(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 November 2007 (15.11.2007)

PCT

(10) International Publication Number
WO 2007/131064 A2

(51) International Patent Classification:
A61B 5/04 (2006.01)

(21) International Application Number:
PCT/US2007/068071

(22) International Filing Date: 2 May 2007 (02.05.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/796,527 2 May 2006 (02.05.2006) US

(71) Applicant *(for all designated States except US)*: **PHYSIOSTREAM, INC.** [US/US]; 75 Fifth Street, NW, Suite 234, Atlanta, GA 30308 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **CHRONOS, Nicholas** [US/US]; 75 Fifth Street, NW Suite 234, Atlanta, GA 30308 (US). **PAPADOPOULOS, Rom** [US/US]; 75 Fifth Street, NW, Suite 234, Atlanta, GA 30308 (US). **CLIFFORD, Gari, D.** [GB/US]; 75 Fifth Street, NW, Suite 234, Atlanta, GA 30308 (US).

(74) Agents: **HILTEN, John, S.** et al.; Mcguirewoods Llp, 1750 Tysons Boulevard, Suite 1800, Mclean, VA 22102-4215 (US).

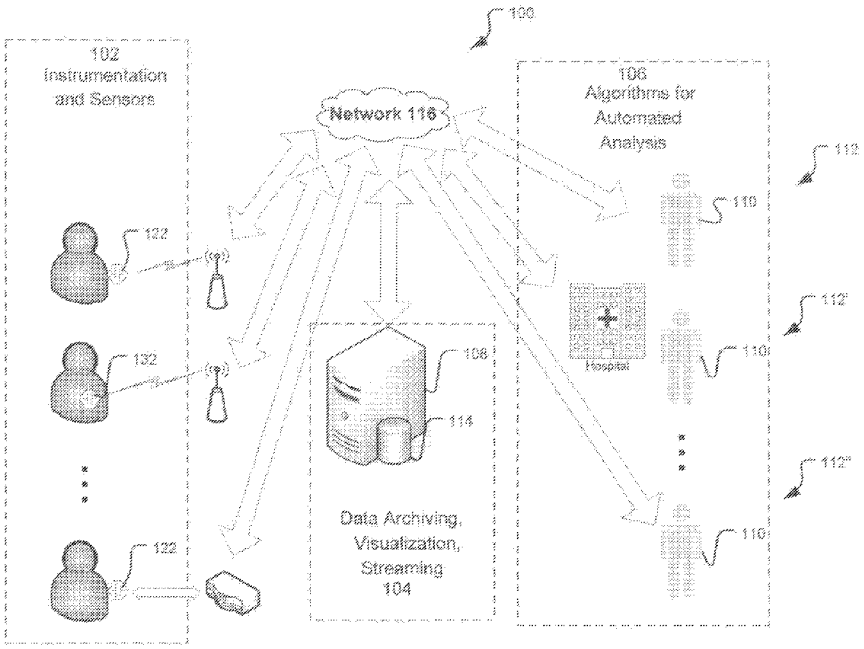
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,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

Published:
— *without international search report and to be republished upon receipt of that report*

[Continued on next page]

(54) **Title:** COLLECTION AND ANALYSIS OF PHYSIOLOGICAL DATA



(57) **Abstract:** A device and process for the collection and analysis of physiological data includes obtaining physiological data concerning at least one subject from at least one sensor, transmitting the physiological data to a centralized location, and streaming the physiological data from the central location to at ieast two remote locations, and analyzing the physiological data with at least one algorithm during, prior to, and/or subsequent to the one or more of the obtaining, streaming, and analyzing steps.

WO 2007/131064 A2

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

COLLECTION AND ANALYSIS OF PHYSIOLOGICAL DATA

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority under 35 U.S.C. §119(e) to provisional U.S. Patent Application No. 60/796,527, filed on May 2, 2006 the disclosure of which is expressly incorporated by reference herein in its entirety.

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0002] The invention is directed to a method and system for improving the effectiveness, efficiency, and economics of the collection and analysis of physiological data for subject monitoring and, more particularly, to improving the efficacy of pre-clinical, clinical trials and the efficiency of diagnostics and disease management through the automation of long-term, real-time physiological data mining and trend analysis.

2. Related Art

[0003] Currently, the collection and analysis of physiological data requires the use of high cost data acquisition with sensors and systems. These sensors and systems have a limited capacity, yet generate very high volumes of sensor data. There is also significant manual cleaning and/or manipulation of the data generated by such sensors and systems that is required before effective use of the data can be made. Such manual cleaning results in low throughput, short-term, retrospective studies and diagnostics of the data. Moreover, this manual cleaning is very labor intensive and requires various known manual analysis processing techniques. This resulting database cleaning is typically carried out by a single user, single sight type architecture. The result is a very limited monitoring window (limited amount of monitoring time) of physiological data. Such limited monitoring is prone to missing prior or subsequent events of interest.

[0004] One example of a specific application of requiring collection and analysis in the monitoring of patients for use in the studies related to the development of new drugs. More specifically, the development of new drugs by the pharmaceutical industry is a costly and lengthy process, with the time from concept to final product typically lasting ten years. Perhaps the most critical stage of this process is the phase one study, where the drug is administered to humans for the first time. During

this stage, each subject is carefully monitored for any unexpected adverse effects that may be brought about by the drug. Of particular interest is the electrocardiogram (ECG) of the patient, which provides detailed information about the state of the patient's heart. By examining the ECG signal in detail, it is possible to derive a number of informative measurements from the characteristic ECG waveform. These characteristics can then be used to assess the medical well-being of the patient, and more importantly, detect any potential side effects of the drug on the patient's cardiac rhythm. The most important of these measurements is the QT interval. In particular, drug-induced prolongation of the QT interval can result in a very fast, abnormal heart rhythm known as *torsade de pointes*, which is often followed by sudden cardiac death.

[0005] In practice, QT interval measurements are carried out manually by trained ECG analysts. This is an expensive and time-consuming process, which is susceptible to mistakes by the analysts and provides no associated degree of confidence (or accuracy) in the measurements. This problem was highlighted in the case of the antihistamine terfenadine, which has the side-effect of significantly prolonging the QT interval in a number of patients. Unfortunately, this side-effect was not detected in the clinical trials and only came to light after a number of people had unexpectedly died while taking the drug.

[0006] Numerous other physiological signals are in need of better monitoring including neural activity, blood pressure, central venous pressure, pulmonary arterial pressure, pulse oximetry (SAO2), cardiac sounds, non-cardiovascular signals such as EEG K-complexes, muscular activity, acoustic waveforms, and speech waveforms.

[0007] Accordingly, there is a need to improve the effectiveness, efficiency and economics of the collection and analysis of the physiological data, as well as, to improve the efficacy of pre-clinical, clinical trials and the efficiency of diagnostics with automated long-term, real-time physiological data mining and trend analysis.

SUMMARY OF THE INVENTION

[0008] Accordingly, the invention provides a low cost sensor and/or data acquisition system together with a very high throughput, high capacity data acquisition, storage, and automated analysis system, which provides for long-term, real-time studies and diagnostics that may include multiple-site web access for visualization, analysis, and

collaboration. The sensors may be implantable, wearable, and/or on the surface of the skin.

[0009] The invention may be implemented in a number of ways.

[0010] According to one aspect of the invention a system for the collection and wherein analysis of physiological data includes a computer system configured to receive physiological data obtained via one of a wearable sensor and an implantable sensor from a network, a storage device configured to archive the physiological data, and the computer system is configured to stream the physiological data over the network to a plurality of locations for the collaborative analysis thereof.

[0011] The computer system and/or a processor may be configured to execute an algorithm to analyze the physiological data. The sensor may be structured and arranged to sense at least one of blood pressure, central venous pressure, pulmonary arterial pressure, pulse oximetry (SAO2), cardiac sounds, non-cardiovascular signals such as EEG K-complexes, muscular activity, neural activity, acoustic waveforms, and speech waveforms. The physiological data may include an ECG, and the system further may include a processor to generate a nonlinear signal model based on the ECG signal, fit the nonlinear signal model to the ECG signal based on an optimization algorithm, and determine at least one feature of the ECG with the nonlinear signal model, and an output device to output the at least one feature of the ECG based on the nonlinear signal model. The computer system may be configured to receive physiological data from a plurality of wearable sensors and/or implantable sensors from the network. The computer system may include a platform, such as a Hermes™ platform. The storage may include a redundant array of independent disks. The sensor may transmit the physiological data to the computer system via one of a wired connection and a wireless transceiver. The physiological data may include physiological data from one of a human and an animal.

