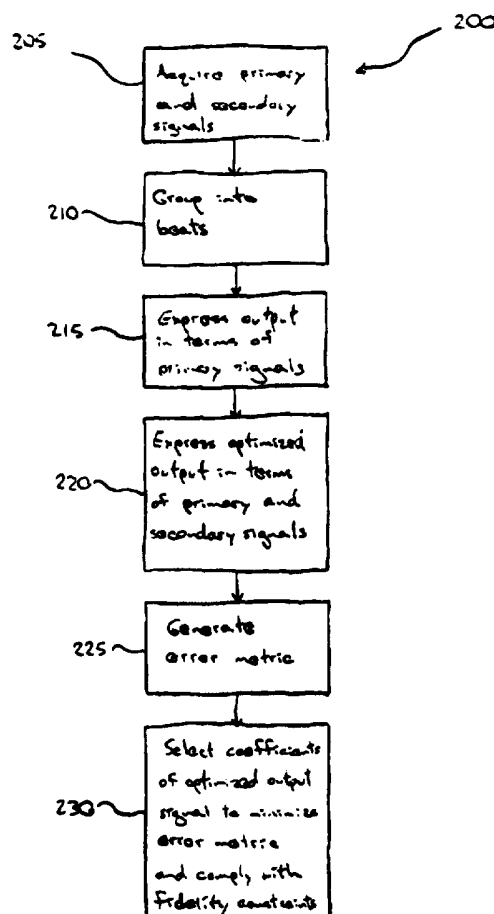# PCT

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(54) Title: USING RELATED SIGNALS TO REDUCE ECG NOISE

(57) Abstract

A method of reducing noise in a signal that represents a physiologic process includes obtaining multiple input signals (205), measuring a relationship between noise content of the input signals (210-225), and combining the input signals in consideration of the measured relationship to produce an output signal having a low noise content (230). The multiple input signals may include, for example, two or more primary physiologic input signals or one or more primary physiologic input signals and two or more secondary input signals that represent noise. The method may further include dividing one or more ECG input signals and secondary input signals into a set of segments, where each set of segments represents a beat of the ECG signal, measuring a relationship between noise content of corresponding points from successive sets of segments, and combining the input signals based on the measured relationship.

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USING RELATED SIGNALS TO REDUCE ECG NOISE

Cross Reference To Related Applications

This application is a continuation-in-part of U.S.
Application Serial No. 08/339,050, entitled "Improved
Method and Apparatus for Assessing Cardiac Electrical
Stability" and filed November 14, 1994; a continuation-
in-part of U.S. Application Serial No. 08/339,032,
entitled "Measuring a Physiologic Signal" and filed
November 14, 1994; and a continuation-in-part of U.S.
Application Serial No. 08/379,375, entitled "Measuring
and Assessing Cardiac Electrical Stability" and filed
January 26, 1995. The disclosures of each of these
applications is incorporated herein by reference.

Background of the Invention

The invention relates to reducing noise in
measurement of a physiologic signal.

Accurate measurement of physiologic signals is
extremely important in many diagnostic and therapeutic
applications. For example, it has been recently
discovered that alternans, a subtle beat-to-beat change
in the repeating pattern of an electrocardiogram (ECG)
waveform can be indicative of electrical instability of
the heart and increased susceptibility to sudden cardiac
death. Alternans results in an ABABAB... pattern of
variation of waveform shape between successive beats in
an ECG waveform, and the level of cardiac stability is
taken as a characterization of an individual's cardiac
electrical stability.

The physiologic signal underlying an ECG waveform
may be obtained through electrodes attached to a
patient's chest. Typically, the electrodes include an
electrically conductive gel that contacts the patient's
skin and detects electrical signals produced by the

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patient's heart. The detected signals are then
transmitted to ECG circuitry for processing and display.

Referring to Fig. 1, an ECG waveform for a single
beat is typically referred to as a PQRST complex.
5 Briefly, the P wave appears at initiation of the beat and
corresponds to activity in the atria, while the QRST
complex follows the P wave and corresponds to ventricular
activity. The QRS component represents the electrical
activation of the ventricles, while the T wave represents
10 the electrical recovery thereof. The ST segment is a
relatively quiescent period. In humans, it has been
found that the T wave is the best interval of the ECG
complex for detecting alternans. That is, a level of
variation in the T waves of alternating beats is the best
15 indicator of a patient's level of alternans.

Typically, the amplitude of an ECG waveform is
measured using an isoelectric point as the zero voltage
reference. The isoelectric point is measured during the
PQ interval between the P wave and QRS complex. The PQ
20 interval is a good approximation to a zero ECG level
because there is no major electrical activity in the
heart at that time. It is important to note that the ECG
waveform has DC content and that the zero ECG level does
not necessarily correspond to zero volts. Thus, any high
25 pass filtering of the waveform will offset the
isoelectric point.

While an ECG waveform typically has a QRS
amplitude measured in millivolts, an alternans pattern of
variation with an amplitude on the order of a microvolt
30 may be clinically significant. Accordingly, the
alternans pattern may be too small to be detected by
visual inspection of the electrocardiogram and often must
be detected and quantified electronically. Such
electronic detection and quantification of the alternans
35 pattern is further complicated by the presence of noise

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in the ECG waveforms, as the noise may result in
beat-to-beat variations in the ECG waveforms that have a
larger magnitude than the alternans pattern of variation.

The noise in an ECG signal can be classified into
5 three categories: baseline noise generated in the
electrode, physiologic noise, and external electrical
noise. The baseline noise is low frequency noise that
appears as an undulating baseline upon which the ECG
rides. Baseline noise is attributable to motion and
10 deformation of the electrode and its associated gel, and
results from low frequency events such as patient
respiration and patient motion. As a result, the
magnitude of baseline noise tends to increase with
exercise. However, many important ECG measurements must
15 be made during exercise. Typically, the frequency
content of baseline noise is below 2 Hz.

Physiologic noise results from other physiologic
processes within the patient that interfere with the ECG
signal, with skeletal muscle activity being the most
20 common source of physiologic noise. The electrical
activity of the skeletal muscles creates potentials that
are additive with respect to the potentials created by
the heart. The frequency content of the skeletal muscle
signals is comparable to the frequency content of the QRS
25 complex, and is typically greater than 10 Hz. When
measuring T wave alternans, additional physiologic noise
may result from changes in the position of the heart due
to respiration or from changes in the projection of the
electrical potential from the heart to the skin surface
30 due to thoracic conductivity changes arising from the
inflation and deflation of the lungs with respiration.

External electrical noise results, for example,
from ambient electromagnetic activity in the room,
electrode cable motion, and variations in amplifiers or
35 other components of the ECG circuitry. External

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electrical noise may be eliminated or reduced through the
use of high quality components and through the reduction
of ambient electromagnetic activity by, for example,
deactivating high power equipment.

5   Noise reduction is of particular importance in
applications that attempt to measure low level ECG
features such as ST segment changes, P waves, or the
fetal ECG, and of even more importance in applications
that attempt to measure microvolt level features of the
10 ECG, such as electrical alternans, His-Purkinje activity,
and late potentials such as might be measured by a signal
averaged ECG (SAECG). Noise in the ECG waveform can
easily mask the presence of alternans. The noise can
also mimic the presence of alternans where there is none.
15 For example, if a patient is breathing at one-half or
one-third of the heart rate, the respiration may
introduce a harmonic signal having the ABABAB... pattern
of alternans. Similarly, motion that repeats with some
periodicity, such as that resulting from exercise, can
20 create electrode noise with a similar pattern.
Furthermore, noise resulting from different sources, such
as respiration and electrode noise, can interact and
produce new periodicities, one of which may mimic
alternans. For all of these reasons, the reduction of
25 interfering noise is of paramount importance for the
measurement of alternans.

        ECG noise reduction strategies have drawn on a
variety of mathematical methods to reduce the noise. The
strategies can be grouped into several categories,
30 including temporal filtering of one dimensional input
signals, spatial filtering of input signals, adaptive
filtering of input signals using a reference input, and
source consistency filtering of input signals.

        The simplest form of temporal filter is a linear
35 filter, such as a low-pass, high-pass, or band-pass

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filter. Some linear filters have been designed with a
time-varying frequency response. For example, the filter
may process the QRS complex differently from the rest of
the ECG complex. Temporal filters also include non-
5 linear filters and cubic spline filters. The cubic
spline filter is a mathematical methodology for
approximating (and then subtracting out) the baseline
noise using only measurements of the isoelectric point
measured in the PQ interval. The methodology uses a
10 third order, discrete time difference equation having
parameters that are determined from the values of the
isoelectric points. The method can be loosely described
as fitting a cubic equation to the isoelectric point of
four beats and subtracting the cubic prediction in the
15 interval between the isoelectric points of the second and
third beats.

    Temporal filtering can exploit the repeating
nature of the ECG complex. The average of multiple ECG
complexes can be used to remove noise while preserving
20 the repeating ECG component. As described in U.S. Patent
No. 5,348,960, singular value decompositions of the ECG
complexes can be used to identify the temporal and
waveform eigenvectors that account for the dominant
features of the ECG complexes. The waveform eigenvectors
25 correspond to the principal components of the beat-to-
beat fluctuations. By reconstructing the original ECG
complexes using only a subset of the dominant
eigenvectors, the ECG complexes may be reproduced while
noise is suppressed.
30   With spatial filtering, ECG signals are
represented as an average of multiple input signals.
Typically, spatial filtering techniques assume that the
ECG signal is present to the same degree in all input
signals so that the input signals can be directly
35 combined. When the input signals cannot be combined

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directly, they can be characterized by the spatial
eigenvectors of the singular value decomposition of the
input signals. As described in U.S. Patent No.
5,348,960, the use of spatial eigenvectors permits the
5 original space of input signals to be reduced to a much
smaller subspace. The spatial eigenvectors can be
combined with the temporal or waveform eigenvectors.

Adaptive filtering uses a reference signal in
combination with an input signal to estimate a filter
10 that removes the noise from the input signal. Adaptive
filters are intended to operate with reference and input
signals which are chosen to be very similar to each
other. With each new sample, an adaptive filter
estimates and updates a filter response to minimize an
15 error signal that is the difference between the filtered
input signal and the reference signal. An adaptive
filter can be used as a noise canceller by defining the
reference signal as the component to be cancelled. For
example, U.S. Patent No. 4,793,361 describes a technique
20 that attempts to enhance P-waves by cancelling the QRS
complex. The P-wave filter functions to reproduce the
dominant component (i.e., the QRS complex), which leaves
the P-wave as a major component of the error signal. The
error signal is then used as the P-wave signal.

25   Source consistency filtering is closely related to
spatial filtering, with the difference being that source
consistency filtering recognizes that the correlation
between input signals is the result of an underlying
single ECG source generator. A source consistency filter
30 described by Mortara in U.S. Patent No. 5,421,342
compares the value of an ECG signal with a predicted
value for that signal, and generates the predicted value
using other ECG signals. The predicted value is based on
a least squares estimate derived from the covariance
35 matrix of the input signals. A filtered ECG signal is

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formed by linearly combining the observed ECG signal and
its predicted value.

Another approach is discussed by Devlin et al. in
"Detecting Electrode Motion Noise in ECG Signals by
5 Monitoring Electrode Impedance", Computers in Cardiology,
1984. In the system described by Devlin et al., an ECG
signal produced by an electrode is collected
simultaneously with a signal related to the impedance of
the electrode/skin interface of the electrode. The
10 impedance signal is then used to estimate noise in the
ECG signal due to electrode motion. Finally, the
estimated noise is employed in an algorithm for reducing
the occurrence of false positive alarms in an automated
arrhythmia detector. According to the algorithm, an
15 estimate of the noise in the ECG signal is made by
determining a transfer function relating the impedance
signal to the ECG signal using a minimum mean square
estimation algorithm and applying the transfer function
to the impedance signal to provide the estimate of the
20 noise. Finally, a peak noise-to-signal ratio is
determined by subtracting the noise estimate from the ECG
signal to produce a "noise free" ECG signal from which an
RMS value is computed, calculating RMS values of the
noise estimate for time windows of the noise estimate,
25 selecting the largest RMS value as the peak noise signal,
and dividing the peak noise signal by the RMS value of
the "noise free" ECG signal to produce the ratio. Devlin
et al. also note that subtracting the noise estimate from
the ECG channel as a means of improving the quality of
30 the ECG channel had been explored.

Summary of the Invention

The invention provides an improved technique for
reducing noise in physiologic signals such as ECG
signals. The noise-reduction technique derives from the

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realization that signals representative of a physiologic
process and signals representative of obscuring noise
appear differently to different types of sensors or to
sensors at different locations and can therefore be
5   accurately separated. In essence, the noise-reduction
technique employs seemingly redundant signals along with
signals that are related to obscuring noise to produce a
signal from which the noise content has been reduced.
        The noise-reduction technique differs from the
10 spatial filtering and source consistency filtering
techniques described above in that it considers the
relationship of the noise content of the input signals
and finds the combination of input signals that minimizes
the noise while preserving the desired features of the
15 signal. The noise-reduction technique does not seek to
blend an original signal with a prediction for that
signal. Thus, unlike the signal produced by the source
consistency filter, the signal produced by the noise-
reduction technique is not a weighted average of an
20 original signal and one or more predicted signals.
Instead, the noise-reduction technique uses each signal
as a vector projection of the underlying ECG generator
onto the body surface and combines the signals in a
manner that optimally reduces the noise while preserving
25 the net vector direction of the ECG generator.
        The noise-reduction technique is implemented using
a generalized procedure that begins by acquiring primary
and secondary input signals. Primary signals are defined
as signals that include part or all of a desired signal
30 from a physiologic process and obscuring noise from one
or more noise processes. Secondary signals are defined
as signals that contain noise which may be related to the
noise in the primary signals. In some instances, only
primary signals may be acquired.

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Once the primary and secondary signals are acquired, a desired output signal is defined as a combination of one or more primary signals. (The term "combination" is used to refer to any mathematical
5 operation that defines a signal in terms of one or more other signals.) The desired output signal includes a desired component and noise. A particular embodiment defines the desired output signal as a linear combination of the primary signals. The manner in which each primary
10 signal contributes to the desired output signal is defined with specificity.

Some or all of the input signals may be processed by transformations and/or combinations prior to their use in modifying the ECG signal. A signal may be created by
15 lagging, filtering, or generally transforming another signal. For example, the impedance signals may be filtered to retain only frequencies known to be related to the baseline noise in the ECG signal. The processing may be general, such as raising the signals to a power,
20 or may involve projection onto other vectors, or decomposition and reconstruction using wavelets. The processed signal may be used to replace part or all of the original signal, or may be included as an additional one of the input signals. One advantage of this
25 generalization is that is permits a linear model approach to incorporate more complicated or even non-linear models.

Next, a model of a low-noise output signal that approximates the desired component of the desired output
30 signal is defined as a combination of the primary and secondary input signals. At this point in the noise-reduction procedure, the parameters of the low-noise output signal (i.e., the degree to which each primary or secondary signal contributes to the low-noise output
35 signal) are left as variable amounts. The model,

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referred to as a noise reduction model, is based on the
realization that there are underlying models (whether
explicit or empirical) for the generation and
characteristics of the physiologic signal and the
5   obscuring noise. The structure of these models acts as a
guide in selecting which primary and secondary signals to
acquire, and in defining the noise reduction model for
creating the low-noise output signal from the input
signals.

10   A noise measure, or error metric, that quantifies
the noise content of the low-noise output signal for
different parameter values of the noise reduction model.
Additional fidelity constraints may also be defined. The
fidelity constraints assure that the desired signal is
15 preserved in the low-noise output signal. The fidelity
constraints can include either direct measures of desired
signal content in the low-noise output signal or direct
constraints on the parameters of the low-noise output
signal, or both.

20   Finally, parameters of the noise reduction model
that minimize the noise measure while satisfying the
fidelity requirements are selected using all or some of
the primary and secondary signals. The selected
parameters are then applied using the noise reduction
25 model to produce the low-noise output signal. The
selected parameters may be applied to an interval of the
low-noise output signal that is the same, shorter or
longer than, or offset in time from, the interval of
input signals used to select the parameters.

