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(71) Applicant *(for all designated States except US)*: **WIDEMED LTD.** [IL/IL]; P.O. Box 12117, 46733 Herzlia (IL).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **TODROS, Koby** [IL/IL]; 79/2 Atad Street, 84847 Beer Sheva (IL). **AMOS, Yariv** [IL/IL]; 14 Hartzfeld Street, 55560 Kiryat Ono (IL). **CHENISKY, Roman** [IL/IL]; 18 Amos De-Shalit Street, 84836 Beer Sheva (IL). **ZONANS, Tomer** [IL/IL]; 22 Dov Gruner Street, 69498 Tel Aviv (IL). **GEVA, Amir** [IL/IL]; 134 Hashalom Street, 85025 Meitar (IL). **REISFELD, Daniel** [IL/IL]; 12 Meir Margalit Street, 69401 Tel Aviv (IL).

(74) Agents: **SANFORD T. COLB & CO.** et al.; P.O. Box 2273, 76122 Rehovot (IL).

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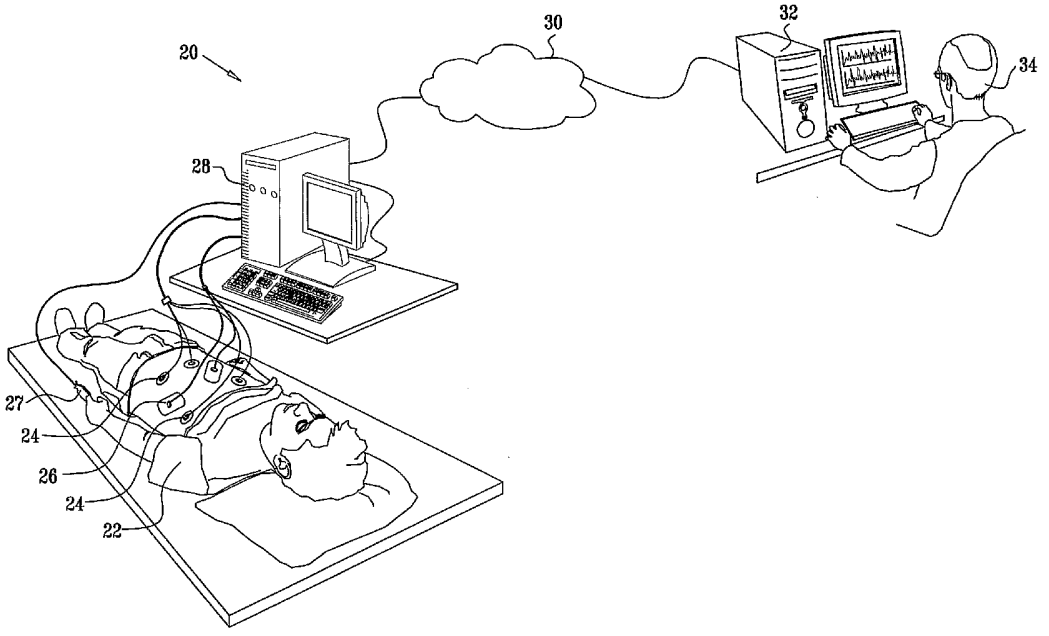

(57) Abstract: A method for diagnosis of a sleep-related condition of a patient. The method includes receiving physiological signals from sensors (24, 26, 27) coupled to the lower body of the patient, and analyzing the physiological signals, independently of any electroencephalogram (EEG) or electro-oculogram (EOG) signals, in order to identify sleep stages of the patient.

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SLEEP STAGING BASED ON CARDIO-RESPIRATORY SIGNALS

CROSS-REFERENCE TO RELATED APPLICATION

This application is a Continuation-In-Part of U.S. Patent Application 10/995,817, filed November 22, 2004. This application is also related to U.S. Patent Application 10/677,176, filed October 2, 2003 (published as US 2004/0073098 A1), and to PCT Patent Application PCT/IL2004/000412, filed May 15, 2003. All of these related applications are assigned to the assignee of the present patent application, and their disclosures are incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates generally to physiological monitoring and diagnosis, and specifically to sleep recording and analysis.

BACKGROUND OF THE INVENTION

Human sleep is generally described as a succession of five recurring stages (plus waking, which is sometimes classified as a sixth stage). Sleep stages are typically monitored using a polysomnograph to collect physiological signals from the sleeping subject, including brain waves (EEG), eye movements (EOG), muscle activity (EMG), heartbeat (ECG), blood oxygen levels (SpO2) and respiration. The commonly-recognized stages include:

- Stage 1 sleep, or drowsiness. The eyes are closed during Stage 1 sleep, but if aroused from it, a person may feel as if he or she has not slept.
- Stage 2 is a period of light sleep, during which the body prepares to enter deep sleep.
- Stages 3 and 4 are deep sleep stages, with Stage 4 being more intense than Stage 3.
- Stage 5, REM (rapid eye movement) sleep, is distinguishable from non-REM (NREM) sleep by changes in physiological states, including its characteristic rapid eye movements.

Polysomnograms show brain wave patterns in REM to be similar to Stage 1 sleep. In normal sleep, heart rate and respiration speed up and become erratic, while the muscles may twitch. Intense dreaming occurs during REM sleep, but paralysis occurs simultaneously in the major voluntary muscle groups.

Although sleep staging is most often performed by a human operator, who reads and scores the polysomnogram, there are also methods known in the art for computerized sleep staging. Penzel et al review such methods in "Computer Based Sleep Recording and

Analysis," *Sleep Medicine Reviews* **4**:2 (2000), pages 131-148, which is incorporated herein by reference. According to this article, the minimum requirements for digital polysomnography as a basis for automatic sleep scoring include measurement of EEG, EOG and EMG, along with respiratory, cardiovascular and movement-related parameters.

Although automated sleep-staging is typically based primarily on analysis of the EEG signal, ECG analysis is frequently used along with the EEG to provide complementary information. For example, Telser et al. describe a method for detecting sleep transitions using ECG signals in "Can One Detect Sleep Stage Transitions for On-Line Sleep Scoring by Monitoring the Heart Rate Variability?" *Somnologie* **8** (2004), pages 33-41, which is incorporated herein by reference. The authors state that analysis of heart rate variability (HRV) can be used to distinguish NREM sleep from REM and wakefulness, but cannot distinguish between wakefulness and REM.

SUMMARY OF THE INVENTION

Embodiments of the present invention provide novel methods and systems for automated sleep staging, without dependence on electroencephalogram (EEG) or electro-oculogram (EOG) signals. In these embodiments, sleep staging is based on physiological signals provided by sensors that are coupled to points on the patient's lower body, i.e., the part of the body from the neck down, such as on the thorax or limbs. Typically, these signals indicate the heart rate and/or respiration rate. The signals are analyzed automatically in order to distinguish between wakefulness, REM sleep and NREM sleep, and possibly between light NREM and deep NREM sleep, as well.

Although EEG monitoring may be considered the "gold standard" of sleep staging, it is cumbersome, uncomfortable and difficult to perform. Therefore, sleep studies are usually performed in a sleep lab or other dedicated facility with EEG capabilities. The methods of the present invention alleviate the need for EEG monitoring in many cases. Therefore, in some embodiments, the principles of the present invention are implemented in a bedside sleep monitoring system, which may be used to collect signals from the patient's thorax during sleep in a home or hospital ward environment. The signals may be analyzed to determine the patient's sleep staging *in situ*, or they may alternatively be transmitted over a communication network for remote analysis. Alternatively or additionally, the methods of analysis described herein may be used in conjunction with a Holter monitoring system or with the telemetry capabilities of an implanted device, such as a pacemaker or intracardiac defibrillator (ICD).

In other embodiments, signal processing methods taught by the present invention may be used in conjunction with EEG and other monitoring modalities.

There is therefore provided, in accordance with an embodiment of the present invention, a method for diagnosis of a sleep-related condition of a patient, the method including:

receiving physiological signals from sensors coupled to a lower body of the patient; and

analyzing the physiological signals, independently of any electroencephalogram (EEG) or electro-oculogram (EOG) signals, in order to identify sleep stages of the patient.

In disclosed embodiments, analyzing the physiological signals includes detecting motion of the patient based on at least one of the physiological signals. Typically, the at least one of the physiological signals includes at least one of an electrocardiogram (ECG) signal, a respiration signal, a heart rate signal, and an oxygen saturation signal.

In some of these embodiments, detecting the motion includes measuring an energy of the at least one of the physiological signals in a selected frequency band as a function of time, finding a respective characteristic of the energy in each of a plurality of time segments, and determining the patient to have moved during one or more of the time segments responsively to the respective variance. Typically, finding the respective characteristic includes finding a respective variance of each of the time segments. Additionally or alternatively, finding the respective characteristic includes performing an adaptive segmentation in order to identify the time segments such that the energy of the at least one of the signals is quasi-stationary during each of the time segments.

Additionally or alternatively, detecting the motion includes identifying a desaturation event caused by the motion in the oxygen saturation signal.

Typically, analyzing the physiological signals includes distinguishing, responsively to detecting the motion, between a waking stage and a REM sleep stage.

In a disclosed embodiment, detecting the motion includes detecting two or more motion events within a time frame of a given length, and combining the two or more motion events into a single fused motion event. Detecting the two or more motion events may include identifying a first motion event responsively to one of the physiological signals, and a second motion event responsively to another of the physiological signals, wherein the first and second motion events overlap in time, and wherein combining the two or more motion events includes

fusing the first and second motion events. Alternatively or additionally, detecting the two or more motion events may include identifying first and second motion events occurring in succession and separated in time by no more than a predetermined duration, and wherein combining the two or more motion events includes fusing the first and second motion events. Further additionally or alternatively, detecting the motion includes determining an average measure of motion in each of a succession of uniform time epochs.

In some embodiments, analyzing the physiological signals includes performing an adaptive segmentation of at least one of the signals so as to identify time segments in which a characteristic of the at least one of the signals is quasi-stationary, and based on the adaptive segmentation, identifying transient events during which the characteristic of the at least one of the signals is not quasi-stationary. In one embodiment, analyzing the physiological signals includes determining at least one of the sleep stages to have been disturbed by occurrence of the transient events during the at least one of the sleep stages.

In some embodiments, analyzing the physiological signals includes detecting an arousal to a wake stage. In one of these embodiments, receiving the physiological signals includes determining a heart rate of the patient, and detecting the arousal includes identifying the arousal responsively to a change in the heart rate over time. In another embodiment, analyzing the physiological signals includes extracting complexity features from the physiological signals, and detecting the arousal includes identifying the arousal responsively to a change in the complexity features over time.

In disclosed embodiments, receiving the physiological signals includes receiving an electrocardiogram (ECG) signal. In some of these embodiments, analyzing the physiological signals includes measuring a variability of a heart rate of the patient responsively to the ECG signal, and identifying at least one of the sleep stages based on the variability. In one embodiment, identifying the at least one of the sleep stages includes computing a variance associated with the variability of the heart rate, and finding, responsively to the variance, a period during which the heart rate was decoupled from a respiratory function of the patient. Typically, identifying the period includes classifying the period as a REM sleep period.

Additionally or alternatively, identifying the at least one of the sleep stages includes measuring first and second energies respectively contained in first and second frequency bands of the variability of the heart rate during a selected epoch, and classifying the sleep stages responsively to a function of the first and second energies. Typically, the function includes a

ratio of the first and second energies. In one embodiment, the first and second frequency bands respectively include low and high frequency bands, and classifying the sleep stages includes distinguishing between light and deep sleep stages based on the function.

In another aspect of the invention, receiving the physiological includes receiving a respiration signal, and analyzing the physiological signals includes analyzing the respiration signal together with the ECG signal in order to identify the sleep stages. Alternatively, the method may include receiving a respiration signal from an airway of the patient, wherein analyzing the physiological signals includes analyzing the respiration signal together with the ECG signal in order to identify the sleep stages.

In some embodiments, receiving the physiological signals includes receiving a respiration signal. In a disclosed embodiment, analyzing the physiological signals includes evaluating a complexity of the respiration signal during a selected epoch, and identifying at least one of the sleep stages responsively to the complexity. Typically, evaluating the complexity includes quantizing and compressing the respiration signal, and measuring the complexity based on an efficiency of compression of the quantized respiration signal. Additionally or alternatively, identifying the at least one of the sleep states includes determining the patient to be in NREM sleep if the complexity is below a predetermined threshold.

In another embodiment, analyzing the physiological signals includes identifying a periodic respiration event, which includes a sequence of individual respiration events that are separated by time gaps whose respective durations are within predetermined limits. Additionally or alternatively, analyzing the physiological signals includes detecting a respiration event in the respiration signal, and identifying an onset of sleep responsively to the respiration event.

In a disclosed embodiment, analyzing the physiological signals includes constructing a hidden Markov model (HMM) having model states corresponding to the sleep stages, and identifying a state sequence in the model that accords with the physiological signals. Constructing the HMM may include associating the patient with a population, and training the HMM using data gathered from members of the population.

In a disclosed embodiment, receiving the physiological signals includes collecting the physiological signals at a bedside of the patient, and analyzing the physiological signals

includes transmitting the physiological signals over a communication network for processing by a diagnostic processor remote from the bedside.

In alternative embodiments, receiving the physiological signals includes collecting the physiological signals from a Holter monitor coupled to the patient, or collecting the physiological signals from a device implanted in the thorax of the patient.

There is also provided, in accordance with an embodiment of the present invention, a method for diagnosis of a sleep-related condition of a patient, the method including:

receiving at least one of an electrocardiogram (ECG) signal and a respiration signal from a sensor coupled to the patient during sleep;

measuring an energy of the at least one of the ECG and respiration signals in a selected frequency band as a function of time;

finding a respective characteristic of the energy in each of a plurality of time segments; and

determining the patient to have moved during one or more of the time segments responsively to the respective characteristic.

Typically, the respective characteristic includes a respective variance of the energy.

In disclosed embodiments, the method includes identifying a sleep stage of the patient during the one or more of the time segments responsively to determining the patient to have moved, wherein identifying the sleep stage includes distinguishing a REM sleep stage from a waking stage.

In an alternative embodiment, the method includes receiving an electroencephalogram (EEG) signal from the patient, wherein identifying the sleep stage includes processing the EEG signal together with the at least one of the ECG and respiration signals.

There is additionally provided, in accordance with an embodiment of the present invention, a method for diagnosis of a sleep-related condition of a patient, the method including:

receiving an electrocardiogram (ECG) signal from a sensor coupled to the patient during sleep;

measuring a variability of a heart rate of the patient responsively to the ECG signal;

computing a characteristic of the variability of the heart rate; and

finding, responsively to the characteristic, a period during which the heart rate was decoupled from a respiratory function of the patient.

Typically, the characteristic includes a variance associated with the variability of the heart rate.

There is further provided, in accordance with an embodiment of the present invention, a method for diagnosis of a sleep-related condition of a patient, the method including:

receiving a signal from a sensor coupled to the patient during sleep, wherein the signal is indicative of at least one of a heart rate and respiration activity of the patient;

evaluating a complexity of the signal during a selected time period; and

identifying a sleep stage of the patient responsively to the complexity.

In a disclosed embodiment, evaluating the complexity includes quantizing and compressing the signal, and measuring the complexity based on an efficiency of compression of the quantized signal. Typically, identifying the sleep stage includes determining the patient to be in NREM sleep if the complexity is below a predetermined threshold.

In another embodiment, evaluating the complexity includes computing a variability of the signal, and extracting a variance of the variability as a measure of the complexity.

In some embodiments, evaluating the complexity includes determining respective values of a set of complexity features in each of a succession of time segments, and identifying the sleep stage includes constructing a complexity feature matrix (CFM), which includes a sequence of feature vectors including the respective values of the complexity features in the succession of time segments, and processing the CFM in order to classify the complexity of the complexity features in each of the time segments. Optionally, processing the CFM includes assigning the patient to a population group, and processing the feature vectors using a probabilistic model of the population group. Typically, the probabilistic model includes a Gaussian mixture model. Additionally or alternatively, processing the CFM includes determining, responsively to the complexity of the complexity features, an average measure of the complexity in each of a succession of uniform epochs.

In an alternative embodiment, the method includes receiving an electroencephalogram (EEG) signal from the patient, wherein identifying the sleep stage includes processing the EEG signal together with the signal received from the sensor.

There is also provided, in accordance with an embodiment of the present invention, a computer-implemented method for diagnosis of a sleep-related condition of a patient, the method including:

receiving a signal that is indicative of breathing activity from a sensor coupled to the patient during sleep;

processing the signal so as to detect individual events that are indicative of disturbance of the breathing;

identifying a periodic event, which includes a sequence of the individual events that are separated by time gaps whose respective durations are within predetermined limits; and

classifying a sleep stage of the patient responsively to the complexity.

Typically, the signal includes at least one of a respiration signal and an oxygen saturation signal.

In one embodiment, identifying the periodic event includes determining that the event was associated with Cheyne-Stokes breathing.

In some embodiments, classifying the sleep stage includes analyzing the periodic event so as to determine whether the periodic event was associated with REM or non-REM sleep. Typically, analyzing the periodic event includes associating the event with REM sleep responsively to at least one of a duration and a symmetry of the event.

There is moreover provided, in accordance with an embodiment of the present invention, apparatus for diagnosis of a sleep-related condition of a patient, the apparatus including:

one or more sensors, coupled to a lower body of the patient, which are adapted to receive physiological signals; and

a diagnostic processor, which is coupled to receive and process the physiological signals, independently of any electroencephalogram (EEG) or electro-oculogram (EOG) signals, in order to identify sleep stages of the patient.