[0012] According to another aspect of the invention a process for the collection and analysis of physiological data includes the steps of obtaining physiological data concerning at least one subject from at least one sensor, transmitting the physiological data to a centralized location, streaming the physiological data from the central location to at least two remote locations, and analyzing the physiological data with at least one algorithm during, prior to, and/or subsequent to the one or more of the obtaining, streaming, and analyzing steps.

[0013] The process may include the step of analyzing the data at one of the plurality of locations. The transmitting step may include transmitting the physiological data from a sensor via at least one of wireless transmission and wired transmission. The obtaining step may include obtaining the physiological data from at least one of implantable sensor and a wearable sensor. The process may include the step of archiving the physiological data at the centralized location. The process may include the step of visualizing the physiological data at the central location. The process may include the step of enabling for the collaborative interaction of a plurality of physicians or analysts at a plurality of locations. The subject may be one of a human and an animal. The physiological data may include an ECG, the process further may include the steps of generating a nonlinear signal model based on the ECG signal, fitting the nonlinear signal model to the ECG signal based on an optimization algorithm, determining at least one feature of the ECG with the nonlinear signal model, and outputting the at least one feature of the ECG based on the nonlinear signal model.

[0014] According to yet another aspect of the invention a system for the collection and analysis of physiological data includes means for receiving physiological data obtained via one of a wearable sensor and an implantable sensor from a network, means for storing and archiving the physiological data, and means for streaming the physiological data over the network to a plurality of locations for the collaborative analysis thereof.

[0015] According to an aspect of the invention a computer readable medium having instructions stored thereon that when executed by a processor operates to provide for the collection and analysis of physiological data includes instructions for obtaining physiological data concerning at least one subject from sensors, instructions for transmitting the physiological data to a centralized location, instructions for streaming the physiological data from the central location to at least two remote locations, and instructions for analyzing the physiological data with at least one algorithm during, prior to, and/or subsequent to the one or more of the obtaining, streaming, and analyzing.

[0016] Additional features, advantages, and embodiments of the invention may be set forth or apparent from consideration of the following detailed description, drawings, and claims. Moreover, it is to be understood that both the foregoing summary of the invention and the following detailed description are exemplary and

intended to provide further explanation without limiting the scope of the invention as claimed.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] The accompanying drawings, which are included to provide a further understanding of the invention, are incorporated in and constitute a part of this specification, illustrate embodiments of the invention and together with the detailed description serve to explain the principles of the invention. No attempt is made to show structural details of the invention in more detail than may be necessary for a fundamental understanding of the invention and the various ways in which it may be practiced. In the drawings:

[0018] Figure 1 schematically illustrates a system for the collection and analysis of physiological data constructed according to the principles of the invention;

[0019] Figure 2 is a flowchart schematically illustrating the collection and analysis of physiological data according to the principles of the invention;

[0020] Figure 3 is a flowchart schematically illustrating a generalized exemplary analysis method for constructing a model fit signal according to the principles of the invention, which may be used with the system of Figure 1;

[0021] Figure 4 shows an original (clean) graphed ECG signal, a model fit signal constructed according to the principles of the invention and the residual error between the two signals;

[0022] Figure 5 shows a model fit to an ECG signal using the principles of the invention under high noise conditions. The underlying signal before noise was added and is shown. Note that the model fit preserves the overall morphology and placement of the onset and offset of the main features;

[0023] Figure 6 shows a ST-elevated waveform and model fit constructed according to the principles of the invention; and

[0024] Figure 7 shows a typical ECG with labels relevant to QT analysis.

DETAILED DESCRIPTION OF THE INVENTION

[0025] The embodiments of the invention and the various features and advantageous details thereof are explained more fully with reference to the non-limiting embodiments and examples that are described and/or illustrated in the accompanying drawings and detailed in the following description. It should be noted that the features illustrated in the drawings are not necessarily drawn to scale, and

features of one embodiment may be employed with other embodiments as the skilled artisan would recognize, even if not explicitly stated herein. Descriptions of well-known components and processing techniques may be omitted so as to not unnecessarily obscure the embodiments of the invention. The examples used herein are intended merely to facilitate an understanding of ways in which the invention may be practiced and to further enable those of skill in the art to practice the embodiments of the invention. Accordingly, the examples and embodiments herein should not be construed as limiting the scope of the invention, which is defined solely by the appended claims and applicable law. Moreover, it is noted that like reference numerals represent similar parts throughout the several views of the drawings.

[0026] Figure 1 schematically illustrates a system for the collection and analysis of physiological data constructed according to the principles of the invention. In particular, a system 100 and associated process may include a combination of instrumentation and sensors 102; data archiving, visualization, and streaming 104; and algorithms for automated analysis 106, each discussed in greater detail below. More specifically the instrumentation and sensors 102 may include wearable and implantable sensor technology. This sensor technology may include wired or wireless type transmission of sensor data. The data archiving, visualization, and streaming 104 may allow for the data acquisition from the sensors that may be digitized, stored, and streamed to remote archiving, analysis servers. Finally, the algorithms for automated analysis 106 may include the capability to analyze data automatically and may further include the capability to have the data reviewed by one or more clinicians via internet or other type of network.

[0027] The instrumentation and sensors 102 of the invention may include wearable devices 122 such as a holter monitor as is known in the art to permit continuous long-term subject monitoring. The holter monitor is also referred to as an ambulatory electrocardiography device that may be a portable device and may allow for continuous monitoring of the heart for up to or more than 24 hours. The holter monitor may include a series of electrodes and may provide recording of the output of the electrodes to a flash memory or the like.

[0028] The sensors noted above may also be implantable 132. The sensor may be implanted and may contain a self-sufficient energy source, such as a battery. The battery may have the ability to be recharged subcutaneously. In another embodiment, the sensor may contain a radio frequency responsive and/or powered circuit energy source. Such sensors allow for ECG monitoring, autonomic

monitoring, peripheral nerve monitoring, systemic glucose monitoring and so on. The implantable type sensors 132 are configured to be small and operate subcutaneously. The implantable type sensor 132 may have a non-invasive arrangement. Both the wearable 122 and implantable sensors 132 provide a robust event monitoring analysis with real-time data capture and streaming. The implantable sensor 132 may have a self-contained form factor, multi-modal sensor and/or analysis capability, and allow for longitudinal data analysis. Both types of sensors may include a housing, memory, operating circuitry, a battery and other components known in the art. The sensors may also be implemented as battery-less sensors that receive power through inductive type circuits. Furthermore, in order to provide wireless transmission of the data, the sensors may include a transceiver and the like. The sensor, may include various input/output connections and the like.

[0029] In particular, the sensor technology used in conjunction with the invention may sense any type of physiological phenomena including electrical, acoustic, vibratory and so on. In particular, any known sensor technology may be used in conjunction herewith, although it is preferred to use electrical sensing sensors.

[0030] A sensor may be used to measure any physiological signal, and, for example, may include blood pressure, central venous pressure, pulmonary arterial pressure, pulse oximetry (SAO2), cardiac sounds, non-cardiovascular signals such as EEG K-complexes, muscular activity, neural activity, acoustic waveforms, and speech waveforms.

[0031] Such types of sensors may include the ability to automatically detect events and transmit data, and may further include real-time data streaming. The data transmission may include transmission directly from a patient's device to an analysis platform by a cellular data network. The platform, as described in greater detail below, may include one or more of a software application, operating system, and hardware. The transmission may include any known protocol including GPRS, EVDO, UNTS, Wimax, WiFi, Bluetooth or the like.

[0032] The data archiving visualization and streaming system 104 may provide for the long-term physiological collection and analysis of the data collected by the instrumentation and sensors 102 noted above. In particular, the data archiving, visualization, and streaming system 104 may allow for the collection, formatting, storage, visualization, automated analysis, annotation, event detection and the like of the physiological data collected by the instrumentation and sensors 102.

[0033] The data archiving, visualization and streaming system 104 may include a platform 108 allowing for the high-speed, high-throughput, multi-channel data collection from the instrumentation and sensors 102. For example, collection may be carried out over, in part, the internet or other type of data transmission network 116. Moreover the platform 108 may allow for efficient high-volume formatting of the data and RAID-based (RAID-Redundant Array of Independent Disks) storage 114 for multiple-user, multiple-site access and archiving. Moreover, the platform 108 may allow for local or remote retrospective or real-time graphical visualization using such processes as a web server process. Additionally, the platform 108 may allow for single or multiple users 110 (collaborative), multiple location annotation of the data. Finally, the platform 108 may include various event detections such as heart rate detection for notification and alarming. The collaborative web-based technology model enables collection of physiological data and analysis of results at many different locations 112, 112', 112". Moreover, the above-described model may allow for a simple existing web-browsing technology for visualization, analysis, and annotation of data. This model as described above may enable a number of remote users 110 to collaborate simultaneously. Additionally, the model allows for a centralized database storage 114 instead of replication at multiple user sites.