30   In a simple example of the noise-reduction
procedure, a low-noise output signal is produced using a
single primary signal and a single secondary signal. The
primary signal is an ECG signal produced by an electrode,
and the secondary signal provides a measure of the
35 impedance of the electrode. The desired output signal is

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the ECG signal at the surface of a patient's skin.
However, in addition to the desired ECG signal, the
primary signal includes baseline noise. For this reason,
noise reduction is performed to separate the baseline
5 noise from the ECG signal and to produce a low-noise
output signal that reflects only the ECG signal.

    Variations in the impedance of an electrode
reflect the baseline noise introduced into the signal
that the electrode produces. As noted above, baseline
10 noise is attributable to motion and deformation of the
electrode and its associated gel, and results from low
frequency events such as patient respiration and patient
motion. In particular, it has been found that baseline
noise results from changes in the structure of the gel-
15 skin interface due from acceleration and compression
forces on the gel and on the gel-skin interface. For
example, respiration is associated with periodic
expansion and contraction of the chest cavity. This
periodic motion of the chest cavity results in periodic
20 expansion and contraction of the gel-skin interface due
to motion of the skin underlying the interface. The gel-
skin interface and the gel-to-connector interface create
a battery-like potential in which the gradient of the
ions across the two sides of the interface is balanced by
25 the potential difference across the interface due to the
imbalance of these charged ions. The ion balance, and
hence the potential across the interface, is sensitive to
changes in the geometry of the interface. As a result,
when the gel is moved or compressed relative to the
30 interface, the ion balance changes and currents flow
across the interface. These currents change the
electrical potential across the interface. The primary
signal includes an ECG-related potential summed with the
potential across the electrode interface. Thus,

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variations in the interface potential affect the primary
signal and constitute baseline noise.

Deformation of the electrode due to the
acceleration and compression of the electrode gel results
5 in variations in the impedance of the electrode and the
gel-skin interface. Because they come from the same
source, the impedance variation is directly related to
the baseline noise, and may be used as an indicator of
the noise. Accordingly, the effects of baseline noise
10 may be eliminated or reduced by modifying the ECG signal
(the primary signal) in view of the monitored impedance
(the secondary signal).

In the simple example of the noise-reduction
technique, the impedance of an electrode (the secondary
15 signal) is measured simultaneously with the primary
signal produced by the electrode. The impedance
measurement is produced by applying one or more high
frequency signals to the electrode and measuring the
output of the electrode. The applied frequencies are
20 selected to be well above the expected frequency of the
ECG signal so that the high frequency signals do not
interfere with the ECG signal. For example, signals
having frequencies of 28 kHz and 56 kHz may be employed.
At these frequencies, the impedance of the electrodes is
25 primarily attributable to the capacitance of the
electrode. Lower or higher frequencies could also be
employed.

Using the noise-reduction technique, the low-noise
output signal is modelled as a combination of the primary
30 signal and the secondary signal. In addition, an error
metric is also defined. The error metric represents a
specific time range of the primary signal. The time
range of the error signal that is used in computing the
metric may depend on, and may vary from, the time range
35 to which the error metric applies.

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When the model for the low-noise output signal is
defined, it includes one or more variable parameters.
Once the error metric is defined, the values of the model
parameters are assigned based on the error metric. For
5 example, the parameters may be assigned values that cause
the error metric to have a low value, and may be varied
as the error metric varies. Depending on the
application, the values of the parameters may be computed
in real time, near real time, or retrospectively.
10 Thereafter, the low-noise output signal is generated
using the values assigned to the parameters.

It also has been determined that the relationship
between baseline noise for an electrode and the impedance
measured for that electrode may be imperfect. For
15 example, motion that influences the baseline noise of an
electrode may not influence the impedance of the
electrode to the same extent. However, the motion may
influence the impedances of other electrodes in a way
that provides a more complete representation of the
20 noise. This provides motivation to use other impedances
from other electrodes that may capture additional
information related to baseline noise. In addition,
trans-thoracic impedance may be measured as a proxy for
baseline noise resulting from respiration. Trans-
25 thoracic impedance provides a measurement which relates
to the motion of the chest because it is strongly
modulated by respiration. Chest motion causes motion of
the electrodes and hence is related to baseline noise.

In a more complicated example of the noise-
30 reduction technique, multiple primary signals and
multiple secondary signals are used to produce a single
low-noise output signal. In particular, a single low-
noise ECG signal is produced using redundant ECG signals
and multiple impedance signals. In the example, the
35 desired output signal is an ECG signal defined as the

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difference between signals produced by two electrodes.
To produce the redundant ECG signals, the electrodes are
implemented using multi-segment electrodes that produce
multiple signals, and the desired output signal is
5 defined as the difference between the signals at the
center segments of the two electrodes. The segments of
the multi-segment electrodes may be biased to different
degrees, or otherwise modified, so that the signals
produced by the segments are affected differently by the
10 baseline noise. Three impedance signals are employed.
The first two impedance signals correspond to the
impedances of segments of the two electrodes such as the
center segments. The third impedance signal corresponds
to trans-thoracic impedance.
15   A noise suppression model is defined to express
the low-noise output signal as a combination of the
redundant ECG signals and the impedance signals. An
error metric and fidelity constraints are then defined.
In this example, a useful fidelity constraint is that the
20 low-noise output signal, when considered over multiple
beats, is comparable to the desired output signal (i.e.,
the average difference between the center segments).
Finally, parameters for the noise suppression model are
selected so as to minimize the error metric and to comply
25 with the fidelity requirements.
        In a variation of the basic technique, low-noise
output signals for use in measuring alternans are
produced using a two-stage noise-reduction technique.
Input signals are produced using a set of multi-segment
30 electrodes and a set of standard electrodes. In a first
noise-reduction stage, the input signals are processed
according to the noise-reduction technique to produce a
set of low-noise electrode signals representing low noise
versions of the signals from each electrode. In
35 particular, the noise-reduction technique is employed to

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produce low-noise output signals for each multi-segment electrode using the redundant ECG signals from the segments of the electrode along with impedance signals for each of the multi-segment electrodes and a trans-
5 thoracic impedance signal representative of respiration. Similarly, the noise-reduction technique is employed to produce a low-noise output signal for each of the standard electrodes using the ECG signal for the standard electrode and the multi-segment electrode and trans-
10 thoracic impedance signals.

The low-noise electrode signals produced in the first noise-reduction stage are used as input signals for a second noise-reduction stage. In the second stage, the noise-reduction technique is applied to produce a set of
15 low-noise signals from the low-noise electrode signals. This set of low-noise signals, is then used to measure alternans.

In one aspect, generally, the invention features reducing noise in a signal that represents a physiologic
20 process by obtaining multiple input signals, measuring a relationship between noise content of the input signals, and combining the input signals in consideration of the measured relationship to produce an output signal having low noise content.

25 Preferred embodiments of the invention may include one or more of the following features. The multiple input signals may include, for example, two or more primary physiologic input signals, one or more primary physiologic input signals and two or more secondary input
30 signals that represent noise. Similarly, the multiple input signals may include one or more ECG input signals and one or more secondary input signals that represent noise, and the method may include dividing the ECG input signals and secondary input signals into set of segments,
35 where each set of segments represents a beat of the ECG

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signal. Thereafter, a relationship between noise content
of corresponding points from successive sets of segments
may be measured for use in combining the signals.

The method may further include defining a desired
5   output signal as a combination of one or more of the
input signals, modelling a low-noise output signal that
approximates the desired output signal as a combination
of two or more of the input signals, with the model of
the low-noise output signal including variable parameters
10 that represent the relative contribution made to the low-
noise output signal by each of the two or more input
signals. Thereafter, based on the relationship between
noise content of the input signals, an error metric that
represents noise content in the low-noise output signal
15 is produced. Finally, values of the variable parameters
that cause the error metric to satisfy a predetermined
condition are determined and the input signals are
combined to produce the low-noise output signal using the
determined values of the variable parameters.

20   Input signals may be obtained using electrodes
applied to a patient's skin, and additional input signals
may represent impedances associated with the electrodes.
Similarly, multiple input signals may be obtained using
segments of a multi-segment electrode. One or more of
25 the input signals may be representative of respiration by
a patient.

Values of the variable parameters may be
determined so that the values reduce or minimize the
value of the error metric. Values may be determined so
30 that the values reduce the value of the error metric
while satisfying an additional condition (i.e., a
fidelity constraint). The additional condition may be a
unit weights fidelity constraint that requires that a sum
of the identified variable parameters associated with the
35 one or more input signals that define the desired output

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signal equal a sum of parameters used in defining the
desired output signal.

The additional condition may also be a dipole
geometry constraint. When the desired output signal
5 represents a physiologic signal sensed at a first
location that is remote from a signal source and the
first location is identified relative to the signal
source by a first vector, and at least two of the input
signals represent the physiologic signal and represent
10 the physiologic signal as sensed at other locations
remote from the signal source and identified relative to
the signal source by corresponding vectors, the
additional condition requires that a sum of the vectors
corresponding to the input signals that represent the
15 physiologic signals, with each vector being weighted by
the identified variable parameter associated with the
corresponding input signal, equals the first vector.

The additional condition may also require that the
low-noise output signal represented by the identified
20 variable parameters has a predetermined relationship with
the desired output signal. The condition may be imposed
by determining an average property of the desired output
signal, determining a corresponding average property of
the low-noise output signal represented by the identified
25 variable parameters, and requiring that the average
property of the low-noise output signal represented by
the determined variable parameters differs from the
average property of the desired output signal by less
than a predetermined amount.

30 The desired output signal may be defined as a
linear combination of two or more of the input signals,
and the desired output signal and the low-noise output
signal may represent an ECG signal.

The low-noise output signal may be used to produce
35 a measurement of alternans.

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The method may be repeated to produce a set of low-noise output signals. These low-noise output signals may be used as input signals for a procedure that produces a further low-noise output signal that may then

5 be used to produce a measurement of alternans.

In another aspect, the invention features measuring two or more primary input signals that include part or all of a desired signal, defining a desired output signal as a combination of one or more of the

10 primary input signals, measuring one or more secondary input signals that include information about noise content in the desired signal, and combining two or more of the primary signals and one or more of the secondary signals to produce an output signal that approximates the

15 desired output signal and has reduced noise relative to the desired output signal.

In another aspect, the invention features measuring one or more primary input signals that include part or all of a desired signal, defining a desired

20 output signal as a combination of one or more of the primary input signals, measuring two or more secondary input signals that include information about noise content in the desired signal, and combining one or more of the primary signals and two or more of the secondary

25 signals to produce an output signal that approximates the desired output signal and has reduced noise relative to the desired output signal.

In another aspect, the invention features a method of reducing noise in an ECG signal by measuring one or

30 more primary input signals that represent the ECG signal, measuring one or more secondary input signals that represent noise in the ECG signal, and dividing the primary and secondary input signals into sets of segments that each represent a beat of the ECG signal. For each

35 set of segments, a relationship between the noise content

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of the primary and secondary input signals is defined and the input signals are combined in a way that produces an output signal having low noise content.

In another aspect, the invention features a method of obtaining a reduced noise physiologic signal by measuring one or more input physiologic signals, producing a model that generates an output signal as a combination of the primary input signals, producing a noise metric that represents noise in the output signal produced by the model, adjusting parameters of the model so as to cause the noise metric to satisfy a predetermined condition, and producing the output signal using the model and the adjusted parameters. The method may further include measuring one or more secondary input signals containing information related to noise in the primary input signals and producing the model to generate the output signal as a combination of the primary input signals and the secondary input signals. In addition, one or more fidelity constraints may be defined, and the parameters of the model may be adjusted so that the parameters of the model and the output signal satisfy the fidelity constraints. Also, a relationship between noise content in each of the primary and secondary input signals may be measured and the parameters of the model may be adjusted in view of the measured relationship to reduce or cancel noise from the output signal.

Other features and advantages of the invention will become apparent from the following description of the preferred embodiment, and from the claims.

Brief Description of the Drawing

Fig. 1 is an ECG potential over a single beat.
Fig. 2 is a block diagram of an ECG system.
Fig. 3 is a placement diagram for electrodes on a patient.

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Fig. 4 is a table illustrating the location and type of the electrodes of Fig. 3 and defining the input signals that are recorded from those electrodes.

Fig. 5 is a flowchart of a procedure for producing a low-noise output signal based on information included in multiple input signals.

Fig. 6A is a table of matrix notations.

Fig. 6B is a table of matrix filter notations.

Fig. 7 is a collection of matrices.

Fig. 8 is a flowchart of a procedure for producing an error metric.

Figs. 9A-9C are graphs of filter outputs relative to input frequency.

Fig. 10 includes plots of signal waveforms over time.

Fig. 11A is a schematic diagram of a heart represented as a dipole source.

Fig. 11B is a schematic diagram of clinical ECG measurements represented as vector projections of a dipole source.

Fig. 12 is an electrode placement diagram for a system having three electrodes.

Fig. 13 is a circuit diagram showing the equivalent circuit for the system of Fig. 12.

Fig. 14 is a circuit diagram of a circuit for measuring a voltage and an impedance of the system of Fig. 12.

Fig. 15 is a diagram of signals produced by the circuit of Fig. 14.

Fig. 16 is a circuit diagram of a circuit for measuring impedances.

Fig. 17 is a circuit diagram showing an equivalent circuit for the system of Fig. 16.

Figs. 18A and 18B are diagrammatic views of components of a multi-segment electrode.

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Fig. 19 is a schematic diagram of a circuit for measuring noise created by movement of a multi-segment electrode.

Fig. 20 is a circuit diagram of a circuit used in generating a low-noise signal.

Fig. 21 is a flowchart of a procedure for producing an alternans measurement.

Fig. 22 is a diagrammatic view illustrating steps for preprocessing input signals.

Fig. 23 is a table defining signal elements of a b(n) matrix.

Fig. 24 is a matrix containing 32 input signals for a particular beat.

Fig. 25 is a table defining coefficients for combining the input signals to create the low-noise output signals.

Figs. 26A-26C are plots of physiologic signals over time.

Description of the Preferred Embodiments

Referring to Fig. 2, an electrocardiogram (ECG) system 100 includes a processor 105 and a set of electrodes 110. The electrodes 100 are attached to a patient's skin and positioned to detect electrical signals produced by the patient's heart. The electrodes include an electrically conductive gel that contacts the patient's skin and conducts to the electrode any electrical signals that are present at the skin. Leads 115 connected between the electrodes 110 and the processor 105 provide the detected signals to the processor 105 for processing and display.

The patient's heart produces an electrical signal that is referred to as an ECG waveform and is illustrated in Fig. 1. Processor 105 analyzes the ECG waveform to detect alternans, a subtle beat-to-beat change in the

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repeating pattern of the ECG waveform that can be
indicative of electrical instability of the heart and
increased susceptibility to sudden cardiac death.
Alternans results in an ABABAB... pattern of variation
5 between the shapes of successive beats in the ECG
waveform. The level of variation is taken as a
characterization of an individual's cardiac electrical
stability.

An ECG waveform for a single beat is typically
10 referred to as a PQRST complex. The P wave appears at
initiation of the beat and corresponds to activity in the
atria, while the QRST complex follows the P wave and
corresponds to ventricular activity. The QRS component
represents the electrical activation of the ventricles,
15 while the T wave represents the electrical recovery
thereof. The ST segment is a relatively quiescent
period. In humans, it has been found that the T wave is
the best interval of the ECG complex for detecting
alternans. That is, a level of variations in the T waves
20 of alternating beats is a good indicator of a patient's
cardiac electrical stability.

The ECG signal produced by the patient's heart
decreases as a function of the distance from the heart at
which it is measured. Accordingly, an ECG signal
25 detected by an electrode 110 will vary from the actual
ECG signal based on the placement of the electrode
relative to the heart. An accurate approximation of the
actual ECG signal may be generated by combining signals
from multiple electrodes having known placement relative
30 to the heart.