In a disclosed embodiment, the apparatus includes a console, which is coupled to collect the physiological signals at a bedside of the patient, and to transmit the physiological signals over a communication network for processing by the diagnostic processor at a location remote from the bedside.

There is furthermore provided, in accordance with an embodiment of the present invention, apparatus for diagnosis of a sleep-related condition of a patient, the apparatus including:

a sensor, which is adapted to be coupled to the patient during sleep so as to receive from the patient at least one of an electrocardiogram (ECG) signal and a respiration signal; and

a diagnostic processor, which is coupled to measure an energy of the at least one of the ECG and respiration signals in a selected frequency band as a function of time, to find a respective characteristic of the energy in each of a plurality of time segments, and to determine the patient to have moved during one or more of the time segments responsively to the respective characteristic.

There is also provided, in accordance with an embodiment of the present invention, apparatus for diagnosis of a sleep-related condition of a patient, the apparatus including:

one or more electrodes, which are adapted to receive an electrocardiogram (ECG) signal from the patient during sleep; and

a diagnostic processor, which is coupled to measure a variability of a heart rate of the patient responsively to the ECG signal, to compute a characteristic of the variability of the heart rate, and to find, responsively to the characteristic, a period during which the heart rate was decoupled from a respiratory function of the patient.

There is additionally provided, in accordance with an embodiment of the present invention, apparatus for diagnosis of a sleep-related condition of a patient, the apparatus including:

a respiration sensor, which is adapted to receive a signal from the patient during sleep, wherein the signal is indicative of at least one of a heart rate and respiration activity of the patient; and

a diagnostic processor, which is coupled to evaluate a complexity of the signal during a selected time period, and to identify a sleep stage of the patient responsively to the complexity.

There is also provided, in accordance with an embodiment of the present invention, apparatus for diagnosis of a sleep-related condition of a patient, the apparatus including:

a sensor, which is adapted to be coupled to the patient during sleep so as to receive from the patient a signal that is indicative of breathing activity; and

a diagnostic processor, which is coupled to process the signal so as to detect individual events that are indicative of disturbance of the breathing, to identify a periodic event, which includes a sequence of the individual events that are separated by time gaps whose respective durations are within predetermined limits, and to classify a sleep stage of the patient responsively to the complexity.

There is further provided, in accordance with an embodiment of the present invention, a computer software product for diagnosis of a sleep-related condition of a patient, the product

including a computer-readable medium, in which program instructions are stored, which instructions, when read by a computer, cause the computer to receive physiological signals from one or more sensors coupled to a lower body of the patient during sleep, and to process the physiological signals, independently of any electroencephalogram (EEG) or electro-oculogram (EOG) signals, in order to identify sleep stages of the patient.

There is moreover provided, in accordance with an embodiment of the present invention, a computer software product for diagnosis of a sleep-related condition of a patient, the product including a computer-readable medium, in which program instructions are stored, which instructions, when read by a computer, cause the computer to receive from the patient at least one of an electrocardiogram (ECG) signal and a respiration signal during sleep, and to measure an energy of the at least one of the ECG and respiration signals in a selected frequency band as a function of time, to find a respective variance of the energy in each of a plurality of time segments, and to determine the patient to have moved during one or more of the time segments responsively to the respective characteristic.

There is also provided, in accordance with an embodiment of the present invention, a computer software product for diagnosis of a sleep-related condition of a patient, the product including a computer-readable medium, in which program instructions are stored, which instructions, when read by a computer, cause the computer to receive an electrocardiogram (ECG) signal from the patient during sleep, and to measure a variability of a heart rate of the patient responsively to the ECG signal, to compute a variance associated with the variability of the heart rate, and to find, responsively to the characteristic, a period during which the heart rate was decoupled from a respiratory function of the patient.

There is additionally provided, in accordance with an embodiment of the present invention, a computer software product for diagnosis of a sleep-related condition of a patient, the product including a computer-readable medium, in which program instructions are stored, which instructions, when read by a computer, cause the computer to receive a signal from the patient during sleep, wherein the signal is indicative of at least one of a heart rate and respiration activity of the patient, and to evaluate a complexity of the signal during a selected time period, and to identify a sleep stage of the patient responsively to the complexity.

There is further provided, in accordance with an embodiment of the present invention, a computer software product for diagnosis of a sleep-related condition of a patient, the product including a computer-readable medium, in which program instructions are stored, which

instructions, when read by a computer, cause the computer to receive from the patient a signal that is indicative of breathing activity, and to process the signal so as to detect individual events that are indicative of disturbance of the breathing, to identify a periodic event, which comprises a sequence of the individual events that are separated by time gaps whose respective durations are within predetermined limits, and to classify a sleep stage of the patient responsively to the complexity.

The present invention will be more fully understood from the following detailed description of the embodiments thereof, taken together with the drawings in which:

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic, pictorial illustration of a system for sleep monitoring, in accordance with an embodiment of the present invention;

Fig. 2 is a flow chart that schematically illustrates a method for processing physiological signals, in accordance with an embodiment of the present invention;

Fig. 3 is a schematic plot of an ECG signal and of a movement signal derived therefrom, in accordance with an embodiment of the present invention;

Fig. 4 is a schematic plot of a respiration signal and of a movement signal derived therefrom, in accordance with another embodiment of the present invention;

Fig. 5 is a flow chart that schematically illustrates a method for processing a heart rate signal, in accordance with an embodiment of the present invention;

Figs. 6A-6D are time plots of event start and end points that schematically illustrate a method for detecting movement events, in accordance with an embodiment of the present invention;

Fig. 7A is a time plot that schematically illustrates start and end points of movement events over a succession of epochs, in accordance with an embodiment of the present invention;

Fig. 7B is a time plot showing averaged movement event scoring based on the movement events of Fig. 7A, in accordance with an embodiment of the present invention;

Figs. 8A and 8B are time plots that schematically illustrate a method for detecting periodic respiration events, in accordance with an embodiment of the present invention;

Fig. 9 is a time plot that schematically shows an oxygen saturation signal, illustrating desaturation events, in accordance with an embodiment of the present invention;

Fig. 10 is a flow chart that schematically illustrates a method for detecting complexity of respiration patterns, in accordance with an embodiment of the present invention;

Fig. 11 is a flow chart that schematically illustrates a method for processing a heart-rate variability (HRV) signal, in accordance with an embodiment of the present invention;

Fig. 12 is a schematic plot illustrating a variance analysis of a HRV signal, in accordance with an embodiment of the present invention;

Fig. 13 is a flow chart that schematically illustrates a method for automated sleep staging, in accordance with an embodiment of the present invention;

Fig. 14A is a schematic plot that schematically illustrates a complexity analysis of a thoracic signal, in accordance with an embodiment of the present invention;

Fig. 14B is a schematic plot of a histogram derived from the complexity analysis of Fig. 14A, in accordance with an embodiment of the present invention;

Fig. 14C is a schematic plot of a manually-scored histogram;

Fig. 15 is a state diagram that schematically illustrates a Hidden Markov Model of sleep states, in accordance with an embodiment of the present invention; and

Fig. 16 is a flow chart that schematically illustrates a method of sleep staging, in accordance with an embodiment of the present invention.

DETAILED DESCRIPTION OF EMBODIMENTS

SYSTEM OVERVIEW

Fig. 1 is a schematic, pictorial illustration of a system 20 for sleep monitoring and diagnosis, in accordance with an embodiment of the present invention. In this embodiment, system 20 is used to monitor a patient 22 in a home or hospital ward environment, although the principles of the present invention may similarly be applied in dedicated sleep laboratories. System 20 receives and analyzes physiological signals generated by the patient's body, including an ECG signal measured by skin electrodes 24, which serve as ECG sensors, and a respiration signal measured by a respiration sensor 26. Optionally, the system also comprises an oxygen saturation sensor 27, which provides a signal indicative of the level of oxygen saturation in the patient's blood and may also be used to provide a heart rate signal. The signals are collected, amplified and digitized by a console 28. No EEG or EOG electrodes are required on the patient's head in system 20, although the techniques of ECG and respiration

monitoring and analysis that are described herein may alternatively be combined with EEG, EOG and other sleep monitoring modalities that are known in the art.

Respiration sensor 26 typically makes electrical measurements of thoracic and abdominal movement. For example, sensor 26 may comprise two or more skin electrodes, which are driven by console 28 to make a plethysmographic measurement of the change in impedance or inductance between the electrodes as a result of the patient's respiratory effort. (It is also possible to use the ECG electrodes for this purpose.) Alternatively, the respiration sensor may comprise a belt, which is placed around the patient's chest or abdomen and senses changes in the body perimeter. Additionally or alternatively, air flow measurement may be used for respiration sensing. For example, the air flow from the patient's nose and/or mouth may be measured using a pressure cannula, thermistor, or CO2 sensor. Any other suitable respiration sensor known in the art may also be used, in addition to or instead of the above sensor types.

Additionally or alternatively, console 28 may gather signals from an existing set of sensors coupled to patient 22. For example, while patient 22 is undergoing Holter monitoring, as is known in the art, the monitored physiological signals may also be used for sleep staging, as described hereinbelow. As another example, implantable cardiac devices, such as pacemakers and ICDs, typically sense the patient's ECG and are capable of transmitting telemetry signals out to a suitable receiver. Such implantable devices sometimes include motion sensors, as well, such as an accelerometer, whose output may also be used, along with the ECG, in sleep staging. Additionally or alternatively, the implantable device may generate and transmit impedance-based respiration measurements (known in the art as "minute ventilation").

Console 28 may process and analyze the ECG, respiration and other signals locally, using the methods described hereinbelow. In the present embodiment, however, console 28 is coupled to communicate over a network 30, such as a telephone network or the Internet, with a diagnostic processor 32. This configuration permits sleep studies to be performed simultaneously in multiple different locations. Processor 32 typically comprises a general-purpose computer with suitable software for carrying out the functions described herein. This software may be downloaded to processor 32 in electronic form, or it may alternatively be provided on tangible media, such as optical, magnetic or non-volatile electronic memory.

Processor 32 analyzes the signals conveyed by console 28 in order to identify sleep stages of patient 22 and to display the results of the analysis to an operator 34, such as a physician.

Typically, processor 32 identifies sleep stages based on a combination of different analyses that are applied to the signals received from patient 22. Exemplary multi-parameter sleep staging methods are shown in Figs. 13 and 16 and are described hereinbelow with reference thereto. Before describing this combined methods, however, a number of the specific analyses that may be used in the method will first be explained.

MOTION DETECTION

Fig. 2 is a flow chart that schematically illustrates a method for detecting motion of patient 22 based on ECG measurements made using electrodes 24, in accordance with an embodiment of the present invention. This motion measurement may be used to distinguish between REM (in which the voluntary muscles are paralyzed) and other states. No dedicated motion sensor is required.

The method of Fig. 2 is based on measuring the energy content of motion-related frequency bands in the ECG signal, at an energy measurement step 40. The inventors have found that the ECG "noise bands," below 2 Hz and above 20 Hz, can be used for this purpose. Alternatively or additionally, other bands that contain motion information may be used. To perform the energy measurement, processor 32 divides the ECG signal into overlapping segments S_i, each δ seconds long, with the starting times of successive segments spaced ε seconds apart. Typically, $\delta = 5$, and $\varepsilon = 0.5$, but other values of these parameters, larger or smaller, may alternatively be used. The noise measure for each segment i is given by:

$$\eta_i = \frac{E_i(0,2) + E_i\left(20, {}^{F_S}\!/_2\right)}{E_i\left(0, {}^{F_S}\!/_2\right)} \qquad (1)$$

wherein E_i is the integrated energy in the range $[x,y]$ (in Hz), and F_S is the sampling rate. An AR (autoregressive) spectrum offers an efficient, accurate means for frequency estimation for short data segments. The inventors have used it for computing the ECG power spectrum and

found that for an ECG sampling rate of 100 Hz, using four AR coefficients gives satisfactory results.

Processor 32 assembles the noise energy values η_i as a time series with a spacing of ε seconds between series elements. The processor may apply spline interpolation, typically with a cubic spline, to interpolate series values between these measured values. For example, the noise energy may initially be computed with 2 Hz resolution, followed by cubic spline fitting to give a continuous noise signal, and concluding with resampling of the continuous noise signal at 6 Hz.

The processor then divides the time series into new segments R_j by an adaptive segmentation process, at a segmentation step 42. Methods of adaptive segmentation that may be applied to physiological signals (particularly in the context of sleep analysis) are described in detail in the above-mentioned PCT Patent Application PCT/IL2004/000412. Briefly, the adaptive segmentation process divides the time series into segments, each of which is characterized by quasi-stationary behavior. "Quasi-stationary" means that certain statistical properties of each segment, such as spectral amplitude variations, are contained within predefined bounds Those segments of the time series that are not quasi-stationary over at least a predefined minimum duration may be identified as transient events.

In one embodiment, processor 32 uses a procedure to define and segment quasi-stationary segments based on a similarity measure D as follows: Let $A=\{a_1 \ldots a_n\}$ and $B=\{b_1 \ldots b_m\}$ be two segments of length n and m respectively. Let σ_A, σ_B be the standard deviations of A and B, respectively, and let σ_{AB} be the standard deviation of the concatenation of A and B. Segments A and B are considered similar if:

$$D(A,B)=\frac{\sigma_A^n \sigma_B^m}{\sigma_{AB}^{n+m}}<T \qquad (2)$$

wherein T is a predefined threshold. Other similarity measures may alternatively be used, for example, $\log D(A,B)$. Now, taking $2l$ to be the minimal length of a quasi-stationary segment

(typically $2l > 5$ sec), and $X = \{x_1, x_2, \ldots\}$ to be the series to be segmented, and denoting the segment $\{x_i, \ldots, x_j\}$ as $[i, j]$, the segmentation procedure at step 42 is expressed as follows:

Initially $i = 1$;

While (signal is not fully segmented) {

Look for $\min j \geq i$ such that $[j, j+l]$ and

$[j+l+1, j+2l]$ are similar

If $(j > i)$ {

$[i, j-1]$ is a non-stationary segment;

$i = j$ }

Else {

Look for $\max j > i+l$ such that $[i, j]$ and

$[j+1, j+l]$ are similar

$[i, j+l]$ is a quasi-stationary segment;

$i = j+l+1;$ }}

Processor 32 next computes the statistical variance of the energy values in each segment R_j, at a variance computation step 44. The variance of each segment is compared to those of its neighboring segments, at a burst detection step 46. If the variance ratio between the neighboring segments is greater than a predetermined threshold, processor 32 concludes that patient 22 moved during the high-variance segment. Typically, the processor compares the noise measure of each segment to that of the closest preceding and subsequent segments that are of at least a predetermined minimum length (typically at least 60 sec). If the noise measure in a given segment is at least 15 times greater than these preceding and succeeding segments, the patient is considered to have moved during the segment. Alternatively, other characteristics of the energy may be used, such as the entropy.

Fig. 3 is a schematic plot showing an ECG signal and a movement signal derived therefrom, in accordance with an embodiment of the present invention. An upper plot 50 shows the ECG signal taken from a patient during sleep. The signal includes a number of

quasi-stationary segments 52 with relatively high variance. A lower plot 54 shows the movement signal derived from the ECG (on a condensed time scale). Segments 52 are reflected in a peak 56 appearing in the movement signal. Processor 32 records this peak as an indication that patient 22 moved during the time frame in question.

The method of Fig. 2 may similarly be applied to detect patient movement based on respiration signals. In this case, at step 40, the high-frequency component of the respiration signal is considered to contain the motion information. Typically, the energy is measured in a high-pass band above 1.5 Hz. An energy time series is thus created, as described above, and adaptively segmented at step 42. The variance of each segment in the energy series is computed at step 44, and high-variance bursts are detected at step 46. Let σ be the variance of a segment S, and let σ_l, σ_r be the variances of previous and succeeding neighboring segments (of sufficient length). The segment S is considered a burst if $\max\left(\frac{\sigma}{\sigma_l}, \frac{\sigma}{\sigma_r}\right) > T$. Typically, a segment meeting this criterion with $T = 5$ is regarded as indicative of patient motion, as long as the neighboring segments are at least 10 sec long.

Fig. 4 is a schematic plot showing a respiration signal and a movement signal derived therefrom, in accordance with another embodiment of the present invention. An upper plot 60 shows the actual respiration signal, including a high-variance segment 62. The corresponding motion signal is shown in a lower plot 64. The high variance of segment 62 is evident in a corresponding segment 66 in the motion signal, indicating that patient motion occurred during this segment.

Fig. 5 is a flow chart that schematically illustrates a method for detecting patient motion based on heart rate measurement, in accordance with an alternative embodiment of the present invention. This method is based on the realization that spontaneous elevation and depression of the heart rate during sleep may be associated with body movements. For the purposes of this method (and other methods described herein that are based on heart rate analysis), the heart rate may be derived from the ECG, oxygen saturation signal, or any other suitable heart rate indicator received from patient 22.

In order to detect heart rate changes that may be indicative of movement, processor 32 eliminates the long-term trend of the heart rate from the heart rate signal, at a trend elimination step 70. Any suitable filtering method may be used for this purpose, for example, Kalman filtering, as is known in the art. The processor then segments the signal remaining after trend

removal into quasi-stationary segments, at a segmentation step 72. This step may use the same sort of technique as was described above for segmentation of ECG signals. The processor computes the duration and variance of each segment, at a segment analysis step 74.

