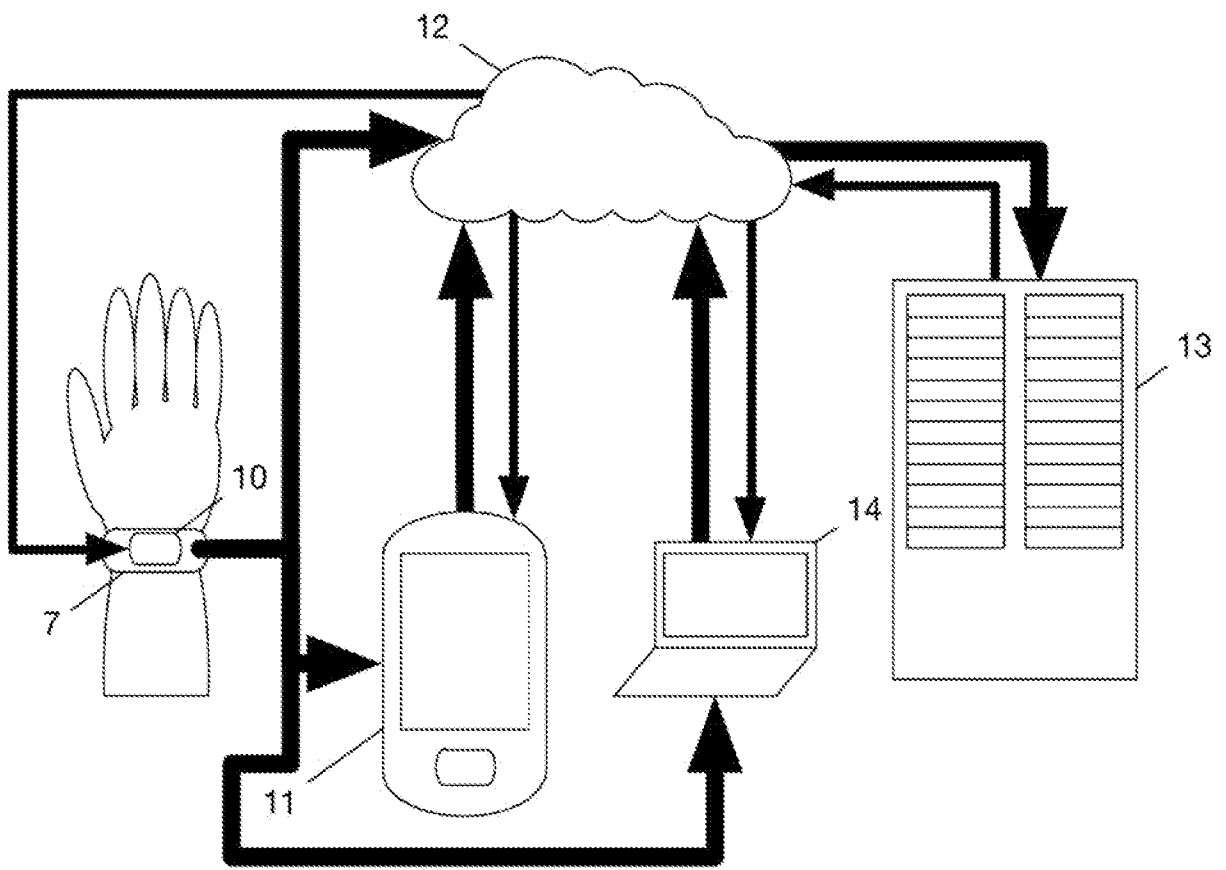


FIG. 3

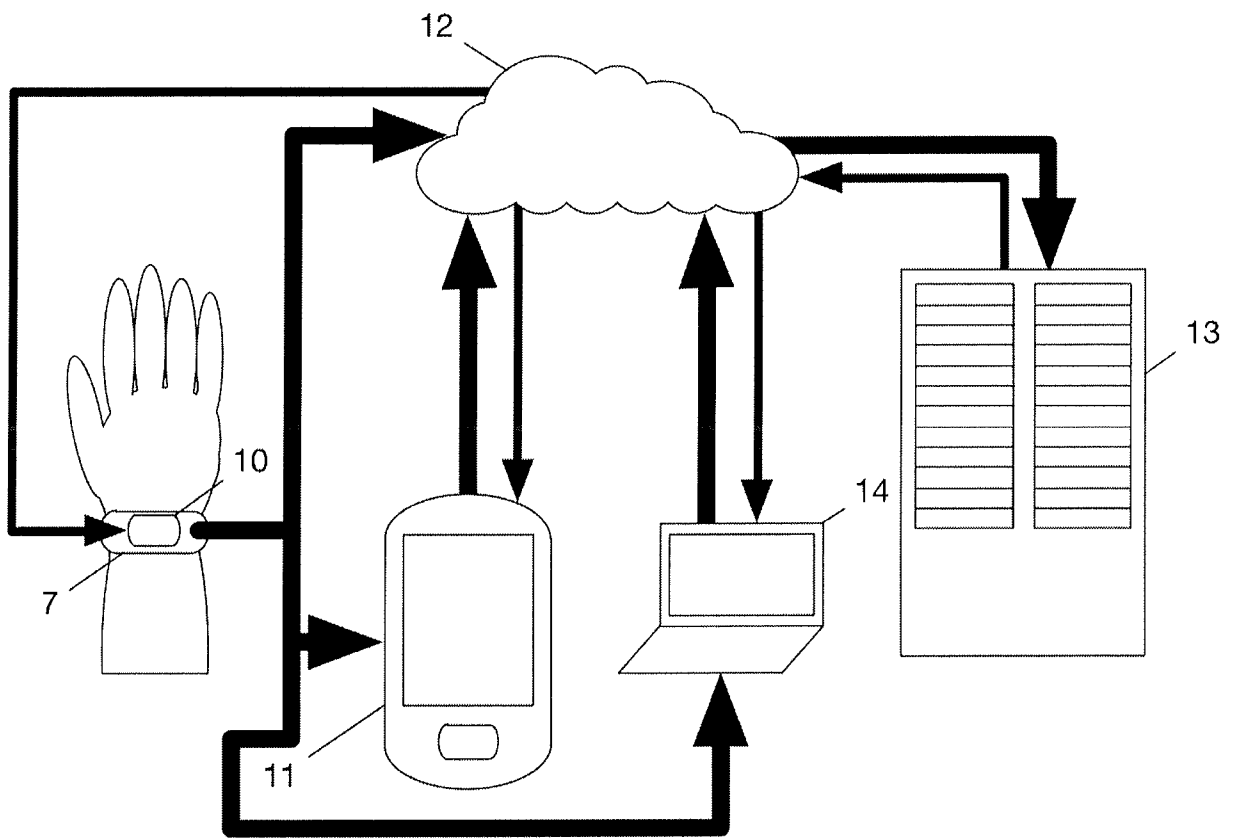


Figure 3

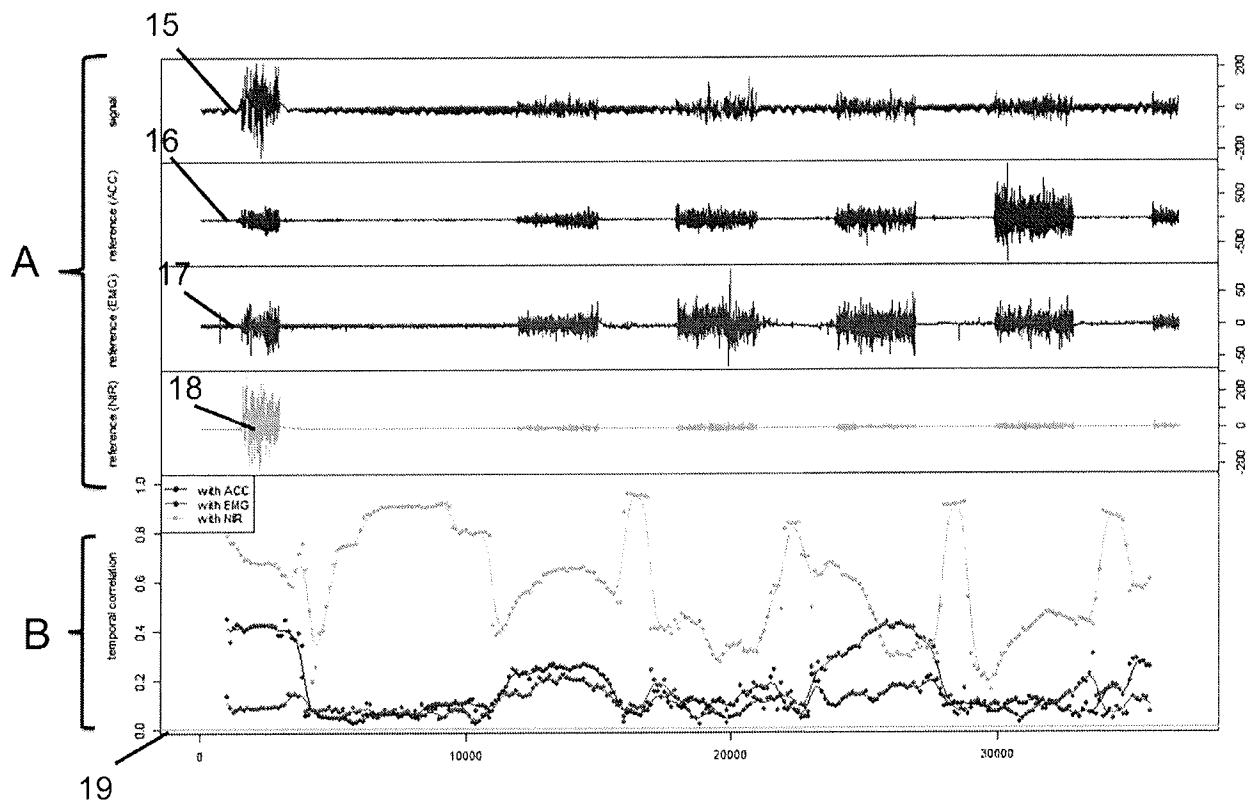


Figure 4

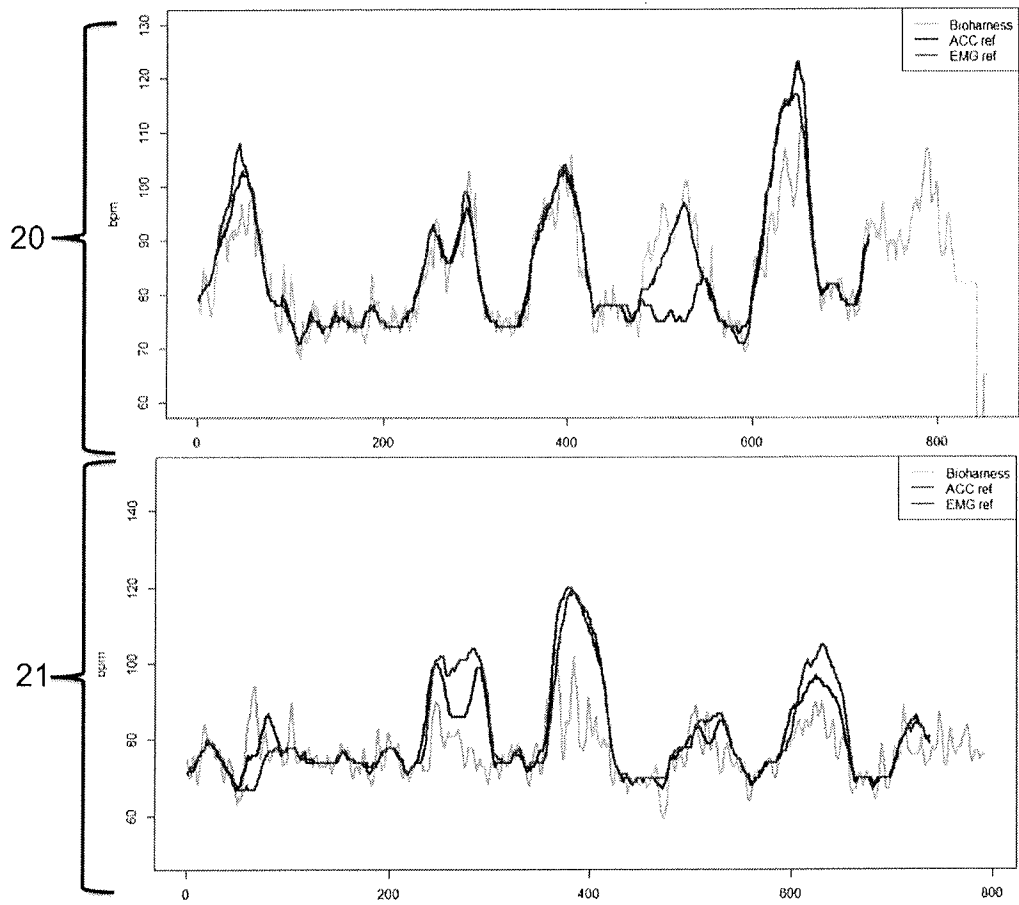


Figure 5

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US15/40543

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61B 5/04, 5/0488 (2015.01)

CPC - A61B 5/04, 5/0488, 5/04886

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(8): A61B 5/04, 5/0488 (2015.01)

CPC: A61B 5/04, 5/04004, 5/0488, 5/04886, 5/72, 5/721, 5/7214, 5/7239

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 practicable, search terms used)