The ECG signal measured at the body surface may be
represented by modelling the heart as a three-dimensional
dipole source that produces an electrical signal which
varies based on the distance from the heart in the X, Y
35 and Z directions. Thus, the voltage detected by an

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electrode M that is located relative to the dipole at a
coordinate given by the vector (x_M, y_M, z_M) will be:

$$M(t) = x_M v_X(t) + y_M v_Y(t) + z_M v_Z(t).$$

Use of the dipole vector model of the heart has lead to
5   the development of clinical systems that measure the X, Y
and Z components of the dipole source through a linear
combination of several electrodes. The most common known
XYZ systems are the Frank lead system and the Bipolar
system. In clinical practice, another common system of
10 electrodes is the twelve lead system. The twelve lead
system places greater emphasis on the electrodes on the
left chest near the heart.

        ECG system 100 includes fourteen electrodes 110
that are placed on the patient as illustrated in Fig. 3.
15 This arrangement combines the electrodes of the Frank and
standard 12 lead systems. The signals produced by the
electrodes, along with their types, are illustrated in
Fig. 4. Seven of the electrodes are conventional ECG
electrodes having a single terminal (and producing a
20 single signal), while the other seven electrodes are
multi-segment electrodes having four terminals (and
producing up to four signals).

        The processor 105 acquires the signals produced by
each of the electrodes by periodically sampling the
25 signals. When recording an ECG signal, the processor 105
uses an isoelectric point of the signal as a zero voltage
reference. The processor 105 measures the isoelectric
point during the PQ interval between the P wave and QRS
complex. The PQ interval is a good approximation to a
30 zero ECG level because there is no major electrical
activity in the heart at that time.

        After acquiring the signals, the processor 105
processes the signals to produce an ECG waveform for

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further analysis or display. While an ECG waveform
typically has a QRS amplitude measured in millivolts, an
alternans pattern of variation with an amplitude on the
order of a microvolt may be clinically significant.

5 Accordingly, the processor 105 must produce the ECG
waveform with extreme accuracy to permit effective
detection of alternans. Achievement of this accuracy is
complicated by the presence of noise in the electrode
signals, as the noise may result in beat-to-beat

10 variations in the ECG waveform that have a larger
magnitude than the alternans pattern of variation.

The noise in an ECG signal can be classified into
three categories: baseline noise generated in the
electrode, physiologic noise, and external electrical

15 noise. The baseline noise is low frequency noise that
appears as an undulating baseline upon which the ECG
rides. Baseline noise is attributable to motion and
deformation of an electrode and its associated gel, and
results from low frequency events such as patient

20 respiration and patient motion. As a result, the
magnitude of baseline noise tends to increase with
exercise. However, it is during exercise that many
important ECG measurements need to be made. Typically,
the frequency content of baseline noise is below 10 Hz.

25 Physiologic noise results from other physiologic
processes within the patient that interfere with the ECG
signal, with skeletal muscle activity being the most
common source of physiologic noise. The electrical
activity of the skeletal muscles creates potentials that

30 are additive with respect to the potentials created by
the heart. The frequency content of the skeletal muscle
signals is comparable to the frequency content of the QRS
complex, and is typically greater than 10 Hz. When
measuring T wave alternans, additional physiologic noise

35 may result from changes in the position of the heart due

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to respiration or from changes in the projection of the electrical potential from the heart to the skin surface due to thoracic conductivity changes arising from the inflation and deflation of the lungs with respiration.

5   External electrical noise results, for example, from ambient electromagnetic activity in the room, electrode cable motion, and variations in amplifiers or other components of the ECG circuitry. External electrical noise may be eliminated or reduced through the
10 use of high quality components and through the reduction of ambient electromagnetic activity by, for example, deactivating high power equipment.

Noise in the ECG waveform can easily mask the presence of alternans. The noise can also mimic the
15 presence of alternans where there is none. For example, if a patient is breathing at one-half or one-third of the heart rate, the respiration may introduce a harmonic signal having the ABABAB... pattern of alternans. Similarly, motion that repeats with some periodicity,
20 such as that resulting from exercise, can create electrode noise with a similar pattern. Furthermore, noise resulting from different sources, such as respiration and electrode noise, can interact and produce new periodicities, one of which may mimic alternans.

25   Noise can also adversely affect the measurement of other ECG parameters, such as the level of the ST segment. Baseline noise can interfere with measurement of the ST level of an ECG signal by misrepresenting the level of the ST segment. Clinically, a change in the ST
30 level of greater than 0.1 millivolts is considered significant. The ST level is typically measured at 80 milliseconds beyond the end of the QRS complex and is measured relative to the isoelectric level determined from the PQ interval. Assuming that the PQ interval is
35 approximately 200 milliseconds away from the ST segment

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point, a low frequency waveform that is changing at a
rate of 0.5 mV per second can misrepresent the ST level
by 0.1 mV (0.5 mV/second * 0.2 second). Muscle noise can
also affect the ST level measurement. Muscle noise

5   appears in bursts coordinated with muscle activity.
Muscle noise can easily be on the order of 0.1 mV RMS,
hence it can introduce a substantial error into the
measurement of the ST level of any single ECG complex.

Similarly, baseline noise can interfere with the T

10 wave alternans measurement because the frequency content
of baseline noise often overlaps with the frequency
content of T wave alternans. T wave alternans occurs at
a frequency of every other beat. Thus, a heart rate of
60 beats per minute corresponds to an alternans

15 repetition rate of 0.5 Hz. Since alternans is typically
measured at heart rates between 60-120 beats per minute,
the alternans rate is typically between 0.5 and 1 Hz.
Baseline noise can have frequency components that occur
at a frequency of every other beat, especially when the

20 noise is driven by a periodic phenomenon such as
respiration. When baseline noise occurs at a frequency
of every other beat, it can mimic alternans. Typically,
however, baseline noise is a broadband signal having a
power spectrum that contains random levels of noise at

25 different frequencies.

Processor 105 measures the level of alternans
(P_{alt}) is measured as the energy level of an ECG signal at
0.5 cycles/beat (referred to as $P_{0.5}$) minus the average
energy level in a noise reference band between 0.43 and

30 0.48 cycles/beat (referred to as P_{noise}):

$$P_{alt} = P_{0.5} - P_{noise}.$$

Alternans is considered significant when P_{alt} is more than
three times the standard deviation of P_{noise}. Processor

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105 reports the alternans results as V_{alt}, which is the square root of P_{alt}, and the alternans ratio, which is P_{alt} divided by the standard deviation of P_{noise}. When there is a random component at the alternans frequency,
5 the component can create a false alternans measurement.

        To effectively detect alternans, processor 105 is configured to reduce the noise in the ECG waveform that it produces. Processor 105 achieves substantial reductions in the noise content of the beats of the ECG
10 waveform by combining one or more ECG signals and one or more other signals in a way that causes the noise content of the signals to combine destructively while preserving the ECG content.

        Referring to Fig. 5, the processor 105 achieves
15 noise reduction by implementing a generalized procedure 200. As a first step in the procedure, the processor acquires primary and secondary signals from the electrodes 110 as discussed above (step 205). Primary signals are signals that are directly related to a
20 desired output signal while secondary signals are signals that provide information about the noise content of one or more primary signals. For example, an ECG signal produced by an electrode 110 may be a primary signal while a voltage related to the impedance of an electrode
25 110 is a secondary signal. It is important to note that the terms "primary" and "secondary" have no functional or mathematical significance, and instead are used solely for ease of description. For example, the impedance signal mentioned above would be a primary signal if the
30 impedance of the electrode was a desired output.

        Since ECG waveforms generally consist of linear combinations of signals, much of the generalized procedure lends itself to description using matrix notation, and such notation is used throughout the
35 application. Other embodiments may employ other

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notations or may employ non-linear signal combinations.
For example, the signals could be considered over time
instead of over the beats. Summaries of the key matrices
and matrix filters employed in the procedure are provided
5 in Figs. 6A and 6B. Matrix notation for a simplified
example is provided in Fig. 7. Matrix notation permits
input signals to be linearly combined by matrix
multiplication. More general formulations that include
non-linear combinations could also be made.

10   The processor 105 groups the samples of the
primary and secondary input signals according to the ECG
beat to which they correspond (step 210). For this
purpose, a beat matrix $B(n)$ is defined as containing
samples of the input signals that are produced during the
15 nth beat. Each row of $B(n)$ corresponds to one signal,
and each column corresponds to one point in time in the
signal. For example, if there are 32 input signals and
measurements are made at 20 locations on each beat, the
nth beat is represented by a beat matrix $B(n)$ that has 32
20 rows and 20 columns. Typically, every entry in a column
of $B(n)$ is produced in one time interval so that each
column includes the values of all of the input signals
for a particular moment in time. As illustrated in Fig.
7, a beat matrix 300 for a system having two primary
25 signals (P1, P2) and one secondary signal (S1) would have
three rows and m columns, where m is the number of
samples in a beat. The $B(n)$ matrices may be processed
prior to their use in the noise-reduction technique. The
processing may be general, such as raising the
30 coefficient of the matrices to a power, or may involve
more complex processes. The processed matrices may be
used to replace part or all of the original matrices, or
may be included as additional information.

          Next, processor 105 expresses the desired output
35 signal S(n) in terms of the primary signals (step 215).

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For this purpose, the processor 105 expresses the desired output signal as a linear combination of one or more of the primary signals. The desired output signal can have one or more dimensions.

5   In the generalized procedure, the matrix F represents the coefficients of the linear combination that defines the desired output signal prior to noise-reduction. The desired output signal $S(n)$ is written as:

$$S(n) = F*B(n),$$

10   where "$*$" denotes a matrix multiplication. Each row of F corresponds to an output dimension of $S(n)$. Each column of F corresponds to the signal in a row of $B(n)$. Typically, processor 105 generates the coefficients of F based on information about the placement of the

15   electrodes, and the coefficients of F are usually the same for all beats.

In the simplest case, where the desired output signal is one of the input signals, all entries in the matrix F are zero except for entries in the column

20   corresponding to that one input signal. An output corresponding to a single lead (where a lead is a combination of the signals from two electrodes 110) such as, for example, an X lead that represents the component of the ECG beat in the X direction, is an example of a

25   one dimensional output. In this example, F includes only one row and $S(n)$ is expressed as:

$$S_X(n) = F_X*B(n).$$

An example of a multi-dimensional output is an output corresponding to a trio of leads such as the X, Y and Z

30   leads (which represent the components of the ECG beat in

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the X, Y and Z direction). In this example, F includes
three rows and S(n) is expressed as:

$$S_{XYZ}(n) = F_{XYZ}*B(n).$$

In this case, the row of F_{XYZ} that corresponds to the X
5 lead is the same as F_X. Here F_{XYZ} defines the
coefficients that constitute the Frank XYZ orthogonal
lead system.

     In the example illustrated in Fig. 7, the desired
output 305 is generated by averaging the two primary
10 signals. Thus, the F matrix 310 includes one row and
three columns, with the coefficients of the first two
columns (corresponding to P1 and P2) being 0.5 and the
coefficient of the third column (corresponding to S1)
being 0.

15   Next, the processor 105 models a low-noise output
signal O(n) as a linear combination of one or more
primary or secondary signals (step 220). The matrix T
represents the coefficients of the linear combination,
and the low-noise output signal O(n) is written as:

20                       $$O(n) = T*B(n)$$

In the example illustrated in Fig. 7, the low-noise
output 315 is generated by combining the two primary
signals and the secondary signal. Thus, the T matrix 320
includes one row and three columns.

25   Once the model of the low-noise output signal O(n)
is defined, the processor 105 considers the error metric
E(n) for different values of T (step 225). The error
metric is usually a measure of the noise content of the
low-noise output signal O(n). Although the error metric
30 can be a general combination of the input signals, it is
common to use simple linear or quadratic error measures.

An example of an error measure composed of linear and quadratic processing is demonstrated below. The processor generates the error metric by first filtering the low-noise output signal $O(n)$ using a filter $h_1(n)$

5 that passes frequency bands corresponding to noise and attenuates other frequencies to create an error signal $C(n)$. Thereafter, the processor squares the error signal $C(n)$ to create a noise correlation matrix $R_C(n)$ that the processor then averages with a filter $h_2(n)$ to produce an

10 average noise correlation matrix $R_E(n)$. The noise correlation matrix expresses a relation between the noise in each of the input signals relative to the noise in the other input signals. To the extent that the noise is caused by underlying mechanical or physiologic processes

15 such as movement, respiration or muscle noise, the noise will be related in the various input signals. $R_E(n)$ as described here embodies this relationship in the form of a correlation matrix optionally weighted by the filter $h_2(n)$, which produces a weighted average of the noise

20 correlation matrix for a range of beats. Finally, the processor 105 generates the error metric $E(n)$, which represents the residual noise power remaining after the input signals are combined using the relationship expressed in the average noise correlation matrix $R_E(n)$.

25   While this procedure is well served with simple linear filters $h_1(n)$ and $h_2(n)$, other approaches may require other, possibly more complicated transformations of the low-noise output signal $O(n)$ to create an error metric $E(n)$.

30   Referring to Fig. 8, the processor 105 creates an error signal $C(n)$ by filtering the low-noise output signal $O(n)$:

$$C(n) = h_1(n) \otimes O(n),$$

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where ⊛ is the convolution operator (step 350). It
should be noted that the filtering here is not over time.
Rather, the filtering is over beats and, as a result,
operates in a frequency domain that is in cycles per
5   beat. Thus, $C(n)$ for a particular beat n may be based on
information for one or more preceding beats (e.g., $n-1$ or
$n-2$) or one or more following beats (e.g., $n+1$ or $n+2$).
The filter operates on the same element of a matrix for
successive beats (i.e., successive values of n). The
10   role of $h_1(n)$ is to retain within the error signal $C(n)$
the frequencies of $O(n)$ that are to be suppressed as
noise. For example, if all frequencies are to be
suppressed equally, then $h_1(n)$ may implemented as an all-
pass filter that retains all frequencies within the error
15   signal $C(n)$:

$$h_1(n) = \delta(k-n),$$

where $\delta(n)$ is a delta function that equals 1 when k
equals n and equals 0 when k has any value other than n.
The frequency response of this filter is illustrated in
20   Fig. 9A. To suppress frequencies near the alternans
frequency (0.5 cycles/beat) to a greater degree than
other frequencies, the filter may be implemented as:

$$h_1(n) = [\delta(k-n) - \delta(k-n-1)]/2,$$

which has the frequency response $\sin(2\pi f)$, where f is in
25   cycles/beat. The frequency response of this filter is
illustrated in Fig. 9B. To suppress frequencies in the
band from 0.25 to 0.5 cycles/beat, the filter may be
implemented as:

$$h_1(n) = 1/8 \ e^{i\pi k/4}, \ for \ k = n - 4 \ to \ n + 3;$$

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$$h_1(n) = 0, \text{ otherwise.}$$

The frequency response of this filter is shown in Fig. 9C. This filter is useful in reducing noise in the band that contains the noise reference for the alternans
5 computation.

The processor 105 then determines the square of the error signal, $R_C(n)$ as:

$$R_C(n) = C(n) * C(n)'.$$

where $C(n)'$ is the transpose of $C(n)$ (step 355).
10 Defining $D(n)$ to be the filtered version of the beat matrix $B(n)$:

$$D(n) = h_1(n) \circledast B(n),$$

and recognizing that

$$C(n) = T * D(n),$$

15 the square of the error signal may be expressed as:

$$R_C(n) = T * R_D(n) * T'$$

where

$$R_D(n) = D(n) * D(n)'.$$

The matrix $R_D(n)$ contains the correlation of the noise
20 between all of the input signals, including the primary signals and the secondary signals.

Next (step 360), the processor 105 generates an averaged noise correlation matrix $R_E(n)$ by filtering $R_D(n)$ with $h_2(n)$:

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$$R_E(n) = h_2(n) \circledast R_D(n).$$

Typically, $h_2(n)$ is a filter that takes the average value
of $R_D(n)$ in a neighborhood around n. The size of the
neighborhood is determined by the length of the impulse
response of $h_2(n)$. Of course, $h_2(n)$ can also be an all
5 pass filter.

Finally (step 365), the processor generates the
error metric for the nth beat, $E(n)$, as:

$$E(n) = tr[T * R_E(n) * T'],$$

10 where $tr[]$ is the trace operator and provides the sum of
the diagonal elements of the given matrix. Since the
diagonal contains the correlation of the signal with
itself, it contains the power of the signal. Thus, $E(n)$
is a measure of the error signal power in the
15 neighborhood of the nth beat. Recognizing that the
correlation matrix $R_E(n)$ expresses the relationship of
the noise between all of the input signals, it becomes
apparent that the error metric $E(n)$ is minimized when the
signals are combined in a way that causes the noise to
20 cancel.

