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METHOD AND APPARATUS FOR DIAGNOSING SLEEP BREATHING DISORDERS WHILE A PATIENT IS AWAKE

STATEMENT OF GOVERNMENT INTEREST

The invention described herein may be manufactured and used by or for the Government of the United States of America for governmental purposes without the payment of any royalties thereon or therefor.

BACKGROUND OF THE INVENTION

(1) Field of the Invention

This invention is generally related to methods and apparatus for performing medical diagnoses and particularly to a method and apparatus for enabling the diagnosis of sleep breathing disorders or other physiological respiratory dysfunction while the patient is awake.

(2) Description of the Prior Art

Sleep breathing disorders and other physiological respiratory dysfunctions in humans constitute an area requiring diagnosis. One such area is called obstructive sleep apnea or sleep disorder breathing. Within the pediatric, infant and newborn population the incidence of apparent life threatening events, sudden infant death syndrome and sleep disorder breathing have all been well documented. Sleep apnea also affects over 25% of apparently healthy adults age 55 and older. Sleep apnea
contributes to daytime fatigue, increased workplace accidents and a number of cardiovascular disorders. The need for a relatively easily implemented procedure exists to provide efficient methods and procedures for diagnosing these various physiological respiratory dysfunctions.

United States Letters Patent No. 4,982,738 to Griebel discloses a diagnostic apnea monitor system that records snoring and respiration sounds made by a patient as well as the patient's heart rate while the patient is sleeping. Signals indicative of snoring sounds and the time intervals therebetween are produced from the recorded respiration. The system generates a first respiration disturbance index representing the number of intervals per hour between episodes of snoring. An average heart rate is also generated in response to the patient's recorded second respiration disturbance index representing the number of episodes per hour in which the patient's heart rate remained at 90% to 109% of its average rate is calculated. A physician then evaluates the first and second disturbance indices to determine whether obstructive sleep apnea is indicated.

United States Letters Patent No. 5,101,831 to Koyama et al. discloses a system for discriminating a sleep state and selectively waking a patient. This system provides variation indices representing the variation of a biological signal on the basis of a first variation amount denoting a tendency of a time series of measured biological signal to increment from the starting time of the measurement and a second variation amount denoting the temporal variation of the biological signal. These
signals enable the discrimination of different sleep states, namely the NREM and REM sleep states, on the basis of the distribution of the density of the variation indices exceeding a predetermined threshold.

United States Letters Patent No. 5,105,354 to Nishimura provides a method and apparatus for correlating respiration and heartbeat variability and particularly a method for forecasting sudden infant death syndrome by investigating the correlation between respiration and heart beat in a normal state and a sleep-apnea state of a newborn. In essence the system detects respiratory information, produces an envelope indicative of the respiration information and samples the envelope to produce a fast Fourier transform spectrum of the envelope information. Simultaneously the system detects cardio-electric information in the form of an EKG, detects the peak value and calculates a sequential R-R interval series that is fast Fourier transformed into a spectrum of the R-R interval variation. These two complex conjugations are multiplied and, through a fast Fourier transform, analyzed to calculate a correlation between respiration and heart beat that can then be evaluated to identify the state just before the normal state of a newborn will convert to the state of sleep apnea and forecast sudden death syndrome.

United States Letters Patent No. 5,385,144 to Yamanishi et al. discloses a respiration diagnosis apparatus that distinguishes between obstructive sleep apnea and central apnea automatically. An analog signal processor generates pulse wave signals based on light received from a light emitting means and
passing through or reflecting off living tissue. A pulse wave line analog signal processor extracts change components of a base line of the generated pulse wave signal. A master microcomputer distinguishes between obstructive apnea and central apnea on the basis of the extracted pulse wave base line change components.

United States Letters Patent No. 5,398,682 to Lynn discloses a method and apparatus for the diagnosis of sleep apnea utilizing a single interface with a human body part. More specifically, the diagnosis identifies the desaturation and resaturation events in oxygen saturation of a patient's blood. The slope of the events is determined and compared against various information to determine sleep apnea.