[0034] The platform 108 may also allow for real-time streaming of physiological data from a large number of remote sensors. The sensors being one or more sensors described above or others as are well known in the art. The platform further may allow for the use of screening algorithms. The screening algorithms may be able to quickly highlight areas of interest in the data that is held by the data archiving, visualization, and streaming platform 108 that was obtained through the instrumentation and sensors 102. The platform may provide a very high volume of capture, storage, and screening of incoming sensor data for automated, long-term testing. One example of a data archiving, visualization, and streaming platform that may be used in the invention is known in the art as a Hermes™ type platform that includes Hermes™ servers, operating system, and so on. The Hermes™ platform may be provided by Hermes Medical Solutions, Inc. Chicago, Illinois, U.S.A. The Hermes™ platform 108 may include any type of processor such as a PC or server, storage system such as a RAID level one (mirror) configuration or the like. The Hermes™ system may further include any form of seamless network integration.

[0035] The algorithms for automated analysis 106 may include any known type of analysis that is algorithm-based or otherwise. In one particular aspect, the analysis

may include an ECG-type analysis as discussed in greater detail below. However, the invention contemplates any type of automated analysis whether based on an algorithm or otherwise. Moreover, the invention contemplates analysis of any type of physiological data including blood pressure, central venous pressure, pulmonary arterial pressure, pulse oximetry (SAO2), cardiac sounds, non-cardiovascular signals such as EEG K-complexes, muscular activity, neural activity, acoustic waveforms, speech waveforms, and so on.

[0036] Figure 2 is a flow chart schematically illustrating the collection and analysis of physiological data process according to the principles of the invention. In particular, Figure 2 shows a collection and analysis process 200 that may be performed by the system 100 in Figure 1 or any other equivalent type system or arrangement.

[0037] In step 202, various targets of interest are provided with wearable type sensor arrangements or implantable type sensor arrangements or other sensors known in the art. The sensors providing sensor output as noted above. The wireless type sensors may output to a wireless access point, cellular tower or the like. The wired type sensors may be configured to connect to some form of network type connection such as the Internet.

[0038] Thereafter, as shown in step 204 the data that is acquired from the targets of interest may then be transmitted over a network such as the Internet to a data archiving, visualization, and streaming type platform 108. In the platform, the data which is the output from the sensors may be archived and stored in a large database, it also may be modified to provide an additional level of analysis and reporting such as a visual imaged-based report.

[0039] Next, in step 206 the data may be streamed to other locations. The other location can include one or more remote or local medical facilities, physicians, analysts, clinicians, and the like. Further the data archiving, data visualization, streaming platform or the various medical analysts may then be able to further apply an algorithm or other type of analysis to the data as shown in step 208. Finally, the various physicians and analysts and the like may then further collaborate together with the information obtained as described above.

[0040] The flowchart of Figure 3 shows a generalized exemplary analysis method for constructing a model according to the invention. In particular, the method of the invention provides a general framework for deriving models of quasi-stationary signals for robust filtering, compression and segmentation of a signal and for

identifying the location of regions of change. As such, the method can be viewed as a type of novel adaptive filter or as a method for correlated source separation in the time domain. In particular, the approach is suited to physiological signals, which are often characterized by oscillations at specific frequencies, and contaminated by in-band noise (which is both periodic and statistical). This approach is set forth in greater detail in copending United Patent Application No. 11/470,506, METHOD AND DEVICE FOR FILTERING, SEGMENTING, COMPRESSING AND CLASSIFYING OSCILLATORY SIGNALS, by Gari D. Clifford, the disclosure of which is incorporated by reference herein in its entirety.

[0041] The assumption in the following method is that the time series under analysis is composed of a set of distinct, yet transient (although not necessarily independent) morphologies. Examples of these include the set of features used to classify sleep from the electroencephalogram, (such as K complexes and sleep spindles), the heart sounds recorded in the phonocardiogram, or the waves in a pulsatile blood pressure waveform. Once a set of general features is identified, a template of each feature may be formed and a mixture of temporally shifted basis functions (such as Gaussians) may be fitted to each major turning point in the signal using an optimization procedure.

[0042] The signal model is a dynamic model, where each turning point in a signal is represented by a Gaussian of varying width and amplitude, centered at different points in time. This novel implementation extends the model by adding a new Gaussian for each asymmetric turning point, then adaptively modifying the parameters to fit a distinct observation. Here, the concept is generalized to model any signal and provide an automatic method for deriving the mode parameters.

[0043] If we assume a transient feature (such as a K complex) is smoothly varying and composed of M symmetric and N asymmetric turning points, then M + 2N Gaussians are required to describe the feature (since a Gaussian is symmetric). For example, an asymmetric turning point requires two Gaussians to be accurately represented. The segment of the signal z, which describes the feature under analysis is given by:

$$z = \sum_{i=1}^{M+2N} k \exp\left(\Delta t_i^2 / 2b_i^2\right) + z_i t \quad (1)$$

where $\Delta t_i = (t - t_i)$, is the relative position of each turning point from the location in time t, of a reference point (fiducial marker), $\kappa = a_i/2b_i$ is a normalization constant (chosen for consistency with the original dynamic model), and the z_i are baseline offset

parameters for each of the turning points. The coefficients a_i govern the magnitude of the turning points and the b_i define the width (time duration) of each turning point. The model is therefore fully described by 3(M + 2N) parameters.

[0044] In order to fit Equation (1) to a feature, an approximate template must be constructed. A general method for this is to apply a coarse matched filter (such as cross correlation with a population independent general template) or an energy thresholding technique (which is common in ECG analysis) to the signal in question. The selection of one technique for this process over another depends on the distribution of the energy of the observation over time. If the signal energy is evenly distributed over time, some a priori knowledge of the features may be used to form a simple template for a matched filter.

[0045] Fiducial markers may then be located at various points in time that provide time-specific reference markers for each candidate feature (segment of signal) as shown in step 302 of Figure 3. By segmenting the time series around each fiducial point, and performing a temporal average, a first template class is generated as shown by step 304. By comparing each candidate feature to the first template class, possible artifacts or patterns belonging to other feature classes may be rejected using a suitable threshold such as a cross-correlation as shown in step 306.

[0046] The first feature class may then be modified to be the average of the non-rejected individual features (to construct a more specific feature). The rejected candidate may then be averaged to form a second feature class template and the process repeated (see arrows A and B) until the number of possible remaining candidates (which were not included in the previous classes) are below some pre-defined threshold, or the inter-pattern variance between the remaining candidate patterns becomes too high to allow the formation of any more distinct groups.

[0047] In the case of an ECG, the first feature class is likely to be a sinus beat (as long as it is the dominant morphology in the time series). Abnormal beats may be rejected and the dominant abnormal beat may become the second feature class. High correlations between the average of this rejected set and each member of the set may identify the new members of the set. Rejected beats may cascade down to the next candidate class.

[0048] For each template class, an initial model must then be derived. The model order O = M + 2N, the number of symmetric plus twice the number of asymmetric turning points in the class. Often, this is a known quantity for most physiological

features, but in some circumstances, an unsupervised method for determining the model order is required.

[0049] One method is as follows: if there are enough feature candidates to form a smooth, low noise template, the number of turning points may be calculated by numerically differentiating the feature and locating the zero crossing points (after allowing for delays in the numerical differentiation function) as shown in step 308.

[0050] The degree of asymmetry for each turning point may then be found by squaring the resultant differential and comparing the resultant two peaks (one for the upslope and one for the downslope) as shown in step 310. If a given pair of peaks are similar in height and width, then the peak is symmetric and only one set of a_i, b_i, and t_i are required for the peak. If the peaks in the squared differential, for a given pair, differ sufficiently (by some predefined threshold that depends on the feature class and signal amplitudes) then the peak is deemed asymmetric and two Gaussians are required to describe the turning point.

[0051] It should be noted that this procedure effectively determines the approximate starting points for fitting the model to each feature candidate (see step 312). However, the height (a_i) and width (b_i) of each Gaussian in the initial model remain to be determined. For most applications, (as long as the t_i are initially limited so that they do not vary significantly) the initialization of the a_i and b_i do not affect the final outcome, and random small values are sufficient. However, in some situations, abnormal local minima in the model fitting procedure are possible and the use of an estimate of the width and height of the turning points not only helps to avoid this, but also allows a significant acceleration in the time for fitting each feature candidate.