Referring again to Fig. 5, once the error metric
$E(n)$ is defined, the processor 105 assigns values to the
coefficients of the matrix T used in producing the low-
noise output signal $O(n)$ (step 230). In assigning the
25 values, the processor 105 attempts to minimize the error
metric while ensuring that the coefficients conform to
certain fidelity constraints. The fidelity constraints
ensure that the coefficients in the matrix T produce a
reasonable low-noise output signal $O(n)$.

30 Fidelity constraints are of two basic kinds. The
first kind, referred to as fidelity to the model
constraints, directly constrain the coefficients of T so

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that the coefficients take on values that embody a priori
knowledge about the reasonableness of the model. The
second kind, referred to as fidelity to the output signal
constraints, constrain the ways that $O(n)$ can differ from
5 $S(n)$. The processor 105 may use either one or both kinds
of fidelity constraints in a particular application.

Fidelity to the model constraints for the linear
matrix formulation may be expressed as:

$$T * P = Q$$

10 This relationship can be understood by considering an
example in which two identical primary ECG signals
contain differing levels of noise and there are no
secondary signals. In this example, the low-noise signal
is a weighted average of the two signals, and the T
15 matrix includes one row and two columns. To include only
one unit of ECG in the low-noise output, the sum of the
two coefficients in T must equal one. Accordingly, the
parameters P and Q are:

$$P = [1 \ 1]' \text{ and } Q = [1].$$

20 This fidelity constraint is called the "unit weights
constraint." The units weight constraint is appropriate
for primary signals that are considered to be equivalent.

The unit weights constraint is illustrated by the
following example. Referring to Fig 10., a desired
25 signal 400 and noise 405 are included in different
amounts in signals 410 and 415. By taking the proper
combination of signals 410 and 415 (i.e., , one half of
each) a resulting signal 420 is created for which the
noise is reduced without distortion of the signal. In
30 this example, the matrix T would be:

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$$T = [0.5 \ 0.5].$$

With P and Q having the values discussed above, T would satisfy the unit weights constraint:

$$T * P = [0.5 \ 0.5] * [1 \ 1]' = [1] = Q.$$

5   The unit weights constraint is applicable to simple systems such as the system illustrated in Fig 10. In that system, the desired signal appeared with equal amplitude and polarity in both signal 410 and signal 415, while the noise had equal amplitude but opposite polarity 10 in the two signals. This permitted a simple average to yield a perfect reconstruction of the signal.

Referring to Figs. 11A and 11B, another fidelity to the model constraint is one based on a dipole generator model of the ECG. In Fig. 11A, the heart 425 15 is depicted at its anatomic position in the chest. As discussed above, the heart is modelled as a three-dimensional dipole source $(v_X(t), \ v_Y(t), \ v_Z(t))$ so that the voltage created by the dipole source at an electrode M located at a coordinate given by the vector (x_M, y_M, z_M) 20 relative to the dipole is:

$$M(t) = x_M v_X(t) + y_M v_Y(t) + z_M v_Z(t).$$

The voltage sensed by any electrode placed on the body surface can be viewed as a linear combination of $v_X(t)$, $v_Y(t)$, and $v_Z(t)$. Furthermore, the combination of 25 the voltages from any two or more electrodes can be viewed in terms of the combination of the vector coordinates of those electrodes. For example, by vector arithmetic it is possible to see that some linear combination of the vectors corresponding to the V3 and V5 30 electrodes should produce a vector that is similar to the

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vector corresponding to the V4 electrode. By contrast, much of the noise influencing each of the electrodes, such as muscle noise, may have a more local source, and may not be as strongly related between electrodes.

5 Hence, if the signal produced by electrode V4 includes an obscuring noise, a suitable combination of the signals produced by electrodes V3, V4 and V5 might be used to reduce the obscuring noise while preserving the underlying signal present at electrode V4. The

10 generalization of this principle is that each electrode contains some amount of $v_X(t)$, $v_Y(t)$ and $v_Z(t)$, and when taken in the proper combination, a group of electrodes can closely approximate or augment the dipole signal at another electrode while helping to cancel out the noise

15 at that electrode.

When the signals produced by multiple electrodes are combined to produce a signal representative of a single electrode, a fidelity to the model constraint may be applied to the combination. This constraint is based

20 on vector addition and requires that, when the vector corresponding to each electrode is weighted based on the coefficients corresponding to that vector, the sum of the weighted vectors equals the vector corresponding to the position of the single electrode for which the signal is

25 being produced. This constraint is called the "dipole geometry constraint." The unit weights constraint is a special case of the dipole geometry constraint in which all of the input signals are assumed to have equivalent vectors.

30 The dipole geometry constraint is based on a matrix P_{XYZ} that is defined to be the dipole projection matrix that gives the X, Y and Z coordinates for each input signal relative to the dipole. P_{XYZ} has three columns corresponding to X, Y and Z. Each row of P_{XYZ}

35 corresponds to an input signal. P_{XYZ} can be generated a

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priori from known positions of the electrodes, or can be
computed from specific measurements of the locations of
the electrodes on the patient. Although P_{XYZ} can be
computed for each beat, it is typically computed only
5 when the underlying conditions of patient heart rate or
position change substantially.

One method for generating a useful dipole
projection matrix P_{XYZ} is to compute it from a correlation
matrix $R_A(n)$ that is the average of one or more
10 correlation matrices $R_B(n)$ given by:

$$R_B(n) = B(n) * B(n)'.$$

Since $B(n)$ is often noisy, it is usually preferable to
filter $B(n)$ by a filter $h_3(n)$ to create an average beat
matrix $A(n)$:

15 $$A(n) = h_3(n) \otimes B(n)$$

from which a correlation matrix $R_A(n)$ is generated as:

$$R_A(n) = A(n) * A(n)'.$$

The average beat matrix $A(n)$ is typically generated using
a simple low-pass filter that averages a group of 50-150
20 beats. The dipole projection matrix P_{XYZ} is then
generated as:

$$P_{XYZ}(n) = R_A(n) * F_{XYZ}' * (F_{XYZ} * R_A(n) * F_{XYZ}')^{-1}$$

where F_{XYZ} is the matrix of coefficients for the triplet
of points corresponding to the X,Y and Z leads as
25 described above and $()^{-1}$ indicates matrix inversion. The
values of P and Q for the dipole geometry constraint are:

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$$P = P_{XYZ} \text{ and } Q = F * P_{XYZ}$$

so that

$$T * P = T * P_{XYZ} = F * P_{XYZ} = Q.$$

The dipole geometry constraint may be applied in reducing
noise from any desired output signal, whether the desired
output signal comes from a single vector or is a signal
derived from a linear combination of signals recorded at
more than one vector coordinate.

It is sometimes desirable to use a priori
information about a known ECG dipole having
characteristics that it is desirable to preserve in the
low-noise output signal if they are present in the input
signals. To achieve this, the correlation matrix $R_A(n)$
is combined with the correlation matrix R_A of the known
dipole.

The second kind of fidelity constraints, fidelity
to the output signal constraints, limit how specific
features of the low-noise output $O(n)$ can differ from the
equivalent features of $S(n)$. These constraints usually
compare only the stable features of $S(n)$ that are least
influenced by noise. Typically, the fidelity to the
output signal constraints aim to preserve features of the
mean of $S(n)$, which can be expressed as:

$$mean[S(n)] = F*A(n),$$

where the mean beat matrix $A(n)$ is often the same as
produced using filter $h_3(n)$ as discussed above.
Similarly, the mean value of the low-noise output signal
$O(n)$ may be expressed as:

$$mean[O(n)] = T*A(n).$$

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The squared difference of the two mean values is a correlation matrix $R_{MD}(n)$ expressed as:

$$R_{MD}(n) = (F-T) * R_A(n) * (F-T)' .$$

The total squared error $E_{TS}(n)$ is the sum of the diagonal
5   elements of the correlation matrix, and is expressed as:

$$E_{TS}(n) = tr[R_{MD}(n)] = tr[(F-T) * R_A(n) * (F-T)'],$$

where $tr[]$ is the trace operator. This error may be
combined with the error metric $E(n)$ to create an
aggregate error metric $E_A(n)$:

10
$$E_A(n) = E(n) + \alpha E_{TS}(n)$$
$$= tr[T * R_E(n) * T' + \alpha (F-T) * R_A(n) * (F-T)'] .$$

The value of T that minimizes $E_A(n)$ is given by:

$$T = Q * T_0 + \alpha F * R_A(n) * R_0 * (I - P * T_0)$$

where I is the identity matrix,

15
$$R_0 = (R_E(n) + \alpha R_A(n))^{-1}$$

and

$$T_0 = (P' * R_0 * P)^{-1} (P' * R_0) .$$

When the error is added to the error metric, it is
referred to as a "morphology cost", since the squared
20 morphology error is traded off against the power of the
error signal.

The matrix $R_A(n)$ embodies the relationship between
the desired output signal components of the input

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signals. As such, it carries information on how signals
may be combined and substituted in a way which preserves
the desired signal while the combination is acting to
reduce the noise by combining signals in a way that
5   causes the noise to cancel.

The fidelity to the output signal can also be
considered as a separate constraint. For example, the
squared error of the mean of the low-noise output signal
relative to the average desired output signal can be
10 constrained so as not to exceed the total power in the
average desired output signal by more than a certain
percentage. The percentage may be expressed as:

$$Err = 100 \ tr[\ (F-T)R_A(n) \ (F-T)' \ ]/ \ tr[FR_A(n)F' \ ],$$

where the total power is given by the quantity
15 $tr[FR_A(n)F' \ ]$. This constraint is referred to as the
"morphology constraint." The solution for T with a
morphology constraint is found using the smallest non-
negative value α that satisfies the equation for
producing a matrix T that minimizes $E_A(n)$ while
20 preventing Err from exceeding 0.9 to 1.1%.

The determination of T is based on some
neighborhood of input signals and is applied to produce
the low-noise output in another neighborhood. In an
adaptive processing implementation, the input
25 neighborhood is some relatively small number of past and
future beats. For example, the matrix T may be derived
using 16 past beats, the current beat, and 15 future
beats. The derived matrix T is then applied to an even
smaller number of beats, and is typically applied only to
30 the current beat.

In a batch processing implementation, the input
and output neighborhoods are similar, if not the same.
The filter $h_2(n)$ may be a simple "boxcar" filter that

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takes the average over the entire group of beats. The resulting matrix T is then applied to the entire group of beats.

Referring to Fig. 12, in a simple case, the processor 105 reduces noise a primary signal produced by a pair of primary electrodes 450 and 455 (RA and LL_1) using a secondary signal produced by a secondary electrode 460 (LL_2). Similar results could also be obtained using only two electrodes. The three electrodes are a subset of the electrodes 110 illustrated in Fig. 3. The first electrode 450 (RA) is positioned just below the patient's right arm. The second electrode 455 (LL_1) is positioned on the patient's left side near the patient's left leg. The electrodes 450 and 455 constitute an ECG lead (LL) with the signal produced by the lead being a voltage difference between the leads that is defined as:

$$LL = RA - LL_1$$

The third electrode 460 (LL_2) is positioned next to the second electrode 455 and provides a secondary signal that is related to the impedance (Z_{LL1}) of the second electrode 455. The third electrode 460 may be implemented as a separate electrode, or may be implemented as a segment of a multi-segment electrode that includes the second electrode 455. The processor 105 uses the impedance of the second electrode 455 to remove the effects of baseline noise from LL to produce a noise-free lead LL'.

An equivalent circuit for the system of Fig. 12 is illustrated in Fig. 13. The circuit includes impedances (Z_{RA}, Z_{LL1}, Z_{LL2}) associated with each of the electrodes 450, 455, 460. The impedance Z_{RA} of the first electrode 450 (RA) is arranged in a series configuration with the impedances Z_{LL1} and Z_{LL2} of the second electrode 455 (LL_1) and the third electrode 460 (LL_2), which are arranged in

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a parallel configuration relative to each other. The
circuit includes an additional impedance Z_P that
represents the impedance of the patient. The impedance
Z_P is arranged in a series configuration relative to the
5   impedances of the electrodes.

Referring to Fig. 14, processor 105 includes
circuitry for measuring LL and Z_{LL1}. The circuitry
includes a current source 465 that is configured and
connected to inject a 56 kHz current between the first
10 electrode 450 (RA) and the second electrode 455 (LL_1).
The current from the current source 465 flows through the
electrode-skin interface of the first electrode 450
(modeled by Z_{RA}), through the patient (modeled by Z_P) and
through the electrode-skin interface of the second
15 electrode 455 (modeled by Z_{LL1}). The measurement
circuitry and the hardware configuration for this example
is similar to the configuration provided by Devlin et al.

The ECG signal ($_{LL}$) is detected by an ECG
amplifier 470 that is connected between the first
20 electrode 450 and the second electrode 455. The
amplifier 470 includes a low-pass filter that blocks the
56 kHz signal and prevents the signal from affecting LL.

A voltage (V_{ZLL1}) corresponding to the impedance
(Z_{LL1}) of the second electrode 455 is produced by a
25 demodulating amplifier 475 that is connected between the
second electrode 455 and the third electrode 460 and is
tuned to measure only the portion of the voltage between
the second and third electrodes that has a frequency of
56 kHz. The demodulating amplifier 475 has a high input
30 impedance so that current flow into the demodulating
amplifier is negligible. Accordingly, there is no 56 kHz
voltage drop across the third electrode 460 (LL_2) and the
voltage (V_{ZLL1}) measured by the demodulating amplifier 475
corresponds to the 56 kHz voltage drop across the second
35 electrode 455 (LL_1). Since the current source 465

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provides a constant level of current, Ohm's law dictates
that the voltage measured by the demodulating amplifier
475 (V_{ZLL1}) is proportional to the impedance (Z_{LL1}) of the
second electrode 455 as:

5 $$Z_{LL1} = V_{ZLL1}/I,$$

where I is the current produced by the current source
465. The output of the ECG amplifier 470 (*LL*) and the
output of the demodulating amplifier 475 (V_{ZLL1}) are
provided to a central processing unit 480 of the
10 processor 105.

Referring to Fig. 15, a signal 485 produced by the
ECG amplifier 470 includes a series of ECG beats (see
Fig. 1) modulated with a low frequency noise signal. A
signal 490 produced by the demodulating amplifier 475
15 includes a low frequency noise signal. The isoelectric
points 495 of beats of the signal 485 vary similarly to
corresponding points 500 in the signal 490.

The processor 105 modifies the output (*LL*) of the
ECG amplifier 470 based on the output (V_{ZLL1}) of the
20 demodulating amplifier 475 according to the procedure 200
discussed above and illustrated in Fig. 5 to produce a
low-noise output signal *O(n)* ($_{LL'}$). After acquiring the
input signals (step 205), the processor 105 defines a
beat matrix *B(n)* that includes two rows and twenty
25 columns, with the first row corresponding to the output
of the ECG amplifier 470 and the second row corresponding
to the output of the demodulating amplifier 475 (step
210).

Next, the processor 105 expresses the desired
30 output signal *S(n)* in terms of the primary signals (step
215). In the described example, the input signals
includes a primary signal (*LL*) that is directly related
to the desired output signal and a secondary signal

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(V_{ZLL1}) that provides information about the noise content
of the primary signal. In particular, the primary signal
(*LL*) includes the true physiologic ECG signal arising
from the heart and baseline noise due to the electrodes

5   and other noise sources, while the secondary signal
(V_{ZLL1}) includes information about the baseline noise.
Accordingly, the processor 105 defines the *F* matrix as:

$$F = [1 \quad 0],$$

which indicates that the desired output signal *S(n)*
10 equals the primary input signal *LL*.