It has also been recognized that cardio and respiratory signals are signals of non-linear dynamical systems. United States Letters Patent No. 5,404,298 to Wang et al. and 5,453,940 to Broomhead et al. disclose dynamical system analyzers or chaos analyzers useful in determining characteristics based upon such dynamical system signals. Additional information on the use of chaos is contained in Strogatz, Steven H., Non-linear Dynamics in Chaos, Reading, MA, Addison Wesley Publishing Company, 1994, p. 379.

United States Letters Patent No. 5,769,084 filed by the same inventors as this application, discloses an apparatus and method for identifying the timing of the onset of and duration of an event characteristic of sleep breathing disorder during a conventional overnight sleep study. Chaotic processing techniques analyze data concerning one or more cardio-respiratory functions,
such as nasal airflow, chest wall effort, oxygen saturation, heart beat and heart activity. Excursions of the resulting signal beyond a threshold provide markers for the timing of such an event that is useful in the diagnosis of obstructed sleep apnea and other respiratory dysfunctions.

Conventional sleep studies require significant resources. Generally they are conducted in special facilities. One patient is located in one room for the night and typically arrives about 8:00 PM and leaves about 6:00 am. At least two trained technicians generally are present for the duration of each test. They attach the various sensors to the head, chest, arms and legs and then monitor the various signals from different patients. The results as multichannel charts and observed events are then reviewed by one or two physicians of different specialties in order to determine the existence of sleep apnea or other respiratory dysfunction conditions. Given this requirement, conventional sleep studies require significant physical plant assets that are not available for other purposes. In addition, the diagnosis is labor intensive.

Katz et al., "A Practical Non-Linear Method for Detection of Respiratory and Cardiac Dysfunction in Human Subjects", SPIE Vol. 2612, Page 189 (1995) hypothesizes the possibility of making a diagnosis while a patient is awake. The paper presents no quantitative results and merely plots a temporal signal dependent on a physiological function. What is needed is a diagnostic test that can screen patients sleeping disorders or other respiratory dysfunctions while the patient is awake thereby to eliminate the
requirement for conventional sleep studies in many patients. Notwithstanding the existence of the foregoing prior art, the current conventional approach for diagnosing sleep apnea continues to be the diagnosis of choice.

**SUMMARY OF THE INVENTION**

Therefore it is an object of this invention to provide a method and apparatus for facilitating the diagnosis of sleep breathing disorders while a patient is awake.

Another object of this invention is to provide a method and apparatus for generating markers that identify the onset and duration of an event characteristic of a sleep breathing disorder while a patient is awake.

In accordance with this invention, a cardio-respiratory function is monitored over time while a patient is awake. A digitized time series representation of each monitored cardio-respiratory function is generated. Chaotic processing of the corresponding time series representation yields a processed signal. Excursions of this signal beyond a corresponding threshold value indicate the time of an onset of an event and its duration.

**BRIEF DESCRIPTION OF THE DRAWINGS**

The appended claims are intended to point out with particularity and to claim distinctly the subject matter of this invention. The various objects, advantages and novel features of this invention will be more fully apparent from a reading of the following detailed description in conjunction with the
accompanying drawings in which like reference numerals refer to like parts, and in which:

FIG. 1 depicts a patient and, in block diagram form, apparatus for implementing this invention;

FIG. 2 is a flow chart representing the method in accordance with this invention employed by the apparatus in FIG. 1;

FIG. 3 is a diagram useful in understanding the operation of the apparatus and methods of FIGS. 1 and 2;

FIGS. 4A and 4B compare signals corresponding to one cardio-respiratory function when a individual is awake (FIG. 4A) and is asleep (FIG. 4B).

DESCRIPTION OF THE PREFERRED EMBODIMENT

Apparatus 10 embodying this invention includes one or more monitors 11, each of which monitors at least one cardio-respiratory function of a patient 12 over time. Each monitor 11 produces signals that a selector 13 can convey to a chaotic processor 14 that converts each selected signal into a time series representation of the monitored cardio-respiratory function and then generates a signal for that function based upon chaotic processing of the time series representation. An output 15 then identifies as a marker each excursion of the signal beyond a corresponding threshold value thereby to indicate the timing of the onset of an event and its duration. FIG. 1 discloses specific embodiments of the monitors 11, chaotic processor 14 and output 15. As shown the selector 13 could act as a multiplexer or switch to sample each of these signals in
seriatim. It will be apparent that the use of the selector is for purposes of explanation only. If the apparatus is designed to monitor only one function, the selector 13 can be eliminated. If on-line results are required and multiple functions are monitored, the components of the chaotic processor 14 could be duplicated either by incorporating multiple chaotic processors or by time sharing programs within the single chaotic processor in a manner synchronized by the selection of signals and known in the art.

