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Osorio et al.

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(54) **SEIZURE DETECTION METHODS, APPARATUS, AND SYSTEMS USING A WAVELET TRANSFORM MAXIMUM MODULUS ALGORITHM**

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A61B 5/00 (2006.01)
A61B 5/048 (2006.01)
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A61B 5/0476 (2006.01)
A61B 5/04 (2006.01)
A61B 5/08 (2006.01)
A61B 5/11 (2006.01)

(52) **U.S. Cl.**
CPC **A61B 5/02055** (2013.01); **A61B 5/048** (2013.01); **A61B 5/4094** (2013.01); **A61B 5/726** (2013.01); **A61B 5/024** (2013.01); **A61B 5/04001** (2013.01); **A61B 5/0476** (2013.01); **A61B 5/0816** (2013.01); **A61B 5/1118** (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

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(57) **ABSTRACT**
Methods for detecting a seizure, by use of a wavelet transform maximum modulus (WTMM) algorithm applied to body data. A non-transitive, computer-readable storage device for storing data that when executed by a processor, perform such a method.

19 Claims, 12 Drawing Sheets

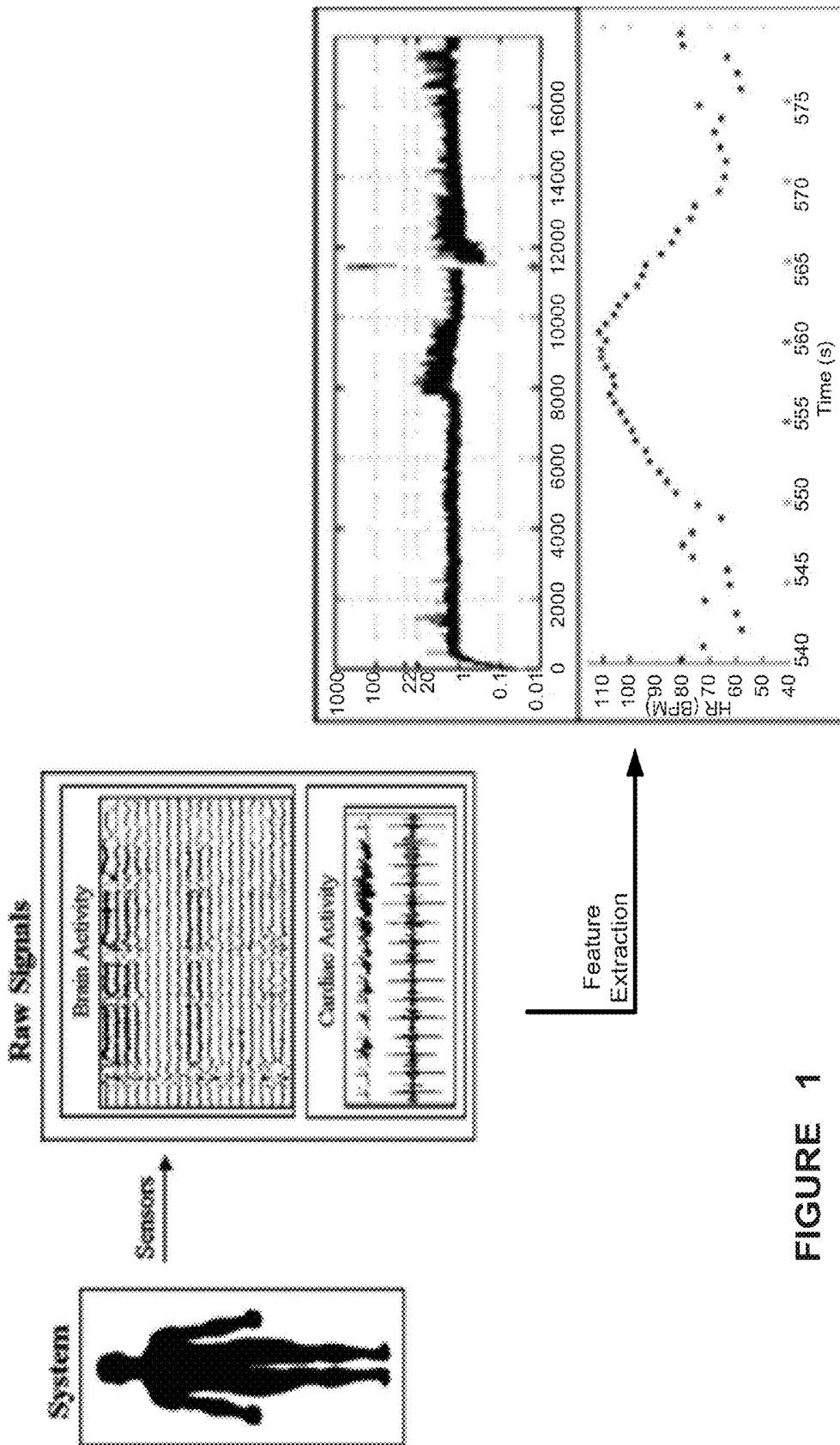


FIGURE 1

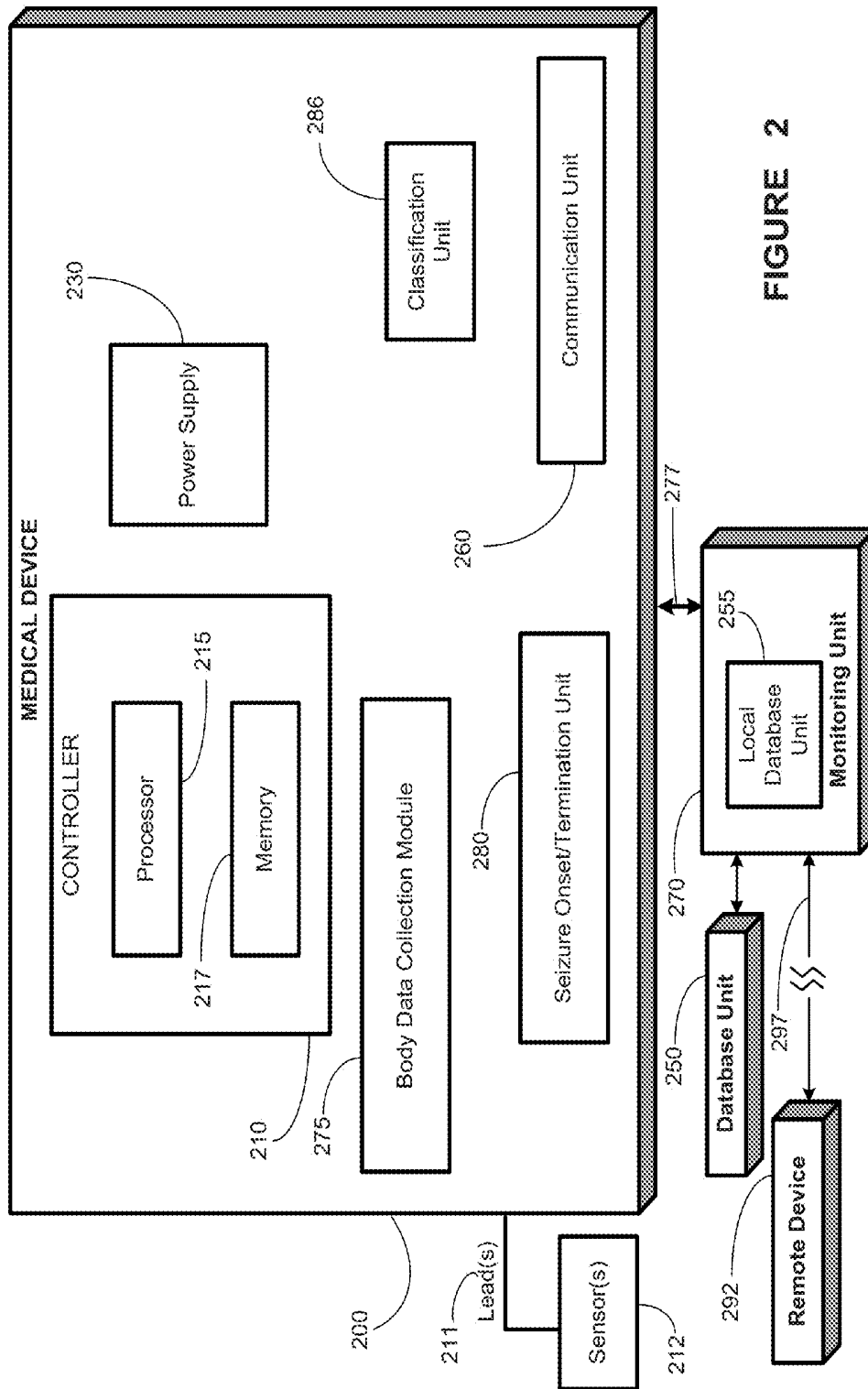


FIGURE 2

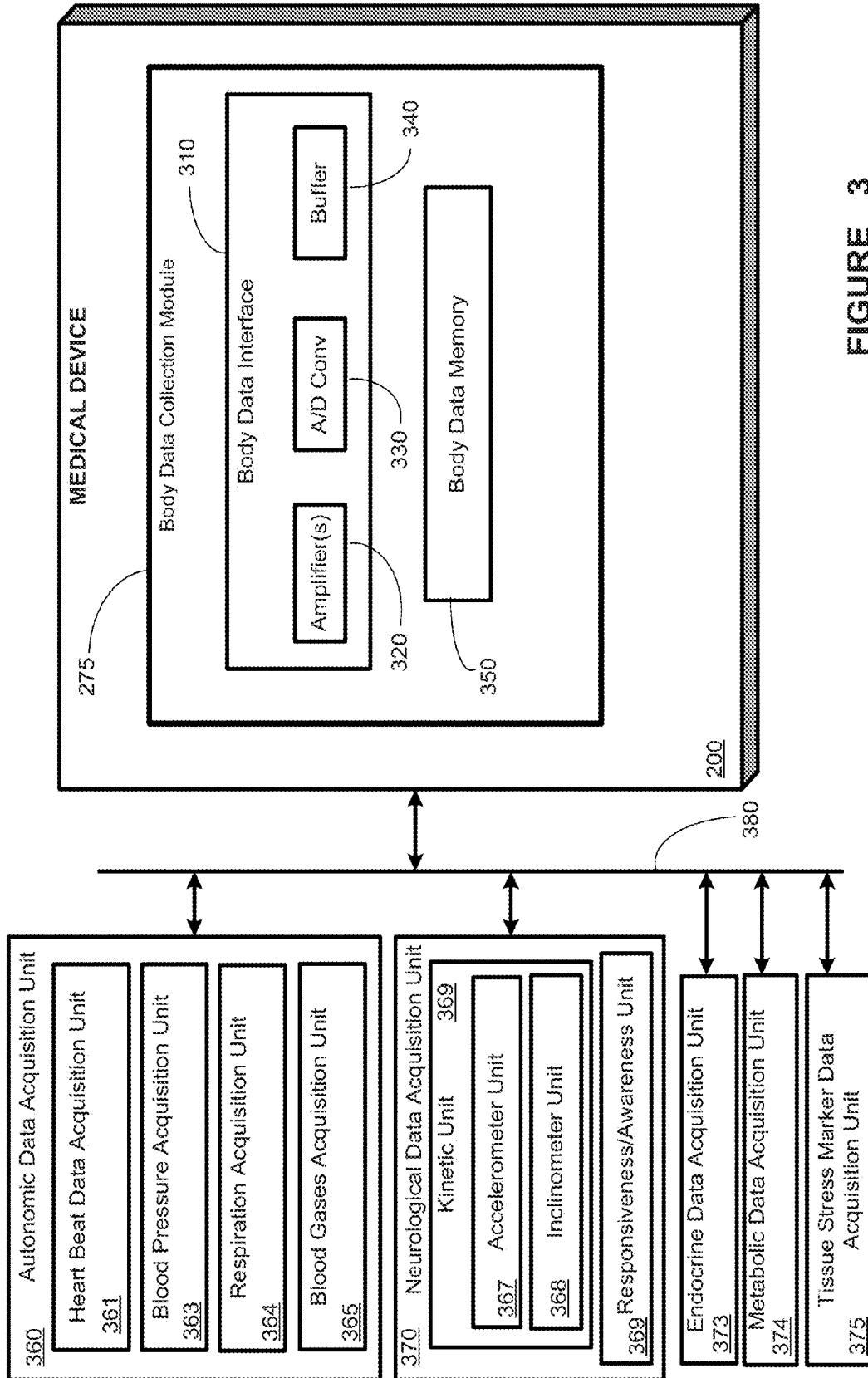


FIGURE 3

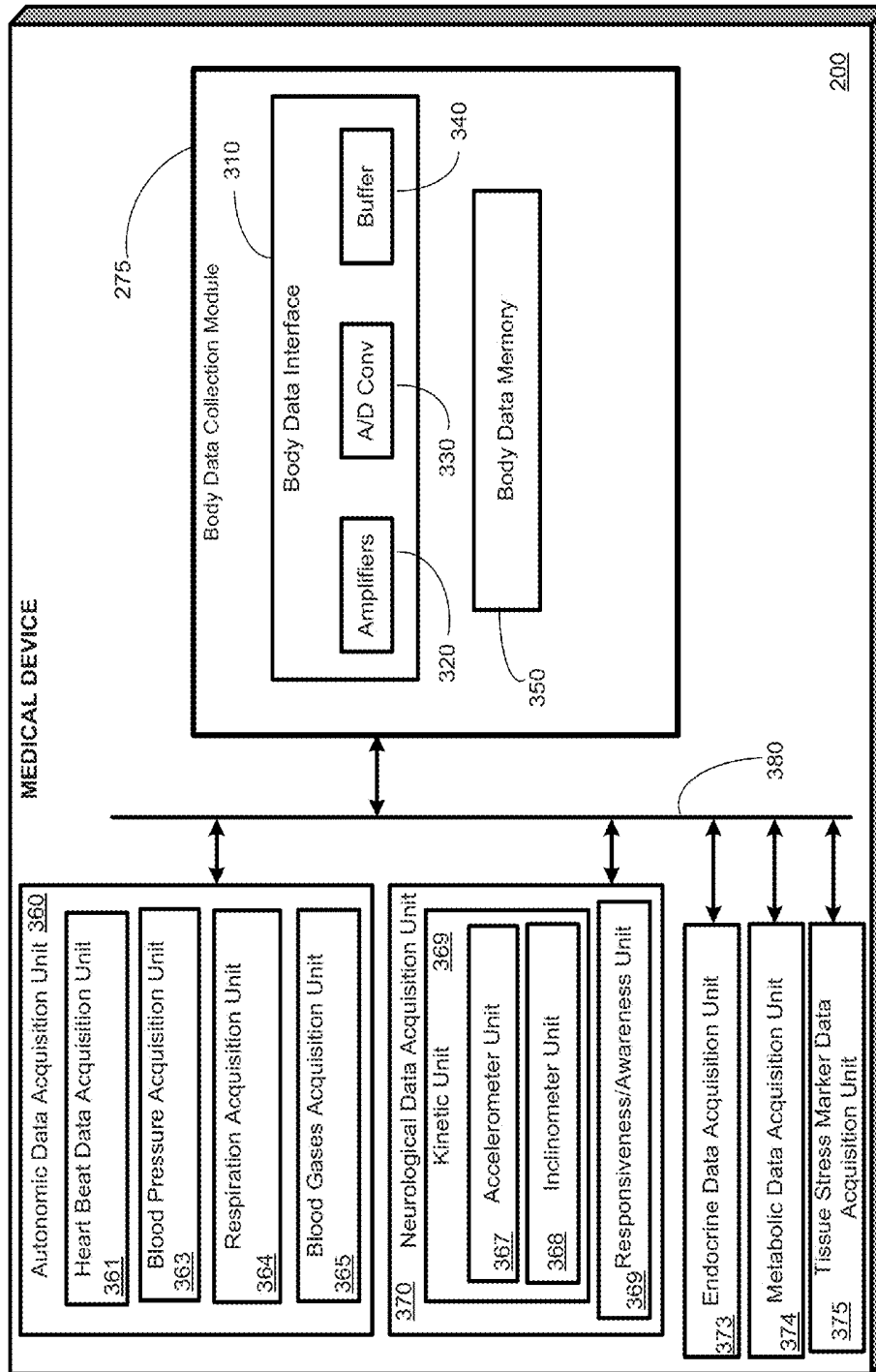


FIGURE 4

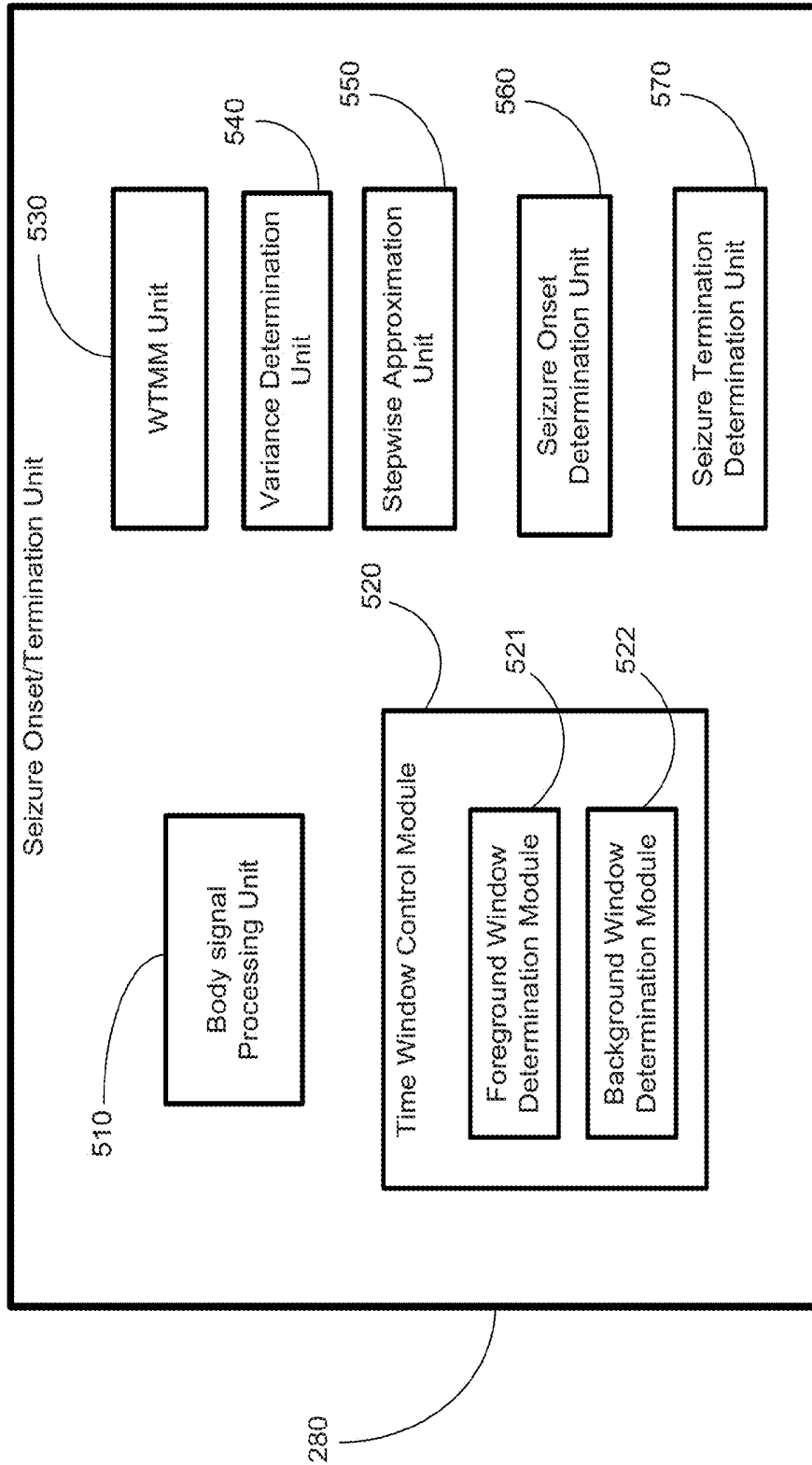


FIGURE 5

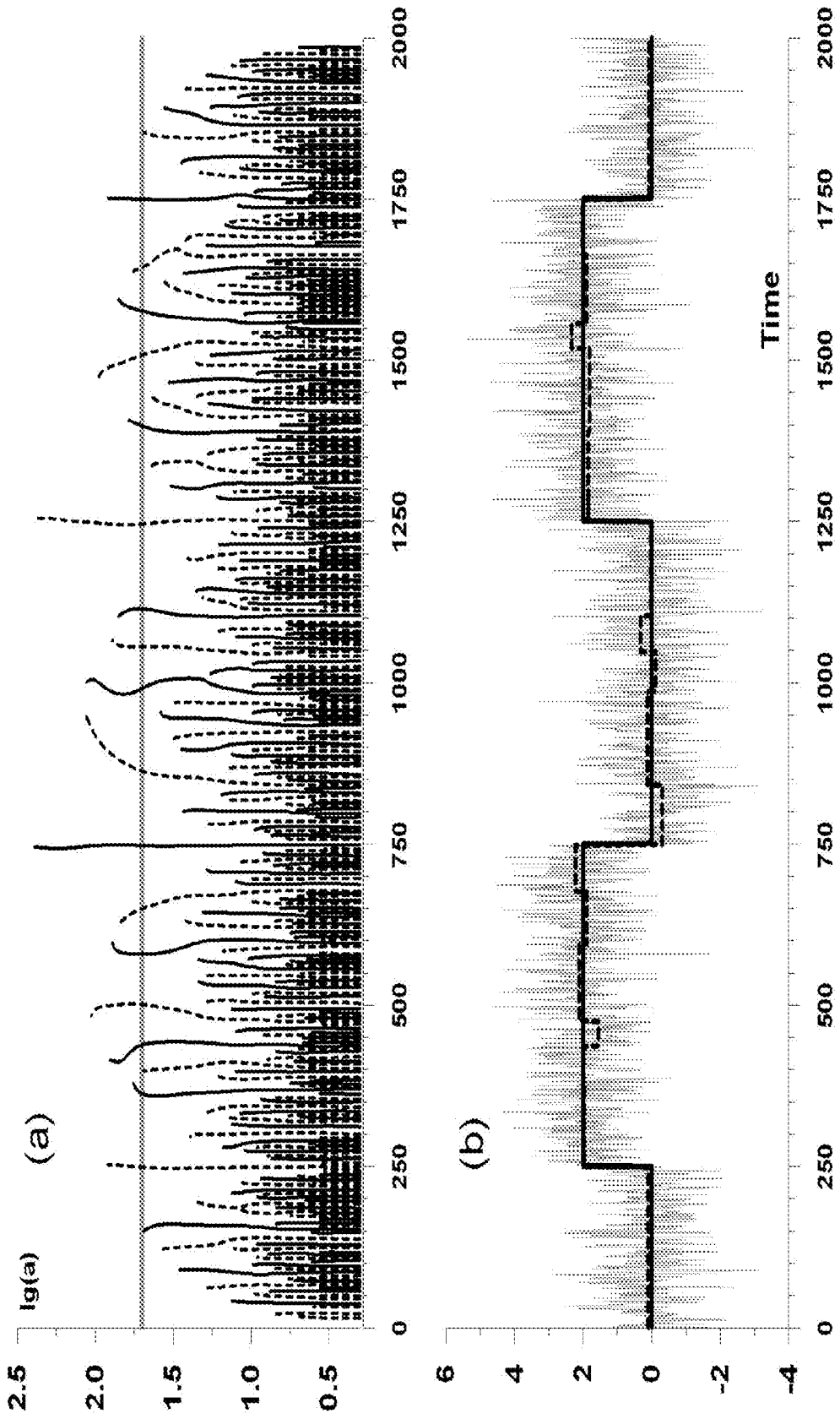


FIGURE 6

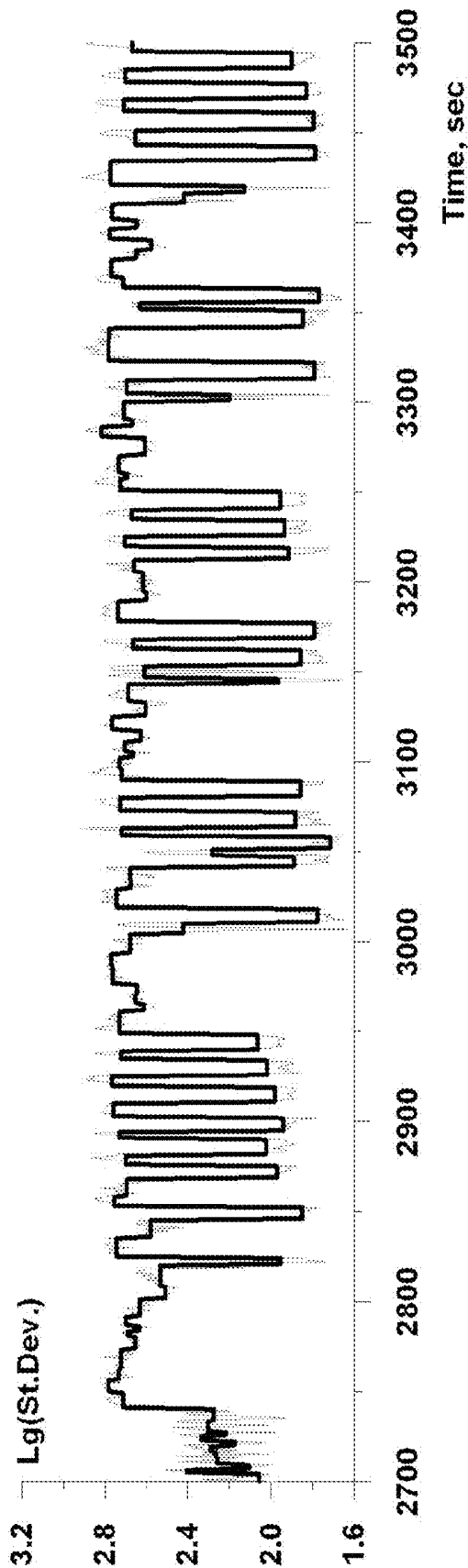


FIGURE 7

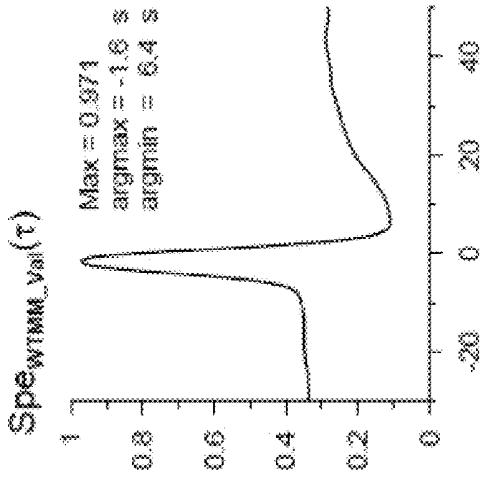


FIGURE 9

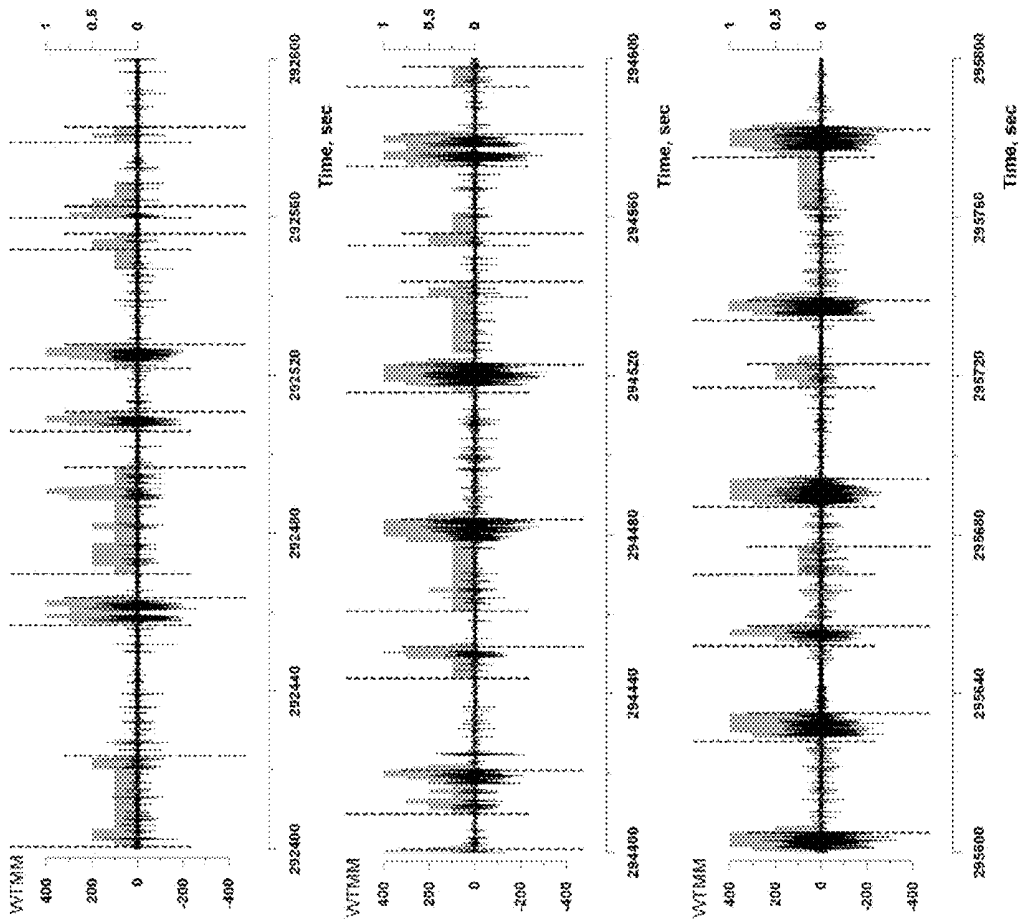


FIGURE 8