Next, the processor 105 expresses the low-noise
output signal *O(n)* (or *LL'*) in terms of the primary and
secondary signals (step 220). As noted above, the signal
485 (*LL*) includes the ECG signal plus noise, while the

15 signal 490 (V_{ZLL1}) is related to noise. Thus, the low-
noise output signal can be expressed as:

$$LL' = LL - con*V_{ZLL1},$$

where *con* is a constant. In matrix notation, this
relationship is expressed as:

20          $$LL' = O(n) = T(n) * B(n)$$

where

$$T(n) = [1 \quad -con(n)],$$

n is a particular beat, and *con(n)* is a constant
applicable to that beat. Thus, the impedance signal is
25 used in a direct linear combinations with the ECG signal.
The impedance signal could be used in other ways. For
example, if the impedance were related to baseline noise

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through a non-linear relationship, that relationship could be employed in modifying the ECG signal. A simple example would be to use both the impedance and the square of the impedance in approximating the baseline noise. In
5 addition, impedance signals measured at different or multiple frequencies could also be used.

Next, the processor 105 defines an error metric for the nth beat (step 225) as the squared deviation of the isoelectric point of $O(n)$ from the neighborhood
10 average in a neighborhood of eight beats. Processor 105 defines the isoelectric point $ISO(n)$ of $O(n)$ from the samples of $O(n)$ in the PQ interval of the beat (see Fig. 1). Processor 105 defines the neighborhood average $A(n)$ for the isoelectric point $ISO(n)$ as:

$$A(n) = \frac{1}{8} \sum_{k=n-7}^{n} ISO(k)$$

15 where the neighborhood includes the beat being considered and seven immediately preceding beats. The error metric $E(n)$ is then defined as:

$$E(n) = \sum_{k=n-7}^{n} (ISO(k) - A(k))^2$$

where the neighborhood is the same as that for $A(n)$.

Finally, the processor 105 reduces noise in the
20 low-noise output signal $O(n)$ by selecting values for $con(n)$ that minimize the error metric (step 230). (Because the ECG signal appears only in the primary signal, the use of "1" as the first entry of the T matrix inherently satisfies the unit weights fidelity
25 constraint.) The value of $con(n)$ that minimizes the error metric $E(n)$ is:

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$$con(n) = \sum_{k=n-7}^{n} ISO(k)\, V_{ZLL1}(k) \Big/ \sum_{k=n-7}^{n} V_{ZLL1}(k)^2$$

The processor 105 uses *con(n)* as the constant for the
isoelectric point for the nth beat. For all other points
in the beat, the processor 105 linearly interpolates
between the value of *con(n)* for the *nth* beat and the
5   value of *con(n)* for the adjacent beat (i.e., *con(n-1)* or
con(n+1)). For example, a point that is halfway between
the isoelectric point of beat *n* and the isoelectric point
of beat *n-1* will have a value for *con(n)* that equals the
average of *con(n)* and *con(n-1)*.

10   Through use of the impedance signal, the processor
105 produces a low-noise output signal *LL'* that has
substantially reduced noise content relative to the
desired output signal *LL*. However, it has been found
that impedance variations for an electrode do not
15 perfectly match the baseline noise for the electrode. It
also has been found that multiple impedance signals may
be used to further improve the quality of the low-noise
output signal. For example, the arrangement illustrated
in Fig. 16 provides three impedance signals for use in
20 noise reduction.

Fig. 16 illustrates two electrodes 110 that, as
shown in Figs. 3 and 4, are multi-segment electrodes
positioned on opposite sides of the patient's thoracic
cavity. Each multi-segment electrode includes a center
25 electrode 505 and a trio of annular segments 510 that are
capacitively coupled to function as a ring electrode for
purposes of impedance measurement. Similar results could
be obtained by replacing each multi-segment electrode
with a pair of traditional electrodes.

30   To produce the impedance signals, a 28 kHz current
source 515 is connected between the center electrodes 505
of the two electrodes to inject a current as discussed

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above. The center electrode 505 and the annular
electrodes 510 of the first electrode 110 (V6) are
capacitively coupled to the input terminals of a
demodulating amplifier 520 that produces an output signal
5 related to the impedance of the center electrode of the
first electrode. Similarly, the center electrode 505 and
the annular electrodes 510 of the second electrode 110
(I) are capacitively coupled to the input terminals of a
demodulating amplifier 525 that produces an output signal
10 related to the impedance of the center electrode of the
second electrode.

The annular electrodes 510 of each electrode 110
are connected to a corresponding input terminal of an
amplifier 530 that produces a signal that corresponds to
15 the patient's trans-thoracic impedance. The trans-
thoracic impedance varies as the patient's lungs inflate
and deflate. Thus, the trans-thoracic impedance is
indicative of respiration by the patient, which, as
previously discussed, is a significant source of baseline
20 noise.

Fig. 17 illustrates an equivalent circuit for the
arrangement of Fig. 16. The circuit includes impedances
(Z_{V6C}, Z_{IC}) associated with each of the center electrodes
505 and impedances (Z_{V6R}, Z_{IC}) associated with each of the
25 ring electrodes 510. The impedance of each center
electrode 505 is arranged in parallel with the impedance
of the corresponding ring electrode 510. The parallel
impedance arrangement for each electrode 110 is arranged
in series with the impedance for the other electrode 110.
30 An additional impedance 535 (Z_P) corresponding to the
trans-thoracic impedance is arranged in series between
the impedances of the two electrodes 110. The input
terminals of the demodulating amplifiers draw essentially
no current. For this reason, no current flows through
35 either of the ring electrodes 510. Thus, the voltage

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difference between the input terminals of demodulating amplifier 520 corresponds to the voltage drop across the center electrode 505 of the first electrode (V6), which corresponds to the impedance (Z_{V6C}) of that electrode.

5 Similarly, the voltage differences between the input terminals of the demodulating amplifiers 525 and 530 correspond, respectively, to the impedance (Z_{IC}) of the center electrode 505 of the second electrode and the impedance 535 (Z_P) of the patient's trans-thoracic
10 cavity.

Referring to Figs. 18A and 18B, multi-segment electrodes are constructed from a film basepad 540 on which is printed silver-chloride ink 545. The ink is patterned to create a center segment 550 and annular
15 segments 555 that provide electrical connection to the electrode gel. The ink pattern also creates traces 560 that continue to the bottom edge 565 of the basepad 540. At the bottom edge of the basepad 540, the traces are brought into a parallel configuration suitable for an
20 edge connector.

A plastic flexible foam 570 is attached to the base pad 540. The foam includes cutout sections that correspond to the electrode segments 505, 510 and create wells that hold electrically conductive gel that makes an
25 electrical connection from the ink to the skin. The surface of the foam is covered with an adhesive that adheres the electrode to the skin of the patient. The foam covers and insulates portions of the traces 560.

Multi-segment electrodes provide a number of
30 advantages. First, an ECG signal typically varies differently (if at all) between segments of the electrode than does baseline noise. This is largely attributable to differences between the physical location of the heart and the locations of sources of noise. It is also
35 attributable to the fact that the segments are all part

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of the same physical structure and are therefore affected
similarly by movement due to respiration or other causes.
In addition, variations in noise due to patient movement
can be adjusted between segments by introducing different
5 DC bias currents at the each segment of the electrode.
Such a biasing system is illustrated in Fig. 19, where
the bias current injected at each segment is related to
the value of a resistor 575 connected to that segment.
Similar results could be obtained by using different
10 electrolyte mixtures in the gel of each segment to vary
the conductivity from segment to segment or by using
different metal combinations on the foam basepad.

Processor 105 also uses the generalized procedure
105 to implement a technique referred to as "electrode
15 noise reduction." In performing electrode noise
reduction, the processor 105 uses multiple equivalent ECG
signals and multiple impedances to reduce noise in an ECG
signal produced by a lead.

Referring to Figs. 5 and 20, processor 105 uses
20 the generalized procedure 200 to produce a low-noise
output signal (X_o) that has substantially reduced
baseline noise and is used in the measurement of
alternans. Processor 105 produces the low-noise output
signal based on eleven signals obtained from electrodes
25 V6, I and RA (see Fig. 3). Eight of the signals ($X1+$,
$X2+$, $X3+$, $X4+$, $X1-$, $X2-$, $X3-$, $X4-$) correspond to ECG
signals sensed by the segments of the electrodes V6 and I
relative to the signal sensed by the electrode RA, and
are produced by amplifiers 580. Each amplifier 580 has
30 one input terminal that is directly connected to a
segment of one of the electrodes V6 and I and another
input terminal that is directly connected to the
electrode RA. The electrodes are not capacitively
coupled to the input terminals of the amplifiers 580.
35 The remaining signals correspond to the center electrode

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impedances (*XI+*, *XI-*) and the trans-thoracic impedance
(*XR*) that are produced by the circuit illustrated in
Figs. 16 and 17 and discussed above.

Processor 105 stores two measurements for each
5 beat (step 205). The first measurement corresponds to
the isoelectric point and equals the average value of
each signal during the PQ interval of the beat. The
second measurement is taken 60 milliseconds after the end
of the QRS complex of the beat and is referred to as the
10 J+60 millisecond point of the ST segment (the J point is
the end of the QRS complex).

Using these measurements, processor 105 generates
a beat matrix *B(n)* having two columns and eleven rows
(step 210). Each of the eleven rows of the beat matrix
15 *B(n)* corresponds to one of the eleven signals, with the
signals arranged in the following order: *X1+*, *X2+*, *X3+*,
X4+, *X1-*, *X2-*, *X3-*, *X4-*, *XI+*, *XI-*, *XR*. The coefficients
of the first column of the beat matrix *B(n)* correspond to
signal values at the isoelectric point, and the
20 coefficients of the second column correspond to signal
values at the J+60 millisecond point.

Next, processor 105 defines the desired output
signal (*X*) in terms of the primary signals (step 215):

$$X = X1+ - X1-.$$

25 In matrix notation, this is expressed as:

$$X = S(n) = F_X * B(n)$$

where

$$F_X = [1\ 0\ 0\ 0\ -1\ 0\ 0\ 0\ 0\ 0\ 0].$$

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Processor 105 then defines the low-noise output
signal $(X_o(n))$ in terms of primary and secondary signals
(step 220):

$$X_o(n) = O(n) = T_X * B(n)$$

5   where the matrix T_X has one row and eleven columns.

The processor 105 then generates an error metric
(step 225). To ensure that the low-noise output signal
includes one unit of the $X+$ (V6) electrode and one unit
of the $X-$ (I) electrode, processor 105 imposes the unit
10 weight fidelity constraint as:

$$P = \begin{bmatrix} 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 & 0 & 0 & 0 \\ 1 & 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}^Y \quad Q = [1 \ 1]$$

Because the low-noise output signal X_o is to be used in
the detection of alternans, processor 105 seeks to
minimize the non-alternans signal content of the error
15 signal $C(n)$. For this reason, processor 105 selects the
filter $h_1(n)$ to have the transfer function illustrated in
Fig. 9B:

$$h_1(n) = [\delta(k-n) - \delta(k-n-1)]/2.$$

Application of this filter results in:

20                         $$C(n) = T_X * D(n)$$

where

$$D(n) = B(n) - B(n-1),$$

$$C(n) = h_1(n) \otimes O(n),$$

and

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$$O(n) = T_X * B(n).$$

Processor 105 then computes the error metric as the square of the error signal over a neighborhood of 32 beats centered around the *nth* beat. Processor does this by defining $h_2(n)$ as:

$$h_2(n) = 1/32 \quad for \ k = [n - 16 \ to \ n + 15]$$
$$= 0, \ otherwise.$$

From this, processor 105 defines $R_E(n)$ as:

$$R_E(n) = h_2(n) \circledast (D(n) * D(n)')$$

or

$$R_E(n) = \frac{1}{32} \sum_{k=n-16}^{n+15} (B(k) - B(k-1)) * (B(k) - B(k-1))'$$

As discussed above, the error metric $E(n)$ equals:

$$E(n) = T * R_E(n) * T'.$$

Finally, processor 105 selects coefficients for $T_X(n)$ that minimize the error metric and satisfy the unit weights fidelity constraint (step 230):

$$T_X(n) = Q * T_0,$$

where

$$T_0 = (P' * R_0 * P)^{-1} * (P' * R_0)$$

and

$$R_0 = [R_E(n)]^{-1}.$$

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Processor 105 generates $T_X(n)$ for each beat, and uses
this value to generate a low-noise output signal $(X_o(n))$
according to:

$$X_o(n) = T_X(n) * B(n),$$

5   where $X_o(n)$ has one row and two columns for each beat,
with the first column corresponding to the isoelectric
point and the second column corresponding to the J+60
millisecond point.

Processor 105 also uses the matrix $T_X(n)$ to modify
10   all samples in the QRST complex of the beat. For this
purpose, processor 105 produces an extended beat matrix
$B_{QRST}(n)$ that has eleven rows and a number of columns that
equals the number of samples in the QRST complex of the
beat. Processor then produces an extended low-noise
15   output signal $X_{QRST}(n)$ as:

$$X_{QRST}(n) = T_X(n) * B_{QRST}(n).$$

In yet another variation, processor 105 imposes a
morphology constraint on the low-noise output signal. As
discussed above, the morphology constraint is a fidelity
20   to the output signal constraint that forces the average
low-noise output signal to conform to the desired output
signal. To implement the morphology constraint,
processor 105 generates $R_A(n)$ using a filter $h_3(n)$ that
averages 100 normal beats over the QRST complexes of the
25   beats. Processor 105 recomputes the $R_A(n)$ matrix for
each new beat. However, processor 105 could obtain
similar results by recomputing the matrix only when the
patient undergoes a significant change in position or
heart rate (conditions under which the average beat would
30   be expected to change). With the morphology constraint,
the solution for $T_X(n)$ becomes:

$$T_X(n) = Q*T_0 + \alpha F*R_A(n)*R_0*(I-(P*T_0)),$$

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where

$$R_0 = (R_E(n) + \alpha R_A(n))^{-1},$$

$$T_0 = (P'*R_0*P)^{-1}*(P'*R_0), \text{ and}$$

I is the identity matrix. Processor 105 selects the
5 smallest suitable non-negative value for the parameter α
by using an iterative search with the condition that:

$$Err = 100(F - T) * R_A(n) * (F - T)' / F * R_A(n) * F'$$

does not exceed the range of 0.9 to 1.1%.

Referring to Fig. 21, processor 105 implements a
10 two-stage noise-reduction procedure 600 to produce an
alternans measurement based on signals from the entire
electrode set illustrated in Figs. 3 and 4. First,
processor 105 preprocesses the input signals (step 605).
Thereafter, processor 105 implements the first noise-
15 reduction stage by performing electrode noise-reduction
(step 610) to produce a set of twelve low-noise ECG
signals (LA, LL, V1, V2, V3, V4, V5, V6, E, I, H and M).
Processor 105 uses the twelve low-noise signals as input
signals for the second noise-reduction stage. In the
20 second noise-reduction stage, processor 105 performs
noise-reduction (step 615) to produce a set of five low-
noise signals (VM, X, Y, Z and V4). VM is a vector
magnitude defined as:

$$VM = \sqrt{X^2 + Y^2 + Z^2}$$

Finally, processor 105 uses the five low-noise signals to
25 produce an alternans measurement (step 620).

Processor 105 obtains thirty two signals from the
fourteen electrodes illustrated in Fig. 3. Of the thirty
two signals, there are twenty four ECG signals, seven

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electrode impedance signals, and one respiratory/trans-
thoracic impedance signal. The impedance signals are
produced using the current injection technique described
above.

5   The twenty four ECG signals are named after their
corresponding electrodes, with the name of the electrode
referring to the center electrode of multi-segment
electrodes and the suffix "a", "b", or "c" referring to
signals from the ring segments of multi-segment
10   electrodes. For most of the multi-segment electrodes,
two or three of the outer ring segments are joined
together to form a larger segment, which reduces the
number of ECG signals that need to be recorded. All the
of ECG signals are recorded relative to the average of
15   the voltages at the RA, LA, and LL electrodes. This
average is commonly referred to as the Wilson's central
terminal.

           The seven impedance signals measure the center
segment impedances of the seven multi-segment electrodes.
20   The impedance signals are named according to their
corresponding electrode followed by the suffix "i".

           As previously discussed, the respiratory signal
(Resp) is a measure of the impedance of the patient's
chest from the right side to the left side. Because air
25   does not conduct electricity as well as body tissues do,
the impedance across the chest changes as the lungs
inflate and deflate due to respiration. Respiration also
introduces baseline noise due to expansion and
compression of the electrodes and changes in the
30   impedance between the heart and the body surface.