[0052] The residual error between the result of the model fitting procedure (described below) and the original feature provides a facility to reject particular fits as shown in step 314. It should also be noted that a classification may be performed by initializing with each possible class (variant of the model) and picking the class with the minimum residual error, or the smallest distance (in parameter space) between a given fit and a cluster center of representative candidates in the same parameter space.

[0053] An efficient method of fitting the signal model (Equation (1)) to a candidate vector s(t), is to minimize the squared error between **s** and the model output, **z**. In other words, one should find

$$\varepsilon_r = \min_{a_i, b_i, \theta_i} \left\| s(t) - z(t) \right\|_2^2$$

over all of the 3(M + 2N) parameters in the model. Equation (1) may be solved using an (3M + 6N)-dimensional nonlinear gradient descent on the parameter space. In general, the problem of multidimensional nonlinear least squares fitting requires the minimization of the squared residuals of n functions, f_j, in p parameters, x_j,

$$\Phi(x) = (1/2)\sum_{j=1}^{n} f_j(x_1,...,x_p)^2$$

$$= (1/2)\|F(x)\|^2$$

all algorithms for achieving the minimization may proceed from an initial guess using the linearization,

$$\psi(p) = \|F(x+p)\| \approx \|F(x) + Jp\|$$

where x is the initial point, p is the next step and J is the Jacobian matrix $J_{jk} = df_j / dx_k$. Additional strategies can be used to enlarge the region of convergence and include requiring a decrease in the norm ||F|| on each step or using a trust region to avoid steps that fall outside the linear regime. This procedure has been implemented in two different libraries: the Gnu Scientific Libraries (GSL) in C, and in Matlab using the function lsqnonlin.

[0054] In one specific application, the invention may be applied in a novel technique for fitting a nonlinear ECG model (a sum of temporally shifted Gaussian waveform morphologies) to the ECG using a nonlinear least squares optimization. Figure 4 illustrates the performance of the fitting procedure for a typical ECG with no noise in the original signal. Figure 3 illustrates the performance of the technique when fitting the model to an extremely noisy beat. Not only does the technique allow a powerful method for filtering the ECG on a beat-by-beat basis even in high noise conditions, but also the use of Gaussian descriptors allows for a statistically meaningful description of wave onset and offset. In particular, this model-fitting procedure provides an excellent method for Q-wave onset and T-wave offset localization.

[0055] The model-based fitting of an ECG allows one to more precisely determine the locations of the P, Q, R, S and T features of each beat, and their respective onsets and offsets (determined as a certain number of standard deviations away from the central point). Furthermore, since noise may not be explicitly encoded in the waveform, the fitting procedure makes for an excellent noise suppression technique. Although the representation of the beat as just 18 coefficients in a nonlinear model means that (lossy) compression is possible, the clustering of these coefficients allows

one to classify beats on this basis. However, perhaps the most useful and immediate application of this model-fitting procedure is in the determination of wave boundaries in noisy conditions to allow robust and accurate QT analysis.

[0056] Accordingly, by fitting a modified version of the model to each beat, and constraining the fit with a time averaged template, a filtering of each beat is performed. The model consists of a sum of Gaussians centered on each wave of the ECG (P, Q, R, S, and T). Each Gaussian is fully specified by three parameters: location in time, amplitude, and broadness. Therefore, the representation of the ECG as a series of Gaussians is also a form of (lossy) compression. Finally, the parameters for each beat may be compared to a normal set of parameters and a classification made.

[0057] Another way to apply the above-noted approach is to describe each feature of the ECG (PQRS & T) by a Gaussian with three parameters: the amplitude a_i, width b_i, and phase $\theta_i = 2\pi/t_i$ (or relative position with respect to the R-peak). The vertical displacement of the ECG, z, is described by an ordinary differential equation,

$$\dot{z}(a_i, b_i, \theta_i) = -\sum_{i\in\{P,Q,R,S,T^-,T^+\}} a_i \Delta\theta_i e^{\frac{-\Delta\theta_i^2}{2b_i^2}} \qquad (3)$$

where $\Delta\theta_i = (\theta - \theta_i)$ is the relative phase. Note that no z -offset exists as the model-fit assumes z=0 at the isoelectric level. Numerical integration of this equation using appropriate set of a_i, b_i, θ_i leads to the familiar ECG waveform.

[0058] Furthermore, an optional extra parameter has been added to the T feature, denoted by a superscripted - or +, to indicate that they are located at values of θ (or t) slightly either side of the original θ_i. By using two sets of { a_i, b_i, θ_i } to represent a particular feature, an asymmetric turning point may be formed. Although this is particularly important for the T-wave on the ECG, it is of negligible importance for the other four features in the ECG. Therefore, six features may be required for the ECG: P, Q, R, S, T^-, T^+.

[0059] Again, an efficient method of fitting the ECG model described above to an observation s(t), is to minimize the squared error between the s(t) and z. That is, one may find

$$\min_{a_i,b_i,\theta_i} \|s(t) - z(t)\|_2^2 \qquad (4)$$

over all six i, with $t_i = 2\pi/\theta_i$. Fortunately, one may analytically integrate (3) to give $\hat{z}(a_i, b_i, t_i) = \sum 2a_i \Delta\theta_i \exp\left(-\theta_i^2 / 2b_i^2\right)$. Equation (4) may then be solved using an eighteen-dimensional gradient descent in the parameter space. The Matlab function lsqnonlin.m or the like may perform the required implementation of this nonlinear least squares optimization.

[0060] To minimize the search space for fitting the parameters (a_i, b_i, and θ_i), a simple peak-detection and time-aligned averaging to form an average beat morphology template is formed over, for example, at least the first 60 beats centered on their R-peaks. (The template window is unimportant, as long as it contains all the PQRST features and does not extend into the next beat). Cross correlation is then performed between each beat and the template to remove outliers (with a linear cross-correlation coefficient less than, for example, 0.95). If more than about 20% of the beats are removed, then another 60 beats may be allowed into the average template, and the outlier rejection procedure is re-iterated. When less than about 20% of the beats are discarded, another average template is then made of the remaining beats. Peak and trough detection is then performed on this template (using refactory constraints for each wave) to find the relative locations of the turning points in time (and hence the θ_i). The values T^- and T^+ may be initialized $\pm$ 40 ms either side of θ_T. By measuring the heights of each peak (or trough) an estimate of the a_i may also be made. Each b_i may be initialized with a value $10 + 5\mu$, where μ is a uniform distribution on the interval [0, . . . , 1]. Each of the values, a_i, and θ_i, were initialized with random perturbations of μ and 20μ respectively.

[0061] Note that it is important that salient features that one wishes to fit (the P-wave and QRS segment in the case of the ECG) are sampled at a high enough frequency to allow them to contribute sufficiently to the optimization. In empirical tests, it has been found that all ECGs below approximately 512 Hz required upsampling (with an appropriate antialiasing filter). This corresponds to about 30 sample points in the QRS complex. Using less than 30 samples in a wave may lead to some extremely bizarre fits that fulfill the optimization criteria.

[0062] Figure 4 shows an original (clean) graphed ECG signal, a model fit signal constructed according to the invention and the residual error between fit and model

signals. In particular, Figure 4 illustrates a real beat (recorded from a V5 lead), a typical fit to a template of real beat, and the residual error.

[0063] Figure 5 illustrates the results of fitting the model to a segment of ECG cleanly recorded and contaminated by electrode motion noise. Note that despite the significant waveform distortion, the locations of the P, Q, R, S, and T peaks match the underlying (uncorrupted signal) to sub-sample precision, even with (F_s > 1 kHz). Note also that the error around the iso-electric point and ST-level are negligible in a clinical sense (< 0.1 mV, or about 5% to 10% of the QRS amplitude for a sinus beat on a V5 lead) (Amplitudes have been scaled by an arbitrary, but consistent factor).

[0064] Filtering of the ECG by fitting equation 3 to small segments of the ECG around each QRS-detection fiducial point is an excellent way to provide an idealistic (zero-noise) representation of the morphology that captures much of the clinical information of that beat. In fact, this approach may be generalized to any band-limited waveform with fewer than F_s oscillations per sample. In particular, the signal we are representing does not need to be periodic and is therefore particularly suited to physiological signals. Since the model is a compact representation of oscillatory signals with few turning points compared to the sampling frequency, it therefore has a band pass filtering effect leading to a lossy transformation of the data into a set of integrable Gaussians distributed over time.