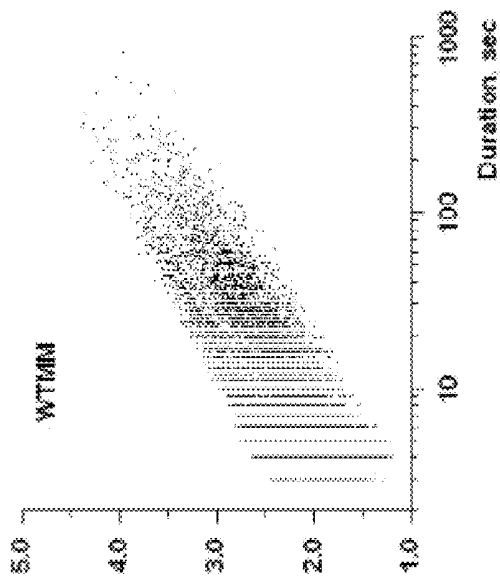


FIGURE 10

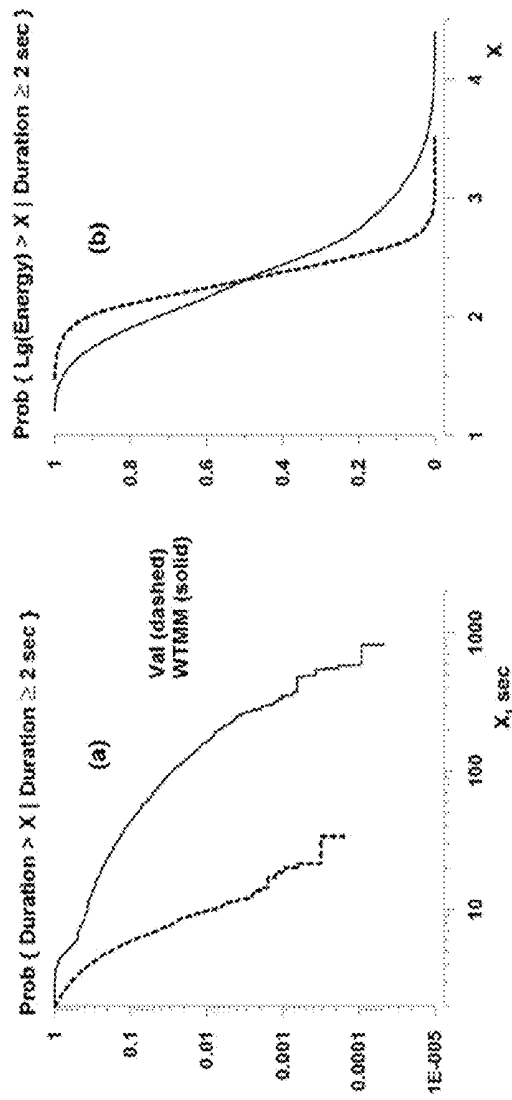


FIGURE 11

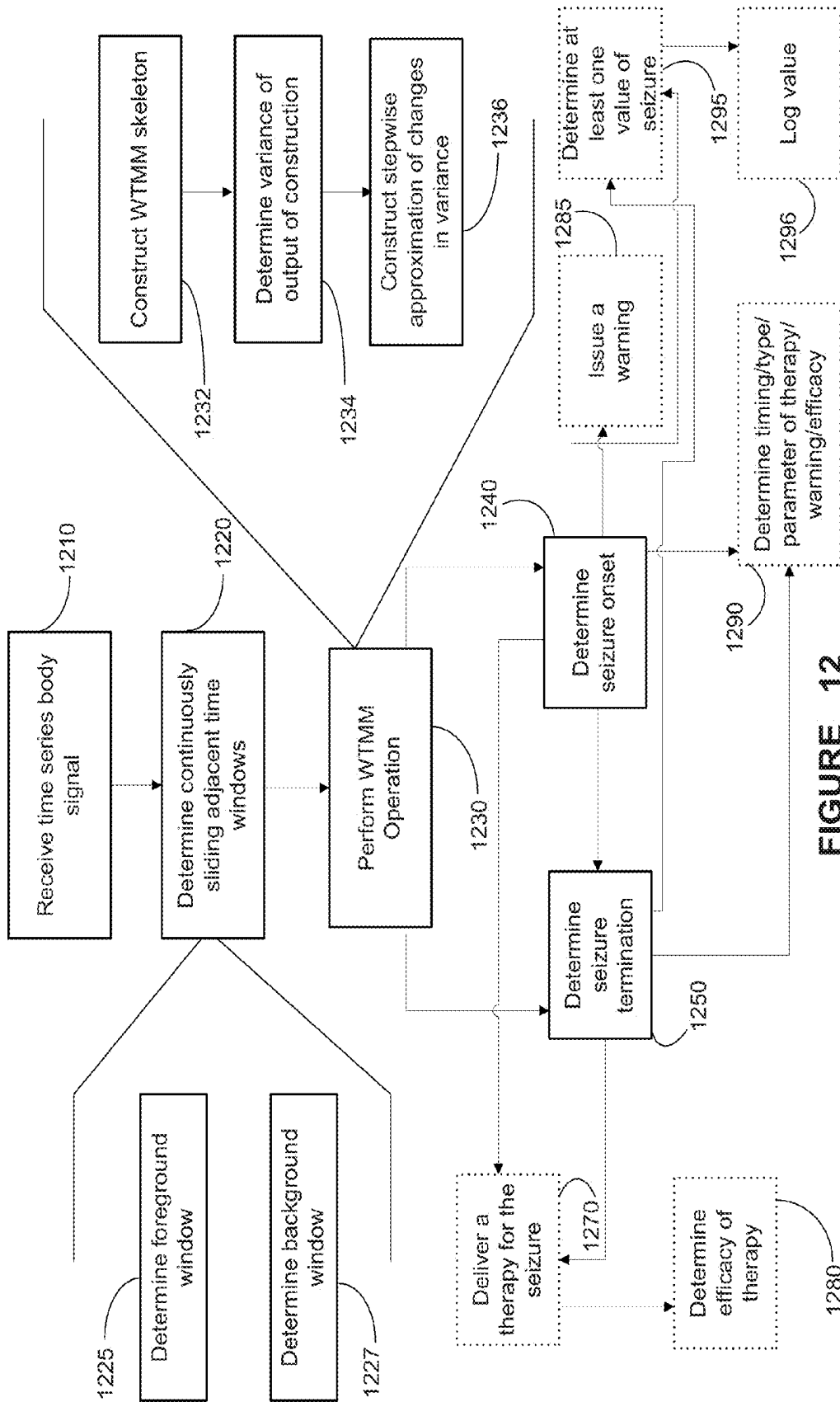


FIGURE 12

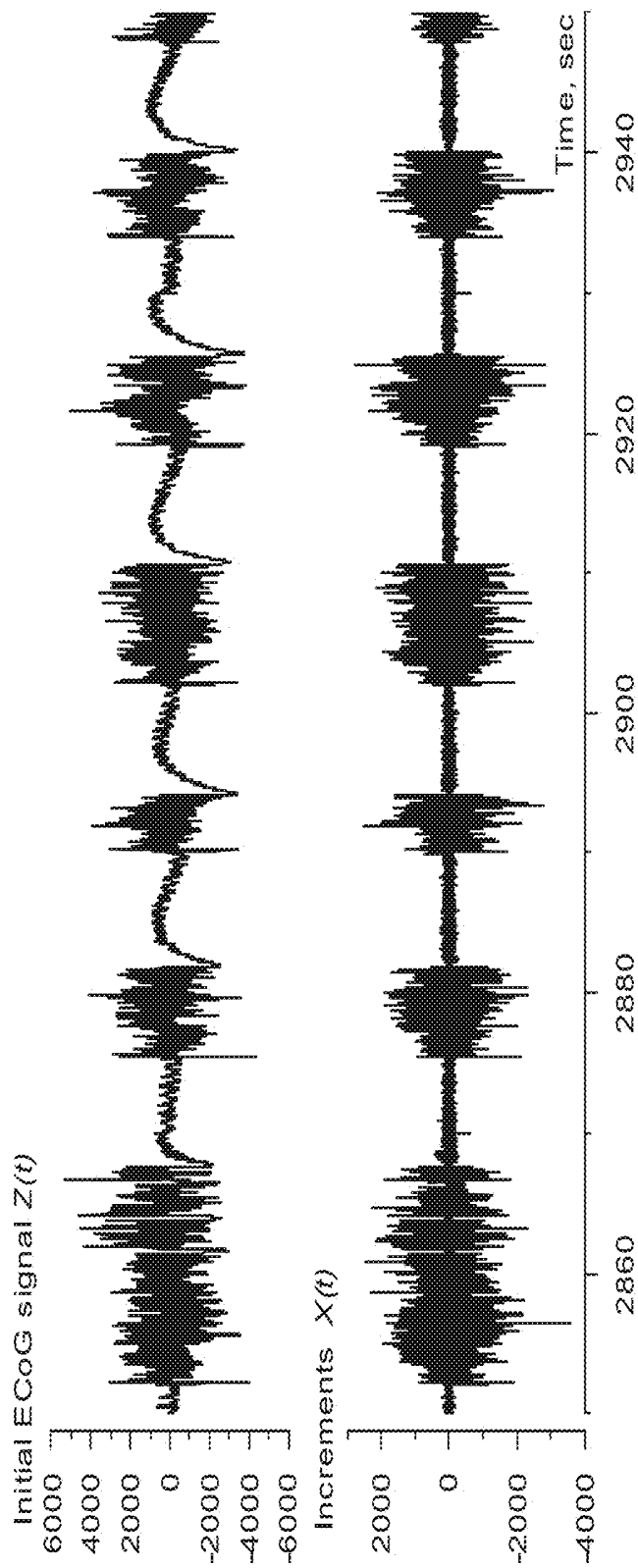


FIGURE 13

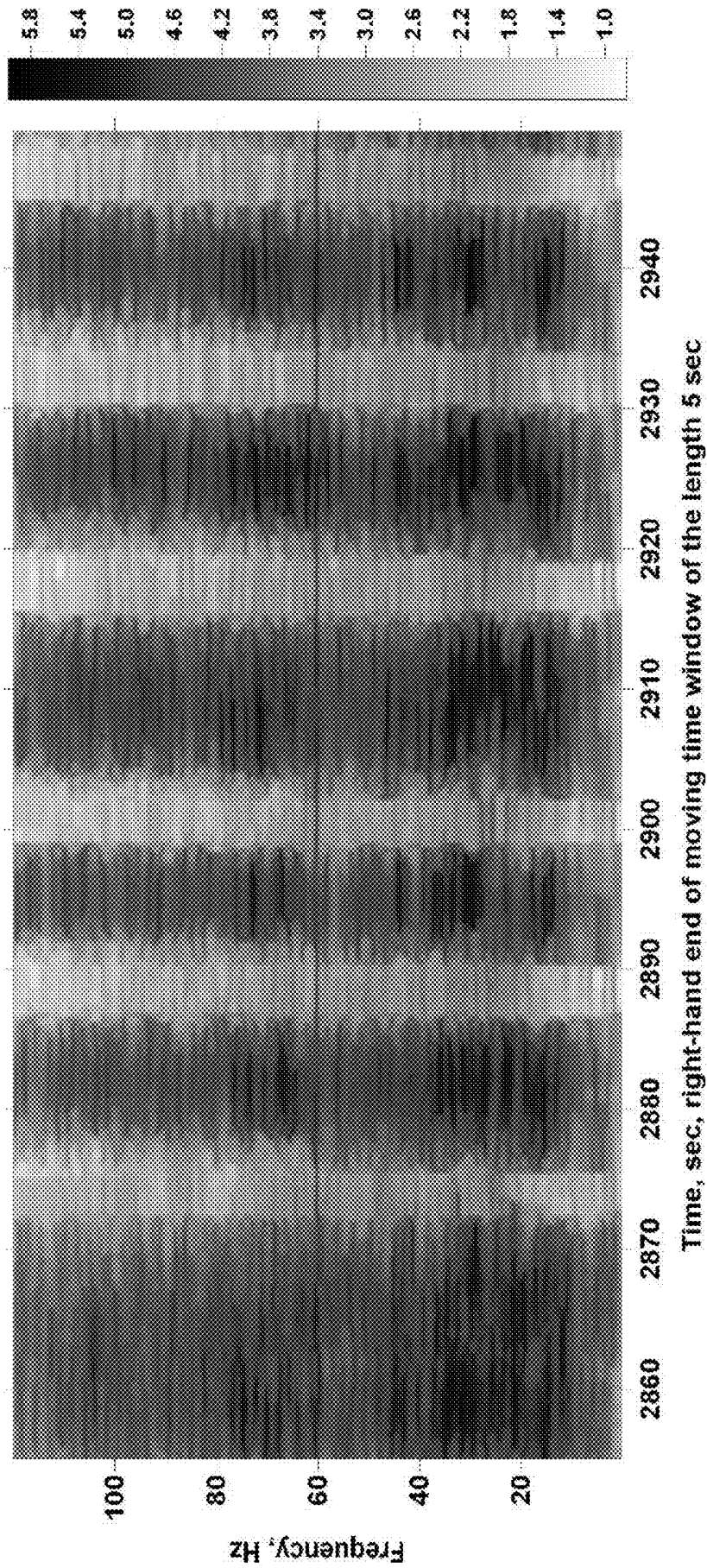


FIGURE 14

**SEIZURE DETECTION METHODS,
APPARATUS, AND SYSTEMS USING A
WAVELET TRANSFORM MAXIMUM
MODULUS ALGORITHM**

The present application claims priority from U.S. provisional patent application Ser. No. 61/547,567, filed on Oct. 14, 2011, which is incorporated herein by reference.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates generally to the field of epileptic event detection. More particularly, it concerns epileptic event detection by use of a wavelet transform maximum modulus (WTMM) algorithm on a time series of patient body signal data.