           The processor 105 preprocesses the signals (step
605) as illustrated in Figs. 22-24. After amplifying and
anti-alias filtering the signals, processor 105 digitizes
the signals at a sampling rate of 1 kHz to create a 32

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signal time series $b(n)$. The contents of the rows of
b(n) are shown in Fig. 23.

Next, processor 105 detects, aligns and classifies
the beats within the time series $b(n)$ to produce a series
5 of beat matrices $B(n)$. The processor 105 aligns each
beat based on the QRS complex of the beat. Thereafter,
processor 105 filters the beat and decimates the beat to
250 Hz around the alignment point. Finally, processor
105 stores the beat in a beat matrix $B(n)$. The
10 decimation allows for some data reduction and lowers the
data storage requirements.

The structure of $B(n)$ is shown in Fig. 24. Row m
of $B(n)$ corresponds to row m of b(n). The columns of
$B(n)$ correspond to successive digital samples over the
15 duration of the beat. The samples start before the
beginning of the P wave and end after the T wave. The
indices K_{P2} and K_{PQ} delineate the PR interval while the
indices K_{T1} and K_{T2} delineate the T wave.

During preprocessing, processor 105 also accounts
20 for matrices corresponding to bad or abnormal beats.
Grossly abnormal waveforms, such as premature atrial and
ventricular beats, disrupt the subtle temporal pattern of
beat-of-beat variability in waveform morphology that is
indicative of alternans.

25   Abnormal beats may be identified by determining if
their morphology differs from the normal waveform
morphology by more than a predetermined threshold or if
the preceding intercycle interval differs from the mean
intercycle interval by more than some predetermined
30 threshold.

Processor 105 can account for matrices that
correspond to abnormal beats in a number of ways. In a
first approach, processor 105 could simply eliminate the
abnormal matrices from the sequence of beats. In another
35 approach, processor 105 could replace the beat matrix

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corresponding to an abnormal beat with a matrix
corresponding to a mean normal beat. In yet another
approach, processor 105 could separately analyze each
sequence of normal beats between abnormal beats and
5 combine the analyses.

     After preprocessing the signals (step 605), the
processor 105 performs electrode noise-reduction (step
610). In particular, processor 105 performs electrode
noise-reduction according to procedure 200 (Fig. 5) for
10 each of the twelve low-noise ECG signals that are
produced in this stage. Five of the twelve low-noise ECG
signals (LA, $V1$, $V2$, $V3$, $V5$) correspond to standard
electrodes. For each of these signals, processor 105
performs procedure 200 using a beat matrix $B(n)$ that has
15 nine rows, with the first row corresponding to the signal
to be processed and the remaining rows corresponding to
the eight impedance signals (LLi, $V4i$, $V6i$, Ii, Hi, Ei,
Mi and $Resp$) (see Fig. 23). The other seven low-noise
ECG signals (LL, $V4$, $V6$, E, I, H and M) correspond to
20 multi-segment electrodes. For each of these signals,
processor 105 performs procedure 200 using a beat matrix
$B(n)$ that includes a row corresponding to each signal of
the electrode and eight rows corresponding to the
impedance signals. Thus, for example, the beat matrix
25 $B(n)$ for $V6$ would include eleven rows, with the first
three rows corresponding to $V6$, $V6a$ and $V6b$, and the
remaining eight rows corresponding to the impedance
signals.

     Processor 105 generates the low-noise output
30 signals based on a neighborhood of thirty two beats in a
manner identical to that described above for the
generation of a low-noise X lead. In addition, processor
105 imposes a 1% morphology constraint. Thus, processor
105 selects the parameter α using an iterative search so
35 that the Err function does not exceed 0.9 to 1.1%. This

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procedure is referred to as "adaptive noise-reduction"
because the T matrices are continually adapted on a beat-
to-beat basis.

5   Next, processor 105 performs noise-reduction using
the twelve low-noise ECG signals (step 615) to produce
low-noise X, Y, Z and $V4$ output signals. The X, Y, and Z
vector signals have the advantage that the vector
magnitude (VM) computed from these signals is immune to
any alternans artifact created by rotation of the heart.
10   The $V4$ signal is representative of the $V1$-$V6$ signals,
which are known to contain information that is not
present in the X, Y and Z signals.

Fig. 25 shows the how the X, Y, Z and $V4$ output
signals are defined in terms of the input signals. The
15   coefficients necessary to create the X, Y, Z, and $V4$
output signals are represented in the row vectors F_X, F_Y,
F_Z, and F_{V4}. The low-noise output signals $S(n)$ are
represented as the matrix products of the F matrix with
$B(n)$.

20   Processor 105 performs noise-reduction every
sixteen beats for a neighborhood of 128 beats. Thus,
processor 105 performs noise-reduction for beats 1-128,
16-144, 32-160, etc.). For each group of 128 beats,
processor 105 computes the matrices T_X, T_Y, T_Z and T_{V4}
25   according to procedure 200. In performing the procedure
200, processor 105 implements the filter $h_1(n)$ as:

$$h_1(n) = 1/8\ e^{i\pi k/4}, \text{ for } k = n-4 \text{ to } n+3,$$
$$= 0, \text{ otherwise.}$$

The frequency response of this filter is shown in Fig.
30   9C. Processor 105 implements filter $h_2(n)$ as a 128 beat
average filter:

$$h_2(n) = 1/128 \text{ for } k = n-64 \text{ to } n+63,$$

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$= 0$, otherwise.

In addition, processor 105 imposes the geometry constraint and the 1% morphology constraint.

Once processor 105 generates the T matrices, it applies the T matrices to all 128 beats of a group. Note that a single beat (e.g., beat number 100) may appear in more than one group of 128 beats (e.g., 1-128 and 16-144) and have a different T matrix applied to it for the two different groups. This is referred to as "batch noise-reduction" because the same T matrix is applied to an entire batch of beats.

After optimizing X, Y, Z, and $V4$, processor 105 computes VM and the alternans measurement for each lead (step 620). Processor 105 then repeats the noise-reduction procedure for the next group of 128 beats (offset from the preceding group by sixteen beats). The sixteen beat offset is dictated by a desire to save computational time and resources, and can be adjusted as desired.

Figs. 26A-26C summarize the method by which processor 105 computes the alternans measurement. First, processor 105 divides the T-wave region of the vector magnitude (VM) beats (Fig. 27A) into a column of points as represented by v(n) (Fig. 27B). Processor 105 then computes the power spectrum of v(n) is computed as V(f). The frequency corresponding to 0.5 cycles per beat is the alternans frequency. The power at the alternans frequency is denoted by $P_{0.5}$ and the noise in the reference band between 0.43 and 0.48 cycles/beat is denoted by P_{noise} as described above. The level of alternans is considered significant if it exceeds the level of noise reference band by an amount equal to three standard deviations of the level in the reference band. The alternans in the X, Y, Z and $V4$ signals is computed

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using the same procedure as that used for computing the
alternans of the vector magnitude signal *VM*.

Other embodiments are within the scope of the
following claims. For example, the error signal has been
5   defined above as the deviation in the isoelectric point
from its mean value. The error signal could be defined
on another part of the PQRST complex, such as, for
example, the ST level in the region of the beat used for
ST analysis or the T wave level in the region of the beat
10 used for alternans analysis. The level may be relative
to a reference feature of the ECG complexes or to a
voltage level. The error signal could also be defined on
an ECG signal from which has been subtracted the mean
PQRST complex, or in terms of the beat-to-beat
15 fluctuations in part or all of the PQRST complex.
Similarly, the error signal could be derived from the
beat-to-beat fluctuations in all or part of the PQRST
complex, applying a different weight to fluctuations at
different frequencies. The different frequencies could
20 be weighed by filtering over multiple beats in the time
range of the error signal used for the error metric.

The error metric could also be modified. In the
described embodiment, the error metric is the mean
squared value of the error signal and is computed over a
25 neighborhood of beats. The error metric could also be
defined as the output of a filter applied to the series
of the error metrics of individual beats. Similarly, the
error metric could be an aggregate metric that cannot be
expressed as a simple combination of the metrics of
30 individual beats. Model parameters that are computed on
the basis of the error metric may be valid for a single
beat, a small group of beats in the neighborhood of beats
used to compute the error metric, or a large group of
beats. In the event that the signals are considered over
35 time instead of over the beats, the error metric could be

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defined as a filter applied over time. For example, a low pass filter could be applied to the output signal and the error metric could be defined as the energy of a signal produced by the filter.

5   In addition, while the described embodiment is directed to the processing of ECG signals, the described procedures could also be used to process other types of physiologic signals. Similarly, the procedures could be implemented without regard to the location of beats or
10 without grouping signals into beats.

Also, while the described embodiment obtains physiologic signals using electrodes, signals could also be obtained using other types of sensors such as motion or pressure sensors. These signals could be used, for
15 example, to supplement or replace the impedance signals.

What is claimed is:

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1.   A method of reducing noise in a signal that
represents a physiologic process, comprising:
        obtaining multiple input signals;
        measuring a relationship between noise content of
5   the input signals; and
        combining the input signals in consideration of
the measured relationship to produce an output signal
having low noise content.

2.   The method of claim 1, wherein the multiple
10 input signals include two or more primary physiologic
input signals.

3.   The method of claim 1, wherein the multiple
input signals include one or more primary physiologic
input signals and two or more secondary input signals
15 that represent noise.

4.   The method of claim 1, wherein the multiple
input signals include one or more ECG input signals and
one or more secondary input signals that represent noise,
the method further comprising dividing the ECG input
20 signals and secondary input signals into set of segments,
wherein each set of segments represents a beat of the ECG
signal; wherein the step of measuring comprises measuring
a relationship between noise content of corresponding
points from successive sets of segments.

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5.   The method of claim 1, further comprising:

defining a desired output signal as a combination of one or more of the input signals;

modelling a low-noise output signal that
5   approximates the desired output signal as a combination of two or more of the input signals, the low-noise output signal including variable parameters that represent the relative contribution made to the low-noise output signal by each of the two or more input signals;

10   based on the relationship between noise content of the input signals, producing an error metric that represents noise content in the low-noise output signal, wherein the noise content in the low-noise output signal and a value of the error metric are affected by values
15   assigned to the variable parameters of the low-noise output signal;

determining values of the variable parameters that cause the error metric to satisfy a predetermined condition; and
20   combining the input signals to produce the low-noise output signal using the determined values of the variable parameters.

6.   The method of claim 5, wherein at least a first input signal of the multiple input signals is
25   obtained using an electrode applied to a patient's skin, wherein the multiple input signals include a second input signal that represents an impedance associated with the electrode, and wherein the step of modelling the low-noise output signal comprises modelling the low-noise
30   output signal as a combination of at least the first and second input signals.

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7.   The method of claim 6, wherein the first input
signal and at least a third input signal are obtained
using segments of a multi-segment electrode.

8.   The method of claim 7, wherein the step of
5   modelling the low-noise output signal comprises modelling
the low-noise output signal as a combination of at least
the first, second and third input signals.

9.   The method of claim 5, wherein at least a
first input signal and a second input signal of the
10   multiple input signals are obtained using segments of a
multi-segment electrode that is applied to a patient's
skin.

10.   The method of claim 9, wherein the step of
modelling the low-noise output signal comprises modelling
15   the low-noise output signal as a combination of at least
the first and second input signals.

11.   The method of claim 5, wherein the step of
determining comprises determining values of the variable
parameters that reduce the value of the error metric.

20   12.   The method of claim 5, wherein the step of
determining comprises determining values of the variable
parameters that reduce the error metric while satisfying
an additional condition.

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13. The method of claim 12, wherein:

the combination of two or more input signals that models the low-noise output signal includes the one or more input signals that define the desired output signal,
5 and

the additional condition satisfied by the step of determining requires that a sum of the identified variable parameters associated with the one or more input signals that define the desired output signal equal a sum
10 of parameters associated with the desired output signal.

14. The method of claim 12, wherein:

the desired output signal represents a physiologic signal sensed at a first location that is remote from a signal source, the first location being identified
15 relative to the signal source by a first vector;

at least two of the input signals represent the physiologic signal;

each input signal that represents the physiologic signal represents the physiologic signal as sensed at a
20 location corresponding to that input signal, the location being remote from the signal source and identified relative to the signal source by a corresponding vector; and

the additional condition satisfied by the step of
25 determining requires that a sum of the vectors corresponding to the input signals that represent the physiologic signals, with each vector being weighted by the identified variable parameter associated with the corresponding input signal, equals the first vector.

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15. The method of claim 12, wherein the additional condition satisfied by the step of determining requires that the low-noise output signal represented by the identified variable parameters have a predetermined
5 relationship with the desired output signal.

16. The method of claim 15, further comprising:
determining an average property of the desired output signal, and
determining a corresponding average property of
10 the low-noise output signal represented by the identified variable parameters,
wherein the additional condition satisfied by the step of determining values for the variable parameters requires that the average property of the low-noise
15 output signal represented by the determined variable parameters differ from the average property of the desired output signal by less than a predetermined amount.

17. The method of claim 5, wherein the step of
20 defining the desired output signal comprises defining the desired output signal as a linear combination of two or more of the input signals.

18. The method of claim 5, wherein the desired output signal and the low-noise output signal represent
25 an ECG signal.

19. The method of claim 18, further comprising using the low-noise output signal to produce a measurement of alternans.

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20. The method of claim 19, wherein at least a first input signal of the multiple input signals is obtained using an electrode applied to a patient's skin, and wherein the multiple input signals include a second
5 input signal that represents an impedance of the electrode.

21. The method of claim 20, wherein the step of modelling the low-noise output signal comprises modelling the low-noise output signal as a combination of at least
10 the first and second input signals.

22. The method of claim 20, wherein the first input signal and at least a third input signal are obtained using segments of a multi-segment electrode.

23. The method of claim 22, wherein the step of
15 modelling the low-noise output signal comprises modelling the low-noise output signal as a combination of at least the first, second and third input signals.

24. The method of claim 19, wherein at least a first input signal and a second input signal of the
20 multiple input signals are obtained using segments of a multi-segment electrode that is applied to a patient's skin.

25. The method of claim 24, wherein the step of modelling the low-noise output signal comprises modelling
25 the low-noise output signal as a combination of at least the first and second input signals.

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26. The method of claim 5, further comprising repeating the defining, modelling, producing, determining and combining steps to produce a set of low-noise output signals.

5   27. The method of claim 26, further comprising:
defining a further desired output signal as a combination of one or more of the low-noise output signals from the set of low-noise output signals;
modelling a further low-noise output signal that
10 approximates the further desired output signal as a combination of two or more of the low-noise output signals, the further low-noise output signal including further variable parameters that represent the relative contribution made to the further low-noise output signal
15 by each of the two or more low-noise output signals;
producing a further error metric that represents noise content in the further low-noise output signal, wherein the noise content in the further low-noise output signal and a value of the further error metric are
20 affected by values assigned to the further variable parameters of the further low-noise output signal;
determining values of the further variable parameters that cause the further error metric to satisfy a predetermined condition; and
25   combining the low-noise output signals to produce the further low-noise output signal using the determined values of the further variable parameters.

28. The method of claim 27, further comprising using the further low-noise output signal to produce a
30 measurement of alternans.

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29. The method of claim 5, wherein a first one of the input signals is representative of respiration by a patient.

30. The method of claim 29, wherein at least a
5 second input signal is obtained using an electrode applied to the patient's skin, and wherein the step of modelling the low-noise output signal comprises modelling the low-noise output signal as a combination of at least the first and second input signals.

10   31. A method of reducing noise in a signal that represents a physiologic process, comprising:
       measuring two or more primary input signals that include part or all of a desired signal;
       defining a desired output signal as a combination
15 of one or more of the primary input signals;
       measuring one or more secondary input signals that include information about noise content in the desired signal;
       combining two or more of the primary signals and
20 one or more of the secondary signals to produce an output signal that approximates the desired output signal and has reduced noise relative to the desired output signal.

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32. A method of reducing noise in a signal that
represents a physiologic process, comprising:
        measuring one or more primary input signals that
include part or all of a desired signal;
5   defining a desired output signal as a combination
of one or more of the primary input signals;
        measuring two or more secondary input signals that
include information about noise content in the desired
signal;
10   combining one or more of the primary signals and
two or more of the secondary signals to produce an output
signal that approximates the desired output signal and
has reduced noise relative to the desired output signal.