[0065] It should be noted that that the fitting procedure effects a (lossy) compression at a rate of $(\frac{F_s}{3k}:1)$ per beat or $(\frac{\overline{RR}}{3}\frac{F_s}{3k}:1)$, where $\overline{RR}$ is the reciprocal of the (average) heart rate, F_s is the sampling frequency, and k = n + 2m is the number of features or turning points used to fit the heart beat morphology (with n symmetric and m asymmetric turning points). For a low ECG sampling rate of 128 Hz, this translates into a compression ratio greater than 7:1 at a heart rate of 60 bpm. However, for high sampling rates (F_s = 1024) this may lead to compression rates of almost 57:1. Reducing k from the full representation of k=18 is often appropriate for tasks which require only the QRS complex (k = 9) or the ST segment (k=12) to be analyzed. High heart rates may reduce this compression unless the dynamic properties of the model are used to encode the heart rate-dependent variations through dynamic shifts in the values of the a_i, b_i, and θ_i. For a given segment of τ

seconds with an average heart rate of $\frac{60}{RR}$, the compression ratio rises by a factor $\frac{\tau}{RR}$.

[0066] The above model is just an approximation and therefore the compression becomes even more lossy. One should also note that no explicit accounting of abnormal beats has been made in these calculations and a new set of parameters must be derived, possibly for each new abnormal beat encountered in the ECG record.

[0067] The above-described method for simultaneously filtering, compressing, and classifying a physiological signal, such as the ECG, from a subject may work in real time on a modern desktop PC and the like. The PC may execute a signal processing program such as Matlab™ (Available from: The MathWorks, Inc., Natick, MA 01760-2098) or the like to perform the above-noted method as is known in the art. By fitting a set of six Gaussians, each specified by three parameters in an ordinary differential equation, and performing a constrained nonlinear optimization, it has been shown that in-band noise may be removed. One advantage of using prior knowledge concerning beat morphology is that a fitting error may be calculated with respect to the model, and thus we have an in-line measure of how well the procedure has filtered the ECG segment. By measuring the distance between the fitted parameters and pre-trained clusters in the 18-dimensional parameter space, classification is possible.

[0068] It should be noted that the real test of the filtering properties is not the residual error, but how distorted the clinical parameters of the ECG (such as the ST-level and QT interval) really are and whether they cause an abnormal beat to be erroneously classified as a normal beat. The methods of the invention produce insignificant distortion in clinical parameters for high levels of noise. For instance the model-based filter may introduce insignificant clinical distortion in the QT interval and QRS width down to an SNR ≥ 0dB for 1/f^Beta noise for Beta < 2. The fiducial point location may be insignificantly distorted (< 1 ms) for an SNR ≥ 2dB, and the ST-level may be stable down to SNR > 12dB. The PR-interval may be more sensitive to noise due to the low amplitude nature of the P-wave, but still robust to noise. In general, the filter performance may be degraded by increasing Beta.

[0069] The method of producing confidence intervals for a particular fit, or classification is an important step in determining the performance of a particular

algorithm. In-line methods such as these may facilitate the robust interpretation of data and algorithms, reducing the number of false alarms that are triggered. In particular, the smooth nature of the fitted waveform allows for simple and robust detection of clinical features such as the iso-electric point, QT-interval, and ST level. The residual error from the fitting procedure then provides a confidence measure for the model-derived values of these features.

[0070] The above-described model has been generalized to allow modeling of turning points that exhibit asymmetries (such as the T-wave) by allowing such a feature to be described by two Gaussians. The model as such, may now be used to represent any waveform. However, the model complexity increases considerably for stochastic processes that inherently have many fluctuations compared to the sampling frequency. The main utility of the method detailed herein lies in the fact that the model represents smooth oscillations with few turning points compared to the sampling frequency, and therefore has a morphology-specific multi-band pass filtering effect leading to a lossy transformation of the data into a set of integrable Gaussians distributed over time. Each clinical feature of the ECG waveform is represented by a known and limited set of parameters. This allows for a very compact representation of the ECG morphology and makes the description mathematically tractable and completely generalizable to any semi-periodic signal.

[0071] Testing of the invention has resulted in accurate QT interval estimates. In contrast, it has been found that ECG analysts consistently pick the T offset to be early, since the analysts are unable to discern T-wave ends from the noise in the data. Accordingly, adaptation of the Gaussian model-based algorithm to locate Q-onset and T-offset points in a robust fashion, allows an accurate method for QT interval measurement, even in high noise situations.

[0072] It is further contemplated that the invention may utilize extra information with 12 leads with the use of a multi-channel QT analysis system, with noise rejection using Independent Component Analysis, Principal Component Analysis and Frank lead reconstruction (using the (inverse) Dower transform). By determining the noise content of each lead and using these dimensionality reduction techniques, the sensitivity of QT analysis to varying levels and types of noise may be evaluated, to provide a principled on-line confidence index for each QT interval evaluation. The relationship between the QT interval, preceding and following RR intervals, and other ECG model parameters (P, Q, R, S, and T amplitude and duration) such as U wave

detection and characterization, T-wave height, and T-wave asymmetry are also contemplated by the invention.

[0073] The algorithm and analytic framework discussed above may also be adapted in the following ways:

-if Bi-phasic QRS complex and P waves are employed, two Gaussians can be used either when there is a substantial asymmetry (skew greater than a given lead dependent threshold for the P wave or T wave) or when there are two significant peaks for each conventional point (P, Q, R, S, T, or U).

-The asymmetry of each wave (T in particular) may be well modeled by a log-normal distribution. Therefore, other embodiments of this approach may consider log-normal distributions also. Disadvantages exist in that the probabilistic interpretation is not so well defined, but there are fewer parameters to fit.

-QT interval determination may be made using probabilities - as well as using the zero-gradient criterion, to more accurately mimic the more conservative human tendency to under-estimate the end of repolarization using the M-sigma point of the two Gaussians in the T wave. This may be calculated using (for N Gaussians):

mu_T = a_(N-1)*mu_(N-1)+a_N*mu_N

sigma_T = (a_(N-1)^2*sig_(N-1)^2 + a_N^2*sig_N^2)^1/2.

and the end of the T wave is taken to be mu_T+M*sigma_T, where M=2 for most leads, but can take other values.

-More sensitive QT analysis is also possible with the model of the invention. There may be considerable overlap in QT/QTc between normal and non-normal patient groups. See e.g., "The Spectrum of Symptoms and QT Intervals in Carriers of the Gene for the Long-QT Syndrome," G. M. Vincent, K. W. Timothy, M. Leppert, M. Keating, N Engl J Med. 1992; 327: 846–852. More sensitive measures of other repolarization-related properties may be used to reveal a more sensitive metric for classifying patients as normal or not normal, including:

- Measure of T-wave amplitude or relative T-wave amplitude (such as the R-peak divided by T-wave peak height);
- Asymmetry of the T-wave (such as the skewness of the jT segment);
- Length of the jT segment (as measured by the 2 sigma point defined above: sigma_T = (a_(N-1)^2*sig_(N-1)^2 + a_N^2*sig_N^2)^1/2.
- Peakiness of the T-wave (such as the kurtosis of the jT segment).

-Short QT syndrome (SQTS) leads to an abbreviated QTc interval and predisposes patients to life-threatening arrhythmias. To date, three forms of the

disease have been identified: SQT1, caused by a gain of function substitution in the HERG (IKr) channel, SQT2, caused by a gain of function substitution in the KvLQT1 (Iks) channel, and, SQT3, which has a unique ECG phenotype characterized by asymmetrical T waves. See, e.g. "A Novel Form of Short QT Syndrome (SQT3) Is Caused by a Mutation in the KCNJ2 Gene," Silvia G. Priori, Sandeep V. Pandit, Ilaria Rivolta, Omer Berenfeld, Elena Ronchetti, Amit Dhamoon, Carlo Napolitano, Justus Anumonwo, Marina Raffaele di Barletta, Smitha Gudapakkam, Giuliano Bosi, Marco Stramba-Badiale, and José Jalife, Circ. Res. 96: 800-807. Therefore, the above discussion of height, skew, width and kurtosis variables as above may be used in a SQTS application to help improve the sensitivity of short QT analysis significantly.