Processor 32 compares the variance of each segment to those of its neighboring segments, at a movement detection step 76, in similar fashion to the comparison used in step 46 (Fig. 2). If the duration of a given high-variance segment is greater than a predetermined minimum, and the variance ratio between the high-variance segment and its neighboring segments is greater than a predetermined threshold, processor 32 concludes that patient 22 moved during the high-variance segment. For example, the minimum duration may be set to 5 sec, and the threshold ratio may be set to 125%. Alternatively, other thresholds and other characteristic measures of segment energy may be used

The heart rate signal may also be used to detect arousals. For this purpose, processor 32 detects peaks in the heart rate, and then seeks the nadir point in the heart rate within a certain time window prior to each peak. If the ratio of the peak value to the corresponding nadir value of the heart rate is greater than a certain threshold, the peak is considered to indicate an arousal. For example, the inventors have found that a peak/nadir ration of 120% over a time window of 5 min is a good indicator of patient arousal. This arousal indicator may be used in conjunction with other indicators in automated sleep staging, using the method of Fig. 13 or Fig. 16, for example.

Additionally or alternatively, patient movement may be detected using oxygen saturation values, such as those provided by saturation sensor 27. De-saturation events that are characterized by high de-saturation slope and low subsequent saturation level are typically indicative of patient movement. A method for detection of de-saturation events that may be used in this context is described by Taha et al., in "Automated Detection and Classification of Sleep-Disordered Breathing from Conventional Polysomnography," *Sleep* **20**:11 (1997), pages 991-1001, which is incorporated herein by reference.

Figs. 6A-6D are time plots of event start and end points, which schematically illustrate a method for detecting movement events, in accordance with an embodiment of the present invention. This method emulates the behavior of a human sleep scorer in fusing movement indications from different sources, such as ECG, respiration, heart rate and saturation signals.

By way of example, let Figs. 6A and 6B represent movement events from two different sources, A and B, such as respiration and ECG. Two events 80 and 82 were detected in the

signals from source A, and two events 88 and 90, overlapping in time with events 80 and 82, were detected in the signals from source B. Processor 32 marks each event with a respective start point 84 and end point 86. The processor then projects all the start and end points onto a common time axis, as shown in Fig. 6C. When events from different sources overlap in time, they are fused into a single event that starts with the earliest start point and ends with the last end point in the group. An algorithm for fusing events in this manner could be expressed as follows:

(a) Open event at first start; set score = 1.
(b) Get next boundary point (start or end).
(c) If start, then increment score; else decrement score.
(d) If score = 0, close event; else go to (b).

The result of the fusion process is shown in Fig. 6D, in which events 80 and 88 have resulted in a fused movement event (FME) 92, and events 82 and 90 have resulted in another FME 94.

Additionally or alternatively, processor 32 may fuse movement events that are closely spaced in time into a single FME. Typically, if the time span between the end point of a first event and the start point of the next event is less than a predetermined threshold, the two events are fused into one FME. The start point of the FME in this case is that of the first event, while the end point is that of the second event. This process may be repeated to fuse the FME with the next event in the sequence if the time span until the next event is also short. Typically, however, a maximum event length is set, and processor 32 refrains from fusing a given event (whether an original, single event or a FME) with another event if the given event is longer in duration than the maximum event length.

Fig. 7A is a time plot showing fused movement events 92 and 94 projected onto a time axis that is divided into uniform epochs, in accordance with an embodiment of the present invention. The epochs are of uniform, 30 sec duration, in order to emulate the 30 sec epochs used by human scorers in manual sleep staging. Alternatively, different epoch lengths may be used. For each epoch in Fig. 7A, processor 32 determines the relative duration of fused movement events and scores the epoch according to the relative duration. For example, as shown in the figure, assuming start point 84 of FME 92 to have occurred at time = 15 sec, and

end point 86 of this FME to have occurred at time = 75 sec, processor 32 assigns an averaged FME (AFME) score of 50% to each of the first and third epochs, and an AFME score of 100% to the second epoch (meaning that the entire epoch was filled with a movement event). Subsequent epochs are scored in like manner.

Fig. 7B is a time plot that shows the result of this event scoring, in accordance with an embodiment of the present invention. The AFME scores determined in Fig. 7A are shown as a function of time in 30 sec epochs. Each epoch is thus rated in terms of the relative amount of patient movement occurring during the epoch.

DETECTION OF PERIODIC EVENTS

Fig. 8A is a time plot that schematically illustrates a periodic sequence of respiration events 100, 102, 104, 106, 108, 110, in accordance with an embodiment of the present invention. Such respiration events may comprise, for example, periods during which processor 32 detected a cessation of breathing (apnea), or other types of disturbed breathing patterns. Periodic respiration events, such as that shown in Fig. 8A, are common in sleep states of patients suffering from sleep-disturbed breathing. Detection of such events is useful, *inter alia*, in distinguishing between sleep and wake states of such patients.

Fig. 8B shows a periodic respiration event (PRE) 112 detected by processor 32 on the basis of the event sequence shown in Fig. 8A, in accordance with an embodiment of the present invention. The processor detects a PRE upon the occurrence of a certain minimum number of successive respiratory events, with certain regular time gaps between successive events. For example, a PRE may be defined as a sequence of at least five consecutive respiration events, such that the mean of the time gaps between the end point of each event and the start point of the succeeding event is no greater than a certain threshold length, and the standard deviation of the time gaps is no greater than a certain maximum variance. The inventors have found that setting the threshold length for the mean gap between events to 4 min, while setting the maximum variance of the gaps to 20 sec, gives good results in automatically detecting PREs.

Periodic respiratory events may further be classified into REM-oriented and non-REM (NREM) oriented PREs. Typically, the duration of PREs in NREM sleep is longer than that in REM sleep, because the muscular paralysis in REM sleep makes it more difficult for the body to recover from respiration events. PREs in REM sleep are also typically more symmetrical, in terms of onset and recovery times, than in NREM sleep.

On the other hand, periodic Cheyne-Stokes respiration events, which are common in patients suffering from congestive heart failure (CHF), for example, occur only in NREM sleep. (Cheyne-Stokes is a breathing pattern marked by shallow breathing alternating with periods of rapid heavy breathing found in some medical conditions and also occurring at high altitude.) Processor 32 determines that a certain PRE is a periodic Cheyne-Stokes respiration event by computing the time gaps between the peaks in the respiration rate that correspond to the start and end points of each respiration event in the succession of respiration events making up the PRE. If the mean of these time gaps is within a certain range, and the standard deviation of the time gaps is no greater than a certain maximum value, and if the amplitude envelope of the respiration signal during the PRE is sinusoidal, then the PRE is considered to be a Cheyne-Stokes PRE. The inventors have gotten good results by setting processor 32 to detect a Cheyne-Stokes PRE when the mean time gap between respiration peaks in each event is between 88 and 92 sec, with a standard deviation no greater than 2 sec.

Based on the criteria explained above, processor 32 detects PREs and classifies them into REM- and NREM-oriented types. For this purpose, the processor typically separates out the Cheyne-Stokes PREs (if any), and then uses fuzzy clustering to group the remaining PREs into long- and short-duration clusters. As noted above, the long-duration PREs are classified as REM-oriented, and the short-duration PREs are classified as NREM-oriented, as are the Cheyne-Stokes PREs. The PREs are projected onto a time axis of uniform epochs, and are used to compute average REM and NREM PRE scores per epoch in the manner shown above in Figs. 7A and 7B.

Fig. 9 is a time plot that schematically illustrates a blood oxygen saturation signal received from sensor 27, in accordance with an embodiment of the present invention. The signal exhibits desaturation events 120 and 122, which are detected on the basis of significant drops in the blood oxygen saturation level. Each of events 120 and 122 has a start time a_i, an end time c_i, and a nadir time b_i ($i = 1$ for event 120, and $i = 2$ for event 122), which may be detected by processor 32 using any suitable method of signal processing known in the art. The duration of each desaturation event is given by $c_i - a_i$; the depth of each event is given by the difference between the baseline saturation value and the value at b_i; and the symmetry of each event is given by:

$$Sym(i) = \frac{\left|(c_i - b_i) - (b_i - a_i)\right|}{(c_i - a_i)} \quad (3)$$

Patients with sleep-disturbed breathing may also exhibit periodic desaturation events (PDEs), which are similar in many respects to the PREs described above. A PDE may be defined, like a PRE, as a sequence of at least five consecutive desaturation events, such that the mean of the time gaps between the end point of each event and the start point of the succeeding event is no greater than a certain threshold length, and the standard deviation of the time gaps is no greater than a certain maximum variance. The same sort of parameter values that were defined above for detecting PREs may be applied in detecting PDEs.

PDEs may also be classified into REM-oriented and NREM-oriented clusters, depending on the duration, depth and symmetry of the desaturation events in each PDE. As in the case of PREs, REM-oriented PDEs tend to be longer, deeper and more symmetrical than NREM-oriented PDEs, due to the muscular paralysis that occurs during REM. Processor 32 therefore uses fuzzy clustering to group the PDEs according to these criteria into REM and NREM group, and then computes average REM and NREM scores per epoch based on the PDE classification, in the manner described above.

DETECTION OF COMPLEXITY OF RESPIRATION PATTERNS

Complexity of the patient's respiration patterns, based on the signal measured by respiration sensor 26 and/or other respiration signals, gives another useful indication of the patient's sleep stage in system 20. NREM sleep is known to be characterized by even breathing, i.e., low-complexity respiration signals, whereas waking and REM typically have more complex, irregular breathing patterns. Various methods may be used to calculate a measure of signal complexity in order to distinguish between these states.

In an exemplary embodiment, processor 32 divides the respiration signal into time segments, and determines the measure of complexity for each segment. The segments may be quasi-stationary time segments, determined by adaptive segmentation, as described above. Alternatively, the segments may be overlapping segments of fixed length, for example, segments 30 sec long with a time offset between successive segments of 1 sec. As the first step in finding the signal complexity, the processor finds the mean m and the standard

deviation σ for each segment, and uses the values of m and σ to quantize the respiration signal s in each segment into n levels, for example, $n = 4$:

$$s = \begin{cases} 'a' & x \geq m + \sigma \\ 'b' & m + \sigma > x \geq m \\ 'c' & m > x > m - \sigma \\ 'd' & m \leq m - \sigma \end{cases} \tag{4}$$

The processor then compresses the string of quantized signal values in the segment using a complexity-dependent compression scheme. For example, the processor may use Lempel-Ziv compression, as described by Lempel et al., in "A Universal Algorithm for Sequential Data Compression," IEEE Transactions on Information Theory, **IT-23**:3 (1977), pages 337-349. The signal complexity may be defined in terms of the compression efficiency ε:

$$\varepsilon = \frac{L \log_n N}{N} \tag{5}$$

wherein N is the length of the segment, and L is the length of the compressed string. A typical calculation of respiratory signal complexity over time is illustrated below in Fig. 14A.

Alternatively or additionally, processor 32 may compute other measures of complexity of the segmented respiration signal, such as the fractal dimension or entropy of each segment.

Further alternatively or additionally, the processor may compute the respiration rate variability (RRV) over time. The processor then segments the RRV (into either quasi-stationary or fixed-length segments) and computes the variance of each segment as a measure of its complexity.

Fig. 10 is a flow chart that schematically illustrates a method for classifying complexity of respiration patterns, in accordance with an embodiment of the present invention. For this purpose, the respiration complexity is represented in terms of a respiratory complexity feature matrix (CFM), which is generated by processor 32 at a CFM generation step 130. To generate the CFM, processor 32 segments the respiration signal and then extracts from each segment one or more complexity features, such as those described above. The complexity feature values for each segment are arranged in a feature vector, and the feature vectors are arranged in

sequential order to form the CFM. Thus, each column of the matrix corresponds to a successive segment, and each row contains the successive values of one of the features.

In preparation for classifying the complexity of the CFM, the patient is assigned to a population group, at a patient assignment step 132. This assignment is desirable because of the characteristic variation in respiration sleep behavior with age, gender and severity of sleep-disturbed breathing (SDB). As a result of this variation, a certain sleep pattern might be classified as complex in one population group and non-complex in another. The patient may be classified at step 132 based either on *a priori* information or using a probabilistic (Bayesian) classification method, based on estimated probability density functions that have been computed in advance for different population groups.

The estimated probability density functions $P(\mathbf{X}|C_k)$ for each population group C_k $(k=1,...,K)$ are computed in advance based on CFMs $\mathbf{X}$ that have been gathered from a large number of representatives of the population group in question. Let $\mathbf{X}=[\mathbf{x}_1,...,\mathbf{x}_N]$, wherein $\mathbf{x}_n$ denotes the nth feature vector. Assuming that the vectors $\{\mathbf{x}_n\}_{n=1}^{N}$ are identical independently distributed (i.i.d.), then $P(\mathbf{X}|C_j)=\prod_{n=1}^{N}P(\mathbf{x}_n|C_j)$. The probability density function $P(\mathbf{x}|C_j)$ may be modeled using a Gaussian mixture model (GMM):

$$P(\mathbf{x}|C_j)=\sum_{p=1}^{M}\hat{\gamma}_{p,j}N(\mathbf{x};\hat{\boldsymbol{\mu}}_{p,j};\hat{\boldsymbol{\Psi}}_{p,j}) \qquad (6)$$

Here $\{\hat{\gamma}_{p,j}\}_{p=1}^{M}$ is the set of estimated weights of the Gaussian functions N in the model of the j^{th} population, and M is the model order (i.e., the number of Gaussians used in the model). The form of the Gaussians is $N(\mathbf{x};\hat{\boldsymbol{\mu}}_{p,j};\hat{\boldsymbol{\Psi}}_{p,j})=\det(2\pi\hat{\boldsymbol{\Psi}}_{p,j})^{-0.5}\exp\left[-(\mathbf{x}-\hat{\boldsymbol{\mu}}_{p,j})^{T}\hat{\boldsymbol{\Psi}}_{p,j}^{-1}(\mathbf{x}-\hat{\boldsymbol{\mu}}_{p,j})\right]$, wherein the sets $\{\hat{\boldsymbol{\mu}}_{p,j}\}_{p=1}^{P}$ and $\{\hat{\boldsymbol{\Psi}}_{p,j}\}_{p=1}^{P}$ contain the estimated mean vectors and covariance matrices

of the Gaussians, respectively. The values of the GMM parameters are estimated from equation (6) using an expectation maximization (EM) algorithm, as described, for example by Verbeek et al., in "Efficient Greedy Learning of Gaussian Mixture Models," *Neural Computation* **5**:2 (2003), pages 469-485, which is incorporated herein by reference.

To perform Bayes classification at step 132, the specific CFM of the patient in question, $\mathbf{X}$, is classified into population group k using the formula:

$$k = \arg\max_j P\left(\mathbf{X} \mid C_j\right) P\left(C_j\right) \quad j = 1,\ldots,K \tag{7}$$

wherein $P\left(C_k\right)$ is the *a priori* probability of being related to population C_k.

After the patient has been assigned to one of the population groups, processor 32 adaptively classifies each of the feature vectors in the patient's CFM as either complex or non-complex, at a feature classification step 134. For this purpose, the probability density function $P\left(\mathbf{x} \mid C_j\right)$ may be written as:

$$P\left(\mathbf{x} \mid C_k\right) = P\left(W_c \mid C_k\right) P\left(\mathbf{x} \mid C_k; W_c\right) + P\left(W_{nc} \mid C_k\right) P\left(\mathbf{x} \mid C_k; W_{nc}\right) \tag{8}$$

wherein W_c and W_{nc} respectively denote the complex and non-complex classes. The probability density functions $P\left(\mathbf{x} \mid C_k; W_c\right)$ and $P\left(\mathbf{x} \mid C_k; W_{nc}\right)$ are typically estimated in advance using the above-mentioned EM algorithm for GMM parameter estimation. The *a priori* probabilities $P\left(W_c \mid C_k\right)$ and $P\left(W_{nc} \mid C_k\right)$ are also estimated in advance using the formula:

$$P\left(W_c \mid C_k\right) = \frac{D_c^{(k)}}{D^{(k)}} \text{ and } P\left(W_{nc} \mid C_k\right) = 1 - P\left(W_c \mid C_k\right) \tag{9}$$

wherein $D_c^{(k)}$ is the total duration of complex respiration segments in a specified population, and $D^{(k)}$ is the total duration of all respiration segments in the same population.

Processor 32 models $\mathbf{x}$ using a GMM, with probability density function $f(\mathbf{x}) = \sum_{m=1}^{M} \hat{w}_{m,j} N\left(\mathbf{x}; \hat{\boldsymbol{\mu}}_{m,j}; \hat{\boldsymbol{\Psi}}_{m,j}\right)$. In this case, $\left\{\hat{\boldsymbol{\mu}}_{m,j}\right\}_{m=1}^{M}$ and $\left\{\hat{\boldsymbol{\Psi}}_{m,j}\right\}_{m=1}^{M}$ are the mean vectors and covariance matrices of the Gaussian functions N in the model of the population group to which the patient was classified at step 132. $\left\{\hat{w}_{m,j}\right\}_{m=1}^{M}$ is the set of estimated weights of the Gaussians, which may be determined using the above-mentioned EM algorithm.