        33. A method of reducing noise in an ECG signal,
15 comprising:
        measuring one or more primary input signals that
represent the ECG signal;
        measuring one or more secondary input signals that
represent noise in the ECG signal;
20   dividing the primary and secondary input signals
into sets of segments, wherein each set of segments
represents a beat of the ECG signal;
        for each set of segments, defining a relationship
between the noise content of the primary and secondary
25 input signals;
        for each set of segments, combining the input
signals in a way that produces an output signal having
low noise content.

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34. A method of obtaining a reduced noise
physiologic signal, comprising:

measuring one or more input physiologic signals;

producing a model that generates an output signal
5 as a combination of the primary input signals;

producing a noise metric that represents noise in
the output signal produced by the model;

adjusting parameters of the model so as to cause
the noise metric to satisfy a predetermined condition;
10 and

producing the output signal using the model and
the adjusted parameters.

35. The method of claim 34, further comprising
measuring one or more secondary input signals containing
15 information related to noise in the primary input
signals, wherein the step of producing the model
comprises producing the model to generate the output
signal as a combination of the primary input signals and
the secondary input signals.

20   36. The method of claim 35, further comprising
defining one or more fidelity constrains, wherein the
step of adjusting comprises adjusting the parameters of
the model so that the parameters of the model and the
output signal satisfy the fidelity constraints.

25   37. The method of claim 36, further comprising
measuring a relationship between noise content in each of
the primary and secondary input signals, wherein the step
of adjusting comprises adjusting the parameters of the
model in view of the measured relationship to reduce or
30 cancel noise from the output signal.

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38. The method of claim 35, further comprising
measuring a relationship between noise content in each of
the primary and secondary input signals, wherein the step
of adjusting comprises adjusting the parameters of the
5 model in view of the measured relationship to reduce or
cancel noise from the output signal.

39. The method of claim 34, further comprising
defining one or more fidelity constraints, wherein the
step of adjusting comprises adjusting the parameters of
10 the model so that the parameters of the model and the
output signal satisfy the fidelity constraints.

40. The method of claim 34, further comprising
measuring a relationship between noise content in each of
the primary input signals, wherein the step of adjusting
15 comprises adjusting the parameters of the model in view
of the measured relationship to reduce or cancel noise
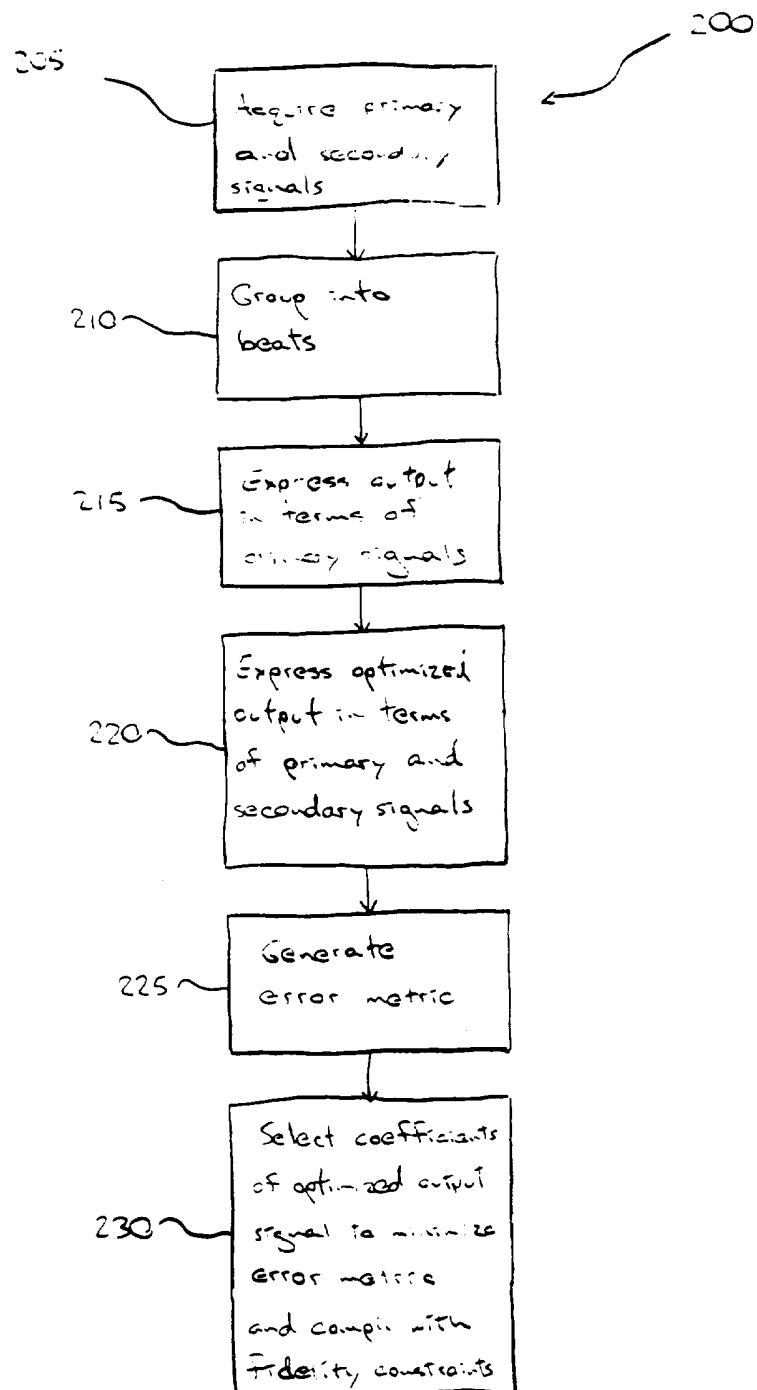from the output signal.

Fig. 1

Fig. 2

H

RA   LA

V1 V2
M   V3
I   E   V4 V5 V6

RL   LL
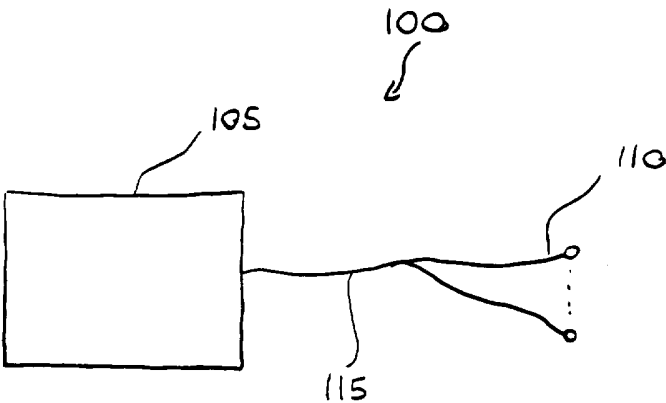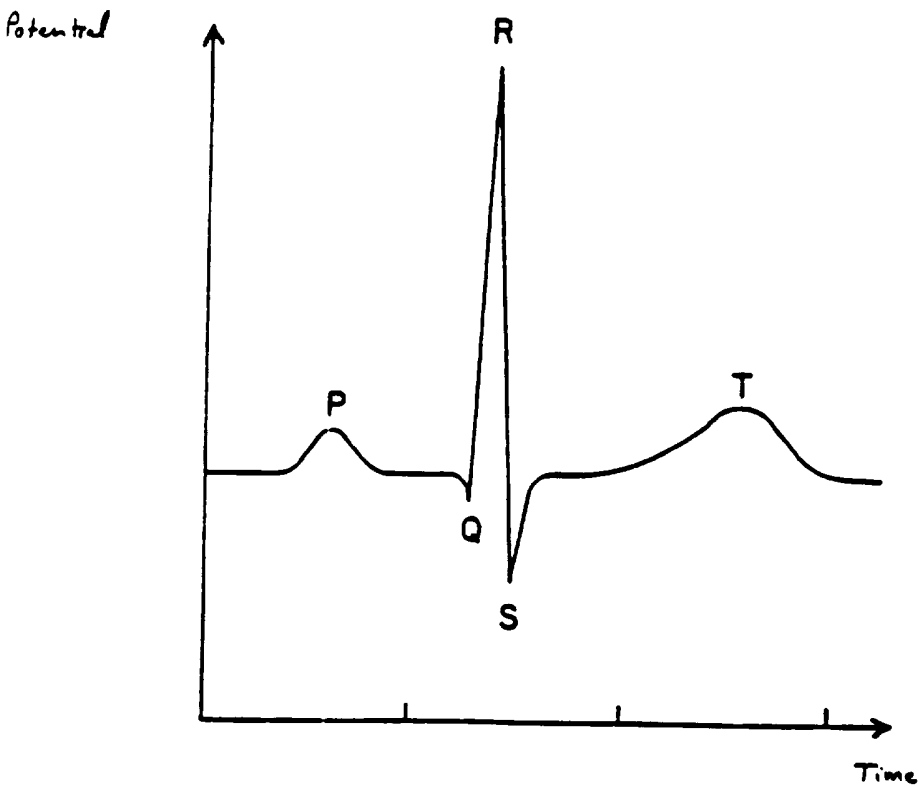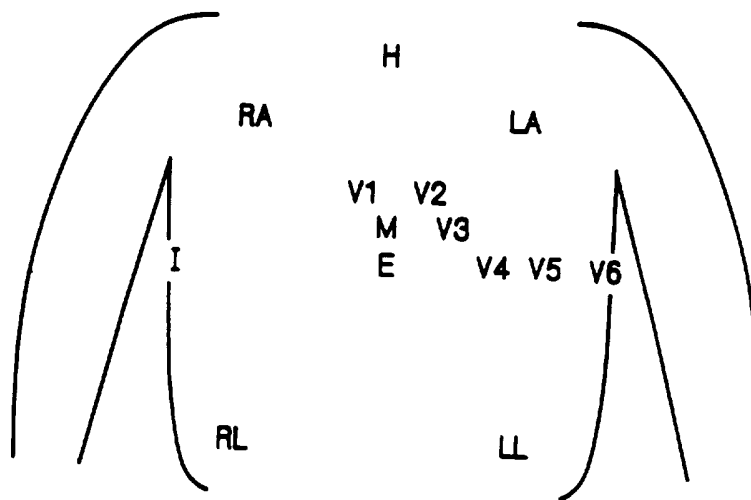
Fig. 3

Electrode Name	Electrode Location	Type	Available Signals
RL	R. ILLIAC CREST	STANDARD	(DRIVEN GROUND)
RA	RIGHT SHOULDER	STANDARD	(REFERENCE)
LA	L. SHOULDER	STANDARD	LA
LL(F)	L. ILLIAC CREST	MULTIPLE	LLa, LLb, LLc, LLi
V1	V1	STANDARD	V1
V2	V2	STANDARD	V2
V3	V3	STANDARD	V3
V4(C)	V4	MULTIPLE	V4, V4a, V4i
V5	V5	STANDARD	V5
V6(A)	V6	MULTIPLE	V6, V6a, V6b, V6i
I	R. V6 POSITION	MULTIPLE	I, Ia, Ib, Ii
H	BELOW NECK	MULTIPLE	H, Ha, Hi
E	BETWEEN A & I	MULTIPLE	E, Ea, Ei
M	BACK	MULTIPLE	M, Ma, Mb, Mi

Fig. 4

Fig. 5

205

200

Acquire primary
and secondary
signals

210

Group into
beats

215

Express output
in terms of
primary signals

220

Express optimized
output in terms
of primary and
secondary signals

225

Generate
error metric

230

Select coefficients
of optimized output
signal to minimize
error metric
and comply with
fidelity constraints

Matrix	Size	Description
$B(n)$	$L \times M$	Beat matrix containing the samples of the nth beat.
F	$K \times L$	Matrix of coefficients defining the output signal $S(n)$ from $B(n)$.
T	$K \times L$	Matrix of coefficients defining the output signal $O(n)$ from $B(n)$.
$S(n)$	$K \times 1$	The output signal computed as $S(n) = F*B(n)$.
$O(n)$	$K \times 1$	The optimized output signal computed as $O(n) = L*B(n)$.
$C(n)$	$K \times 1$	The optimized output signal computed as $c(n) = h_1(n) \otimes O(n)$.
$R_C(n)$	$L \times L$	Correlation matrix which is the "square" of $C(n)$: $R_C(n) = C(n)*C'(n)$.
$D(n)$	$L \times L$	A filtered version of $B(n)$ that retains only frequency content to be eliminated from the output signal: $D(n) = h_1(n) \otimes B(n)$.
$R_D(n)$	$L \times L$	Correlation matrix that is the "square" of $D(n)$: $R_D(n) = D(n)*D'(n)$.
$R_E(n)$	$L \times L$	Correlation matrix obtained by taking a weighted average of $R_D(n)$: $R_E(n) = h_2(n) \otimes R_D(n)$.
$E(n)$	1×1	Error metric for the nth beat. Computed as the trace of $R_E(n)$. May include other terms.
$A(n)$	$L \times M$	Mean beat computed as a weighted average of $B(n)$: $A(n) = h_3(n) \otimes B(n)$.
$R_A(n)$	$L \times L$	Correlation matrix that is the "square" of $A(n)$: $R_A(n) = A(n)*A'(n)$.

Fig. 6A

Filter	Size	Description
$h_1(n)$		Filter that creates $D(n)$ from $B(n)$; passes the frequency bands that are to be removed from the output.
$h_2(n)$		Filter that creates $R_E(n)$ from $R_D(n)$; takes a weighted average of $R_D(n)$ over a range of beats.
$h_3(n)$		Filter that creates $A(n)$ from $B(n)$; passes the frequency bands that are to be preserved in the output; creates a weighted average over a range of beats.

Fig. 6B

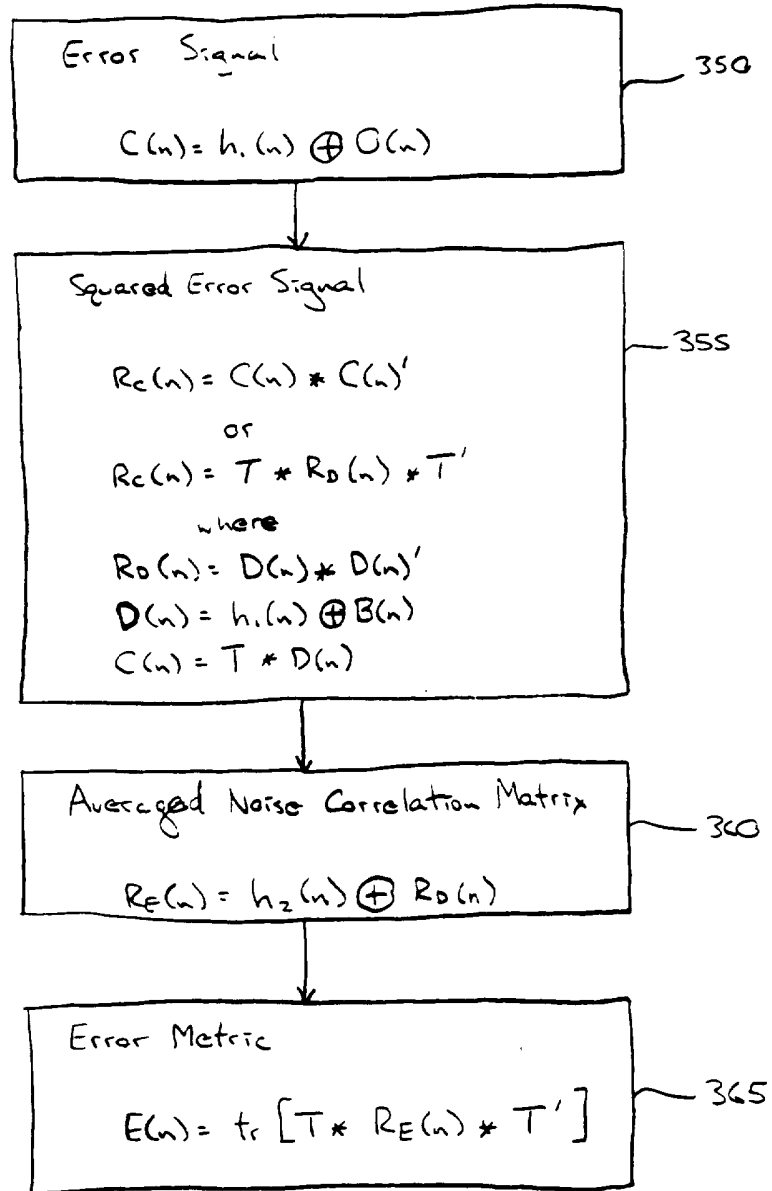$$\text{Fig. 7}$$

$$B(n) = \begin{bmatrix} P1_1 & P1_2 & \ldots & P1_m \\ P2_1 & P2_2 & \ldots & P2_m \\ S1_1 & S1_2 & \ldots & S1_m \end{bmatrix} \overset{300}{}$$