One of the monitors 11 in FIG. 1 is an air flow monitor 16 that monitors oral nasal airflow. Any of a number of different flow and pressure transducer-based monitors can be used to provide a signal that accurately models the air flow from the patient 11. The output of the air flow monitor 16 may generate a strip chart and the function of the selector 13 could be provided by apparatus that automatically or with manual intervention provides an input to a digital-to-analog converter or otherwise enables the signal to be submitted into the chaotic processor in an analog form. Alternatively and preferably the analog signals from the air flow monitor 16 could be digitized immediately for storage in a local memory.

Before discussing the process of a signal from one of the monitors 11 and their respective signals it will be helpful to review the operation of the chaotic processor 14. Essentially in accordance with one aspect of this invention, the chaotic processor converts an analog signal from a monitor 11 into a chaotic radius signal and a differential radius signal. FIG. 2
1 depicts the steps in one method for analyzing such a signal to
determine the timing of the onset of an event characteristic of a
sleep breathing disorder and its duration. Particularly, as an
initial step, the system uses the signal from the oral-nasal air
flow monitor 16 to measure nasal air flow as a cardio-respiratory
function. This measurement is made while the patient is in a
comfortable position and is awake. The measurement may last for
any arbitrary time. It is expected that measurements will be
made for up to one hour or so. A time sample A/D converter 22 in
the chaotic processor 14 converts the measured function into a
digitized time series of samples of the monitored function at a
sampling frequency.

The sampling frequency must be selected to provide adequate
sampling so that the following steps in the process will have
sufficient data for providing reliable results with a reasonable
temporal resolution. Oversampling is preferable to undersampling
although this will increase the burdens of the processing time
and complexity. It has been found that the minimum sampling
frequency ought to be greater than the greatest frequency of
physiologic relevance with respect to the monitored cardio-
respiratory function. As a general rule, a sampling frequency of
two to five times the Nyquist sampling frequency for linear
signals provides good results. A sampling frequency between 10
Hz and 40 Hz provides adequate sampling for nasal air flow.
Sampling rates above 40 Hz have been found to be effective for
monitoring other non-linear physiological parameters.
Still referring to FIGS. 1 and 2, the converter 22 and step
23 produce a digitized representation of the incoming cardio-
respiratory function signal in the form of a scalar time series
having the general form:

\[ v(n) = v(t + ndt) \]  (1)

where "t" is the start time for the diagnosis, "dt" is the sample
interval (e.g., 0.10 seconds at a 10Hz sampling frequency) and
"n" is the sample number and \( n = 1, 2, 3, \ldots N \).

A vector time delay interval generator 24 in FIG. 1
processes this scalar time series to determine an interval at
which a series of vectors should be generated. This process can
use several known techniques. Step 25 in FIG. 2 depicts a
preferred alternative that uses a known process based upon
average mutual information (AMI), represented by an AMI module 26
in FIG. 1, to determine the vector time delay. As known, average
mutual information quantitates the information theoretic
properties of chaotic systems. More specifically, average mutual
information indicates how much information exists in the form of
a time series, such as shown in Equation 1, about the measurement
of that signal and shown in FIG. 1 concerning the measurement of
that signal at a time \( Tdt \) later. That is, a time series \( v(n) \) for
average mutual information indicates how much information will be
available to predict the voltage level at a time \( Tdt \) later, i.e.,
the value \( v(n+T) \). Average mutual information processes

distribute the measurements \( v(n) \) and \( v(n+T) \) over the set of
measured data and determine the joint distribution of
measurements of these two quantities. The first of these
distributions is $P(v(n))$, the second is $P(v(n+T))$, and the third
is $P(v(n), v(n+T))$. The mutual information between these
measurements is:

$$\ln \left[ \frac{P(v(n), v(n+T))}{P(v(n))P(v(n+T))} \right]$$

(2)

where "ln" is the natural logarithm. For $N$ observations, the
average over all measurements is the AMI given by:

$$AMI = \sum_{n=1}^{N} \left[ \frac{P(v(n), v(n+T))}{P(v(n))P(v(n+T))} \ln \frac{P(v(n), v(n+T))}{P(v(n))P(v(n+T))} \right]$$