2. Description of Related Art

There have been various advancements in the area of seizure detection, which remains a fairly subjective endeavor. The task of automated detection of epileptic seizures is intimately related to and dependent on the definition of what is a seizure, definition which to date is subjective and thus inconsistent within and among experts. The lack of an objective and universal definition not only complicates the task of validation and comparison of detection algorithms, but possibly more importantly, the characterization of the spatio-temporal behavior of seizures and of other dynamical features required to formulate a comprehensive epilepsy theory.

The current state of automated seizure detection is, by extension, a faithful reflection of the power and limitations of visual analysis, upon which it rests. The subjectivity intrinsic to expert visual analysis of seizures and its incompleteness (it cannot quantify or estimate certain signal features, such as power spectrum) confound the objectivity and reproducibility of results of signal processing tools used for their automated detection. What is more, several of the factors, that enter into the determination of whether or not certain grapho-elements should be classified as a seizure, are non-explicit (“gestalt-based”) and thus difficult to articulate, formalize and program into algorithms.

Most, if not all, existing seizure detection algorithms are structured to operate as expert electroencephalographers. Thus, seizure detection algorithms that apply expert-based rules are at once useful and deficient; useful as they are based on a certain fund of irreplaceable clinical knowledge and deficient as human analysis biases propagate into their architecture. These cognitive biases which pervade human decision processes and which have been the subject of formal inquiry are rooted in common practice behaviors such as: a) The tendency to rely too heavily on one feature when making decisions (e.g., if onset is not sudden, it is unlikely to be a seizure because these are paroxysmal events); b) To declare objects as equal if they have the same external properties (e.g., this is a seizure because it is just as rhythmical as those we score as seizures) or c) Classify phenomena by relying on the ease with which associations come to mind (e.g., this pattern looks just like the seizures we reviewed yesterday).

Seizure detection algorithms’ discrepant results make attainment of a unitary or universal seizure definition ostensibly difficult; the notion that expert cognitive biases are the main if not only obstacle on the path to “objectivity” is rendered tenuous by these results. These divergences in objective and reproducible results may be attributable in part, but not solely, to the distinctiveness in the architecture

and parameters of each algorithm. The fractal or multi-fractal structures of seizures accounts at least in part for the differences in results and draws attention to the so-called “Richardson effect.” Richardson demonstrated that the length of borders between countries (a natural fractal) is a function of the size of the measurement tool, increasing without limit as the tool’s size is reduced. Mandelbrot, in his seminal contribution “How long is the coast of Britain,” stressed the complexities inherent to the Richardson effect, due to the dependency of particular measurements on the scale of the tool used to perform them. Although defining seizures as a function of a detection tool would be acceptable, this approach may be impracticable when comparisons between, for example, clinical trials or algorithms are warranted. Another strategy to bring unification of definitions is to universally adopt the use of one method, but this would be to the detriment of knowledge mining from seizure-time series and by extension to clinical epileptology.

To date, meaningful performance comparisons among myriad existing algorithms have not been feasible due to lack of a common and adequate database. However, even if adequate databases were available, the value of such “comparisons” would be limited by the absence of a universally accepted definition of what is a “seizure.” The previously noted cognitive biases and architectural/parametric distinctions among algorithms impede achievement of consensus and in certain cases even of majority agreement in classifying particular events as seizures or non-seizures. Because expert visual analysis provides the benchmarks (seizure onset and termination times) from which key metrics (detection latency in reference to electrographic and clinical onset time (“speed of detection”), sensitivity, specificity and positive predictive value) are derived, the effects of cognitive biases propagate beyond the seizure/non-seizure question into other aspects of the effectiveness of a particular seizure detection algorithm.

SUMMARY OF THE INVENTION

In one aspect, the present disclosure relates to a method, comprising receiving a time series of a first body signal of the patient; determining at least two sliding adjacent time windows for said time series of said first body signal comprising a foreground window and a background window; extracting at least one first long chain from said foreground window and at least one second long chain from said background window; applying a continuous wavelet transform to each of said long chains, to yield a wavelet transform maximum modulus (WTMM) skeleton for each window; determining a first variance of the WTMM skeleton from said foreground window and a second variance of the WTMM skeleton from said background window; generating a stepwise approximation of changes in said variance; determining a seizure onset in response to a determination that an output of the stepwise approximation of changes in said first variance has reached an onset threshold; and determining a seizure termination in response to a determination that an output of the stepwise approximation of changes in said second variance has reached a termination threshold.

In one aspect, the present disclosure relates to a non-transitory computer readable program storage unit encoded with instructions that, when executed by a computer, perform a method as described above or herein.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention may be understood by reference to the following description taken in conjunction with the accompanying drawings, in which like reference numerals identify

elements, and in which:

FIG. 1 illustrates a medical device system for detecting and classifying seizure events related to epilepsy from sensed body data processed to extract features indicative of aspects of the patient's epilepsy condition;

FIG. 2 illustrates a medical device system, according to an illustrative embodiment of the present disclosure;

FIG. 3 provides a stylized diagram of a medical device and different data acquisition units that may provide output(s) used by other unit(s) of the medical device, in accordance with one illustrative embodiment of the present disclosure;

FIG. 4 provides a stylized diagram of a medical device and different data acquisition units that may provide output(s) used by other unit(s) of the medical device, in accordance with one illustrative embodiment of the present disclosure;

FIG. 5 provides a stylized diagram of a seizure onset/termination unit, in accordance with one illustrative embodiment of the present disclosure;

FIG. 6 presents WTMM chains constructed from a signal, in accordance with one illustrative embodiment of the present disclosure;

FIG. 7 presents a logarithmic standard deviation of an ECoG time series and a WTMM-stepwise approximation thereof, in accordance with one illustrative embodiment of the present disclosure;

FIG. 8 illustrates the output of the WTMM algorithm in reference to an Average Indicator Function (AIF) making use of four algorithms, including the WTMM algorithm, in accordance with one illustrative embodiment of the present disclosure;

FIG. 9 shows a graph of a specificity function for the WTMM method as a function of time with respect to a validated algorithm's time of seizure detection, in accordance with one illustrative embodiment of the present invention;

FIG. 10 shows a plot of the decimal logarithm of the dependence of seizure energy on seizure duration, in accordance with one illustrative embodiment of the present disclosure;

FIG. 11 shows the empirical "tail" of the conditional probability distribution functions for: (a) Seizure durations (minimum duration: 2 sec); and (b) the logarithm of seizure energy as estimated with four different methods, in accordance with one illustrative embodiment of the present disclosure;

FIG. 12 provides a flowchart depiction of a method, in accordance with one illustrative embodiment of the present disclosure;

FIG. 13 shows ECoG before (upper panel) and after differentiation (lower panel), in accordance with one illustrative embodiment of the present disclosure; and

FIG. 14 shows temporal evolution of the decimal logarithm of the power spectrum of differentiated ECoG.

DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

In one aspect, the present disclosure provides several new seizure detection algorithms that may be applied to one or more streams of body data. Some of these algorithms rely principally on power variance for detection of seizures, while others rely mainly on power spectral shape.

In another aspect, the present disclosure exploits the simultaneous application of two or more individual seizure detection algorithms to derive a probabilistic measure of seizure activity (PMSA), which may be used to issue detections by majority or consensus of a plurality of the two or more seizure detection algorithms, depending on safety factors and others such as detection speed, sensitivity, specificity or any other performance measures and the clinical application(s) at hand. Real-time ("on the run") automated seizure detection provides the only means through which contingent warning to minimize risk of injury to patients, delivery of a therapy for control of seizures, or logging of the date, time of onset and termination and severity may be performed.

This disclosure, in one embodiment, provides a wavelet transform maximum modulus (WTMM) algorithm suitable for use in epileptic event detection, by operation on a time series of patient body signal data. Such a WTMM algorithm may be used by itself, as part of a Probabilistic Measure of Seizure Activity (PMSA), or, by performing stepwise approximations of the WTMM, as a single algorithm capable of providing a PMSA.

More generally, this disclosure: a) draws attention to the intricacies inherent to the pursuit of a universal seizure definition even when powerful, well understood signal analysis methods are utilized to this end; b) identifies this aim as a multi-objective optimization problem and discusses the advantages and disadvantages of adopting or rejecting a unitary seizure definition; c) introduces a Probabilistic Measure of Seizure Activity to manage this thorny issue.

Seizure detection belongs to a class of optimization problems known as "multi-objective" due to the competing nature between objectives: improvements in specificity of detection invariably degrade sensitivity, and vice-versa. Attempts to achieve a universal seizure definition using objective, quantitative means, are likely to be fraught with similar competing objectives. In one aspect, the present invention involves the application of tools from the field of multi-objective optimization, among others to make the problems caused by competing objectives more tractable.

Achieving a unitary seizure definition would be difficult, as consensus among epileptologists as to what grapho-elements are classifiable as ictal, is rare. In the absence of a universal definition, issuing seizure warnings for certain cases will be problematic and unsafe. For example, if a patient with seizures wishes to operate power equipment or a motor vehicle, the absence of a universal agreement on when the patient has had a seizure may preclude any viable way of ensuring, using seizure detection algorithms that the patient's seizures are under sufficient control to allow such activities to occur. To manage the difficulties of a consensus seizure definition, substantive gains are feasible through steps entailing, for example, the application of advanced signal analysis tools to ECoG, to hasten the identification of properties/features that would lead to the probabilistic discrimination of seizures from non-seizures with worthwhile sensitivity and specificity for the task at hand. However, to even have a modicum of success, such an approach should not ignore the non-stationarity of seizures and, should strike some sort of balance between supervised (human) and unsupervised machine-learning) approaches. The resulting multidimensional parameter space, expected to be broad and intricate, may also foster discovery of hypothesized (e.g. pre-ictal) brain sub-states.

The challenges posed by the attempt to define seizures unitarily using objective means (distinct from visual analysis) may be partly related to their fractal properties and

understood through a simplistic analogy to the so-called “Richardson effect”. A revision of the time-honored subjective definition of seizures may be warranted to further advance epileptology.

The present inventors propose a Probabilistic Measure of Seizure Activity (PMSA) as one possible strategy for characterization of the multi-fractal, non-stationary structure of seizures, in an attempt to eschew the more substantive limitations intrinsic to other alternatives.

The PMSA may make use of “indicator functions” (IFs) denoted χ_{algo} for each algorithm ‘algo.’ In one embodiment, the PMSA may also make use of an Average Indicator Function (AIF). In one embodiment, the AIF is defined as:

$$AIF(t) = (\chi_{Val}(t) + \chi_{r^2}(t) + \chi_{STA/LTA}(t) + \chi_{WTMM}(t)) / 4$$

The subscripts Val, r^2 , STA/LTA and WTMM refer to four different algorithms, particular embodiments of which are described herein and/or in other related applications. One or more of these algorithms may be used to detected seizures from one or more body data streams including, but not limited to, a brain activity (e.g., EEG) data stream, a cardiac (e.g., a heart beat) data stream, and a kinetic (e.g., body movement as measured by an accelerometer) data stream.

“Val” refers to an algorithm for seizure detection using ECoG data that has been validated by experts without reaching a universal consensus about its performance (e.g., false positive, false negative and true positive detections). An “ r^2 ” algorithm may also be referred to herein as an “ r^2 ,” “autoregression,” or “autoregressive” algorithm. A “STA/LTA” algorithm refers to an algorithm characterized by the ratio of a Short-Term Average to a Long-Term Average. A “WTMM” algorithm refers to a Wavelet Transform Maximum Modulus algorithm.

For determination of an AIF from the foregoing formula, an algorithm’s IF equals 1 for time intervals (0.5 sec in this application) “populated” by ictal activity and 0 by inter-ictal activity. The IF’s are used to generate four stepwise time functions, one for each of: a) a 2^{nd} order auto-regressive model (r^2); b) the Wavelet Transform Maximum Modulus (WTMM); c) the ratio of short-to-long term averages (STA/LTA) and d) a Validated algorithm (Val). With these IFs, the AIF is computed (its values may range between [0-1] with intermediate values of 0.25, 0.5 and 0.75 in this embodiment). (Intermediate AIF values are functions of the number of algorithms applied to the signal. Since in this study 4 methods were used and the range of the indicator function is [0-1], the intermediated values are [0.25, 0.5, 0.75]). These values [0-1] are estimates of the probability of seizure occurrence at any given time. In another embodiment, the values of each algorithm’s IF may be weighted differently, and a composite IF (e.g., a Weighted Indicator Function or WIF) different from the AIF may be computed.

Data obtained from one subject undergoing evaluation for epilepsy surgery with intracranial electrodes was selected for analyses. The ECoG was recorded using electrodes implanted into the amygdala, pes hippocampus and body of hippocampus bilaterally through the temporal neocortex and had a duration of 6.9 days (142’923’853 samples; 239.75 Hz sampling rate).

For efficient analyses, ECoG signal differentiation was performed, so as to minimize the non-stationarity present in them. If $Z(t)$ is raw ECoG, then its difference is $X(t) = Z(t) - Z(t-1)$, where (t) corresponds to a sample time increment. This linear operation is exactly invertible and, unlike band-pass filtering or detrending, does not suppress low frequency fluctuations, but decreases their overall influence. FIG. 13 illustrates the effect of this operation on raw ECoG. The

differentiated ECoG is less non-stationary (chiefly at low frequencies) than the undifferentiated one (x-axis: time in sec.; y-axis: amplitude in microvolts). FIG. 14 shows a time-frequency map of the evolution of the power spectra of differentiated ECoG segments (as shown in FIG. 13, bottom panel). The power spectra are estimated within 5 sec moving windows of length. Six brief seizures appear as marked power spectrum increases (red and specks of white) in the 10-100 Hz. band (x-axis: time in sec.; y-axis: frequency (Hz); color scale to the right of main graph).

Continuous Wavelet Transform Maximum Modulus (WTMM)

The WTMM technique exploits the large, sudden changes in the variance of signal features, such as amplitude and frequency that characterize most epileptic seizures. These features are calculated within a hierarchy of sequences of short contiguous windows of equal length and are extracted in the form of chains of continuous Wavelet Transform Maximum Modulus (WTMM), using a mother wavelet defined as the 1st order derivative of the Gaussian function $\sim \exp(-t^2)$. The construction of long chains to form a WTMM-skeleton is a commonly used method for detecting changes in the mean value of noisy signals such as edge detection in vision computer programs. WTMM relies on three parameters: a) The length of the window used to calculate the sequence of variance values; b) A parameter a^* that defines which WTMM-chains are long and, c) The threshold ΔU for the stepwise approximation of the logarithmic variance curve for detecting the onsets and ends of seizures.