Each mean vector in the set $\left\{\hat{\boldsymbol{\mu}}_{m,j}\right\}_{m=1}^{M}$ is classified into the complex/non-complex classes according to the Bayesian rule:

$$u = \arg\max_{t} P\left(\boldsymbol{\mu}_{m,j} \mid C_k; W_t\right) P\left(W_t \mid C_k\right) \quad t = 0,1 \tag{10}$$

wherein u is a class index such that $u = 0$ refers to the complex class, and $u = 1$ refers to the non-complex class. The patient-adaptive probability density functions for each class are then given by:

$$f\left(\mathbf{x} \mid W_t\right) = \sum_{m \in S_t} \phi_{m,t} N\left(\mathbf{x}; \hat{\boldsymbol{\mu}}_{m,j}; \hat{\boldsymbol{\Psi}}_{m,j}\right) \tag{11}$$

wherein $\phi_{m,t} = \dfrac{\hat{w}_{m,j}}{\sum_{m \in S_t} \hat{w}_{m,j}}$, and $S_0 \in [1,..,M]$ and $S_1 \in [1,..,M]$ are the sets of indices of the mean vectors that have been classified into the non-complex and complex classes, respectively.

The *a priori* probability of each class is taken to be $f\left(W_t\right) = \sum_{m \in S_t} \hat{w}_{m,j}$. Each feature vector in the CFM of the given patient is then classified according to:

$$u_n = \arg\max_{t} f\left(\mathbf{x}_n \mid W_t\right) f\left(W_t\right) \quad t = 0,1 \tag{12}$$

Step 134 thus results in a sequence of binary values, indicating the complexity or non-complexity of each successive feature vector in the CFM. This sequence is projected onto a uniformly-spaced time axis, at a projection step 136. The sequence is projected, in a manner similar to that shown above in Figs. 7A and 7B, by computing the relative duration of complex respiration segments within non-overlapping time frames, which are typically 30 sec epochs. The outputs of this process is the averaged complexity ratio (ACR) of the respiration signal.

DETECTION OF HEART RATE COMPLEXITY AND RESPIRATORY DECOUPLING

Complex heart rate (HR) patterns may be detected and classified in the same manner as that described above for respiration patterns. In this case, the HR complexity feature matrix is processed to generate a HR complexity sequence, which may then be projected onto a uniform time axis to determine an averaged complexity ratio of the HR. Alternatively or additionally, heart rate complexity may be determined on the basis of the heart-rate variability (HRV) signal, as described hereinbelow.

Reference is now made to Figs. 11 and 12, which schematically illustrate a method for detecting respiratory decoupling in the HRV signal, in accordance with an embodiment of the present invention. This method is based on the observation that during NREM sleep, the heart rate varies, typically in synchronization with the patient's respiration. In REM, however, the heart rate is decoupled from respiration, i.e., it fails to exhibit the variation characteristic of NREM sleep. Fig. 11 is a flow chart showing the steps in the present method, while Fig. 12 shows a plot 180 of a HRV signal to which the method is applied. HRV is expressed and plotted in terms of the length (in seconds) of the R-R interval (RRI) in the ECG signal.

Processor 32 processes the ECG signal received from electrodes 24 to detect the R waves and thus measure the HRV, at a HRV measurement step 170. The processor then filters the HRV signal that it has derived, at a HRV processing step 172. Typically, at this step, the processor uses a bandpass filter with a passband corresponding to the respiratory frequency range, for example, 0.15 to 0.4 Hz. The processor then calculates the second derivative of the filtered HRV signal. It calculates the variance of this second derivative signal, at a variance computation step 174. Typically, the variance is computed over a series of overlapping time frames, for example, 30 sec time frames with starting times spaced 1 sec apart.

Processor 32 analyzes the time sequence of variance values to identify periods of low variance, at a variance analysis step 176. Typically, for this purpose, the processor uses a

hierarchical clustering algorithm to divide the time sequence into segments. In other words, the processor recursively partitions the time sequence into smaller and smaller segments until it finds a period or periods whose variance is lower than the neighboring periods by a predetermined ratio, or until it reaches a minimal segment length. Let σ_A be the variance of a segment of length n, let σ_B be the variance of a neighboring segment of length m, and let σ_{AB} be the variance of the concatenated segment. As noted earlier, the two segments may be considered similar if $\log\frac{\sigma_A^n\sigma_B^m}{\sigma_{AB}^{n+m}} < T$. The similarity threshold, T, for identifying a low variance segment is typically 15, i.e., similarity in excess of this threshold indicates that respiratory decoupling occurred during this segment. Low-variance segments 182 of this sort, indicative of respiratory decoupling, can be seen in Fig. 12.

The output of this phase is the respiration decoupling sequence (RDS), which may be projected onto a uniformly-spaced time axis to find the averaged RDS, in the manner described above.

AUTOMATIC SLEEP STAGING

Fig. 13 is a flow chart that schematically illustrates a method for automated sleep staging using the signal processing techniques described above, in accordance with an embodiment of the present invention. In this sleep staging process, processor 32 analyzes the ECG and respiration data in epochs of 30 sec each, at an epoch input step 190. This period is chosen because it is the standard epoch length used in manual sleep staging.

The processor determines whether the ECG and respiratory signals were quasi-stationary (as defined above) within the current epoch, at a stationarity evaluation step 192. If quasi-stationarity was not maintained for at least a minimal, predetermined length of time (typically 5 sec) in the epoch, then the processor notes the possible occurrence of a transient event. The processor may further analyze this transient event to identify short-term variations in the patient's sleep state, such as micro-arousals. The processing and significance of transient events are further described in the above-mentioned PCT Patent Application PCT/IL2004/000412.

Assuming the signals to have been quasi-stationary in the epoch under analysis, processor 32 next computes the complexity of the respiratory signal, at a complexity

evaluation step 194. The method of computation is described above. If the average complexity over the epoch is less than a predetermined threshold, for example, 0.6, then the patient is determined to be in NREM sleep.

Optionally, the frequency content of the ECG signal may be evaluated in order to determine the depth of NREM sleep, at a frequency assessment step 196. It has been found that a low range of HRV frequencies (in the 0.04-0.15 Hz range, referred to hereinbelow as the LF range) is associated with baroreflex sympathetic control, encountered in light sleep; while a higher range (0.15-0.4 Hz, referred to hereinbelow as the HF range) is associated with parasympathetic control, which is characteristic of deep sleep. Results of this sort are reported, for example, by Akselrod et al., in "Power Spectrum Analysis of Heart Rate Fluctuation: A Quantitative Probe of Beat-to-Beat Cardiovascular Control," *Science* **213** (1981), pages 220-222, which is incorporated herein be reference. Thus, at step 196, processor 32 measures the energy contained in the LF and HF ranges of the HRV during the current epoch and computes the ratio of energies in the two bands, LF energy/HF energy. If the ratio is greater than a predetermined threshold, for example, 1.8, the patient is considered to be in light sleep, i.e., stage 1 or 2. Otherwise, the patient is considered to be in deep sleep, stage 3 or 4.

Alternatively or additionally, the HRV time series may be segmented into quasi-stationary segments, and the LF/HF ratio may calculated from the power spectrum of each segment to give a LF/HF time sequence. The values in this sequence are then compared to a threshold in order to give a binary sequence indicating which segments had high LF/HF ratio. The binary sequence is projected onto a uniformly-spaced time axis and then averaged over non-overlapping time frames, in the manner described above. These averaged LF/HF values may be used in step 196 or in other sleep staging methods described hereinbelow.

Returning now to step 194, if processor 32 finds the average complexity of the respiratory signal over the current epoch to be greater than the complexity threshold, the processor concludes that the patient is not in NREM sleep, and checks whether the patient has moved during this epoch or the preceding or succeeding epoch, at a movement checking step 198. Movement may be assessed, for example, by applying the method of Fig. 2 to ECG or respiration signals, as described above. If the patient is determined to have moved, the processor concludes that the patient is awake. Typically, average movement activity over 30 sec greater than 0.5, coupled with respiration signal complexity greater than 0.6, is indicative of a state of wakefulness.

If the patient is found at step 198 not to have moved during the current epoch, processor 32 checks the HRV signal for respiratory decoupling, at a decoupling detection step 200. Respiratory decoupling may be detected using the method described above with reference to Fig. 11. If the HRV variance, as defined above, is sufficiently low to qualify as decoupling, and is accompanied by an absence of movement, the processor then classifies the current epoch as REM sleep. If the HRV variance is not low, despite the lack of movement, processor 32 marks the current epoch as anomalous. Such anomalies may occur, for example, due to sleep apneas.

As noted above, processor 32 detects transient events in the ECG and/or respiratory signals at step 192. After classifying a given epoch as belonging to a REM or NREM sleep state, the processor checks the record of transient events to determine whether the patient's sleep in the current epoch has been interrupted by such events, at an interruption checking step 202. If the current epoch is uninterrupted, it is classified as normal sleep. If one or more transient events interrupted the current epoch, however, processor 32 notes that the quality of sleep during this epoch was disturbed. This information may be used in diagnosing certain pathological conditions affecting the quality of sleep of patient 22.

Figs. 14A-14C are schematic plots showing the results of sleep staging performed by processor 32, in accordance with an embodiment of the present invention. Fig. 14A shows the results of a computation of complexity of the respiration signal received from sensor 26, as determined at step 194 (Fig. 13) and described above. Fig. 14B shows a hypnogram, generated automatically by processor 32 using the method of Fig. 13, and based on the complexity signal shown in Fig. 14A, along with other respiratory and ECG data. The computer-generated hypnogram is compared with a hypnogram generated manually by an expert human scorer, which is shown in Fig. 14C.

In this embodiment, the LF/HF ratio (step 196) was not computed, and the processor was thus unable to distinguish between different stages of NREM sleep. Therefore, Fig. 14B shows only stages 0 (wakefulness), 2 (representing all NREM sleep stages) and 5 (REM sleep). With this reservation, there is still a good correlation between the sleep stages derived automatically, as shown in Fig. 14B, and the manual scoring results shown in Fig. 14C. As noted above, this result was achieved based on thoracic measurements only, without the use of EEG or EOG signals.

In another embodiment of the present invention, processor 32 uses the processed signals described above in a two-phase process of automatic sleep staging. In the first phase, the processor performs macro-analysis, to classify each epoch as wake, light sleep, deep sleep or REM using a Continuous Hidden Markov Model (CHMM) classifier. In the second phase, the processor performs micro-analysis in order to fine-tune the sleep stages.

Fig. 15 is a state diagram showing a HMM used in classifying patient sleep stages, in accordance with an embodiment of the present invention. The model includes a wake state 220, a light sleep state 222, a deep sleep state 224, and a REM state 226. Each state is connected to every other state by a positive transition coefficient a_{ij}, so that the state transition probability matrix is given by:

$$A=\begin{bmatrix} \mathbf{a}_{11} & \mathbf{a}_{12} & \mathbf{a}_{13} & \mathbf{a}_{14} \\ \mathbf{a}_{21} & \mathbf{a}_{22} & \mathbf{a}_{23} & \mathbf{a}_{24} \\ \mathbf{a}_{31} & \mathbf{a}_{32} & \mathbf{a}_{33} & \mathbf{a}_{34} \\ \mathbf{a}_{41} & \mathbf{a}_{42} & \mathbf{a}_{43} & \mathbf{a}_{44} \end{bmatrix} \tag{13}$$

Every state j has a respective GMM probability density function b_j for determining the likelihood that a given feature vector $\mathbf{y}_n$ is associated with that state:

$$b_j(\mathbf{y}_n)=\sum_{k=1}^{M} c_{jk} N(\mathbf{y}_n, \hat{\boldsymbol{\mu}}_{jk}, \hat{\Psi}_{jk}),\ j=1,2,3,4 \tag{14}$$

wherein the mixture weights c_{jk} satisfy the stochastic constraint $\sum_{k=1}^{M} c_{jk}=1,\ c_{jk}\geq 0,\ j=1,2,3,4,\ 1\leq k\leq M$. For convenience, we denote the HMM as $\lambda=(A,B,\pi)$, wherein $B=\{b_j(\mathbf{y}_n)\}$ is the observation probability distribution, and $\pi=\{\pi_i\}$ is the initial state vector, i.e., the set of probabilities of being initially in each state i.

The unknown parameters of λ_p for each population p are determined based on the training data (feature matrices) that have been gathered from members of each population,

resulting in $\{\lambda_p\}_{p=1}^{P}$ models. The model order M for each state is also defined in the training phase. The model parameters may be estimated, for example, using the Baum-Welch algorithm, as described by Rabiner in "A Tutorial on Hidden Markov Models and Selected Applications in Speech Recognition," *Proceedings of the IEEE* 77:2 (1989), pages 257-286, which is incorporated herein by reference.

The feature matrix used in training the HMM (and subsequently in classifying sleep stages of patient 22) may include any of the features described above, as well as other features derived from monitoring the patient during sleep. In an exemplary embodiment, the feature matrix $\mathbf{Y}=[\mathbf{y}_1,...,\mathbf{y}_N]$ comprises successive vectors of the following features:

- Averaged fused movement events
- Averaged NREM periodic respiration events
- Averaged REM periodic respiration events
- Averaged NREM periodic desaturation events
- Averaged REM periodic desaturation events
- Averaged complexity ratio of respiration
- Averaged complexity ratio of heart rate
- Averaged respiration decoupling sequence
- Averaged LF/HF ratio sequence

Fig. 16 is a flow chart that schematically illustrates a method for automated sleep staging using the HMM of Fig. 15, in accordance with an embodiment of the present invention. Once the HMM has been suitably trained for each population of interest, processor 32 collects signals from patient 22, and processes the signals to produce a sequence of feature vectors, $\{\mathbf{y}_n\}_{n=1}^{N}$, at a vector collection step 230. The patient is assigned to one of the predefined population groups, based either on *a priori* information or Bayesian classification, as described above, at a patient classification step 232. Processor 32 then compares the feature vector sequence to the HMM λ_p of the assigned population group in order to choose the sequence of sleep states that best fits the observed sequence of feature vectors, at a fitting step 234. Any suitable algorithm known in the art may be used at step 234, such as the well-known Viterbi algorithm. The result of this step is a hypnogram, similar to that shown above in Fig. 14B.

The hypnogram derived at step 234 includes nominal points of sleep onset, generally at transitions from state 220 (wake) to state 222 (light sleep). Processor 32 may next perform micro-analysis in order to more accurately identify the point of sleep onset, at a hypnogram refinement step 236. This step may use, for example, detailed analysis of the respiration signal in the following manner:

1. Processor 32 finds the first respiration central event in the period immediately preceding the nominal point of sleep onset. The "immediately preceding" period may typically be taken to be approximately 5 min long. A "central event" refers to an event related to 100% of flow and effort reduction, which is typically detected upon occurrence of simultaneous flow reduction in the flow and effort respiration channels if the reduction in the respiration volume is greater than 100% and there is no respiration within the boundaries of the suspected event.
2. When such a respiration event is found during a given epoch in the allotted period, the processor identifies the next epoch as sleep onset and scores this next epoch as stage 1 (light sleep).
3. The processor scores the next epoch after sleep onset as stage 3 (deep sleep).

Processor 32 may next use arousal and/or movement signals, such as the heart rate-derived signals and/or respiration-derived signals described above, in order to more accurately identify wake states in the hypnogram, at an arousal identification step 238. Some of the rules applied by the processor at this step may depend on changes in certain feature vectors. For this purpose, the percentage of change D between successive feature vectors $\mathbf{x}$ and $\mathbf{y}$ may be defined as follows:

$$D(\mathbf{x},\mathbf{y}) = \frac{\langle \mathbf{x},\mathbf{y} \rangle}{\langle \mathbf{x},\mathbf{x} \rangle \langle \mathbf{y},\mathbf{y} \rangle} \cdot 100 \qquad (15)$$

wherein $\langle \mathbf{a},\mathbf{b} \rangle$ denotes the correlation coefficient of vectors $\mathbf{a}$ and $\mathbf{b}$. The respiratory complexity feature vectors may be defined, for example, as $\mathbf{x} = \begin{bmatrix} \text{mean RRV} \\ \text{mean peak to peak amplitude} \end{bmatrix}$.

In an exemplary embodiment, processor 32 applies the following rules at step 238:

1. If the respiration signal is indicative of an arousal lasting more than 50% of an epoch, processor 32 scores the epoch as wake stage.
2. If the respiration or heart rate complexity feature vectors change by more than a threshold percentage over at least a certain time period before and after an arousal event, processor 32 scores the epochs following the arousal as wake stage. In an exemplary embodiment, the threshold percentage may be set to 10%, and the minimum time period during which the change must take place is one 30 sec epoch. When the complexity feature vectors subsequently change again by at least the threshold percentage, the processor determines that the wake stage has ended.
3. If the change in the complexity feature vectors during the time period before and after an arousal is less than the threshold percentage, processor 32 scores the epoch following the arousal as stage 1 sleep, and then scores the next epoch as either REM or stage 3 sleep, depending upon the stage of sleep prior to the arousal.

Although the embodiments described above rely only on measurements made using certain sensors, particularly on the patient's thorax and other parts of the lower body, the principles of the present invention may similarly be applied to measurements of heart rate, respiration and/or oxygen saturation using sensors of other types and in other locations. The measurements and signal processing techniques taught by the present invention may also be combined with collection and processing of other physiological signals, including EEG and EOG. It will thus be appreciated that the embodiments described above are cited by way of example, and that the present invention is not limited to what has been particularly shown and described hereinabove. Rather, the scope of the present invention includes both combinations and subcombinations of the various features described hereinabove, as well as variations and modifications thereof which would occur to persons skilled in the art upon reading the foregoing description and which are not disclosed in the prior art.

CLAIMS

1. A computer-implemented method for diagnosis of a sleep-related condition of a patient, the method comprising:

receiving physiological signals from sensors coupled to a lower body of the patient; and

analyzing the physiological signals, independently of any electroencephalogram (EEG) or electro-oculogram (EOG) signals, in order to identify sleep stages of the patient.