(3)

For independent measurements, each term in the above sum
vanishes due to factorization of the joint probability
$P(a, b) = P(a)P(b)$. For the case $T=0$, $I(0)$ is large because there
is full knowledge of the measurements. Generally, however, $I(T)
will be greater than zero. The objective becomes determining an
intermediate value of $T$ that will preserve the information in the
system without overburdening the process. With average mutual
information, one approach is to choose the value for $T$ that
corresponds to the first minimum of $I(T)$, although any value of $T
near the first minimum should suffice. As will be apparent the
value of $T$ can be any arbitrary number. Normally, the value will
be refined so that it corresponds to an integer multiple of the
sampling integral established in the converter 22.

Once the value $T$ has been obtained, step 27 in FIG. 2 uses a
time series vector representation generator 28 in the chaotic
processor 14 to convert the digitized samples into a time series
vector representation that has a sampling interval of $T$. Each
vector points to the scalar value at an interval "T" later. More
specifically the time series vector generator 28 in FIG. 1 operating in accordance with step 27 in FIG. 2 generates a d-dimensional set of vectors from a sequence of fixed vector time delays, T, in the form:

\[ y(n) = [v(n), v(n+T), v(n+2T), \ldots, v(n+(d-1)T)] \]  

where:

- \( v(n) \) is the original time series datum at time index \( n \);
- \( v(n+T) \) is datum from the same time series offset in the positive direction by the vector time delay interval \( T \);
- \( v(n+2T) \) is datum from the same time series offset in the positive direction by the vector time delay interval \( 2T \);
- \( v(n+(d-1)T) \) is the datum offset by the vector delay interval \( (d-1)T \) where \( d \) is an embedding dimension to be obtained from an embedding delay value generator 30 in FIG. 1 as it processes step 31 in FIG. 2; and
- \( n \) is an index number for time series datum where \( n = 1, 2, 3 \ldots N \) and the maximum number of indices. \( N \), may be selected to be any arbitrary large value. Typical values are 900 or greater.

These time delays are presented as having a positive direction. As apparent, they also can be taken as having a negative direction.

The resulting time series vector is then analyzed to determine a minimum embedding function, "d". As with respect to the generation of the vector time delay interval, alternate approaches are available for determining the embedding delay.
value. A preferred approach that has produced reliable results utilizes a known "global false nearest neighbor" process that is implemented in the generator 30 by an GFNN module 32. Basically this process is based upon the concept that when points of higher dimension are projected down to a space of lower dimension, there are overlapping orbits in the low dimension space such that if the process were reversed and given space were projected to a higher dimension it could be reasonably expected that neighboring points along a trajectory would separate. Basically the process starts with a first dimension, unfolds the time series vector representation to higher and higher dimensions while keeping track of the percentage of nearest neighbors that spread apart at each integer increase of dimension. When the quality of the predictions or motions of neighbors become independent of the dimensions, the resulting delay for one representation to the other producing the desired result constitutes the minimum embedding value.

More specifically the process determines the dimension "d" with points made out of the vector representation in which the nearest neighbors ynn(n) of the point y(n) is given by:

$$ynn(n) = [vnn(n), vnn(n+T) \ldots vnn(n+(d-1)T)]$$ (5)

The process determines whether or not these points remain near in dimension (d+1), whether vector y(n) is augmented by a component v(n+dT) and ynn(n) is augmented by vnn(n+dT). For small distances the neighbors are true neighbors. For large distances false neighbors exist. When the percentage of false neighbors
drops to zero, the resulting delay is the minimum embedding
dimension or delay value.