-QTd (QT dispersion) is defined as the difference between the maximum and minimum QT intervals of any of 12 leads. QTd is sometimes thought to be a marker of myocardial electrical instability and has been proposed as a marker of the risk of death for those awaiting heart transplantation. See e.g., "Development of Automated 12-Lead QT Dispersion Algorithm for Sudden Cardiac Death," M. B. Malarvili, S. Hussain, Ab. Rahim Ab. Rahman, The Internet Journal of Medical Technology, 2005, Volume 2 Number 2. In a similar way to QT intervals, QTd takes a Gaussian histogram of values for a particular population. There is a significant cross-over between normal and those at risk of sudden cardiac death (SCD). The mean value of QTd±1SD is 37.28 ± 11.13ms ($p < 0.05$) for a non-MI group and 66.17 ± 13.95ms ($p < 0.05$) for the MI group. With QTd < 50ms is the threshold for normality, but this would lead to 20-30% of the normals being classified as MI and ~20% being classified as non-MI. Using the height, skew, width and kurtosis variables as above would improve the sensitivity significantly.

[0074] The algorithm and analytic framework discussed above may also be used to perform very sensitive analysis of any feature of an ECG, including to:

- filter ECGs
- compress ECGs for efficient storage, transmission, and reconstruction
- perform P-wave detection (and hence atrial beat/rhythm classification)
- perform amplitude and QRS axis analysis (for deriving respiration)
- perform beat classification (from clustering the parameters)
- perform robust QT interval analysis
- perform robust ST-segment analysis
- perform PQRST subtraction for high frequency QRS analysis for diagnosis of ischemic heart disease, respiration related issues, and the like

- perform PQRST subtraction for late potential analysis
- perform T-wave alternan classification
- perform rhythm analysis

[0075] In accordance with various embodiments of the invention, the methods described herein are intended for operation with dedicated hardware implementations including, but not limited to, PCs, PDAs, semiconductors, application specific integrated circuits (ASIC), programmable logic arrays, and other hardware devices constructed to implement the methods described herein. Moreover, various embodiments of the invention described herein are intended for operation as software programs running on a computer processor. Furthermore, alternative software implementations including, but not limited to, distributed processing, component/object distributed processing, parallel processing, virtual machine processing, any future enhancements, or any future protocols thereof may also be used to implement the methods described herein.

[0076] It should also be noted that the software implementations of the invention as described herein are optionally stored on a tangible storage medium, such as: a magnetic medium such as a disk or tape; a magneto-optical or optical medium such as a disk; or a solid state medium such as a memory card or other package that houses one or more read-only (non-volatile) memories, random access memories, or other re-writable (volatile) memories. A digital file attachment to email or other self-contained information archive or set of archives is considered a distribution medium equivalent to a tangible storage medium. Accordingly, the invention is considered to include a tangible storage medium or distribution medium, as listed herein and including art-recognized equivalents and successor media, in which the software implementations herein are stored.

[0077] While the invention has been described in terms of exemplary embodiments, those skilled in the art will recognize that the invention can be practiced with modifications in the spirit and scope of the appended claims. These examples given above are merely illustrative and are not meant to be an exhaustive list of all possible designs, embodiments, applications, or modifications of the invention. For example, the invention may fit a set of alternate basis functions to the signal, perhaps using some other form of optimization; may use other signals other than physiological signals; may use any set of basis functions, not just Gaussians; may use any optimization routine to fit the basis functions to the observation – least squares, nonlinear least squares, gradient descent with any cost function and any

activation function (such as tanh or softmax in a neural network). Moreover, IIR/FIR filters, Independent Component Analysis (ICA); Principal Component Analysis (PCA) / Singular Value Decomposition (SVD) / Karhunen Loeve Transform (KLT) / Hotelling Transform; Auto-Regressive (AR) modeling – equivalent to Fourier Transform; and Wavelet Analysis (Laguna et al, Hughes et al.) approaches may also be used for further pre-processing or post-processing.

WHAT IS CLAIMED:

1. A system for the collection and analysis of physiological data comprising:

a computer system configured to receive physiological data obtained via one of a wearable sensor and an implantable sensor from a network;

a storage device configured to archive the physiological data; and

said computer system being configured to stream the physiological data over the network to a plurality of locations for the collaborative analysis thereof.

2. The system according to claim 1 wherein one of said computer system and a processor is configured to execute an algorithm to analyze the physiological data.

3. The system according to claim 1 wherein said sensor is structured and arranged to sense at least one of blood pressure, central venous pressure, pulmonary arterial pressure, pulse oximetry (SAO2), cardiac sounds, non-cardiovascular signals such as EEG K-complexes, muscular activity, neural activity, acoustic waveforms, and speech waveforms.

4. The system according to claim 1 wherein the physiological data comprises an ECG, the system further comprising:

a processor to generate a nonlinear signal model based on the ECG signal, fit the nonlinear signal model to the ECG signal based on an optimization algorithm, and determine at least one feature of the ECG with the nonlinear signal model; and

an output device to output the at least one feature of the ECG based on the nonlinear signal model.

5. The system according to the claim 1 wherein said computer system is configured to receive physiological data from a plurality of wearable sensors and/or implantable sensors from the network.

6. The system according to the claim 1 wherein said computer system comprises a platform.

7. The system according to the claim 6 wherein said platform comprises a Hermes platform.

8. The system according to claim 1 wherein said storage comprises a redundant array of independent disks.

9. The system according to claim 1 wherein the sensor transmits the physiological data to said computer system via one of a wired connection and a wireless transceiver.

10. The system according to claim 1 wherein the physiological data comprises physiological data from one of a human and an animal.

11. A process for the collection and analysis of physiological data comprising the steps of:

obtaining physiological data concerning at least one subject from at least one sensor;

transmitting the physiological data to a centralized location;

streaming the physiological data from the central location to at least two remote locations; and

analyzing the physiological data with at least one algorithm during, prior to, and/or subsequent to the one or more of the obtaining, streaming, and analyzing steps.

12. The process according to claim 11 further comprising the step of analyzing the data at one of the plurality of locations.

13. The process according to claim 11 wherein the transmitting step comprises transmitting the physiological data from a sensor via at least one of wireless transmission and wired transmission.

14. The process according to claim 11 wherein the obtaining step comprises obtaining the physiological data from at least one of implantable sensor and a wearable sensor.

15. The process according to claim 11 further comprising the step of archiving the physiological data at the centralized location.

16. The process according to claim 11 further comprising the step of visualizing the physiological data at the central location.

17. The process according to claim 11 further comprising the step of enabling for the collaborative interaction of a plurality of physicians or analysts at a plurality of locations.

18. The system according to claim 11 wherein the subject is one of a human and an animal.

19. The process according to claim 11 where the physiological data comprises an ECG, the process further comprising the steps of:

generating a nonlinear signal model based on the ECG signal;

fitting the nonlinear signal model to the ECG signal based on an optimization algorithm;

determining at least one feature of the ECG with the nonlinear signal model; and

outputting the at least one feature of the ECG based on the nonlinear signal model.

20. A system for the collection and analysis of physiological data comprising:

means for receiving physiological data obtained via one of a wearable sensor and an implantable sensor from a network;

means for storing and archiving the physiological data; and

means for streaming the physiological data over the network to a plurality of locations for the collaborative analysis thereof.

21. A computer readable medium having instructions stored thereon that when executed by a processor operates to provide for the collection and analysis of physiological data comprising:

instructions for obtaining physiological data concerning at least one subject from at least one sensor;

instructions for transmitting the physiological data to a centralized location;

instructions for streaming the physiological data from the central location to at least two remote locations; and

instructions for analyzing the physiological data with at least one algorithm during, prior to, and/or subsequent to the one or more of the obtaining, streaming, and analyzing steps.