2. The method according to claim 1, wherein analyzing the physiological signals comprises detecting motion of the patient based on at least one of the physiological signals.

3. The method according to claim 2, wherein the at least one of the physiological signals comprises at least one of an electrocardiogram (ECG) signal, a respiration signal, a heart rate signal, and an oxygen saturation signal.

4. The method according to claim 2, wherein detecting the motion comprises:

measuring an energy of the at least one of the physiological signals in a selected frequency band as a function of time;

finding a respective characteristic of the energy in each of a plurality of time segments; and

determining the patient to have moved during one or more of the time segments responsively to the respective variance.

5. The method according to claim 4, wherein finding the respective characteristic comprises finding a respective variance of each of the time segments.

6. The method according to claim 4, wherein finding the respective characteristic comprises performing an adaptive segmentation in order to identify the time segments such that the energy of the at least one of the signals is quasi-stationary during each of the time segments.

7. The method according to claim 2, wherein detecting the motion comprises identifying a desaturation event caused by the motion in the oxygen saturation signal.

8. The method according to claim 2, wherein analyzing the physiological signals comprises distinguishing, responsively to detecting the motion, between a waking stage and a REM sleep stage.

9. The method according to claim 2, wherein detecting the motion comprises detecting two or more motion events within a time frame of a given length, and combining the two or more motion events into a single fused motion event.

10. The method according to claim 9, wherein detecting the two or more motion events comprises identifying a first motion event responsively to one of the physiological signals, and a second motion event responsively to another of the physiological signals, wherein the first and second motion events overlap in time, and wherein combining the two or more motion events comprises fusing the first and second motion events.

11. The method according to claim 9, wherein detecting the two or more motion events comprises identifying first and second motion events occurring in succession and separated in time by no more than a predetermined duration, and wherein combining the two or more motion events comprises fusing the first and second motion events.

12. The method according to claim 2, wherein detecting the motion comprises determining an average measure of motion in each of a succession of uniform time epochs.

13. The method according to claim 1, wherein analyzing the physiological signals comprises:

performing an adaptive segmentation of at least one of the signals so as to identify time segments in which a characteristic of the at least one of the signals is quasi-stationary; and

based on the adaptive segmentation, identifying transient events during which the characteristic of the at least one of the signals is not quasi-stationary.

14. The method according to claim 13, wherein analyzing the physiological signals comprises determining at least one of the sleep stages to have been disturbed by occurrence of the transient events during the at least one of the sleep stages.

15. The method according to claim 1, wherein analyzing the physiological signals comprises detecting an arousal to a wake stage.

16. The method according to claim 15, wherein receiving the physiological signals comprises determining a heart rate of the patient, and wherein detecting the arousal comprises identifying the arousal responsively to a change in the heart rate over time.

17. The method according to claim 15, wherein analyzing the physiological signals comprises extracting complexity features from the physiological signals, and wherein detecting

the arousal comprises identifying the arousal responsively to a change in the complexity features over time.

18. The method according to any of claims 1-17, wherein receiving the physiological signals comprises receiving an electrocardiogram (ECG) signal.

19. The method according to claim 18, wherein analyzing the physiological signals comprises measuring a variability of a heart rate of the patient responsively to the ECG signal, and identifying at least one of the sleep stages based on the variability.

20. The method according to claim 19, wherein identifying the at least one of the sleep stages comprises computing a variance associated with the variability of the heart rate, and finding, responsively to the variance, a period during which the heart rate was decoupled from a respiratory function of the patient.

21. The method according to claim 20, wherein identifying the period comprises classifying the period as a REM sleep period.

22. The method according to claim 19, wherein identifying the at least one of the sleep stages comprises measuring first and second energies respectively contained in first and second frequency bands of the variability of the heart rate during a selected epoch, and classifying the sleep stages responsively to a function of the first and second energies.

23. The method according to claim 22, wherein the function comprises a ratio of the first and second energies.

24. The method according to claim 22, wherein the first and second frequency bands respectively comprise low and high frequency bands, and wherein classifying the sleep stages comprises distinguishing between light and deep sleep stages based on the function.

25. The method according to claim 18, wherein receiving the physiological signals comprises receiving a respiration signal, and wherein analyzing the physiological signals comprises analyzing the respiration signal together with the ECG signal in order to identify the sleep stages.

26. The method according to claim 18, and comprising receiving a respiration signal from an airway of the patient, wherein analyzing the physiological signals comprises analyzing the respiration signal together with the ECG signal in order to identify the sleep stages.

27. The method according to any of claims 1-17, wherein receiving the physiological signals comprises receiving a respiration signal.

28. The method according to claim 27, wherein analyzing the physiological signals comprises evaluating a complexity of the respiration signal during a selected epoch, and identifying at least one of the sleep stages responsively to the complexity.

29. The method according to claim 28, wherein evaluating the complexity comprises quantizing and compressing the respiration signal, and measuring the complexity based on an efficiency of compression of the quantized respiration signal.

30. The method according to claim 28, wherein identifying the at least one of the sleep states comprises determining the patient to be in NREM sleep if the complexity is below a predetermined threshold.

31. The method according to claim 27, wherein analyzing the physiological signals comprises identifying a periodic respiration event, which comprises a sequence of individual respiration events that are separated by time gaps whose respective durations are within predetermined limits.

32. The method according to claim 27, wherein analyzing the physiological signals comprises detecting a respiration event in the respiration signal, and identifying an onset of sleep responsively to the respiration event.

33. The method according to any of claims 1-17, wherein analyzing the physiological signals comprises constructing a hidden Markov model (HMM) having model states corresponding to the sleep stages, and identifying a state sequence in the model that accords with the physiological signals.

34. The method according to claim 33, wherein constructing the HMM comprises associating the patient with a population, and training the HMM using data gathered from members of the population.

35. The method according to any of claims 1-17, wherein receiving the physiological signals comprises collecting the physiological signals at a bedside of the patient, and wherein analyzing the physiological signals comprises transmitting the physiological signals over a communication network for processing by a diagnostic processor remote from the bedside.

36. The method according to any of claims 1-17, wherein receiving the physiological signals comprises collecting the physiological signals from a Holter monitor coupled to the patient.

37. The method according to any of claims 1-17, wherein receiving the physiological signals comprises collecting the physiological signals from a device implanted in the body of the patient.

38. A computer-implemented method for diagnosis of a sleep-related condition of a patient, the method comprising:

receiving at least one of an electrocardiogram (ECG) signal and a respiration signal from a sensor coupled to the patient during sleep;

measuring an energy of the at least one of the ECG and respiration signals in a selected frequency band as a function of time;

finding a respective characteristic of the energy in each of a plurality of time segments; and

determining the patient to have moved during one or more of the time segments responsively to the respective characteristic.

39. The method according to claim 38, wherein finding the respective characteristic comprises finding a respective variance of the energy.

40. The method according to claim 38 or 39, and comprising identifying a sleep stage of the patient during the one or more of the time segments responsively to determining the patient to have moved.

41. The method according to claim 40, wherein identifying the sleep stage comprises distinguishing a REM sleep stage from a waking stage.

42. The method according to claim 40, and comprising receiving an electroencephalogram (EEG) signal from the patient, wherein identifying the sleep stage comprises processing the EEG signal together with the at least one of the ECG and respiration signals.

43. A computer-implemented method for diagnosis of a sleep-related condition of a patient, the method comprising:

receiving an electrocardiogram (ECG) signal from a sensor coupled to the patient during sleep;

measuring a variability of a heart rate of the patient responsively to the ECG signal;

computing a characteristic of the variability of the heart rate; and

finding, responsively to the characteristic, a period during which the heart rate was decoupled from a respiratory function of the patient.

44. The method according to claim 43, wherein computing the characteristic comprises determining a variance associated with the variability of the heart rate.

45. The method according to claim 43, and comprising identifying a sleep stage of the patient during the period based on decoupling of the heart rate from the respiratory function.

46. The method according to claim 45, wherein identifying the sleep stage comprises classifying the period as a REM sleep period.

47. The method according to any of claims 43-46, and comprising receiving an electroencephalogram (EEG) signal from the patient, wherein identifying the sleep stage comprises processing the EEG signal together with the ECG signal.

48. A computer-implemented method for diagnosis of a sleep-related condition of a patient, the method comprising:

receiving a signal from a sensor coupled to the patient during sleep, wherein the signal is indicative of at least one of a heart rate and respiration activity of the patient;

evaluating a complexity of the signal during a selected time period; and

identifying a sleep stage of the patient responsively to the complexity.

49. The method according to claim 48, wherein evaluating the complexity comprises quantizing and compressing the signal, and measuring the complexity based on an efficiency of compression of the quantized signal.

50. The method according to claim 48, wherein evaluating the complexity comprises computing a variability of the signal, and extracting a variance of the variability as a measure of the complexity.

51. The method according to any of claims 48-50, wherein evaluating the complexity comprises determining respective values of a set of complexity features in each of a succession of time segments, and wherein identifying the sleep stage comprises constructing a complexity feature matrix (CFM), which comprises a sequence of feature vectors comprising the respective values of the complexity features in the succession of time segments, and

processing the CFM in order to classify the complexity of the complexity features in each of the time segments.

52. The method according to claim 51, wherein processing the CFM comprises assigning the patient to a population group, and processing the feature vectors using a probabilistic model of the population group.

53. The method according to claim 52, wherein the probabilistic model comprises a Gaussian mixture model.

54. The method according to claim 51, wherein processing the CFM comprises determining, responsively to the complexity of the complexity features, an average measure of the complexity in each of a succession of uniform epochs.

55. The method according to any of claims 48-50, wherein identifying the sleep stage comprises determining the patient to be in NREM sleep if the complexity is below a predetermined threshold.

56. The method according to any of claims 48-50, and comprising receiving an electroencephalogram (EEG) signal from the patient, wherein identifying the sleep stage comprises processing the EEG signal together with the signal received from the sensor.

57. A computer-implemented method for diagnosis of a sleep-related condition of a patient, the method comprising:

receiving a signal that is indicative of breathing activity from a sensor coupled to the patient during sleep;

processing the signal so as to detect individual events that are indicative of disturbance of the breathing;

identifying a periodic event, which comprises a sequence of the individual events that are separated by time gaps whose respective durations are within predetermined limits; and

classifying a sleep stage of the patient responsively to the complexity.

58. The method according to claim 57, wherein the signal comprises at least one of a respiration signal and an oxygen saturation signal.

59. The method according to claim 57, wherein identifying the periodic event comprises determining that the event was associated with Cheyne-Stokes breathing.

60. The method according to any of claims 57-59, wherein classifying the sleep stage comprises analyzing the periodic event so as to determine whether the periodic event was associated with REM or non-REM sleep.

61. The method according to claim 60, wherein analyzing the periodic event comprises associating the event with REM sleep responsively to at least one of a duration and a symmetry of the event.

62. Apparatus for diagnosis of a sleep-related condition of a patient, the apparatus comprising:

one or more sensors, coupled to a lower body of the patient, which are adapted to receive physiological signals; and

a diagnostic processor, which is coupled to receive and process the physiological signals, independently of any electroencephalogram (EEG) or electro-oculogram (EOG) signals, in order to identify sleep stages of the patient.

63. The apparatus according to claim 62, wherein the diagnostic processor is adapted to detect motion of the patient based on at least one of the physiological signals.

64. The apparatus according to claim 63, wherein the at least one of the physiological signals comprises at least one of an electrocardiogram (ECG) signal, a respiration signal, a heart rate signal, and an oxygen saturation signal.

65. The apparatus according to claim 63, wherein the diagnostic processor is adapted to measure an energy of the at least one of the physiological signals in a selected frequency band as a function of time, to find a respective characteristic of the energy in each of a plurality of time segments, and to determine the patient to have moved during one or more of the time segments responsively to the respective variance.

66. The apparatus according to claim 65, wherein the respective characteristic comprises a respective variance of each of the time segments.

67. The apparatus according to claim 65, wherein the diagnostic processor is operative to perform an adaptive segmentation in order to identify the time segments such that the energy of the at least one of the signals is quasi-stationary during each of the time segments.

68. The apparatus according to claim 63, wherein the diagnostic processor is adapted to detect the motion by identifying a desaturation event caused by the motion in the oxygen saturation signal.

69. The apparatus according to claim 63, wherein the diagnostic processor is adapted to distinguish, responsively to detecting the motion, between a waking stage and a REM sleep stage.

70. The apparatus according to claim 63, wherein the diagnostic processor is adapted to detect two or more motion events within a time frame of a given length, and to combine the two or more motion events into a single fused motion event.

71. The apparatus according to claim 70, wherein the diagnostic processor is adapted to identify a first motion event responsively to one of the physiological signals, and a second motion event responsively to another of the physiological signals, wherein the first and second motion events overlap in time, and to combine the first and second motion events into a single fused event.

72. The apparatus according to claim 70, wherein the diagnostic processor is adapted to identify first and second motion events occurring in succession and separated in time by no more than a predetermined duration, and to combine the first and second motion events into a single fused event.

73. The apparatus according to claim 63, wherein the diagnostic processor is adapted to determine an average measure of motion in each of a succession of uniform time epochs.

74. The apparatus according to claim 62, wherein the diagnostic processor is adapted to perform an adaptive segmentation of at least one of the signals so as to identify time segments in which a characteristic of the at least one of the signals is quasi-stationary, and based on the adaptive segmentation, to identify transient events during which the characteristic of the at least one of the signals is not quasi-stationary.

75. The apparatus according to claim 74, wherein the diagnostic processor is adapted to determine at least one of the sleep stages to have been disturbed by occurrence of the transient events during the at least one of the sleep stages.

76. The apparatus according to claim 62, wherein the diagnostic processor is adapted to analyze the physiological signals so as to detect an arousal to a wake stage.

77. The apparatus according to claim 77, wherein the physiological signals are indicative of a heart rate of the patient, and wherein the diagnostic processor is adapted to identify the arousal responsively to a change in the heart rate over time.

78. The apparatus according to claim 77, wherein the diagnostic processor is adapted to extract complexity features from the physiological signals, and to identify the arousal responsively to a change in the complexity features over time.

79. The apparatus according to any of claims 62-79, wherein the physiological signals comprise an electrocardiogram (ECG) signal.

80. The apparatus according to claim 79, wherein the diagnostic processor is adapted to measure a variability of a heart rate of the patient responsively to the ECG signal, and to identify at least one of the sleep stages based on the variability.

81. The apparatus according to claim 80, wherein the diagnostic processor is adapted to compute a variance associated with the variability of the heart rate, and to find, responsively to the variance, a period during which the heart rate was decoupled from a respiratory function of the patient.

82. The apparatus according to claim 81, wherein the diagnostic processor is adapted to classify the period as a REM sleep period responsively to decoupling of the heart rate from the respiratory function.

83. The apparatus according to claim 80, wherein the diagnostic processor is adapted to measure first and second energies respectively contained in first and second frequency bands of the variability of the heart rate during a selected epoch, and to classify the sleep stages responsively to a function of the first and second energies.

84. The apparatus according to claim 83, wherein the function comprises a ratio of the first and second energies.

85. The apparatus according to claim 83, wherein the first and second frequency bands respectively comprise low and high frequency bands, and wherein the diagnostic processor is adapted to distinguish between light and deep sleep stages based on the function.

86. The apparatus according to claim 79, wherein the physiological signals comprise a respiration signal, and wherein the diagnostic processor is adapted to analyze the respiration signal together with the ECG signal in order to identify the sleep stages.

87. The apparatus according to claim 79, wherein the diagnostic processor is coupled to receive a respiration signal from an airway sensor in an airway of the patient, and wherein the diagnostic processor is adapted to analyze the respiration signal together with the ECG signal in order to identify the sleep stages.

88. The apparatus according to any of claims 62-79, wherein the physiological signals comprise a respiration signal.

89. The apparatus according to claim 88, wherein the diagnostic processor is adapted to evaluate a complexity of the respiration signal during a selected epoch, and to identify at least one of the sleep stages responsively to the complexity.

90. The apparatus according to claim 89, wherein the diagnostic processor is adapted to quantize and compress the respiration signal, and to measure the complexity based on an efficiency of compression of the quantized respiration signal.

91. The apparatus according to claim 89, wherein the diagnostic processor is adapted to determine the patient to be in NREM sleep if the complexity is below a predetermined threshold.

92. The apparatus according to claim 88, wherein the diagnostic processor is adapted to analyze the respiration signal so as to identify a periodic respiration event, which comprises a sequence of individual respiration events that are separated by time gaps whose respective durations are within predetermined limits.

93. The apparatus according to claim 88, wherein the diagnostic processor is adapted to detect a respiration event in the respiration signal, and to identify an onset of sleep responsively to the respiration event.

94. The apparatus according to any of claims 62-79, wherein the diagnostic processor is adapted to process the physiological signals using a hidden Markov model (HMM) having model states corresponding to the sleep stages, and to identify the sleep stages by finding a state sequence in the model that accords with the physiological signals.

95. The apparatus according to claim 94, wherein the patient is associated with a population, and wherein the HMM is trained using data gathered from members of the population.

96. The apparatus according to any of claims 62-79, and comprising a console, which is coupled to collect the physiological signals at a bedside of the patient, and to transmit the physiological signals over a communication network for processing by the diagnostic processor at a location remote from the bedside.

97. The apparatus according to any of claims 62-79, wherein the diagnostic processor is coupled to receive the physiological signals from a Holter monitor coupled to the patient.

98. The apparatus according to any of claims 62-79, wherein the diagnostic processor is coupled to receive the physiological signals from a device implanted in the body of the patient.