Once the minimum embedding delay value has been determined,
step 33 in FIG. 2 and a chaotic radius processor 34 in FIG. 1
compare the magnitude of each term in the time series vector
representation with a term delayed by the embedding delay value
to obtain a chaotic radius for each term. In general terms, the
chaotic radius \( r \) for \( n \) dimensions is given by:

\[
r = \sqrt[2]{X(t)^2 + X(t + p)^2 + \cdots + X(t + (n-1)p)^2}
\]

The chaotic radius processor 34 in FIG. 1 effectively plots the
scalar value of each point in the vector for some value of \( n > 1 \).
FIG. 3 depicts a solution for \( n = 2 \). On a horizontal scale and
a vertical scale, \( X(t) \) and \( X(t+p) \) represent the component
magnitudes of the vector at time "t", points \( X(t+d) \) and \( X(t+d+p) \)
respectively represent the change in magnitude between two
successive points at "t" and at \( (t+d) \). Consequently the chaotic
radius \( r \) for \( n = 2 \) is given by:

\[
r = \sqrt{X(t)^2 + X(t + p)^2}
\]

It will be further evident that the differential radius \( (dr) \)
can be determined by:

\[
gr = \sqrt{[X(t + d) - X(t)]^2 + [X(t + d + p) - X(t + p)]^2}
\]
or by

\[
gr = r(i + 1) - r(i)
\]
Step 35 in FIG. 2 and a differential radius processor 36 in FIG. compute, for each vector in the time series vector representation, a corresponding differential radius, \( dr \), according to either of the foregoing alternatives.

Referring again to FIG. 1, the chaotic radius or the differential radius can transfer from the chaotic radius processor 34 or differential radius processor 36 to a threshold detector 40 in the output 15. A threshold selector 41 can be adjusted for the signal corresponding to chaotic radius or differential chaotic radius for different cardio-respiratory functions in order to provide, on a display 42, a representation of the chaotic radius or differential chaotic radius. Typically the threshold will be set to a value either of two or three standard deviations outside of the mean level for a specified time interval. These have been found to be useful in clinical diagnoses.

With this understanding of the operation of the chaotic processor 14, reference is again made to the patient 12 in FIG. 1 undergoing diagnosis in accordance with this invention. As shown in FIG. 1, the air flow monitor 16 provides an input to the chaotic processor 14. It has been found that a measurement of a single cardio-respiratory function can provide sufficient data for making a diagnosis. In some situations it may desirable to use a measurement of another cardio-respiratory function exclusively of the air flow measurement or as a complement to the air flow measurement. The results from the complementary measurement could then be used to corroborate the signals from
the air flow monitor. Consequently in FIG. 1 additional monitors are shown in phantom. These include an ECG 44 that measures electrical heart activity; a heart rate monitor 45 that measures heart rate; an oximeter that attaches to an individual's index finger and provides an indication of oxygen saturation levels; and a chest wall impedance monitor 47 that measures chest wall effort. Each of the monitors 44 through 47 are well known in the art. The chart recorder 50 may be included with the selector 13 to provide a real-time graphical history of the test by displaying the variations in the signal or signals being used during the diagnosis.

FIGS. 4A and 4B graphically compare the results of analyses made on the same patient while the patient was awake and asleep. Specifically, FIG. 4A depicts a trace 51 of the differential radius produced over a 1.5-minute test interval while the patient was awake. This data can be analyzed statistically to establish a threshold as previously described. Alternatively the threshold can be set at an arbitrary number based upon empirical information. For purposes of this explanation, it is assumed that the threshold is set at -10. FIG. 4A depicts sixteen excursions beyond the threshold represented by dashed line 52. These are identified as excursions A through P.

FIG. 4B depicts a trace 53 of the differential radial trace taken from a 1.5-minute interval of a conventional sleep study. For purposes of comparison, the threshold is again set to -10 as represented by the dashed line 54. During this interval
there are sixteen excursions beyond the threshold 54. They are
designated as excursions A through P.