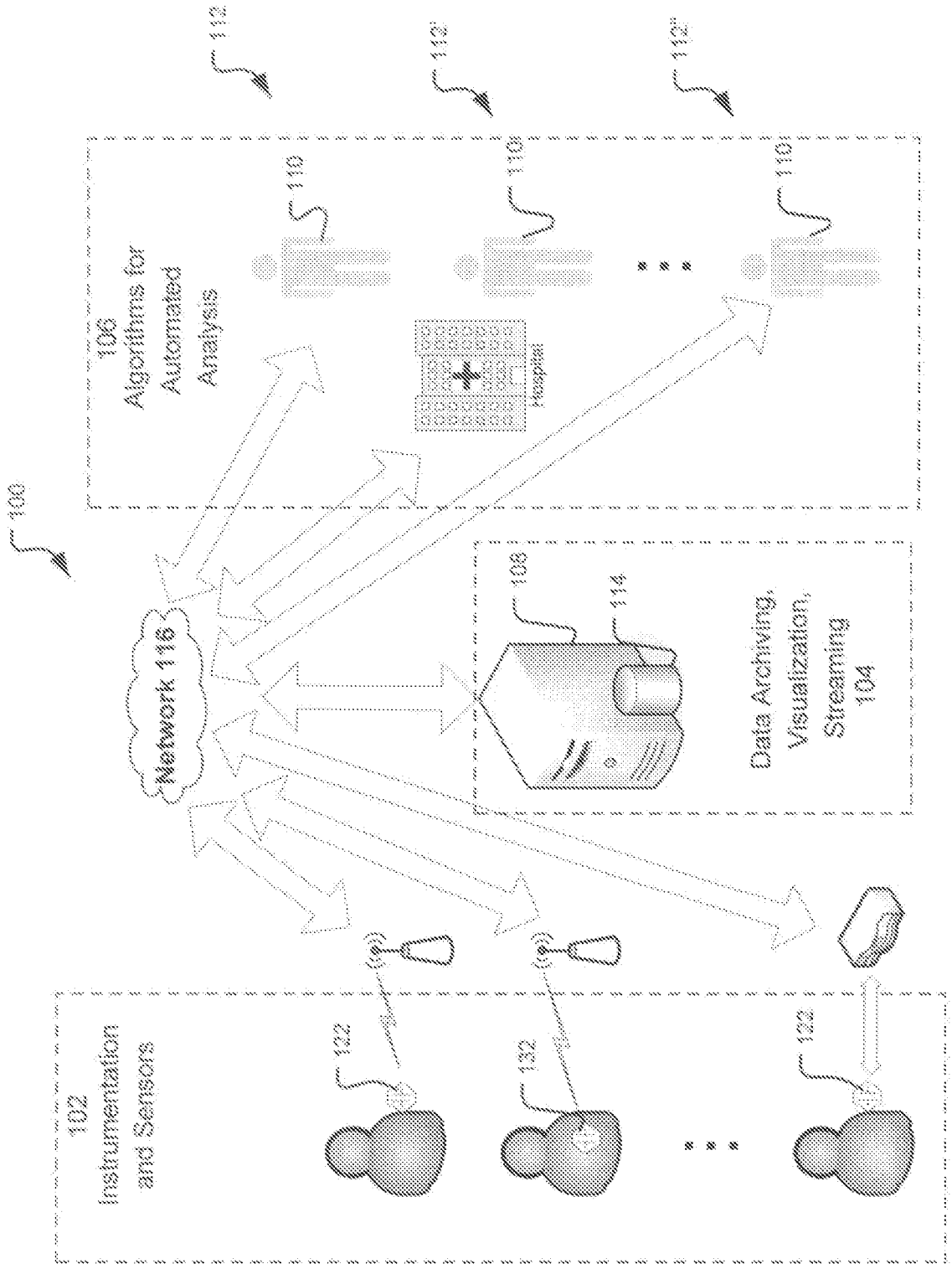

100
102
Instrumentation
and Sensors
122
132
122
Network 116
106
Algorithms for
Automated
Analysis
110
110'
110"
Hospital
112
112'
112"
108
114
Data Archiving,
Visualization,
Streaming
104

FIGURE 1

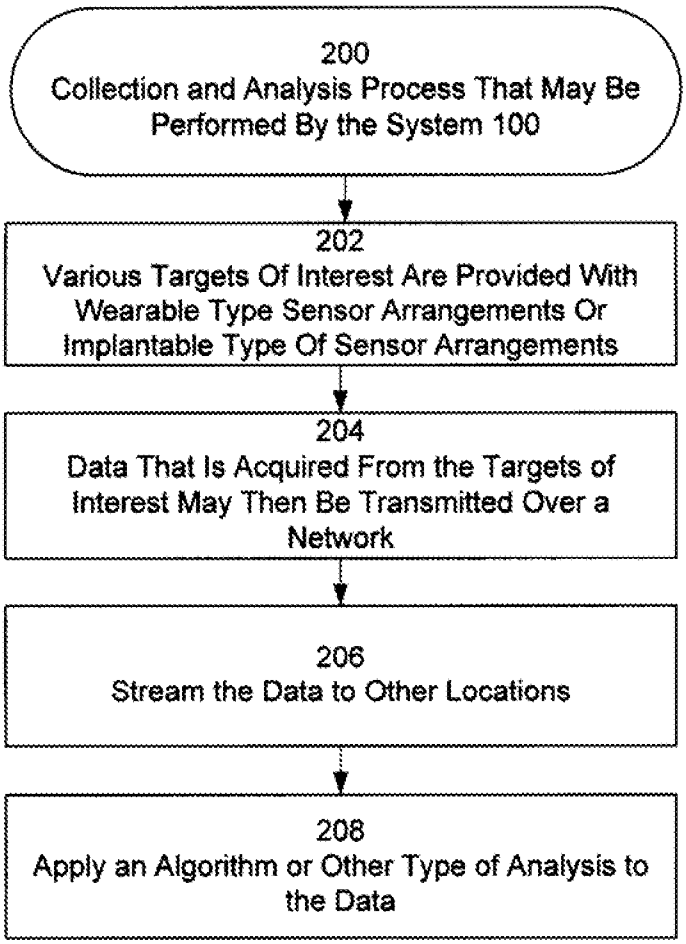

200
Collection and Analysis Process That May Be Performed By the System 100
202
Various Targets Of Interest Are Provided With Wearable Type Sensor Arrangements Or Implantable Type Of Sensor Arrangements
204
Data That Is Acquired From the Targets of Interest May Then Be Transmitted Over a Network
206
Stream the Data to Other Locations
208
Apply an Algorithm or Other Type of Analysis to the Data

FIGURE 2

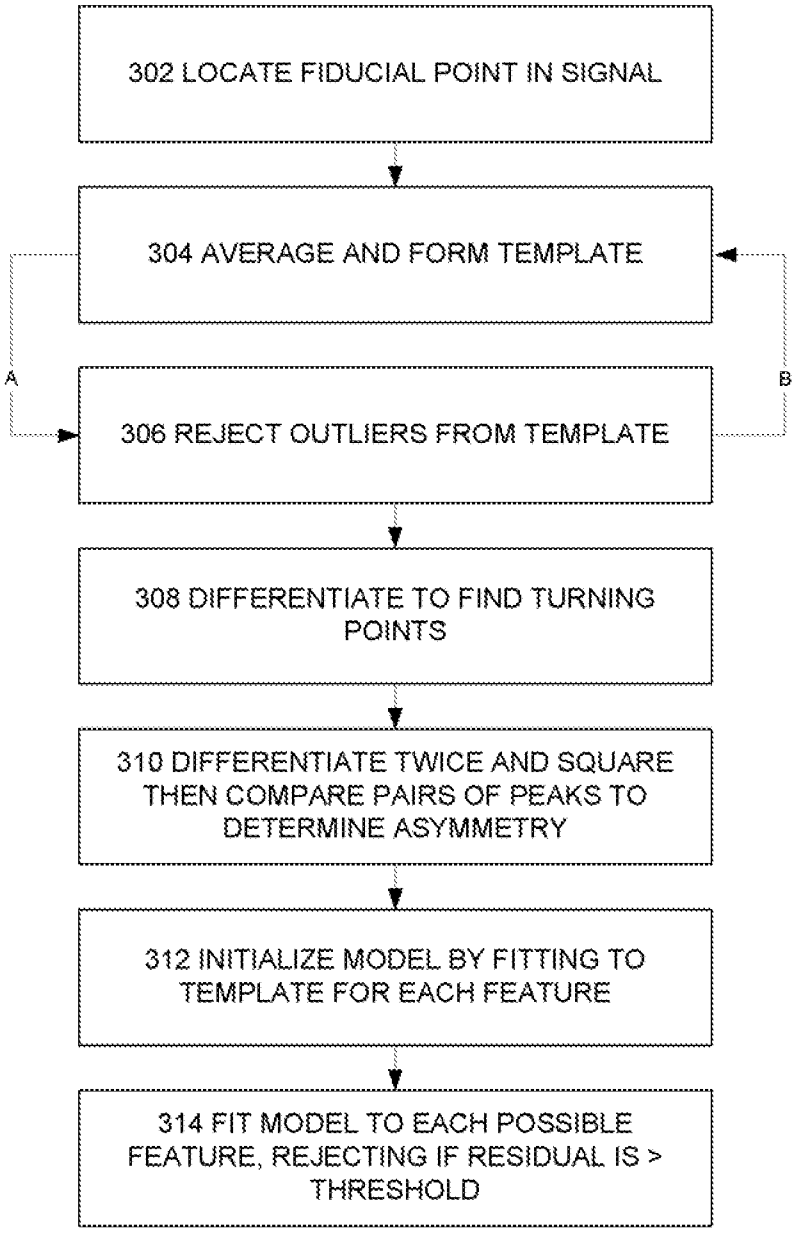

302 LOCATE FIDUCIAL POINT IN SIGNAL
304 AVERAGE AND FORM TEMPLATE
A
B
306 REJECT OUTLIERS FROM TEMPLATE
308 DIFFERENTIATE TO FIND TURNING POINTS
310 DIFFERENTIATE TWICE AND SQUARE THEN COMPARE PAIRS OF PEAKS TO DETERMINE ASYMMETRY
312 INITIALIZE MODEL BY FITTING TO TEMPLATE FOR EACH FEATURE
314 FIT MODEL TO EACH POSSIBLE FEATURE, REJECTING IF RESIDUAL IS > THRESHOLD