The Wavelet Transform (WT) may be conceptualized as a “mathematical microscope” that is well suited to reveal the hierarchy that governs the spatial distribution of singularities of multifractal measures. The role of the scaling parameter a^* is similar to that of the magnification setting in a microscope: the larger the value of a^* , the larger the scale of the signal’s structure under investigation. By using wavelets instead of boxes, the smoothing effect of polynomials that might either mask singularities or perturb the estimation of their strength (Holder exponent) is avoided. This approach remedies one of the main failures of the classical multifractal methods such as the box-counting algorithms in the case of measures and of the structure function method in the case of functions. Another advantage of this method is that the skeleton defined by the WTMM provides an adaptive space-scale partitioning from which to extract the singularity spectrum via the Legendre transform of the scaling exponents (real, positive as well as negative) of some partition functions defined from the WT skeleton. The person of ordinary skill in the art is aware of mathematical description and applications, as well as theoretical treatment, of random multifractal functions.

As originally pointed out for the specific purpose of analyzing the regularity of a function, the redundancy of the WT may be eliminated by focusing on the WT skeleton defined by its modulus maxima only. These maxima are defined, at each scale a , as the local maxima of the set of wavelet transforms over all possible position x at the fixed scale a of the function f denoted $|T_{\psi}[f](x,a)|$. These WTMM points are disposed on connected curves in the space-scale (or time-scale) half-plane, called maxima lines. Let us define $L(a_0)$ as the set of all the maxima lines that exist at the scale a_0 and which contain maxima at any scale $a < a_0$. An important feature of these maxima lines, when analyzing singular functions, is that there is at least one maxima line pointing towards each singularity.

There are almost as many analyzing wavelets as applications of the continuous WT. A commonly used class of analyzing wavelets is defined by the successive derivatives of the Gaussian function:

$$g^{(N)}(x) = \frac{d^N}{dx^N} \exp(-x^2/2) \quad (7)$$

Note that the WT of a signal $f(x)$ with $g^{(N)}$ (Eq. 7) takes the following simple expression:

$$T_{g^{(N)}}[f](x, a) = \frac{1}{a} \int_{-\infty}^{+\infty} f(y) g^{(N)}((y-x)/a) dy = a^N \frac{d^N}{dx^N} T_{g^{(0)}}[f](x, a) \quad (8)$$

Equation (8) shows that the WT computed with $g^{(N)}$ at scale a is nothing but the N -th derivative of the signal $f(x)$ smoothed by a dilated version $g^{(0)}(x/a)$ of the Gaussian function. This property is at the heart of various applications of the WT “microscope” as a very efficient multi-scale singularity tracking technique.

The algorithm described as follows may be used to construct the WTMM-skeleton.

Let $Y(t)$ be an arbitrary signal and consider the corresponding smoothed signal obtained by using a scale-dependent kernel:

$$c_0(t, a) = \int_{-\infty}^{+\infty} Y(t+av) \cdot \psi_0(v) dv / \int_{-\infty}^{+\infty} \psi_0(v) dv \quad (9)$$

where $a > 0$ is a time scale and $\psi_0(t)$ is some function decaying sufficiently fast on both sides of its single maximum; further on, $\psi_0(t) = \exp(-t^2)$ shall be used. The wavelet function is defined as:

$$\psi_n(t) = (-1)^n \cdot \frac{d^n \psi_0(t)}{dt^n} \equiv (-1)^n \cdot \psi_0^{(n)}(t) \quad (10)$$

Using integration by part and exploiting the fast decay of the function $\psi_0(t)$ at $t \rightarrow \pm\infty$, the following formula for the Taylor’s coefficients (the n -th derivative of the smoothed signal, divided by $n!$) of the smoothed signal is obtained:

$$c_n(t, a) \equiv \frac{1}{n!} \frac{d^n c_0(t, a)}{dt^n} = \int_{-\infty}^{+\infty} Y(t+av) \psi_n(v) dv / a^n \int_{-\infty}^{+\infty} v^n \psi_n(v) dv \quad (11)$$

Equation (9) is a particular case of formula (II) for $n=0$.

The WTMM-point (t, a) for $n \geq 1$ is defined as the point for which $|c_n(t, a)|$ has a local maximum with respect to time t for a given time scale a . For $n=0$, the WTMM-points are defined as points of local extremes (maxima or minima) of the smoothed signal $c_0(t, a)$ that may be joined to form chains; the set of all chains creates a WTMM-skeleton of the signal. If $\psi_0(t)$ is a Gaussian function, then a given WTMM-skeleton chain does not end when the scale a is decreased. The WTMM-points for the 1st order derivative $c_1(t, a)$ indicate time points of the maximum trend (positive or negative) of the smoothed signal $c_0(t, a)$ for the given scale. This allows temporal localization of “points” of large and abrupt

changes of the mean value of a noisy signal such as ECoG; these “points” mark the times when rather long WTMM-chains begin to grow.

A stepwise approximation $S_Y(t|a^*)$ for the signal $Y(t)$, is defined as a function which is equal to the sequence of constant values g_k in the successive intervals $t \in [\tau_k(a^*), \tau_{k+1}(a^*)]$. Here $\tau_k(a^*)$ are the beginnings of the WTMM-chains for $c_1(t, a)$ which exceed the threshold time scale a^* and

$$g_k = \sum_{t=\tau_k(a^*)}^{\tau_{k+1}(a^*)} Y(t) / (\tau_{k+1}(a^*) - \tau_k(a^*) + 1) \quad (12)$$

is equal to the mean value of $Y(t)$ within the time interval $[\tau_k(a^*), \tau_{k+1}(a^*)]$.

For example, consider a signal that is a sum $Y(t) = S_0(t) + \epsilon(t)$, $t=1, \dots, 2000$, where $\epsilon(t)$ is a Gaussian white noise with unit standard deviation and

$$S_0(t) = 0 \text{ for } t \in [1, 250], [751, 1250], [1751, 2000];$$

$$S_0(t) = 2 \text{ for } t \in [251, 750], [1251, 1750].$$

The resulting stepwise approximation for this signal using WTMM-chains is shown in FIG. 6, (noting that for both panels, the x -axis represents time (in sec)). (a) y -axis: Wavelet Transform Maximum Modulus-chains constructed using the 1st derivative of the Gaussian wavelet for the signal $S_0(t) + \epsilon(t)$ defined by expression (12) (grey lines in FIG. 3b). The solid lines correspond to WTMM-chains for negative $c_1(t, a)$ values and the dashed lines to WTMM-chains for positive $c_1(t, a)$ values. The thin grey horizontal line indicates the time scale threshold $a^* = 50$; (b) y -axis: The grey lines represent the signal $S_0(t) + \epsilon(t)$ (equation (12)), the solid horizontal line is the pure signal $S_0(t)$ without noise and the dashed horizontal line the reconstructed signal $S_Y(t|a^*)$ using the WTMM method for $a^* = 50$.

Thus, times of abrupt changes of the mean value of the signal of interest can be estimated as instants of rather large steps of the signal $S_Y(t|a^*)$ with an appropriate choice of the time scale threshold a^* .

Seizure Detection with the WTMM-Method

The WTMM-method of constructing a stepwise approximation $S_Y(t|a^*)$ for an arbitrary signal $Y(t)$ may be applied to the task of seizure detection. This is suggested from observations of seizures as intervals of large, abrupt signal variance. Let us calculate sample estimates of the variance of the normalized ECoG $X(t)$ within “small” adjacent time intervals of length L and take the logarithmic values of the standard deviations:

$$U(\xi_j) = \frac{1}{2} \cdot \lg(V_X(\xi_j)), \quad V_X(\xi_j) = \frac{1}{L} \sum_{t=\xi_j-L+1}^{\xi_j} X^2(t), \quad (13)$$

$$\xi_j = j \cdot L, \quad j = 1, 2, \dots$$

Thus, $U(\xi_j)$ is a time series with a sampling time interval which is L times larger than the sampling time interval of the original ECoG. Graphics of U are plotted as a function of the time position of the right end of these time intervals of length L and its stepwise approximation $S_U(\xi_j|a^*)$ is constructed, where a^* is a scale threshold for the decimal logarithms of the variance U (FIG. 7) of the ECoG. Specifically, in FIG. 7, the grey line indicates values of the logarithmic standard deviation of the time series of ECoG in a rat model (Rat48 increments), estimated within adjacent

time intervals of length $L=240$. The thick black line is the WTMM-stepwise approximation of $\text{Lg}(\text{St.Dev.})$ with time scale threshold $a^*=3$.

Seizures onsets and terminations are defined by the following rule:

$$\begin{aligned} \xi_j \text{ is onset if } S_L(\xi_{j+1}|a^*) - S_L(\xi_j|a^*) \geq \Delta U \\ \tau_j \text{ is end if } S_L(\xi_{j+1}|a^*) - S_L(\xi_j|a^*) \leq \Delta U \end{aligned} \quad (14)$$

The time interval length L , the scale threshold a^* for the decimal logarithms of the variance and the threshold value ΔU for the logarithm of the variance of the normalized ECoG are this method's three parameters. In the application shown in FIG. 7, the chosen parameter values are the following: ($L=240$, $a^*=3$, $\Delta U=0.0.25$). The value of the threshold ΔU determines the "strength" required to detect ECoG activity that qualifies as seizures. Given a window $L=240$ for calculating the sequence of $U(\xi_j)$ and a sampling rate of 240 Hz, the time resolution of the WTMM-seizures detection implementation shown in FIG. 7 is 2 s.

The WTMM and Validated algorithms have been described in U.S. provisional patent application Ser. No. 61/547,567, filed on Oct. 14, 2011, which is hereby incorporated by reference herein in its entirety.

The total number of detections, their duration and the percent time spent in seizure over the time series total duration (6.9 days) are presented in Table 1.

TABLE 1

Summary statistics obtained by applying two different detection methods (Validated Algorithm; WTMM). The minimum duration of seizures was set at 2 s.		
	Validated algorithm	WTMM
Total number of seizures with duration ≥ 2 s.	3184	10795
Mean duration, s.	3.8	18.6
Median duration, s.	3.4	6
% time spent in seizure	2	34

FIG. 8 illustrates the output of the WTMM algorithm in comparison with an AIF making use of each of the validated

detect the seizure event. This indicates that the spectral and other properties of seizures are not homogeneous at the onset and termination of seizures, which is consistent with the lack of agreement among human experts (and algorithms) during onset and termination. Left y-axis: ECoG amplitude (in μV); excursions above zero correspond to positive, and below, to negative, polarity.

Table 2 provides further evidence that, at some point in time, the majority of seizures detected by the validated algorithm are also detected by the WTMM method, with WTMM detecting 97% of seizures. More specifically and by way of example, the value 0.971 in Table 2 means that the WTMM method detections encompass 97.1% of seizure time intervals detected with the validated method, with the exception of 1.6 s. that correspond to the delay/lag between them in detecting seizure onsets (see below for details).

Time intervals for which the pairwise product $\chi_{\text{Val}}(t) \chi_{\text{WTMM}}(t)=1$ correspond to seizures detected by both the validated algorithm and WTMM. Dividing the number of time intervals when $\chi_{\text{Val}}(t) \chi_{\text{WTMM}}(t)=1$ by the number of intervals when $\chi_{\text{Val}}(t)=1$, yields the specificity of the WTMM method with respect to the validated algorithm. The specificity functions for the two other methods $\text{Spe}_{r2_Val}(\tau)$ and $\text{Spe}_{STA/LTA_Val}(\tau)$ are identically computed and their maximum value (dependent on τ) may be regarded as the mean value of the time delay of one method's function with respect to another for seizure onset and end times. Since the validated algorithm has an inherent delay of 1 s (the median filter's foreground window is 2 s) and an additional duration constraint of 0.84 s. is imposed before a detection is issued, its onset and end times are "delayed" compared to those yielded by the WTMM method.

The present inventors discovered that the time differences are negative for all three algorithms compared to the validated algorithm; that is, the validated algorithm's detection times lag behind those given by the other methods. More particularly, the mean delay of the validated algorithm is 1.6 s with respect to WTMM. The re-calculated specificity values shifted by τ shown in Table 2 are higher compared to those without shifting.

TABLE 2

Values of specificity of WTMM calculated with respect to the validated method and time lag (as defined in the text) at which the specificity attains its largest value.			
Method	$\text{Spe}_{\text{Method_Val}}(0)$	$\max_{\tau} \text{Spe}_{\text{Method_Val}}(\tau)$	$\text{argmax}_{\tau} \text{Spe}_{\text{Method_Val}}(\tau)$
WTMM	0.823	0.971	-1.6 s

algorithm, and the r2 (AR), STA/LTA and WTMM algorithms. Specifically, FIG. 8 shows results of applying the WTMM seizure detection method to a differentiated ECoG (in black; 200 sec/panel) of a human with pharmaco-resistant epilepsy. The grey boxes represent the values (right y-axis) of an Average Indicator Function in the interval $[0,1]$. Seizures onset and end times determined by the WTMM algorithm are indicated by vertical lines, with onset lines shifted upward and end lines, downward. Notice that the value of the Average Indicator Function is rarely 1, at onset or termination, indicating all methods do not detect the ECoG activity as being ictal in nature at those moments. However, with seizures exceeding certain duration (at least 20 seconds) and intensity thresholds, they converge to all

The information in Table 2 is also depicted graphically in FIG. 9, which illustrates a graph of a specificity function for the WTMM method as a function of time with respect to the Validated algorithm's time of seizure detection. Tau (τ) zero (x-axis) corresponds to the time at which Val issues a detection. Negative τ values indicate "late" detections by the validated algorithm in relation to the WTMM algorithm and positive value the opposite. As shown, WTMM issues earlier detections than Val. Values of the lags τ corresponding to the maximum and minimum values of the function are presented under the names argmax and argmin respectively.

The present inventors also discovered that only 29.5% of seizures recognized as such by the WTMM method were also detected by the validated method, indicating that in its

generic form and by design, the validated algorithm is less sensitive and more specific for seizure detection than the WTMM algorithm.

The WTMM method, along with the other methods mentioned supra, survey different but inter-dependent ECoG signal properties, thus expanding the breadth and perhaps also the depth of insight into the spectral “structure” of epileptic seizures in a clinically relevant manner. The WTMM method is well suited for estimations of changes in power variance within adjacent “short” time windows. The WTMM may be implemented in off-line analysis applications given its relatively high algorithmic complexity. Of course, readily foreseeable advances in the miniaturization, speed, power, and energy efficiency of computational devices indicate the WTMM may be implemented in implantable devices and/or real time applications.