The average repetition rate of the excursions over the test
interval is a key indicator of the onset of sleep apnea or other
respiratory dysfunction. By comparing FIGS. 4A and 4B it will be
apparent that the timing of the different excursions beyond the
thresholds are different. However, the average number is
statistically the same and in this particular case, exactly the
same. Thus the information obtained over the 1.5-minute test
interval while the patient is awake, as shown in FIG. 4A,
provides the same quantitative data as the 1.5-minute interval
shown in FIG. 4B obtained when the patient is undergoing a
conventional sleep study.

Thus FIG. 4A provides essentially the same information in a
short test while the patient is awake as when the patient is
asleep for a long interval. Moreover, it has been found that the
number of measurements that must be taken can be reduced. In
this particular embodiment only nasal airflow was monitored,
eliminatating the myriad sensors utilized in conventional sleep
studies. This further simplifies the diagnostic procedures.

Consequently, the physical assets of a hospital that must be
devoted to such a test can be significantly reduced for the test.

Moreover, even assuming an interval for allowing the patient to
be interviewed, prepared and tested for up to one hour, it should
be possible to run 8 tests during normal working hours in the
same time that would be required to conduct one sleep study after
normal business hours. As a result the number of patients that
can be screened at a given facility can be greatly increased over
the number that can be screened using conventional sleep studies
at a significantly lower cost.

Any number of available chaotic processing systems can be
utilized to generate the information provided by the chaotic
processor 14 shown in FIG. 1. The individual components in FIG.
1, particularly those in the processor 13 and threshold detector
40 may comprise discrete structures or software modules in a data
processing system or a hybrid. The display 42 of the system in
FIG. 1 can comprise a simple graphical display of the
differential radius or radius over time or could superimpose
either signal against a threshold. Alternatively a circuit for
comparing the values of the differential chaotic radius or
chaotic radius against the thresholds and automatically marking
the time of such an excursion could also be produced in
conjunction with the information contained in the chaotic
processor 14.

This invention has been disclosed in terms of certain
embodiments. It will be apparent that many modifications can be
made to the disclosed apparatus without departing from the
invention. For example, temperature measurements of air flow
could be modified to pressure measurements of air flow to yield
similar information. Therefore, it is the intent
to cover all such variations and modifications as come
within the true spirit and scope of this invention.
METHOD AND APPARATUS FOR DIAGNOSING SLEEP
BREATHING DISORDERS WHILE A PATIENT IS AWAKE

ABSTRACT OF THE DISCLOSURE

An apparatus and method for identifying the timing of the onset of and duration of an event characteristic of sleep breathing disorder while a patient is awake. Chaotic processing techniques analyze data concerning a cardio-respiratory function, such as nasal air flow. Excursions of the resulting signal beyond a threshold provide markers for delivering the average repetition rate for such events that is useful in the diagnosis of obstructed sleep apnea and other respiratory dysfunctions.
MEASURE, WHILE THE PATIENT IS AWAKE, A CARDIO-RESPIRATORY PARAMETER (E.G., NASAL AIR FLOW)

CONVERT THE MEASURED PARAMETER INTO A DIGITIZED SERIES OF SAMPLES AT A SAMPLING FREQUENCY

ANALYZE THE SERIES OF SAMPLES USING AVERAGE MUTUAL INFORMATION TO DETERMINE A VECTOR TIME DELAY VALUE FOR THE PARAMETER

GENERATE A TIME SERIES VECTOR REPRESENTATION OF THE SERIES OF SAMPLES TAKEN AT INTERVALS CORRESPONDING TO THE VECTOR TIME DELAY VALUE

ANALYZE THE TIME SERIES VECTOR REPRESENTATION USING CHAOTIC PROCESSING TO IDENTIFY AN EMBEDDING DELAY VALUE

COMPARE THE MAGNITUDE OF EACH TERM IN THE TIME SERIES VECTOR REPRESENTATION WITH A TERM DELAYED BY THE EMBEDDING DELAY VALUE TO OBTAIN A CHAOTIC RADIUS OF DIMENSION "n"

DETERMINE A DIFFERENTIAL RADIUS FROM THE CHAOTIC RADIUS

FIG. 2
\[ X(t+d+p) \]

\[ X(t+p) \]

\[ X(t) \]

\[ X(t+d) \]

\[ d = \text{SAMPLE INTERVAL} \]

\[ p = \text{DELAY T} \]

FIG. 83