99. Apparatus for diagnosis of a sleep-related condition of a patient, the apparatus comprising:

a sensor, which is adapted to be coupled to the patient during sleep so as to receive from the patient at least one of an electrocardiogram (ECG) signal and a respiration signal; and

a diagnostic processor, which is coupled to measure an energy of the at least one of the ECG and respiration signals in a selected frequency band as a function of time, to find a respective characteristic of the energy in each of a plurality of time segments, and to determine the patient to have moved during one or more of the time segments responsively to the respective characteristic.

100. The apparatus according to claim 100, wherein the characteristic comprises a respective variance of the energy in each of the plurality of time segments.

101. The apparatus according to claim 100 or 101, wherein the diagnostic processor is adapted to identify a sleep stage of the patient during the one or more of the time segments responsively to determining the patient to have moved.

102. The apparatus according to claim 102, wherein the diagnostic processor is adapted to distinguish a REM sleep stage from a waking stage.

103. The apparatus according to claim 102, wherein the diagnostic processor is coupled to receive an electroencephalogram (EEG) signal from the patient, and to process the EEG signal together with the at least one of the ECG and respiration signals.

104. Apparatus for diagnosis of a sleep-related condition of a patient, the apparatus comprising:

one or more electrodes, which are adapted to receive an electrocardiogram (ECG) signal from the patient during sleep; and

a diagnostic processor, which is coupled to measure a variability of a heart rate of the patient responsively to the ECG signal, to compute a characteristic of the variability of the heart rate, and to find, responsively to the characteristic, a period during which the heart rate was decoupled from a respiratory function of the patient.

105. The apparatus according to claim 104, wherein the characteristic comprises a respective variance associated with the variability of the heart rate.

106. The apparatus according to claim 104, wherein the diagnostic processor is adapted to identify a sleep stage of the patient during the period based on decoupling of the heart rate from the respiratory function.

107. The apparatus according to claim 106, wherein the processor is adapted to classify the period as a REM sleep period based on the decoupling.

108. The apparatus according to any of claims 104-107, wherein the diagnostic processor is coupled to receive an electroencephalogram (EEG) signal from the patient, and to process the EEG signal together with the ECG signal.

109. Apparatus for diagnosis of a sleep-related condition of a patient, the apparatus comprising:

a respiration sensor, which is adapted to receive a signal from the patient during sleep, wherein the signal is indicative of at least one of a heart rate and respiration activity of the patient; and

a diagnostic processor, which is coupled to evaluate a complexity of the signal during a selected time period, and to identify a sleep stage of the patient responsively to the complexity.

110. The apparatus according to claim 109, wherein the diagnostic processor is adapted to quantize and compress the signal, and to measure the complexity based on an efficiency of compression of the quantized signal.

111. The apparatus according to claim 109, wherein the diagnostic processor is adapted to compute a variability of the signal, and to extract a variance of the variability as a measure of the complexity.

112. The apparatus according to any of claims 109-111, wherein the diagnostic processor is adapted to determine respective values of a set of complexity features in each of a succession of time segments, and to construct a complexity feature matrix (CFM), which comprises a sequence of feature vectors comprising the respective values of the complexity features in the succession of time segments, and to process the CFM in order to classify the complexity of the complexity features in each of the time segments.

113. The apparatus according to claim 112, wherein the patient is assigned to a population group, and wherein the diagnostic processor is adapted to process the feature vectors using a probabilistic model of the population group.

114. The apparatus according to claim 113, wherein the probabilistic model comprises a Gaussian mixture model.

115. The apparatus according to claim 112, wherein the diagnostic processor is adapted to determine, responsively to the complexity of the complexity features, an average measure of the complexity in each of a succession of uniform epochs.

116. The apparatus according to any of claims 109-111, wherein the diagnostic processor is adapted to determine the patient to be in NREM sleep if the complexity is below a predetermined threshold.

117. The apparatus according to any of claims 109-111, wherein the diagnostic processor is coupled to receive an electroencephalogram (EEG) signal from the patient, and to process the EEG signal together with the signal received from the sensor.

118. Apparatus for diagnosis of a sleep-related condition of a patient, the apparatus comprising:

a sensor, which is adapted to be coupled to the patient during sleep so as to receive from the patient a signal that is indicative of breathing activity; and

a diagnostic processor, which is coupled to process the signal so as to detect individual events that are indicative of disturbance of the breathing, to identify a periodic event, which comprises a sequence of the individual events that are separated by time gaps whose respective durations are within predetermined limits, and to classify a sleep stage of the patient responsively to the complexity.

119. The apparatus according to claim 118, wherein the signal comprises at least one of a respiration signal and an oxygen saturation signal.

120. The apparatus according to claim 118, wherein the diagnostic processor is adapted to determine that the periodic event was associated with Cheyne-Stokes breathing.

121. The apparatus according to any of claims 118-120, wherein the diagnostic processor is adapted to analyze the periodic event so as to determine whether the periodic event was associated with REM or non-REM sleep.

122. The apparatus according to claim 121, wherein the diagnostic processor is adapted to associate the event with REM sleep responsively to at least one of a duration and a symmetry of the event.

123. A computer software product for diagnosis of a sleep-related condition of a patient, the product comprising a computer-readable medium, in which program instructions are stored, which instructions, when read by a computer, cause the computer to receive physiological signals from one or more sensors coupled to a lower body of the patient during sleep, and to process the physiological signals, independently of any electroencephalogram (EEG) or electro-oculogram (EOG) signals, in order to identify sleep stages of the patient.

124. A computer software product for diagnosis of a sleep-related condition of a patient, the product comprising a computer-readable medium, in which program instructions are stored, which instructions, when read by a computer, cause the computer to receive from the patient at least one of an electrocardiogram (ECG) signal and a respiration signal during sleep, and to measure an energy of the at least one of the ECG and respiration signals in a selected frequency band as a function of time, to find a respective variance of the energy in each of a plurality of time segments, and to determine the patient to have moved during one or more of the time segments responsively to the respective characteristic.

125. A computer software product for diagnosis of a sleep-related condition of a patient, the product comprising a computer-readable medium, in which program instructions are stored, which instructions, when read by a computer, cause the computer to receive an electrocardiogram (ECG) signal from the patient during sleep, and to measure a variability of a heart rate of the patient responsively to the ECG signal, to compute a variance associated with the variability of the heart rate, and to find, responsively to the characteristic, a period during which the heart rate was decoupled from a respiratory function of the patient.

126. A computer software product for diagnosis of a sleep-related condition of a patient, the product comprising a computer-readable medium, in which program instructions are stored, which instructions, when read by a computer, cause the computer to receive a signal from the patient during sleep, wherein the signal is indicative of at least one of a heart rate and respiration activity of the patient, and to evaluate a complexity of the signal during a selected time period, and to identify a sleep stage of the patient responsively to the complexity.

127. A computer software product for diagnosis of a sleep-related condition of a patient, the product comprising a computer-readable medium, in which program instructions are stored, which instructions, when read by a computer, cause the computer to receive from the patient a signal that is indicative of breathing activity, and to process the signal so as to detect individual events that are indicative of disturbance of the breathing, to identify a periodic event, which comprises a sequence of the individual events that are separated by time gaps whose respective durations are within predetermined limits, and to classify a sleep stage of the patient responsively to the complexity.

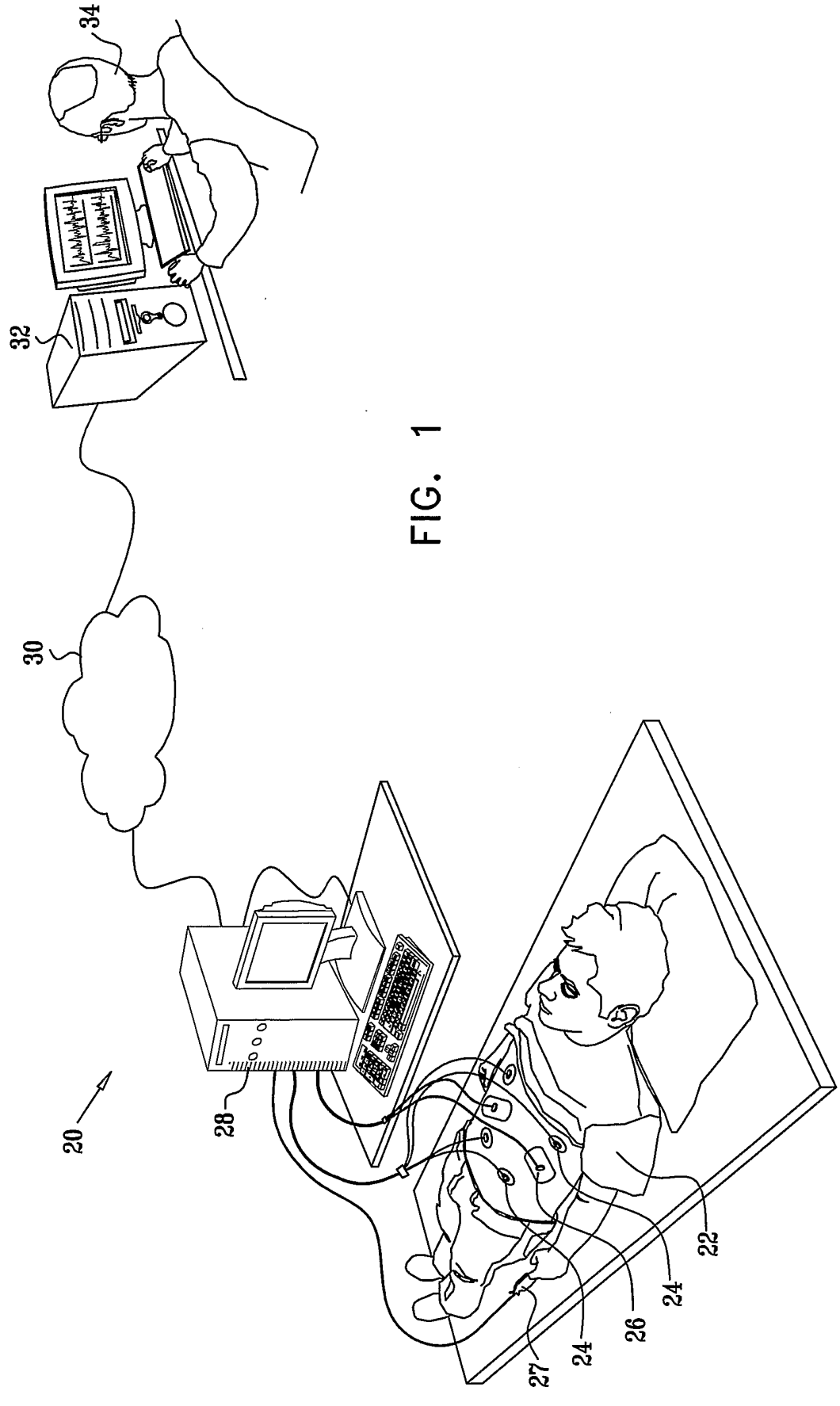


FIG. 1

FIG. 2

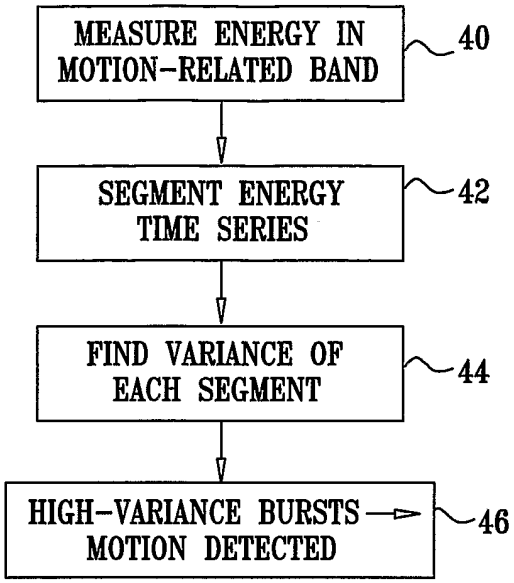

MEASURE ENERGY IN MOTION-RELATED BAND
40
SEGMENT ENERGY TIME SERIES
42
FIND VARIANCE OF EACH SEGMENT
44
HIGH-VARIANCE BURSTS MOTION DETECTED
46

FIG. 3

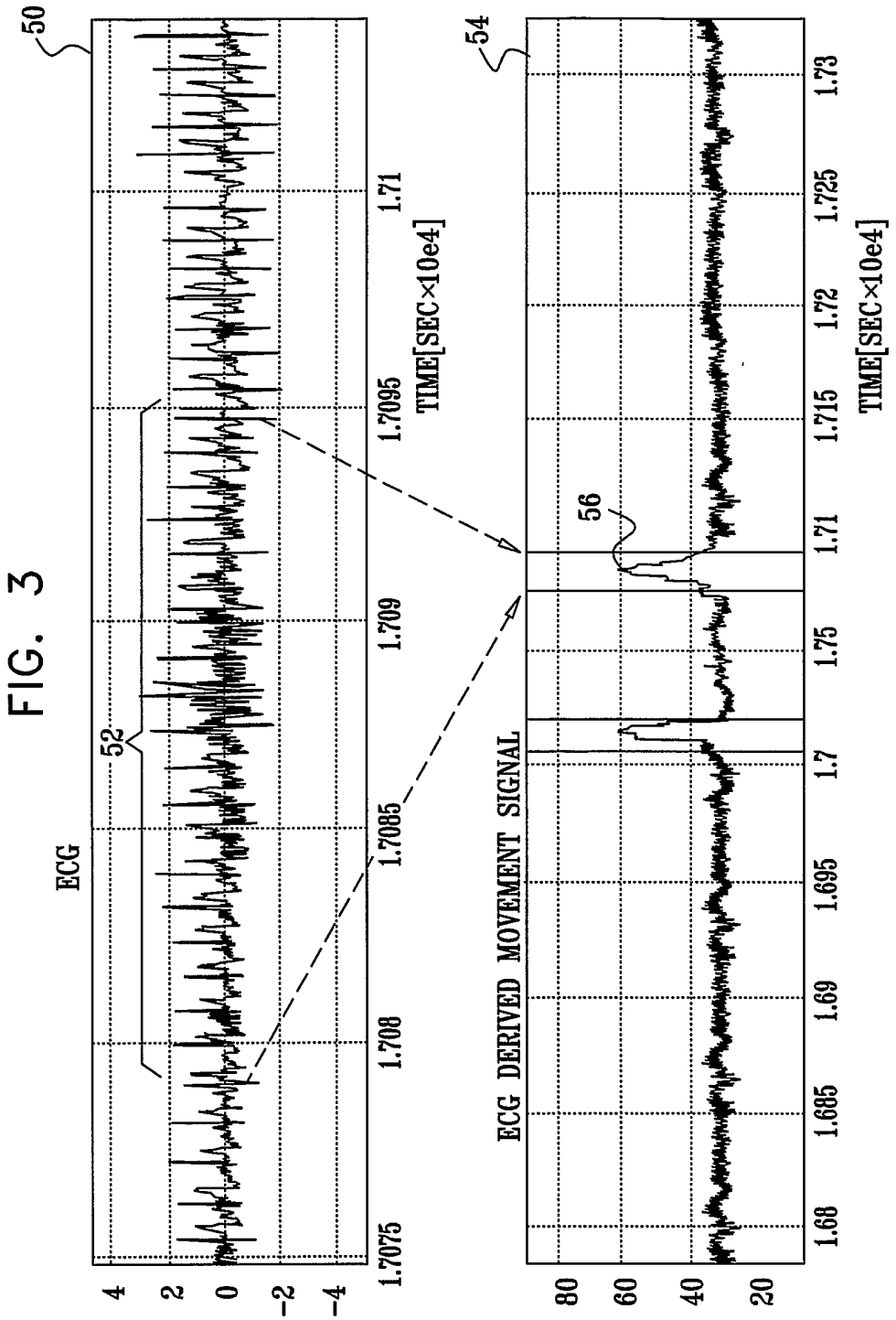

50
ECG
52
4
2
0
−2
−4
1.7075
1.708
1.7085
1.709
1.7095
1.71
TIME[SEC×10e4]
54
ECG DERIVED MOVEMENT SIGNAL
56
80
60
40
20
1.68
1.685
1.69
1.695
1.7
1.75
1.71
1.715
1.72
1.725
1.73
TIME[SEC×10e4]