Algorithmic and visual expert analysis consensus as to what grapho-elements define a ‘seizure’ seems to be highly dependent on when during the course of a ‘seizure’ a decision is made. In this context, it is noteworthy that AIF frequently reached a value of 1, indicative of concordance among all detection methods sometime after seizure onset and before its termination (as determined by any of the methods), provided said seizures reached a certain duration (20-30 s.) as discussed in more detail in U.S. provisional patent application Ser. No. 61/547,567, filed on Oct. 14, 2011. In short, seizure onsets and terminations may be under certain conditions universally undefinable by algorithmic or expert visual analysis. A systematic investigation of the differences in signal spectral properties between the “preface”/“epilogue” and the “main body” of seizures was not performed. It is speculated that the presence of “start-up transients” (in a dynamical sense) and of temporo-spatial dispersion of the ictal signal (which impacts S/N) may be most prominent at the onset and termination of seizures. These and local and global state-dependencies of certain signal features, account in part for the temporal fluctuations in algorithmic detection performance that characterize these results.

Defining seizure energy as the product of the standard deviation of the power of ECoG by its duration (in seconds), reveals that the WTMM algorithm identifies as a continuum seizures that the validated algorithm detects as clusters of short seizures. The lack of correspondence between a certain percentage of detections (2.9% for the WTMM method) and the validated algorithm may be partially attributed to brief discontinuities in seizure activity as shown in FIG. 8. This phenomenon (“go-stop-go”) appears to be inherent to seizures (e.g., it is a general feature of intermittency associated with many dynamical systems). These discontinuities are also an “artifact” caused by the architecture of and parameters used in each algorithm. For example, the longer the foreground window and the higher the order statistical filter (e.g., median vs. quartile), in the validated algorithm, the higher the probability that “gaps” in seizure activity will occur. Clustering of detections is a strategy to manage dynamical or artifactual ictal “fragmentation,” and in this sense the WTMM algorithm avoids the subjective biases and arbitrariness associated with human-imposed clustering rules.

The dependencies of seizure energy (defined as the product of the standard deviation of the differentiated ECoG signal and seizure duration, in sec.) on seizure duration, for the set of icti detected by the WTMM method is depicted in FIG. 10. A subset of seizures detected by all methods obeys a simple law of proportionality between energy (y-axis) and duration (x-axis, log scale, seconds), that is, the longer the

seizure, the larger its energy. However, this relationship is not invariably linear for other detection algorithms, indicating the presence of interesting scaling properties of seizure energy.

FIG. 11 shows the empirical “tail” of the conditional probability distribution functions for: (a) Seizure durations (minimum duration: 2 sec); (b) the logarithm of seizure energy as estimated with the Validated method (dashed) and the Wavelet Transform Maximum Modulus (solid).

The conditional probabilities of durations (FIG. 11a) and of the logarithm of energy of seizures (FIG. 11b) provide additional support that their properties are partly a function of the method used for their detection. The validated and STA/LTA algorithms yield similar durations but different from those of the WTMM and r^2 methods, which are analogous to each other (FIG. 11a). The distributions of the logarithm of seizure energies as identified by each of the methods (FIG. 11b) reveals additional discrepancies as evidenced by the much narrower and shorter “tail” distribution of the validated algorithm compared to the others.

The medical and psycho-socio-economic burden imposed upon patients, caregivers and health systems by pharmacoresistant epilepsies is enormous. Intracranial devices for automated detection, warning and delivery of therapy, the presently preferred “line of attack” for an abundance of weighty reasons, would be insufficient to adequately address said burden at a global scale. Reliance on signals that while extra-cerebral are under cortical modulation or control such as cardiac or motor and are altered by seizures, emerges as a viable research direction with potentially fruitful clinical applications.

The greater ease of implementation and lower cost of automated real-time detection, warning and therapy systems based on extra-cerebral signals, compared to those requiring intracranial placement, makes them worthy of investigation.

Cortical electrical activity has been the primary, if not sole, source of signals for visual or automated detection and quantification of seizures in clinical use. The inextricable link between brain and epilepsy has historically impelled clinical neuroscientists to leave unexploited the equally inextricable link between brain and body. The brain-epilepsy link has distracted us from certain severe limitations (for certain applications) inherent to the recording of cortical signals from scalp or even directly from its surface, such as marked cortical signal attenuation and filtering and limited access to neural sources (only about one-third of the neocortex is surveyable by scalp electrodes and subdural electrodes record little activity from the lateral and bottom walls of sulci). Yet, readily accessible sources that provide indirect but valuable information about the state of the brain, particularly during the ictal or postictal state, remain largely untapped.

The growing emphasis on widely accessible, cost-effective, good quality health care in the context of expanding populations, especially in age-groups above 60 yr. in whom the incidence of epilepsy is high, and the shrinking financial resources to support the required infra-structure, pose an enormous challenge to patients whose seizures are pharmacoresistant as well as to epileptologists and functional neurosurgeons. The properly placed emphasis on implantable intracranial devices for automated seizure detection, warning and delivery of therapy in patients with drug-resistant seizures should be viewed in the context that even if economic resources were unlimited, human resources are starkly small. Given the number of functional neurosurgeons in the United States (one source puts the number at 300, of which about 100 work in epilepsy) is it realistic to pursue

exclusively intracranial devices to address the unmet needs of pharmaco-resistant patients conservatively estimated (in the US) at 600,000? The deleterious medical, and psychosocial impact of intractable epilepsy and its high cost of care, along with the sophisticated human and technological resources needed to address them, qualifies this, in these authors opinions, as a public health care problem. Indeed, scientific advances regardless of their value may not translate into improved care of epilepsy and lessen its burden, unless devices are broadly accessible; in short the challenge of ameliorating the global burden of drug-resistant epilepsies may exceed scientific and technological ones. If the answer to the question put forth a few lines above is in the negative (intracranial devices will not meet the global burden) viable alternatives must be sought.

The utilization of certain extra-cerebral signals looms as one such alternative. Cardiac (e.g., heart rate, EKG morphology) and motor (speed, direction and force of joint movements) signals are prime candidates for the following reasons: 1. Structures that form part of the central autonomic nervous system or are strongly interconnected with it, are common sites of epileptogenesis (e.g., amygdalae-hippocampi); 2. Spread of seizures out of the primary epileptogenic zone, is prevalent in pharmaco-resistant patients so that even if the site of origin is not part of the central autonomic network, invasion of it by ictal activity is quite common; 3. Partial seizures particularly if complex, are characterized by either positive (e.g., motor automatism, hypermotoric behavior, clonic/myoclonic activity, focal increase in anti-gravitatory muscle tone) or negative (e.g., motionless, focal loss of antigravitatory muscle tone) phenomena that are stereotypical across seizures originating from the same site and appear relatively early in the course of seizures; 4. Cardiac and motor signals are highly robust, easily recordable as they do not require implantable devices or development of ground breaking technology; EKG, actigraphs, 3-D accelerometers are widely available commercially and are considerably less costly than those required for use in the central nervous system (CNS); 5. Signals of cardiac and motor origin lack the high complexity or large dimensionality of those generated by the brain's cortex, are simpler to process and analyze, and, thus, are less computationally expensive. Ease of computation allows the use of simpler, smaller devices compared to those required for computation of cortical signals and as they use less power, battery recharging or replacements are less frequent; 6. The neurosurgical procedures and potential associated complications make implantable devices unappealing to a majority of pharmaco-resistant patients that responded to a survey.

Among the numerous extra-cerebral signals usable for seizure detection, cardiac, have been the most extensively investigated. Tachycardia is a common manifestation of partial seizures, occurring in almost 90% of seizures of mesial temporal origin and precedes electrographic (as determined with scalp electrodes) and clinical onset in the majority of these seizures. (Tachycardia invariably occurs in primarily/secondarily generalized tonic-clonic seizures being higher in magnitude and longer duration than in partial seizures. Tachycardia with tonic-clonic seizures is multifactorial: neurogenic, metabolic, and exertional.) From a cardiac rhythm perspective, the increases in heart rate temporally correlated with seizures are rarely pathologic, being of sinus origin; additionally their magnitude is unlikely to compromise cardiac output in healthy individuals. Ictal tachycardia has a strong neurogenic component reflective of either an increase in sympathetic or withdrawal of parasympathetic activity; while increases in motor activity in refer-

ence to the interictal state would augment its magnitude, tachycardia occurs in subjects in whom seizures manifest with motionless. Bradycardia also occurs with seizures, albeit with much lower prevalence than tachycardia; so called "temporal lobe syncope", denoting the loss of consciousness (without convulsive activity) during partial seizures is caused by profound bradycardia.

In light of the potential to apply cardiac signals, and in particular of exploiting changes in heart rate (increases or decreases relative to an interictal baseline) for automated seizure detection, algorithms are being developed and tested to this end. In addition to detection and warning of seizures, heart rate changes may be used to quantify: a) Relative duration defined as the time said changes spend above or below an interictal reference value(s); b) Relative intensity corresponding to the area under the curve or to the product of peak/bottom heart rate and duration (in sec.); c) Seizure frequency/unit time (e.g., month). The challenge of this detection modality for ambulatory clinical applications, is the ubiquitousness of heart rate changes with daily life activities that may translate into large numbers of false positive detections. Arousal from sleep, standing up from a recumbent position, climbing stairs, are but a few of the myriad daily life activities associated with relative or absolute changes (e.g., increases) in heart rate. The discriminating power or positive predictive value (ictal vs. exertional) of this detection modality is currently the subject of investigation in epilepsy monitoring units. Heart rate, among other (rate of change/slope; P-QRS-T morphology) markers, during seizures, are recorded, analyzed and compared to those associated with protocolized motor activities (e.g., walking on a treadmill). Preliminary results show that the magnitude of ictal increases in heart rate is sufficiently large compared to non-strenuous exercises, so as to allow accurate differentiation and, consequently, detection of certain types of partial seizures. It would be naive and incorrect to presume that univariate (e.g., heart rate changes alone) automated detection of seizures would yield worthwhile positive predictive power (PPV=number of true positive detections/total number of detections) in ambulatory patients. Multivariate-based detection would be required to achieve satisfactory performance in a sufficiently large number of patients; ictal (reversible) changes in EKG morphology while less prevalent than in heart rate, have higher specificity and may increase considerably speed of detection (e.g., to within 3 heart beats). Visual analysis of peri-ictal R-R plots, has led to the discovery of heart rate patterns with characteristic morphology that are reproducible among seizures sharing a common epileptogenic zone and appear to be a specific ictal marker. One of these patterns resembles the letter "M" and indicates heart rate changes during seizures may not be unidirectional or monotonic: in this example, heart rate elevation is followed by a return towards its interictal baseline, which in turn gives way to a second elevation in rate. These fluctuations may be attributable, in part to the co-existence of parasympathetic and cholinergic neurons within the same autonomic nervous system structure; specifically, components of the central autonomic network such as the Dorsal Medial Hypothalamus, the Paraventricular Nucleus of the hypothalamus and the Nucleus Tractus Solitarius have dual cholinergic and noradrenergic innervation. Heart rate changes are also expected to be dependent on time of day (circadian), level of consciousness (awake vs. asleep), patient's fitness level, activity level (walking vs. jogging), and emotional and cognitive states, as well as on ingestion of drugs with adrenergic or cholinergic actions.

Ictal motor activity (movement amplitude, direction, velocity and type and number of muscles groups involved) recorded with actigraphs/3-D accelerometers would enhance specificity of cardiac-based detection, as it is stereotypical across seizures originating from the same structure(s). Use of ictal motor movements to detect seizures independent of heart rate or other sensors is actively under investigation. For example, a wrist accelerometer accurately detected seven of eight tonic-clonic seizures, and nonseizure movements were readily identified by patients thereby reducing the consequence of false detections. As wearable technologies advance, so do opportunities for more precise measurement of complicated seizure-related movements such as automatisms.

Respiratory rate is markedly increased (also a neurogenic phenomenon) during seizures manifesting with tachycardia and its specificity may be higher than heart rate changes as its magnitude and pattern differ amply from exertional increases in ventilation. Electrodermal (e.g. skin resistance, sudomotor) or vocal (e.g., non-formed vocalizations) activity, eyelid and ocular movements (gaze deviation, nystagmus), metabolic (e.g., profound normokalemic lactic acidosis with convulsions, hormonal (prolactin elevations with convulsion or certain partial seizures) or tissue stress (lactic acid, CK) indices may aid in extracerebral seizure detection.

Paradoxically, a potentially important hurdle in the path to adoption of extra-cerebral detection of seizures is the markedly low sensitivity and other limitations of patient diaries, the universal “gold” metric or “ground truth” in epileptology. The rate of automated seizure detection, whether cerebrally or extra-cerebrally based, will be higher, possibly much higher in certain cases, than obtainable with diaries as not only clinical, but also “subclinical” seizures will be logged. This “limitation” or “inconvenience” that may discourage patients and epileptologists, is compounded by the absence of simultaneously recorded cortical activity, since direct proof cannot be furnished that a change in extra-cerebral indices, was indeed caused by a seizure. A simple, but powerful means to overcome this hurdle is through the administration of complex reaction time tests implementable in real-time, into hand-held devices and triggered by changes in extra-cerebral signals such as EKG; in a cooperative, motivated patient, cardiac activity changes in the context of an abnormal response or failed test will be classified as clinical seizures, while those with a preserved response as either subclinical seizures or false positive detections.

Based on the existing evidence and body of work, it may be stated that extra-cerebral automated detection, warning, logging of seizures and delivery of therapy, looms as a useful, cost-effective and widely accessible option to better manage pharmaco-resistant epilepsies.

An embodiment of a medical device adaptable for use in implementing some aspects of embodiments of the present invention is provided in FIG. 1. As shown in FIG. 1, a system may involve a medical device system that senses body signals of the patient—such as brain or cardiac activity—and analyzes those signals to identify one or more aspects of the signal that may identify the occurrence of a seizure. The signal may be processed to extract (e.g., mathematically by an algorithm that computes certain values from the raw or partially processed signal) features that may be used to identify a seizure when compared to the inter-ictal state. As shown in the right side of FIG. 1, the features may also be graphically displayed either in real time or subsequent to the event to enable visual confirmation of the

seizure event and gain additional insight into the seizure (e.g., by identifying a seizure metric associated with the seizure).

Turning now to FIG. 2, a block diagram depiction of a medical device 200 is provided, in accordance with one illustrative embodiment of the present invention. In some embodiments, the medical device 200 may be implantable, while in other embodiments the medical device 200 may be completely external to the body of the patient.