PatSeer (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC Data); Google/Google Scholar; IP.com; PubMed/MEDLINE; physiolo\*, heartrate\*, heart rate\*, photoplethys\*, PPG\*, BCG\*, ECG\*, surface electromyo\*, EMG\*, sEMG\*, motion\*, artifact\*, raw\*, signal\*.

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y	US 2014/0094675 A1 (LUNA, M et al.) April 3, 2014; abstract; figures 2, 7-8; paragraphs [0017], [0034], [0044]-[0045], [0048]-[0049], [0051]	1, 3-4, 6-9, 11-12, 14-15, 17-21 -- 2, 5, 10, 13, 16
Y	US 2010/0113960 A1 (SCHEIB, C) May 6, 2010; abstract; paragraph [0063]	2, 10
Y	US 5630425 A (PANESCU, D et al.) May 20, 1997; abstract	5, 13
X -- Y	US 2004/0073098 A1 (GEVA, A et al.) April 15, 2004; abstract; paragraphs [0017], [0021], [0029], [0033]	1, 9 -- 16
A	WO 2012/061707 A2 (THE CLEVELAND CLINIC FOUNDATION) May 10, 2012; entire document	1-21
A	US 2011/0028823 A1 (GILMORE, LD et al.) February 3, 2011; entire document	1-21
A	US 2003/0125635 A1 (MAALOUF, KJ et al.) July 3, 2003; entire document	1-21
A	US 2007/0129915 A1 (BLOMBERG, U et al.) June 7, 2007; entire document	1-21
A	US 7433718 B2 (MANABE, H et al.) October 7, 2008; entire document	1-21
A	US 6224549 B1 (DRONGELEN, WV) May 1, 2001; entire document	1-21

 Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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	

Date of the actual completion of the international search

21 September 2015 (21.09.2015)

Date of mailing of the international search report

13 OCT 2015

Name and mailing address of the ISA/

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents  
P.O. Box 1450, Alexandria, Virginia 22313-1450  
Facsimile No. 571-273-8300

Authorized officer

Shane Thomas

PCT Helpdesk: 571-272-4300  
PCT OSP: 571-272-7774