FIG. 4

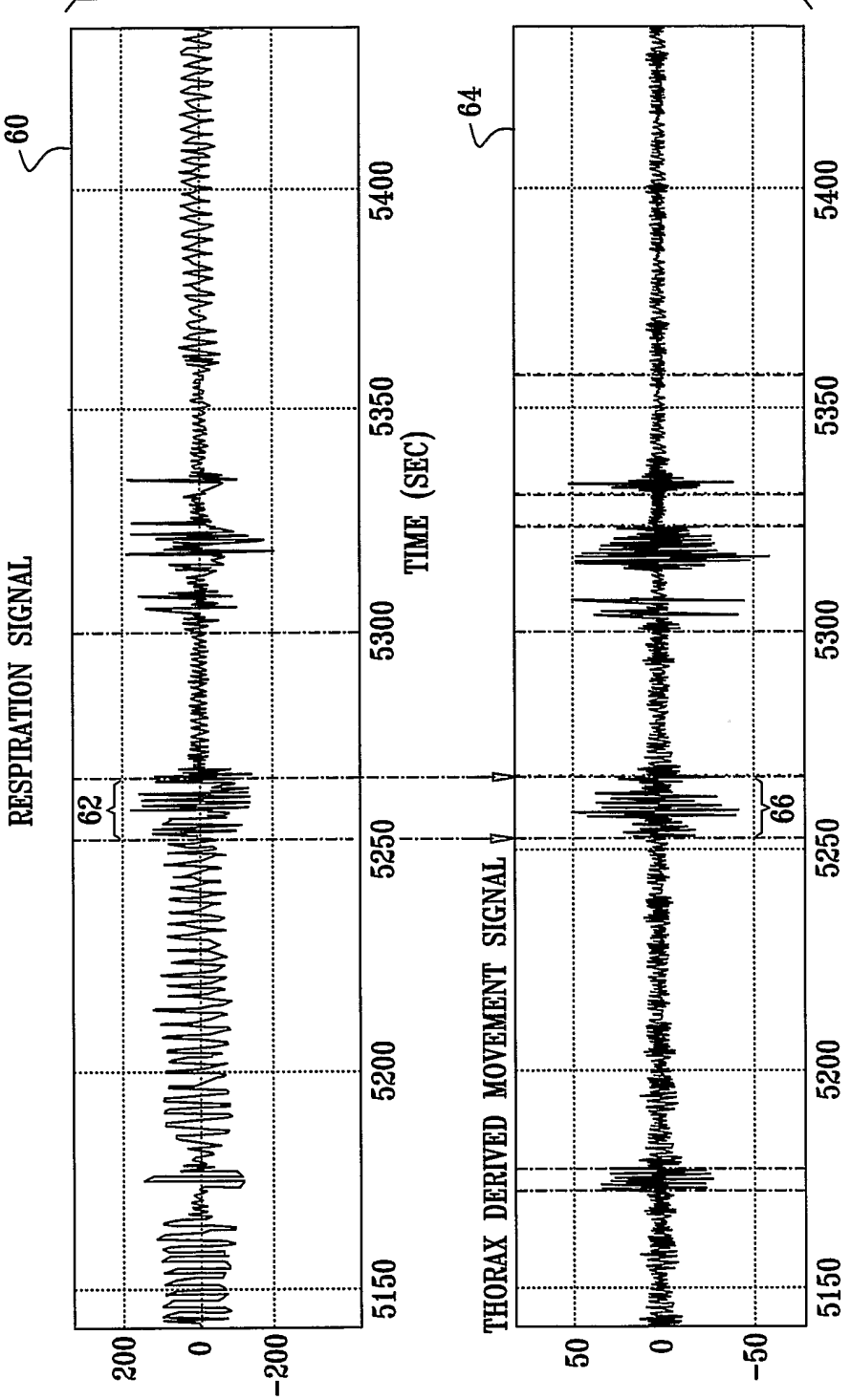

RESPIRATION SIGNAL
60
62
200
0
-200
5150
5200
5250
5300
5350
5400
TIME (SEC)
THORAX DERIVED MOVEMENT SIGNAL
64
66
50
0
-50
5150
5200
5250
5300
5350
5400