The medical device 200 may comprise a controller 210 capable of controlling various aspects of the operation of the medical device 200. The controller 210 is capable of receiving internal data or external data, and in one embodiment, is capable of causing a stimulation unit (not shown) to generate and deliver an electrical signal, a drug, cooling, or two or more thereof to one or more target tissues of the patient’s body for treating a medical condition. For example, the controller 210 may receive manual instructions from an operator externally, or may cause an electrical signal to be generated and delivered based on internal calculations and programming. In other embodiments, the medical device 200 does not comprise a stimulation unit. In either embodiment, the controller 210 is capable of affecting substantially all functions of the medical device 200.

The controller 210 may comprise various components, such as a processor 215, a memory 217, etc. The processor 215 may comprise one or more microcontrollers, microprocessors, etc., capable of performing various executions of software components. The memory 217 may comprise various memory portions where a number of types of data (e.g., internal data, external data instructions, software codes, status data, diagnostic data, etc.) may be stored. The memory 217 may comprise one or more of random access memory (RAM), dynamic random access memory (DRAM), electrically erasable programmable read-only memory (EEPROM), flash memory, etc.

The medical device 200 may also comprise a power supply 230. The power supply 230 may comprise a battery, voltage regulators, capacitors, etc., to provide power for the operation of the medical device 200, including delivering the therapeutic electrical signal. The power supply 230 comprises a power source that in some embodiments may be rechargeable. In other embodiments, a non-rechargeable power source may be used. The power supply 230 provides power for the operation of the medical device 200, including electronic operations and the electrical signal generation and delivery functions. The power supply 230 may comprise a lithium/thionyl chloride cell or a lithium/carbon monofluoride (LiCFx) cell if the medical device 200 is implantable, or may comprise conventional watch or 9V batteries for external (i.e., non-implantable) embodiments. Other battery types known in the art of medical devices may also be used.

The medical device 200 may also comprise a communication unit 260 capable of facilitating communications between the medical device 200 and various devices. In particular, the communication unit 260 is capable of providing transmission and reception of electronic signals to and from a monitoring unit 270, such as a handheld computer or PDA that can communicate with the medical device 200 wirelessly or by cable. The communication unit 260 may include hardware, software, firmware, or any combination thereof.

The medical device 200 may also comprise one or more sensor(s) 212 coupled via sensor lead(s) 211 to the medical device 200. The sensor(s) 212 are capable of receiving signals related to a physiological parameter, such as the patient’s heart beat, blood pressure, and/or temperature, and

delivering the signals to the medical device **200**. The sensor **212** may also be capable of detecting kinetic signal associated with a patient's movement. The sensor **212**, in one embodiment, may be an accelerometer. The sensor **212**, in another embodiment, may be an inclinometer. In another embodiment, the sensor **212** may be an actigraph. In one embodiment, the sensor(s) **212** may be the same as implanted electrode(s) **126**, **128**. In other embodiments, the sensor(s) **212** are external structures that may be placed on the patient's skin, such as over the patient's heart or elsewhere on the patient's torso. The sensor **212**, in one embodiment is a multimodal signal sensor capable of detecting various autonomic and neurologic signals, including kinetic signals associated with the patient's movement.

The seizure onset/termination module **280** is capable of detecting an epileptic event based upon one or more signals provided by body data collection module **275**. The seizure onset/termination module **280** can implement one or more algorithms using the autonomic data and neurologic data in any particular order, weighting, etc. The seizure onset/termination module **280** may comprise software module(s) that are capable of performing various interface functions, filtering functions, etc. In another embodiment, the seizure onset/termination module **280** may comprise hardware circuitry that is capable of performing these functions. In yet another embodiment, the seizure onset/termination module **280** may comprise hardware, firmware, software and/or any combination thereof.

The seizure onset/termination unit **280** is capable of determining an epileptic event by application of a WTMM algorithm to one or more signals provided by body data collection module **275** and/or seizure onset/termination module **280**. The seizure onset/termination unit **280** may comprise software module(s) that are capable of performing various interface functions, filtering functions, etc. In another embodiment, the seizure onset/termination unit **280** may comprise hardware circuitry that is capable of performing these functions. In yet another embodiment, the seizure onset/termination unit **280** may comprise hardware, firmware, software and/or any combination thereof.

In addition to components of the medical device **200** described above, a medical device system may comprise a storage unit to store an indication of at least one of seizure or an increased risk of a seizure. The storage unit may be the memory **217** of the medical device **200**, another storage unit of the medical device **200**, or an external database, such as a local database unit **255** or a remote database unit **250**. The medical device **200** may communicate the indication via the communications unit **260**. Alternatively or in addition to an external database, the medical device **200** may be adapted to communicate the indication to at least one of a patient, a caregiver, or a healthcare provider.

In various embodiments, one or more of the units or modules described above may be located in a monitoring unit **270** or a remote device **292**, with communications between that unit or module and a unit or module located in the medical device **200** taking place via communication unit **260**. For example, in one embodiment, one or more of the body data collection module **275** or the seizure onset/termination module **280** may be external to the medical device **200**, e.g., in a monitoring unit **270**. Locating one or more of the body data collection module **275** or the seizure onset/termination module **280** outside the medical device **200** may be advantageous if the calculation(s) is/are computationally intensive, in order to reduce energy expenditure and heat generation in the medical device **200** or to expedite calculation.

The monitoring unit **270** may be a device that is capable of transmitting and receiving data to and from the medical device **200**. In one embodiment, the monitoring unit **270** is a computer system capable of executing a data-acquisition program. The monitoring unit **270** may be controlled by a healthcare provider, such as a physician, at a base station in, for example, a doctor's office. In alternative embodiments, the monitoring unit **270** may be controlled by a patient in a system providing less interactive communication with the medical device **200** than another monitoring unit **270** controlled by a healthcare provider. Whether controlled by the patient or by a healthcare provider, the monitoring unit **270** may be a computer, preferably a handheld computer or PDA, but may alternatively comprise any other device that is capable of electronic communications and programming, e.g., hand-held computer system, a PC computer system, a laptop computer system, a server, a personal digital assistant (PDA), an Apple-based computer system, a cellular telephone, etc. The monitoring unit **270** may download various parameters and program software into the medical device **200** for programming the operation of the medical device, and may also receive and upload various status conditions and other data from the medical device **200**. Communications between the monitoring unit **270** and the communication unit **260** in the medical device **200** may occur via a wireless or other type of communication, represented generally by line **277** in FIG. 2. This may occur using, e.g., wand **155** to communicate by RF energy with an implantable signal generator **110**. Alternatively, the wand may be omitted in some systems, e.g., systems in which the MD **200** is non-implantable, or implantable systems in which monitoring unit **270** and MD **200** operate in the MICS bandwidths.

In one embodiment, the monitoring unit **270** may comprise a local database unit **255**. Optionally or alternatively, the monitoring unit **270** may also be coupled to a database unit **250**, which may be separate from monitoring unit **270** (e.g., a centralized database wirelessly linked to a handheld monitoring unit **270**). The database unit **250** and/or the local database unit **255** are capable of storing various patient data. These data may comprise patient parameter data acquired from a patient's body, therapy parameter data, seizure severity data, and/or therapeutic efficacy data. The database unit **250** and/or the local database unit **255** may comprise data for a plurality of patients, and may be organized and stored in a variety of manners, such as in date format, severity of disease format, etc. The database unit **250** and/or the local database unit **255** may be relational databases in one embodiment. A physician may perform various patient management functions (e.g., programming parameters for a responsive therapy and/or setting references for one or more detection parameters) using the monitoring unit **270**, which may include obtaining and/or analyzing data from the medical device **200** and/or data from the database unit **250** and/or the local database unit **255**. The database unit **250** and/or the local database unit **255** may store various patient data.

One or more of the blocks illustrated in the block diagram of the medical device **200** in FIG. 2 may comprise hardware units, software units, firmware units, or any combination thereof. Additionally, one or more blocks illustrated in FIG. 2 may be combined with other blocks, which may represent circuit hardware units, software algorithms, etc. Additionally, any number of the circuitry or software units associated with the various blocks illustrated in FIG. 2 may be combined into a programmable device, such as a field programmable gate array, an ASIC device, etc.

Turning now to FIG. 3, a block diagram depiction of an exemplary implementation of the body data collection mod-

ule 275 is shown. The body data collection module 275 may include hardware (e.g., amplifiers, accelerometers), tools for chemical assays, optical measuring tools, a body data memory 350 (which may be independent of memory 117 or part of it) for storing and/or buffering data. The body data memory 350 may be adapted to store body data for logging or reporting and/or for future body data processing and/or statistical analyses. Body data collection module 275 may also include one or more body data interfaces 310 for input/output (I/O) communications between the body data collection module 275 and sensors 112. Body data from memory 350 and/or interface 310 may be provided to one or more body index calculation unit(s) 355, which may determine one or more body indices.

In the embodiments of FIG. 3, sensors 112 may be provided as any of various body data units/modules (e.g., autonomic data acquisition unit 360, neurological data acquisition unit 370, endocrine data acquisition unit 373, metabolic data acquisition unit 374, tissue stress marker data acquisition unit 375, and physical fitness/integrity determination unit 376) via connection 380. Connection 380 may be a wired connection a wireless connection, or a combination of the two. Connection 380 may be a bus-like implementation or may include an individual connection (not shown) for all or some of the body data units.

In one embodiment, the autonomic data acquisition unit 360 may include a cardiac data acquisition unit 361 adapted to acquire a phonocardiogram (PKG), EKG, echocardiography, apexcardiography and/or the like, a blood pressure acquisition unit 363, a respiration acquisition unit 364, a blood gases acquisition unit 365, and/or the like. In one embodiment, the neurologic data acquisition unit 370 may contain a kinetic unit 366 that may comprise an accelerometer unit 367, an inclinometer unit 368, and/or the like; the neurologic data acquisition unit 370 may also contain a responsiveness/awareness unit 369 that may be used to determine a patient's responsiveness to testing/stimuli and/or a patient's awareness of their surroundings. Body data collection module 275 may collect additional data not listed herein, that would become apparent to one of skill in the art having the benefit of this disclosure.

The body data units ([360-370], [373-377]) may be adapted to collect, acquire, receive/transmit heart beat data, EKG, PKG, echocardiogram, apexcardiogram, blood pressure, respirations, blood gases, body acceleration data, body inclination data, EEG/ECOG, quality of life data, physical fitness data, and/or the like.

The body data interface(s) 310 may include various amplifier(s) 320, one or more A/D converters 330 and/or one or more buffers 340 or other memory (not shown). In one embodiment, the amplifier(s) 320 may be adapted to boost and condition incoming and/or outgoing signal strengths for signals such as those to/from any of the body data acquisition units/modules (e.g., ([360-370], [373-377])) or signals to/from other units/modules of the MD 100. The A/D converter(s) 330 may be adapted to convert analog input signals from the body data unit(s)/module(s) into a digital signal format for processing by controller 210 (and/or processor 215). A converted signal may also be stored in a buffer(s) 340, a body data memory 350, or some other memory internal to the MD 100 (e.g., memory 117, FIG. 1) or external to the MD 100 (e.g., monitoring unit 170, local database unit 155, database unit 150, and remote device 192). The buffer(s) 340 may be adapted to buffer and/or store signals received or transmitted by the body data collection module 275.

As an illustrative example, in one embodiment, data related to a patient's respiration may be acquired by respiration unit 364 and sent to MD 100. The body data collection module 275 may receive the respiration data using body data interface(s) 310. As the data is received by the body data interface(s) 310, it may be amplified/conditioned by amplifier(s) 320 and then converted by A/D converter(s) into a digital form. The digital signal may be buffered by a buffer(s) 340 before the data signal is transmitted to other components of the body data collection module 275 (e.g., body data memory 350) or other components of the MD 100 (e.g., controller 110, processor 115, memory 117, communication unit 160, or the like). Body data in analog form may be also used in one or more embodiments.

Body data collection module 275 may use body data from memory 350 and/or interface 310 to calculate one or more body indices in body one or more body index calculation unit(s) 355. A wide variety of body indices may be determined, including a variety of autonomic indices such as heart rate, blood pressure, respiration rate, blood oxygen saturation, neurological indices such as maximum acceleration, patient position (e.g., standing or sitting), and other indices derived from body data acquisition units 360, 370, 373, 374, 375, 376, 377, etc.

Turning now to FIG. 4, an MD 100 (as described in FIG. 3) is provided, in accordance with one illustrative embodiment of the present invention. FIG. 4 depicts the body data acquisition units similar to those shown in FIG. 3, in accordance with another embodiment, wherein these units are included within the MD 100, rather being externally coupled to the MD 100, as shown in FIG. 3. In accordance with various embodiments, any number and type of body data acquisition units may be included within the MD 100, as shown in FIG. 4, while other body data units may be externally coupled, as shown in FIG. 3. The body data acquisition units may be coupled to the body data collection module 275 in a fashion similar to that described above with respect to FIG. 3, or in any number of different manners used in coupling intra-medical device modules and units. The manner by which the body data acquisition units may be coupled to the body data collection module 275 is not essential to, and does not limit, embodiments of the instant invention as would be understood by one of skill in the art having the benefit of this disclosure. Embodiments of the MD depicted in FIG. 4 may be fully implantable or may be adapted to be provided in a system that is external to the patient's body.

A time series body signal collected by the body data collection module 275 may comprise at least one of a measurement of the patient's heart rate, a measurement of the patient's kinetic activity, a measurement of the patient's brain electrical activity, a measurement of the patient's oxygen consumption, a measurement of the patient's work, a measurement of an endocrine activity of the patient, a measurement of a metabolic activity of the patient, a measurement of an autonomic activity of the patient, a measurement of a cognitive activity of the patient, or a measurement of a tissue stress marker of the patient.

Turning to FIG. 5, the seizure onset/termination unit 280 depicted in FIG. 2 is shown in greater detail. The seizure onset/termination unit 280 may comprise a body signal interface 510 adapted to received collected body data from the body data collection module 275. For example, the seizure onset/termination unit 280 may be adapted to receive a time series of collected body data.

The seizure onset/termination unit 280 may also comprise a time window control module 520. The time window

control module **520** may comprise a foreground window determination module **521**, adapted to determine a sliding time window for the time series body signal comprising a foreground window; and/or a background window determination module **522**, adapted to determine a sliding time window for the time series body signal comprising a background window.