FIGURE 3

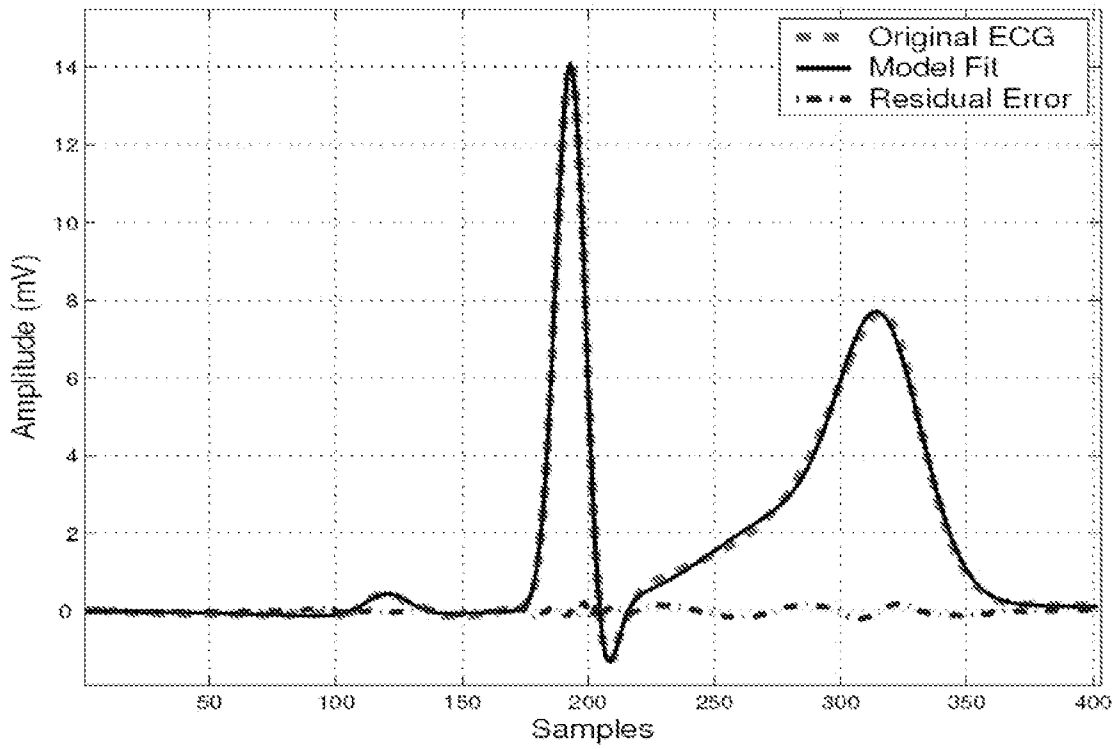

Original ECG
Model Fit
Residual Error
Amplitude (mV)
Samples
0
2
4
6
8
10
12
14
50
100
150
200
250
300
350
400

FIGURE 4

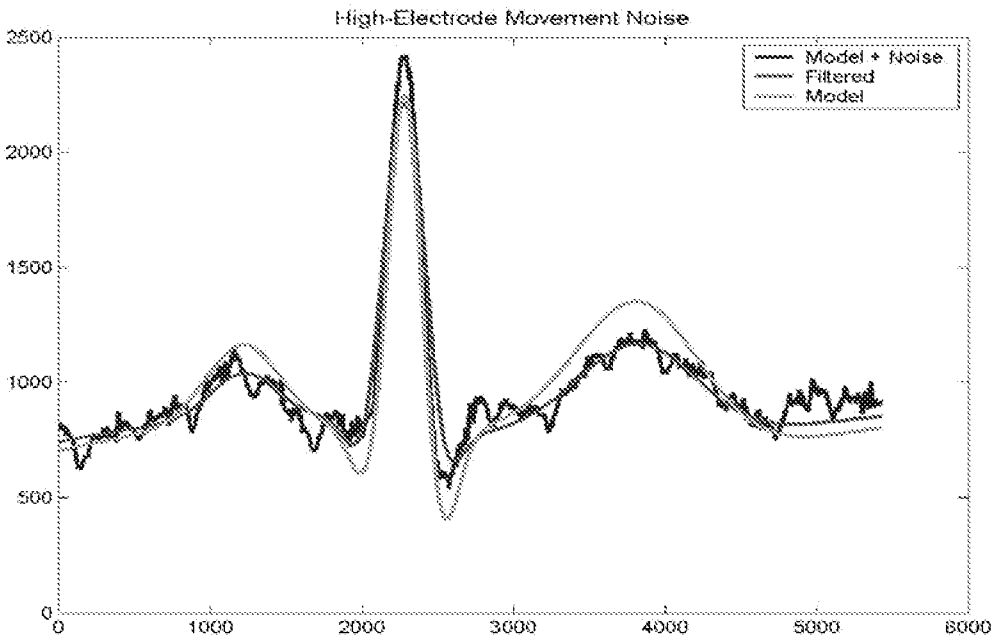

High-Electrode Movement Noise
Model + Noise
Filtered
Model
2500
2000
1500
1000
500
0
0
1000
2000
3000
4000
5000
6000

FIGURE 5


ST-Elevation Fit
data1
Model
Original
2500
2000
1500
1000
500
0
500
1000
1500
2000
2500

FIGURE 6

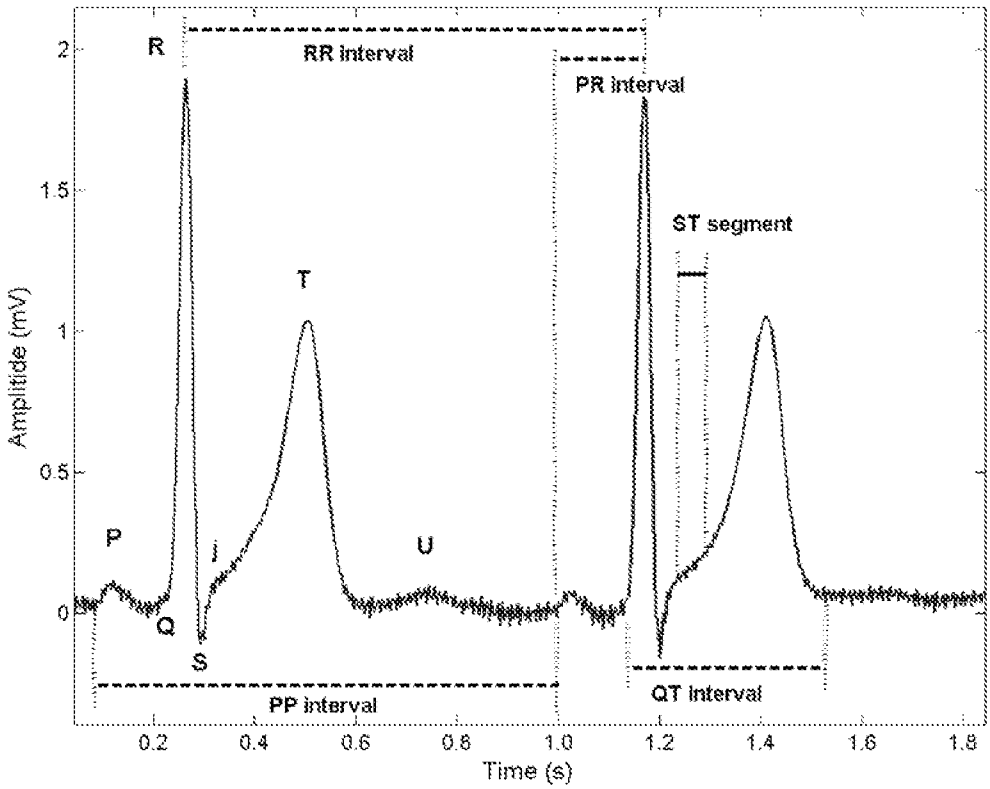

R
RR interval
PR interval
ST segment
T
P
Q
S
j
U
PP interval
QT interval
Amplitide (mV)
Time (s)
2
1.5
1
0.5
0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8

FIGURE 7