FIG. 5

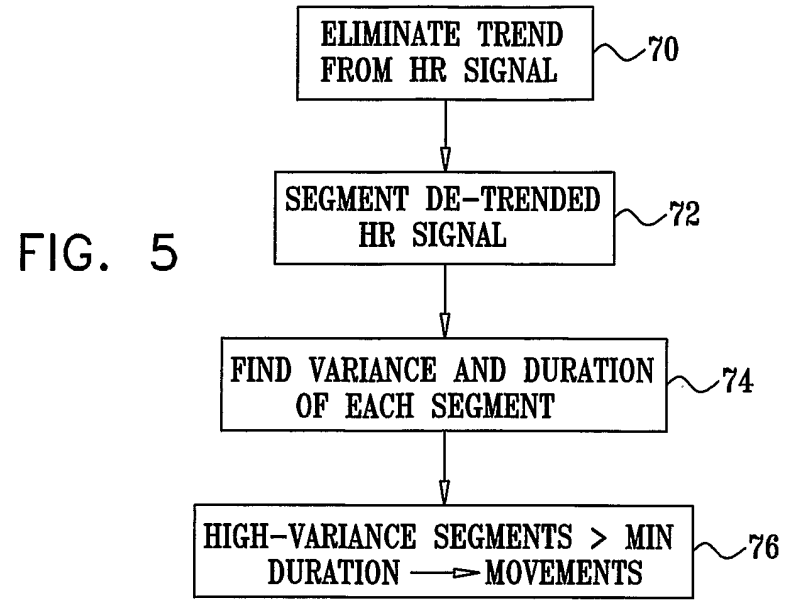


FIG. 6A

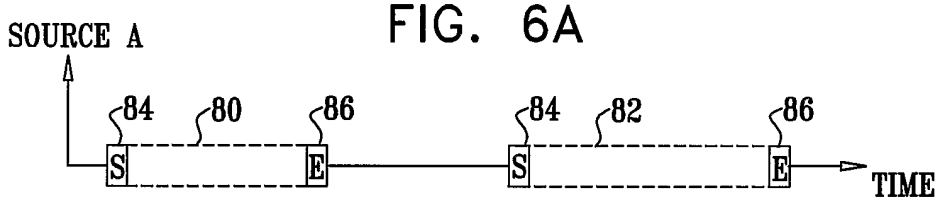


FIG. 6B

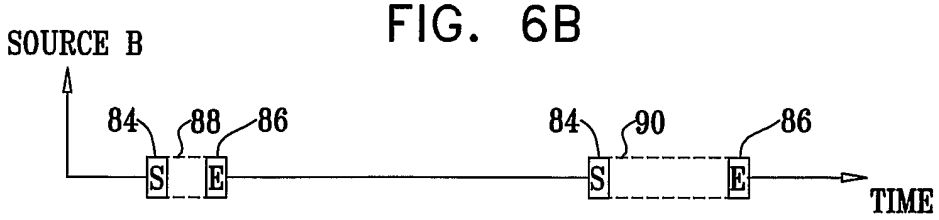


FIG. 6C

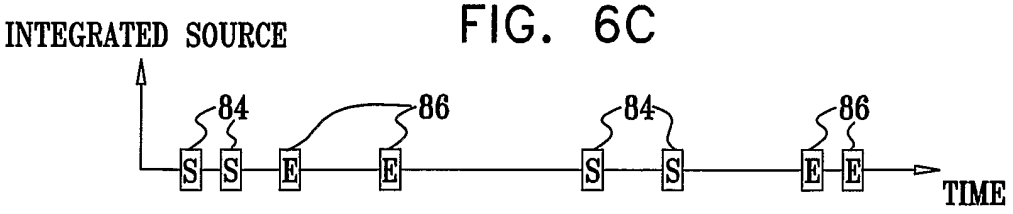


FIG. 6D

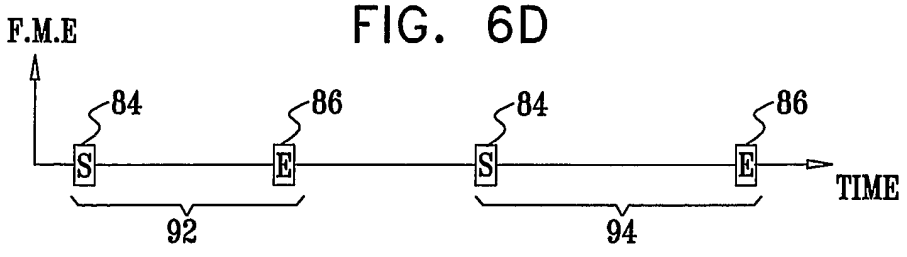


FIG. 7A

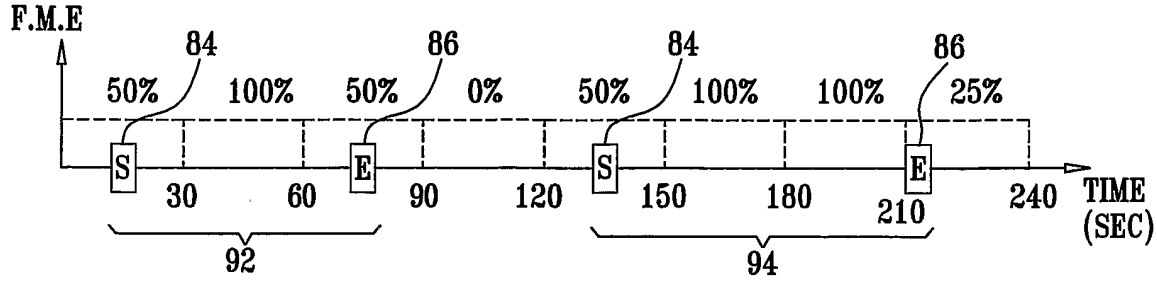


FIG. 7B

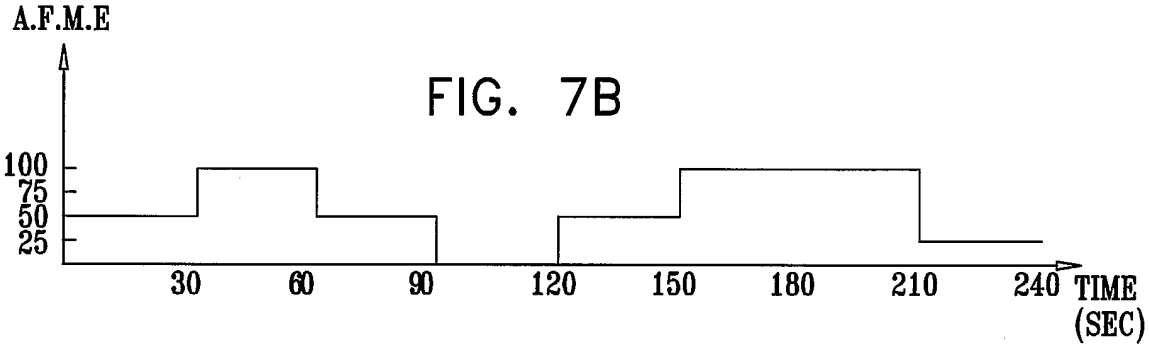


FIG. 8A

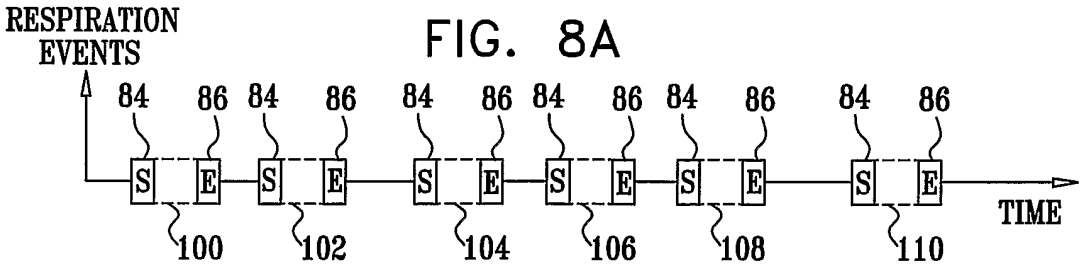


FIG. 8B

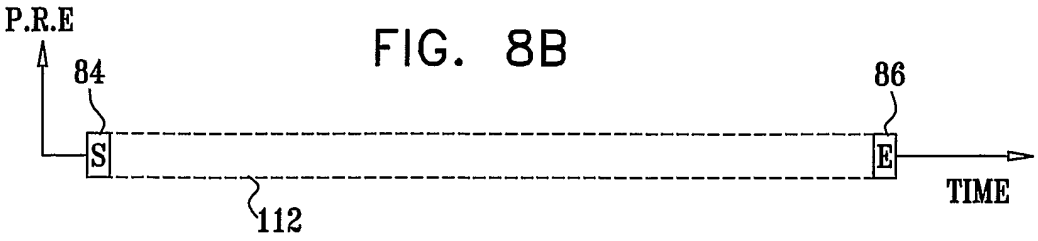


FIG. 9

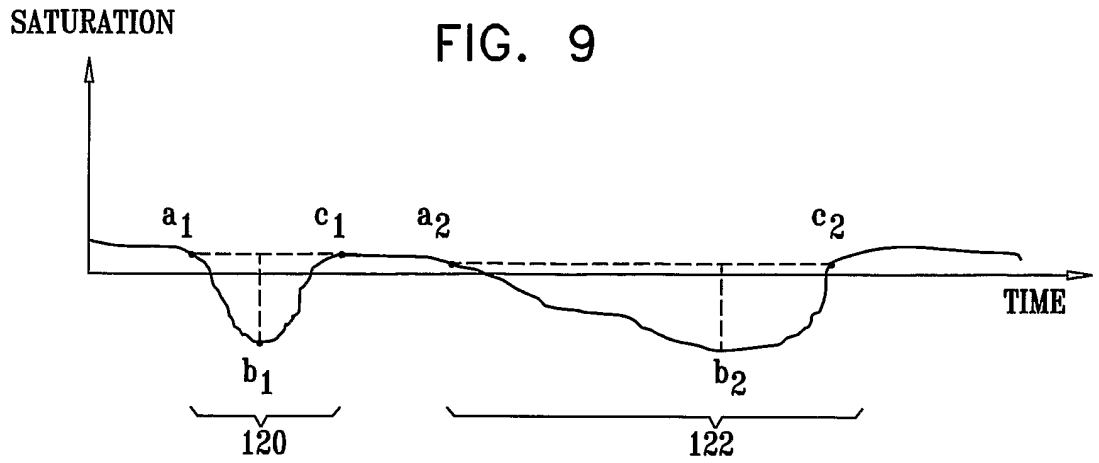


FIG. 10

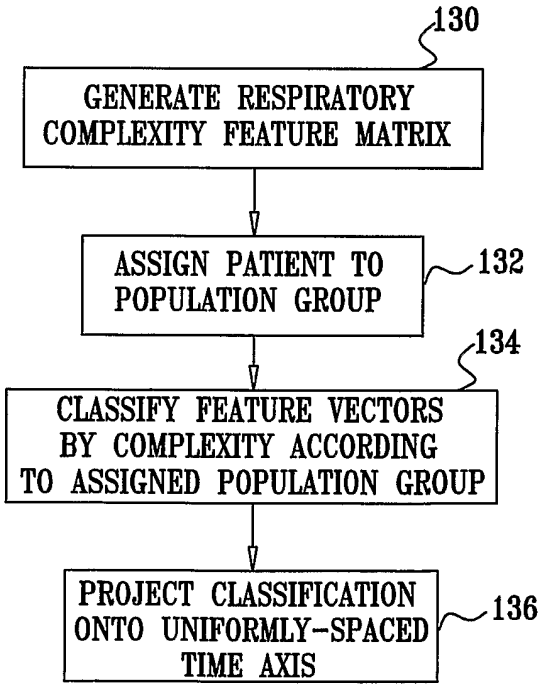


FIG. 11

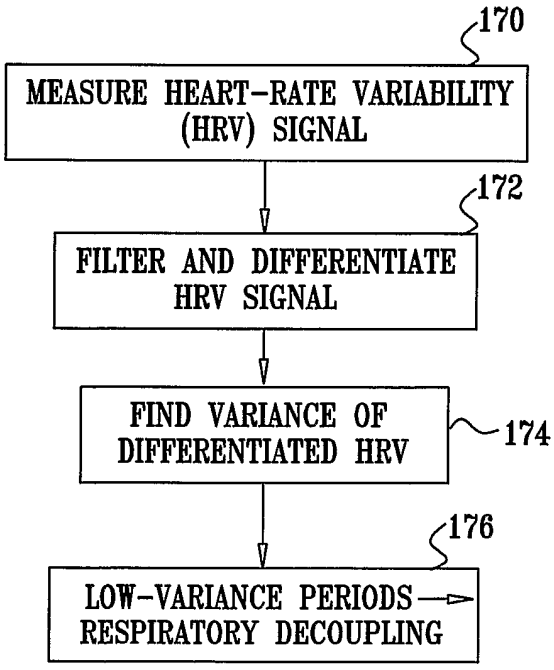


FIG. 12

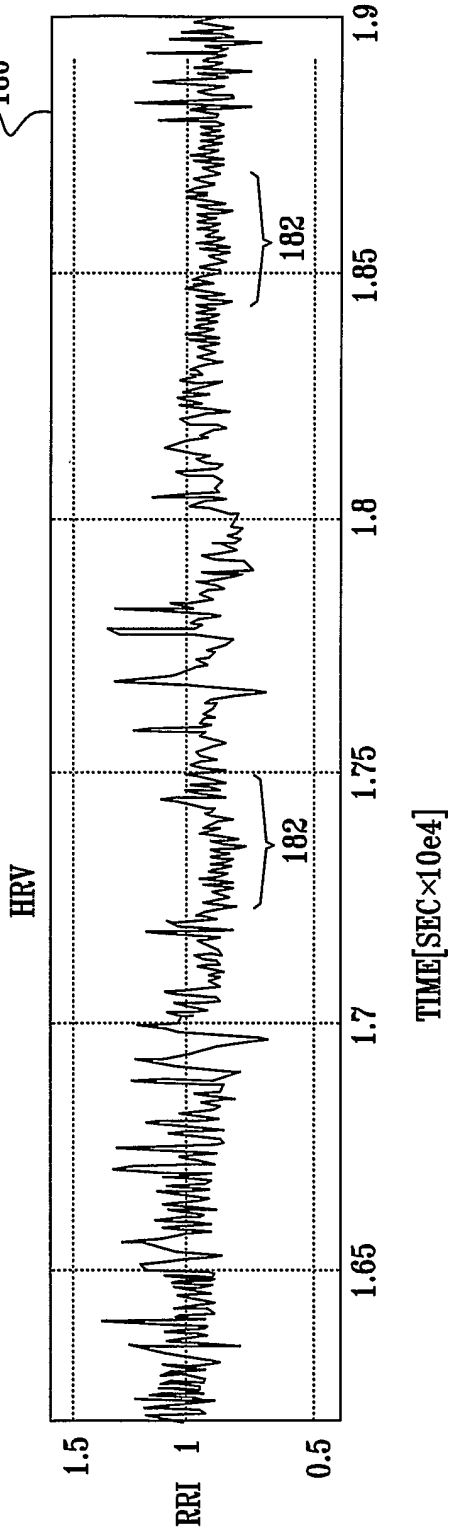
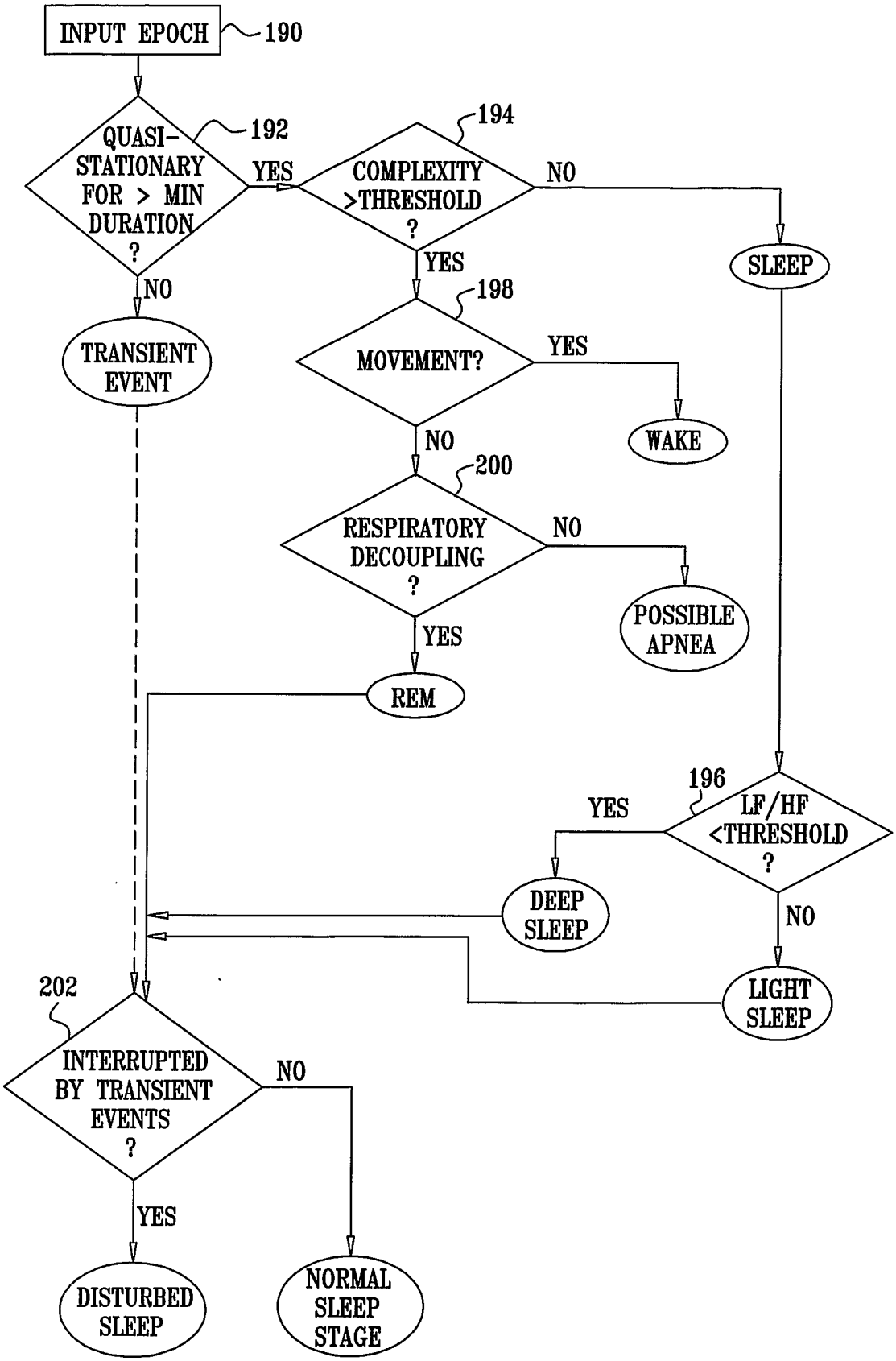


FIG. 13


INPUT EPOCH
190
QUASI-STATIONARY FOR > MIN DURATION ?
192
YES
NO
TRANSIENT EVENT
COMPLEXITY >THRESHOLD ?
194
NO
SLEEP
YES
MOVEMENT?
198
YES
WAKE
NO
RESPIRATORY DECOUPLING ?
200
NO
POSSIBLE APNEA
YES
REM
LF/HF <THRESHOLD ?
196
YES
DEEP SLEEP
NO
LIGHT SLEEP
INTERRUPTED BY TRANSIENT EVENTS ?
202
NO
YES
DISTURBED SLEEP
NORMAL SLEEP STAGE

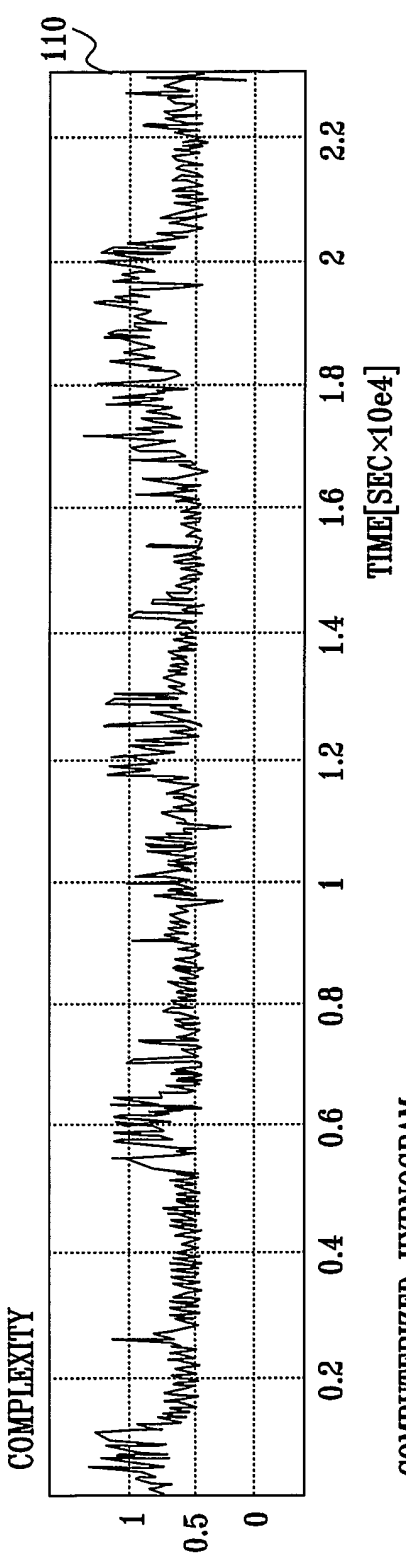


FIG. 14A

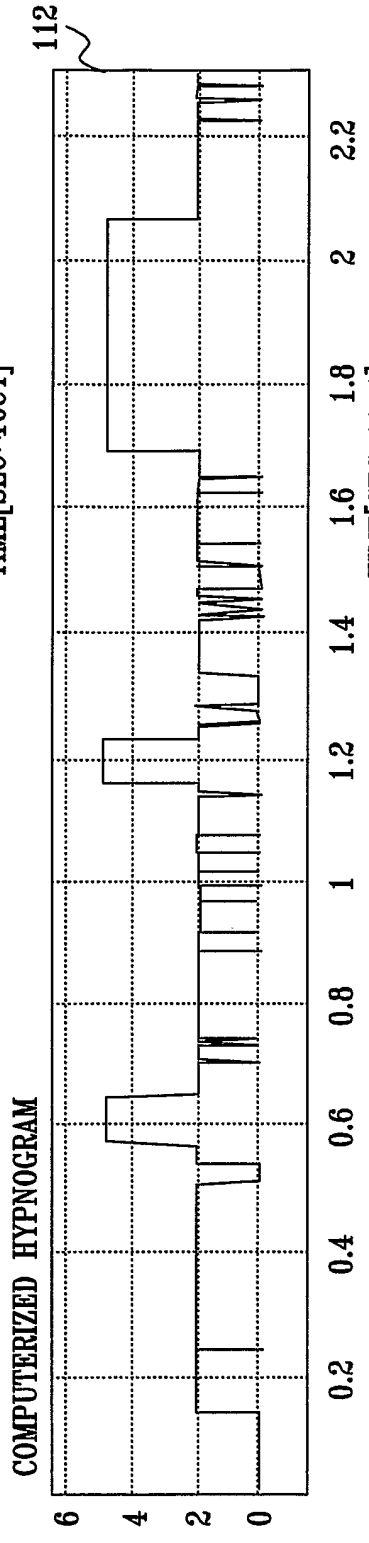


FIG. 14B

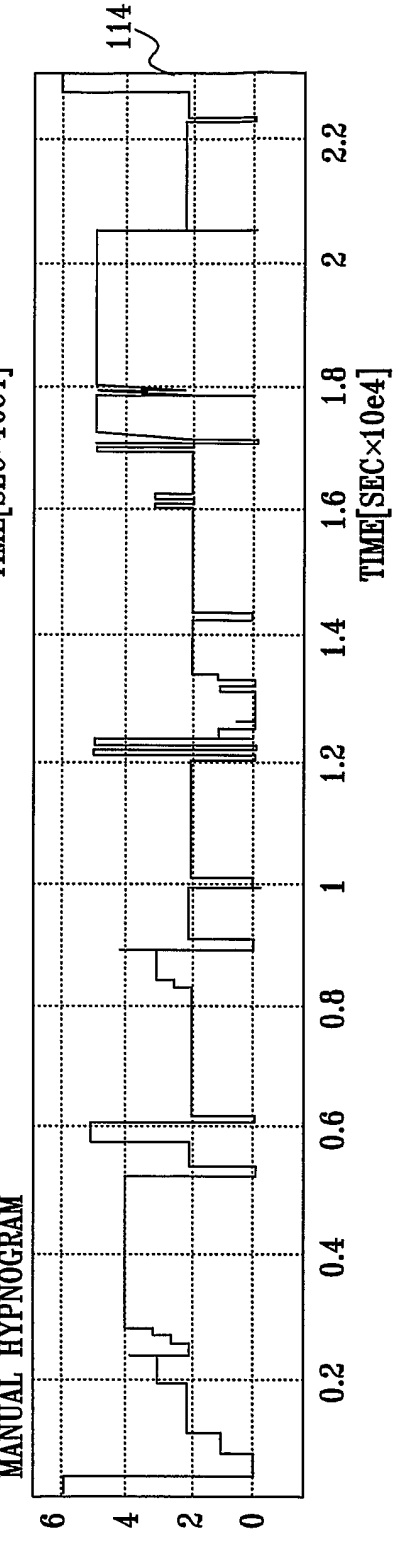


FIG. 14C

FIG. 15

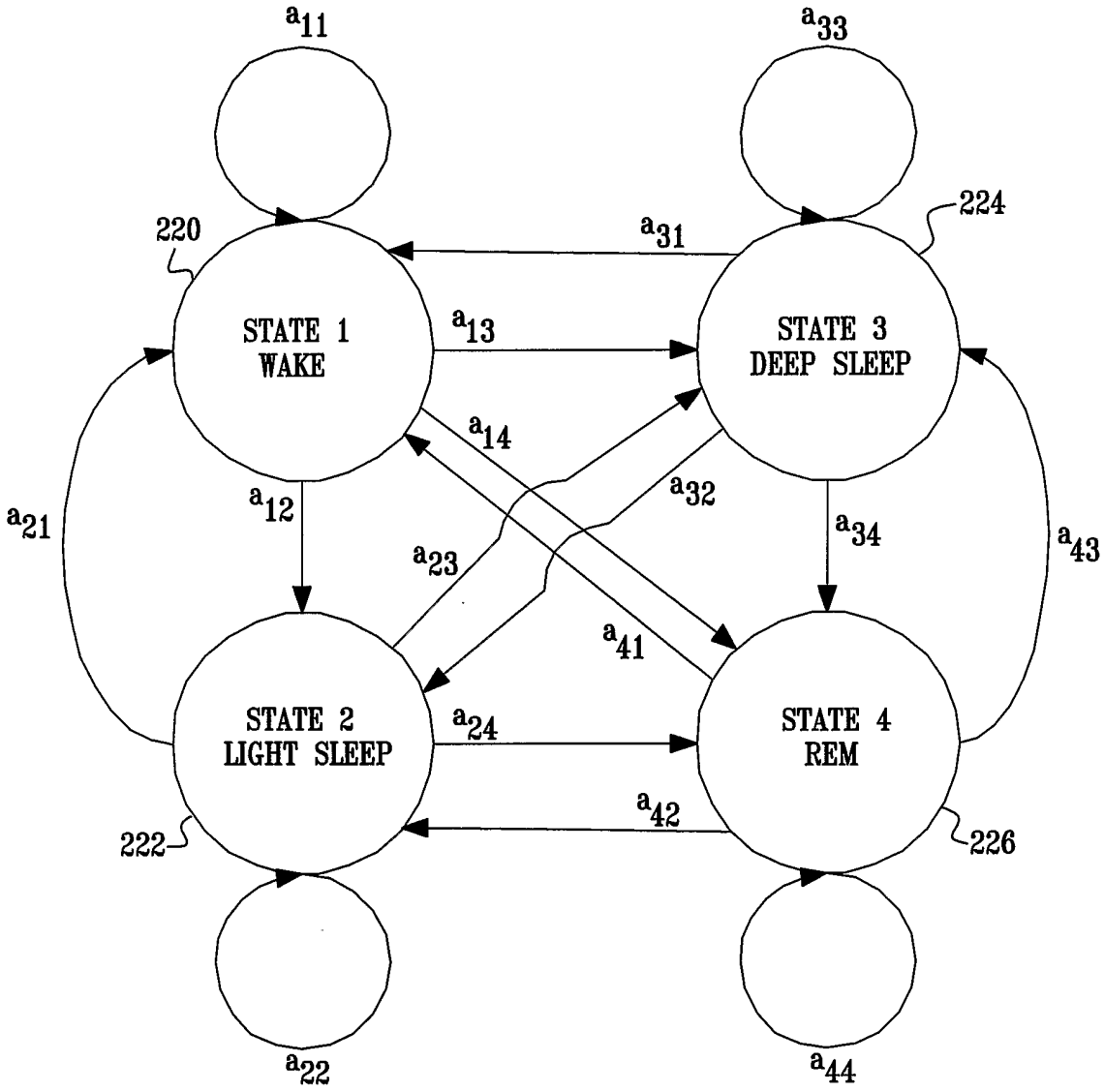
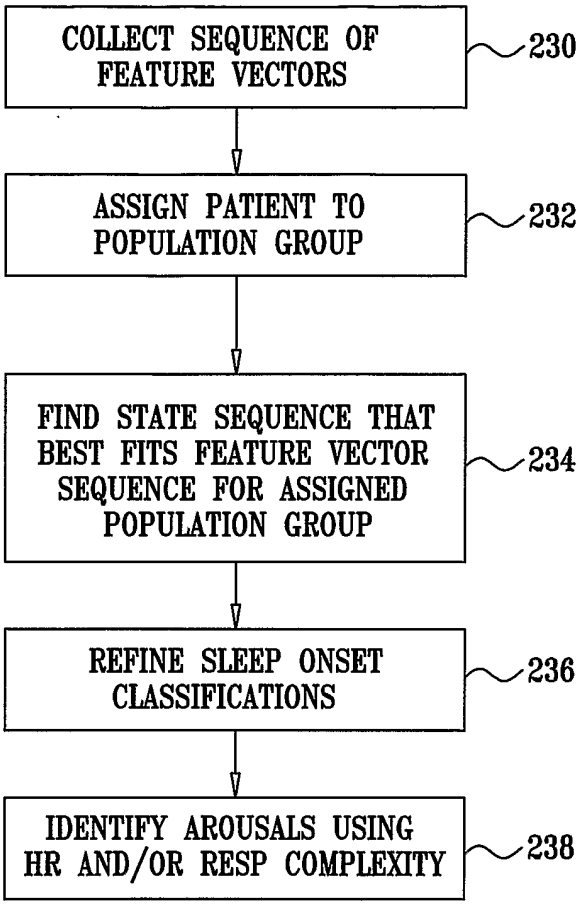

a11
a33
220
224
a31
STATE 1
WAKE
a13
STATE 3
DEEP SLEEP
a14
a12
a32
a21
a34
a43
a23
a41
STATE 2
LIGHT SLEEP
a24
STATE 4
REM
a42
222
226
a22
a44

FIG. 16


COLLECT SEQUENCE OF FEATURE VECTORS
230
ASSIGN PATIENT TO POPULATION GROUP
232
FIND STATE SEQUENCE THAT BEST FITS FEATURE VECTOR SEQUENCE FOR ASSIGNED POPULATION GROUP
234
REFINE SLEEP ONSET CLASSIFICATIONS
236
IDENTIFY AROUSALS USING HR AND/OR RESP COMPLEXITY
238