In other embodiments (not shown), any time window used herein may be a moving time window, not necessarily a sliding time window. As used herein, a “sliding” time window moves over continuous points of a time series and the present (e.g., foreground) and past (e.g., background) are contiguous in time, if not overlapping. For example, if the foreground window is 5 s and the background 60 s in length, and the current time is 10:00:00 AM, the temporal location of the foreground window may be 10:00:00-10:00:05 and that of the background, 09:59:00-10:00:00. A “moving” time window may move over continuous points of the time series or “jump” over discontinuous points. For example, a moving window may be chosen from past data that optimizes sensitivity, specificity, or speed of detection as required by the patient’s prevailing conditions, activities, or time of day, said time being discontinuous from that of the foreground window. Using the example cited immediately above, in this example, the foreground window of 5 s at 10:00:00 AM may be compared to a 60 s background recorded 6 hr. earlier (04:00:00-04:01:00). A moving window may also be the average or median of several windows.

The seizure onset/termination unit **280** may also comprise a WTMM unit **530**. The WTMM unit **530** may be adapted to apply a WTMM skeleton to at least one long chain extracted from the windowed signals using a continuous wavelet transform.

The parameters of the WTMM may comprise at least one window length of 1 second, a scale for selecting chain length of 3, and a variance increment of 0.25.

The parameters of the WTMM model may be selected based on at least one of a clinical application of said detection; a level of safety risk associated with an activity; at least one of an age, physical state, or mental state of the patient; a length of a window available for warning; a degree of efficacy of therapy and of its latency; a degree of seizure control; a degree of circadian and ultradian fluctuations of said patient’s seizure activity; a performance of the detection method as a function of the patient’s sleep/wake cycle or vigilance level; a dependence of the patient’s seizure activity on at least one of a level of consciousness, a level of cognitive activity, or a level of physical activity; the site of seizure origin; a seizure type suffered by said patient; a desired sensitivity of detection of a seizure, a desired specificity of detection of a seizure, a desired speed of detection of a seizure, an input provided by the patient, or an input provided by a sensor.

In various embodiments, the selected parameters may reflect the degree of certainty of detections desired by the patient, a caregiver, a medical professional, or two or more thereof. Such person(s) are expected to have biases regarding their desire for certainty of detection, and variation in their risk-proneness and/or aversion to risk. Thus, in one embodiment, the patient, caregiver, and/or medical professional may be allowed to change (within certain limits and for certain activities only, if desired) the sensitivity, specificity, and/or speed of detection of the algorithms.

The seizure onset/termination unit **280** may also comprise a variance determination unit **540**. The variance determina-

tion unit **540** may be adapted to determine a variance of the output of the WTMM unit **530** based upon the WTMM skeleton.

The seizure onset/termination unit **280** may also comprise a stepwise approximation unit **550**. The stepwise approximation unit **550** may be adapted to generate a stepwise approximation of the changes in variance of the windowed signal as analyzed by the WTMM unit **530** and/or the variance determination unit **540**.

The seizure onset/termination unit **280** may also comprise a seizure onset determination module **560**. The seizure onset determination module **560** may be configured to determine an onset of a seizure in response to a determination that an output of the stepwise approximation of the changes in variance in the foreground window has reached an onset threshold.

The seizure onset/termination unit **280** may also comprise a seizure termination determination module **570**. The seizure termination determination module **570** may be adapted to determine a termination of a seizure in response to a determination that an output of the stepwise approximation of the changes in variance in the background window has reached a termination threshold.

Turning to FIG. **12**, a flowchart depiction of a method for detecting an onset and a termination of an epileptic event from a patient body signal is shown. A time series body signal of a patient may be received at **1210**. Sliding first and second time windows for the time series body signal may be determined at **1220**. The determination at **1220** may comprise determining a foreground window at **1225** and/or determining a background window at **1227**. A WTMM operation may be performed at **1230** to each of the sliding adjacent time windows. The performance at **1230** may comprise constructing at **1232** a WTMM skeleton, determining at **1234** a variance of the output of the construction, and/or constructing at **1236** a stepwise approximation of change in the variance.

An onset of a seizure may be determined at **1240** based on the stepwise approximation and/or the variance. A termination of a seizure may be determined at **1250** based on the stepwise approximation and/or the variance.

Optionally, the method depicted in FIG. **12** may comprise other activities. The method may further involve delivering a therapy for the seizure at a particular time at **1270**, wherein at least one of the therapy, the particular time, or both may be based upon the determination of the seizure onset.

Alternatively or in addition, the method may further involve determining at **1280** an efficacy of the therapy.

Alternatively or in addition, the method may further involve issuing at **1285** a warning for the seizure, wherein the warning may be based upon the determination of the seizure onset.

In one embodiment, at least one of the delivered therapy or the issued warning is based at least in part on at least one of the type of activity engaged in by the patient at the time of seizure onset, the seizure type, the seizure severity, or the time elapsed from the last seizure.

Alternatively or in addition, the method may further involve determining at **1290** at least one of a timing of delivery of therapy, a type of therapy, at least one parameter of the therapy, a timing of sending a warning, a type of warning, a duration of the warning, or an efficacy of said therapy, based upon a timing of said determination of said seizure onset, said determination of said seizure termination, or both.

Alternatively or in addition, the method may further involve determining at **1295** at least one value selected from

the duration of the epileptic event, the severity of the epileptic event, the intensity of the epileptic event, the extent of spread of the epileptic event, an inter-seizure interval between the epileptic event and a prior epileptic event, a patient impact of the epileptic event, or a time of occurrence of the epileptic event. The method may further comprise logging at 1296 the at least one value.

A method, such as that depicted in FIG. 12, may be implemented by a non-transitory computer readable program storage unit encoded with instructions that, when executed by a computer, perform the method.

An activity, such as walking, swimming, driving, etc., may be allowed or terminated, a warning may be issued or not issued, or a therapy may be delivered or not delivered, based on the determination of seizure onset, seizure termination, or both, either from a WTMM algorithm alone or a PMSA value calculated at least in part from an indicator function derived from the WTMM algorithm.

An "efficacy index" may be used herein to refer to any quantification of an efficacious result of a therapy. In one example, if a patient's seizures typically present an increase in heart rate from a resting rate of 80 beats per minute (BPM) to a peak ictal heart rate of 160 BPM, and upon administering a therapy to the patient, the patient's peak ictal heart rate is 110 BPM, this result may be quantified as an efficacy index of 50 (on a scale of non-therapy peak ictal heart rate-peak ictal heart rate after therapy), 0.625 (50 BPM reduction from peak ictal heart rate/80 BPM increase from resting rate to peak ictal heart rate in the absence of therapy), etc.

The invention claimed is:

1. A system, comprising:

a body data collection module configured to collect body data comprising a time series of a first body signal of a patient, wherein said first body signal is a cardiac signal or a kinetic signal,

a non-transitory computer readable program storage unit encoded with instructions that, when executed by a computer, perform a method, comprising:

receiving a said time series of a said first body signal of a patient from said body data collection module,

determining at least two sliding adjacent time windows for said time series of said first body signal comprising a foreground window and a background window;

extracting at least one first long chain from said foreground window and at least one second long chain from said background window;

applying a continuous wavelet transform to each of said long chains, to yield a wavelet transform maximum modulus (WTMM) skeleton for each window;

determining a first variance of the WTMM skeleton from said foreground window and a second variance of the WTMM skeleton from said background window;

generating a stepwise approximation of changes in said variance;

determining a seizure onset in response to a determination that an output of the stepwise approximation of changes in said first variance has reached an onset threshold; and

determining a seizure termination in response to a determination that an output of the stepwise approximation of changes in said second variance has reached a termination threshold; and

an implantable medical device comprising an electrical signal generator, a lead assembly attached at a first end to said electrical signal generator, and an electrode assembly attached to a second end of said lead assembly, wherein said electrode assembly is configured for

surgical coupling to a cranial nerve of said patient, wherein said implantable medical device is configured to deliver an electrical signal for treating said seizure at a particular time, wherein said particular time is based upon said determination of said seizure onset, wherein said seizure onset is determined faster than a seizure onset determined by a validated algorithm.

2. The system of claim 1, including data that when executed by a processor performs the method of claim 1, wherein parameters of the wavelet transform maximum modulus comprise at least one window length of 1 second, a scale for selecting chain length of 3, and a variance increment of 0.25.

3. The system of claim 1, including data that when executed by a processor performs the method of claim 1, wherein at least one of said onset threshold or said termination threshold is based on at least one of a clinical application of at least one said determination; a level of safety risk associated with an activity; at least one of an age, physical state, or mental state of the patient; a length of a window available for warning; a degree of efficacy of therapy and of its latency; a degree of seizure control; a degree of circadian and ultradian fluctuations of said patient's seizure activity; a performance of the detection method as a function of the patient's sleep/wake cycle or vigilance level; a dependence of the patient's seizure activity on at least one of a level of consciousness, a level of cognitive activity, or a level of physical activity; the site of seizure origin; a seizure type suffered by said patient; a desired sensitivity of detection of a seizure, a desired specificity of detection of a seizure, a desired speed of detection of a seizure, an input provided by the patient, or an input provided by a sensor.

4. The system of claim 3, including data that when executed by a processor performs the method of claim 3, wherein the method further comprises adaptively establishing at least one of said onset threshold or said termination threshold.

5. The system of claim 1, including data that when executed by a processor performs the method of claim 1, wherein at least one of the delivered therapy or an issued warning is based at least in part on at least one of a type of activity engaged in by the patient at a time of seizure onset, a seizure type, a seizure severity, or a time elapsed from the last seizure.

6. The system of claim 1, including data that when executed by a processor performs the method of claim 1, wherein the method further comprises determining at least one of:

a timing of delivery of therapy, a duration of a therapy, a type of therapy, at least one parameter of the therapy, a timing of sending a warning, a type of warning, or a duration of the warning;

based upon said seizure onset, said seizure termination, or both.

7. The system of claim 1, including data that when executed by a processor performs the method of claim 1, wherein the method further comprises:

determining at least one value selected from the duration of said seizure, the severity of said seizure, the intensity of said seizure, the extent of spread of said seizure, an inter-seizure interval between said seizure and a prior seizure, a patient impact of said seizure, or a time of occurrence of said seizure; and

logging said at least one value.

8. The system of claim 1, including data that when executed by a processor performs the method of claim 1,

wherein the method further comprises estimating the degree of nonstationarity of said first body signal.

9. A method for treating a seizure, comprising:

collecting, by a body data collection module, body data comprising a time series of a first body signal of a patient, wherein said first body signal is a cardiac signal or a kinetic signal,

determining at least two sliding adjacent time windows for said time series of said first body signal comprising a foreground window and a background window;

applying a wavelet transform maximum modulus (WTMM) skeleton to at least one long chain extracted from said windowed signals using a continuous wavelet transform;

determining a variance of the output of the previous step based upon the WTMM skeleton;

generating a stepwise approximation of changes in variance of the windowed signal as analyzed using previous steps;

determining a seizure onset in response to a determination that an output of the stepwise approximation of changes in variance in the foreground window has reached an onset threshold;

determining a seizure termination in response to a determination that an output of the stepwise approximation of changes in said second variance has reached a termination threshold; and

delivering an electrical signal for treating said seizure at a particular time, wherein said particular time is based upon said determination of said seizure onset, wherein said seizure onset is determined faster than a seizure onset determined by a validated algorithm.

10. The method of claim 9, wherein the parameters of the wavelet transform maximum modulus comprise at least one window length of 1 second, a scale for selecting chain length of 3, and a variance increment of 0.25.

11. The method of claim 9, wherein at least one of said onset threshold or said termination threshold is based on at least one of a clinical application of at least one said determination; a level of safety risk associated with an activity; at least one of an age, physical state, or mental state of the patient; a length of a window available for warning; a degree of efficacy of therapy and of its latency; a degree of seizure control; a degree of circadian and ultradian fluctuations of said patient's seizure activity; a performance of the detection method as a function of the patient's sleep/wake cycle or vigilance level; a dependence of the patient's seizure activity on at least one of a level of consciousness, a level of cognitive activity, or a level of physical activity; the site of seizure origin; a seizure type

suffered by said patient; a desired sensitivity of detection of a seizure, a desired specificity of detection of a seizure, a desired speed of detection of a seizure, an input provided by the patient, or an input provided by a sensor.

12. The method of claim 11, further comprising allowing at least one of the patient, a caregiver, or a medical professional to change at least one of the sensitivity, specificity, or speed of seizure detection.

13. The method of claim 9, further comprising:

determining an efficacy of said therapy; or

issuing a warning for said seizure, wherein said warning is based upon said determination of said seizure onset; wherein said seizure onset is determined faster than a seizure onset determined by a validated algorithm.

14. The method of claim 13, wherein at least one of the delivered therapy or the issued warning is based at least in part on at least one of the type of activity engaged in by the patient at the time of seizure onset, the seizure type, the seizure severity, or the time elapsed from the last seizure.

15. The method of claim 9, further comprising determining at least one of:

a timing of delivery of therapy, a duration of a therapy, a type of therapy, at least one parameter of the therapy, a timing of sending a warning, a type of warning, or a duration of the warning;

based upon said seizure onset, said seizure termination, or both.

16. The method of claim 9, further comprising:

determining at least one value selected from the duration of said seizure, the severity of said seizure, the intensity of said seizure, the extent of spread of said seizure, an inter-seizure interval between said seizure and a prior seizure, a patient impact of said seizure, or a time of occurrence of said seizure; and

logging said at least one value.

17. The method of claim 9, further comprising estimating the degree of nonstationarity of said first body signal.

18. The system of claim 1, including data that when executed by a processor performs the method of claim 1, wherein the method further comprises at least one responsive action selected from:

determining an efficacy of said therapy; or

issuing a warning for said seizure, wherein said warning is based upon a determination of said seizure onset; wherein said seizure onset is determined faster than a seizure onset determined by a validated algorithm.

19. The system of claim 18, wherein said warning is further based on at least one of a determination of duration of said seizure or a determination of a type of said seizure.

* * * * *

专利名称(译)	使用小波变换最大模数算法的癫痫发作检测方法，装置和系统		
公开(公告)号	US9549677	公开(公告)日	2017-01-24
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[标]申请(专利权)人(译)	奥索里奥IVAN lyubushin阿列克谢 Didier Sornette		
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IPC分类号	G01N33/50 A61B5/0205 A61B5/00 A61B5/048 A61B5/11 A61B5/08 A61B5/04 A61B5/0476 A61B5/024		
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外部链接	Espacenet USPTO		

摘要(译)

用于通过使用应用于身体数据的小波变换最大模量 (WTMM) 算法来检测癫痫发作的方法。一种用于存储当由处理器执行时执行这种方法的数据的非传递性计算机可读存储设备。

the 20th Annual International Conference of the IEEE Engineering in Medicine and Biology Society, vol. 20, No. 3, 1998, 3 pages.
International Application No. PCT/US2012/060029, PCT Search Report and Written Opinion dated Dec. 21, 2012, 15 pages.