$$S(n) = F * B(n) = \overset{305}{}[0.5 \quad 0.5 \quad 0] * \overset{310}{}B(n) \overset{300}{}$$

$$= [0.5 P1_1 + 0.5 P2_1, \quad 0.5 P1_2 + 0.5 P2_2 \quad \ldots \quad 0.5 P1_m + 0.5 P2_m] \overset{305}{}$$

$$O(n) = \overset{315}{}T * \overset{320}{}B(n) = \overset{300}{}[T_{P1} \quad T_{P2} \quad T_{S1}] * \overset{320}{}B(n) \overset{300}{}$$

$$= [T_{P1} P1_1 + T_{P2} P2_1 + T_{S1} S1_1 \quad T_{P1} P1_2 + T_{P2} P2_2 + T_{S1} S1_2 \quad \ldots \overset{315}{}$$
$$T_{P1} P1_m + T_{P2} P2_m + T_{S1} S1_m]$$
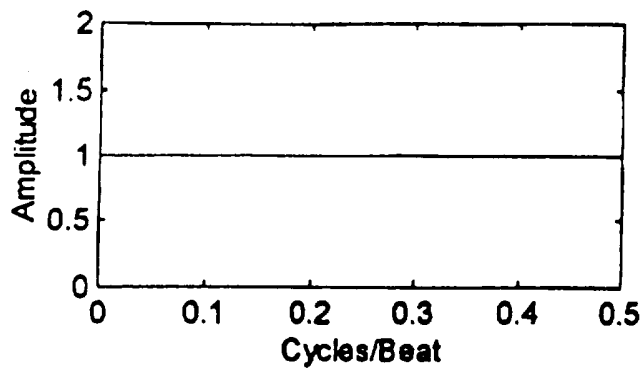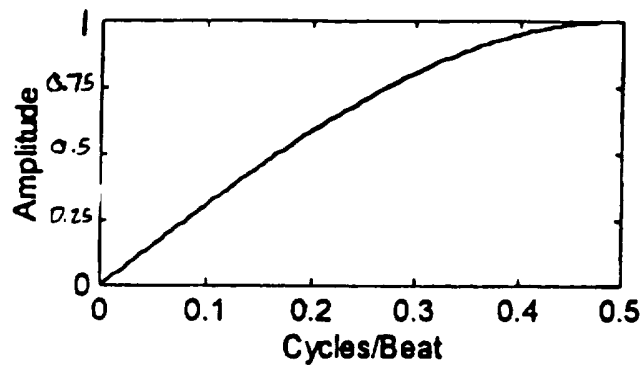
Fig. 8

$$C(n) = h_1(n) \oplus O(n)$$

Error Signal — 350

Squared Error Signal — 355

$$R_C(n) = C(n) * C(n)'$$

or

$$R_C(n) = T * R_D(n) * T'$$

where

$$R_D(n) = D(n) * D(n)'$$
$$D(n) = h_1(n) \oplus B(n)$$
$$C(n) = T * D(n)$$

Averaged Noise Correlation Matrix — 360

$$R_E(n) = h_2(n) \oplus R_D(n)$$

Error Metric — 365

$$E(n) = tr\left[T * R_E(n) * T'\right]$$

Fig. 9A

Fig. 9B

Fig. 9C

400

405

410

0.5   1 Part Signal, 1 Part Noise

415

+

0.5   1 Part Signal, -1 Part Noise

=

420

1.0   1 Part Signal

Fig. 10

Fig. 11A

$$M = [x_M, y_M, z_M] \qquad M(t) = x_M v_x(t) + y_M v_Y(t) + z_M v_Z(t)$$

$v_Z(t)$

425

Left

Right

$v_X(t)$

$v_Y(t)$

Front

Fig. 11B

M

425

I

V6

V5

V4

V1

V2

V3

Fig. 12

Fig. 13

Fig. 15

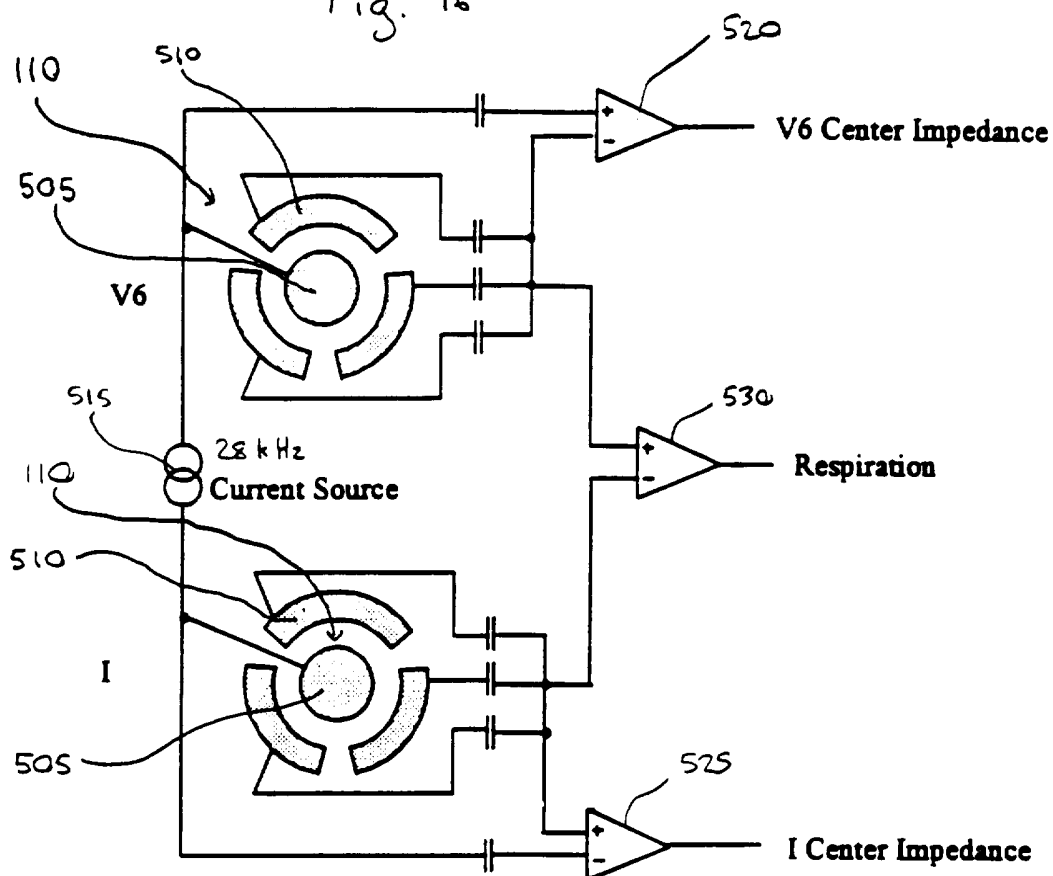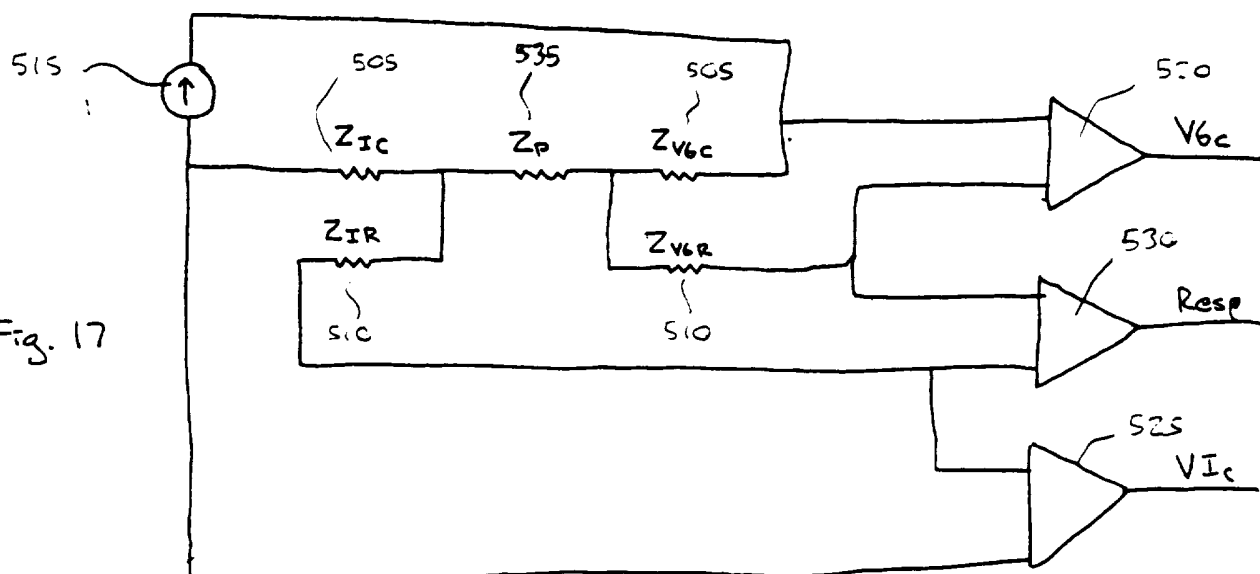Fig. 16

V6 Center Impedance

28 kHz
Current Source

Respiration

I Center Impedance
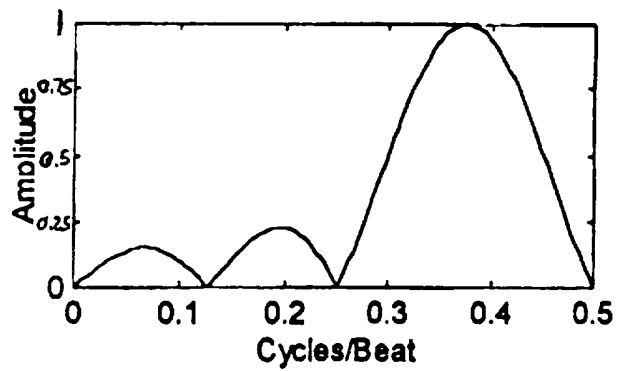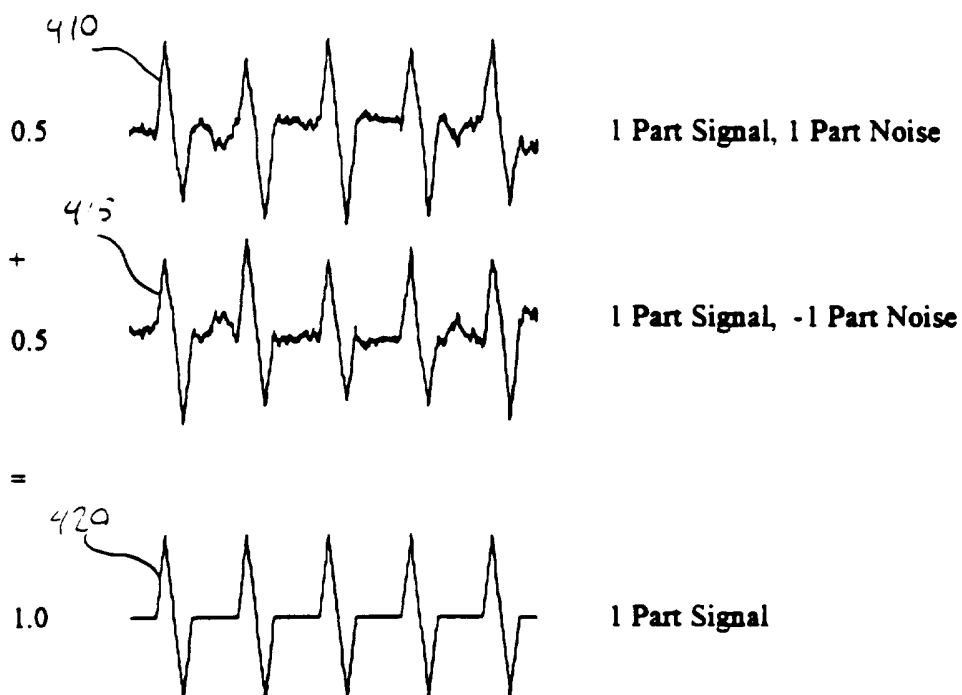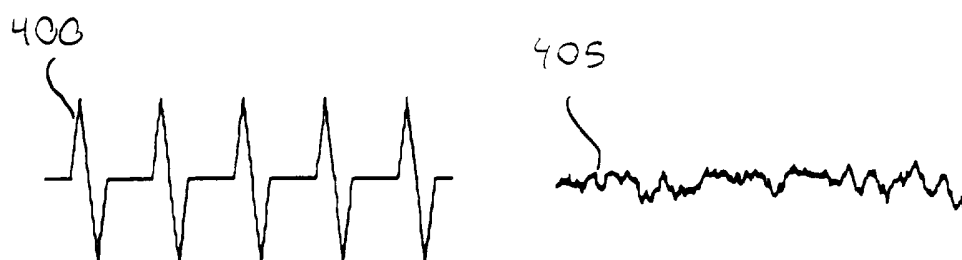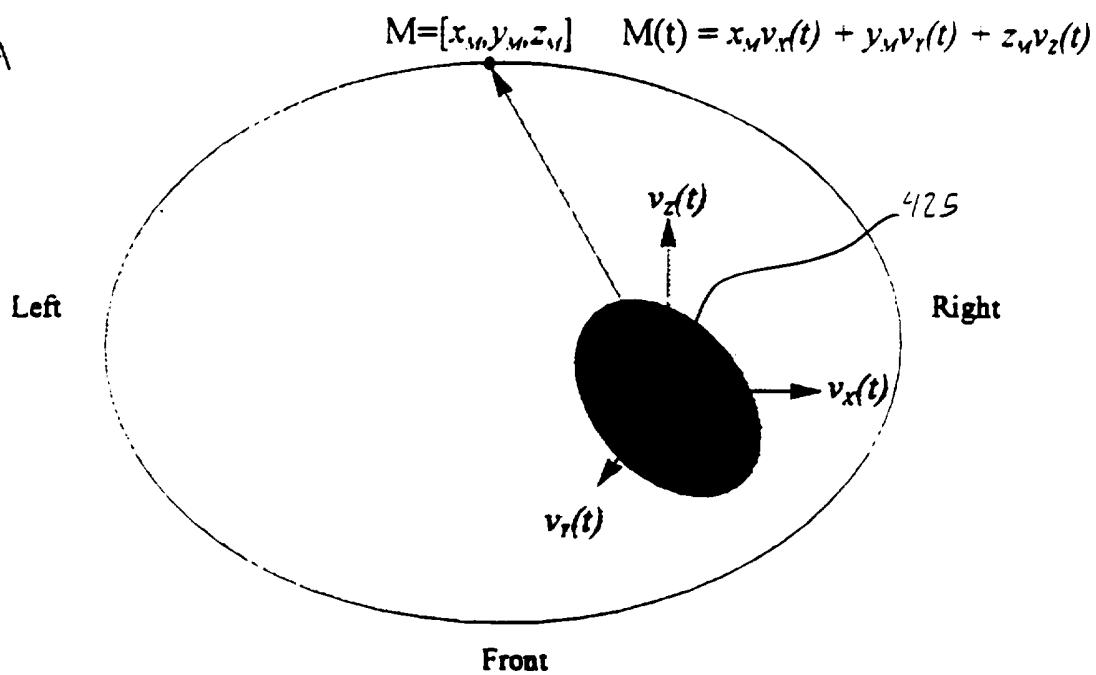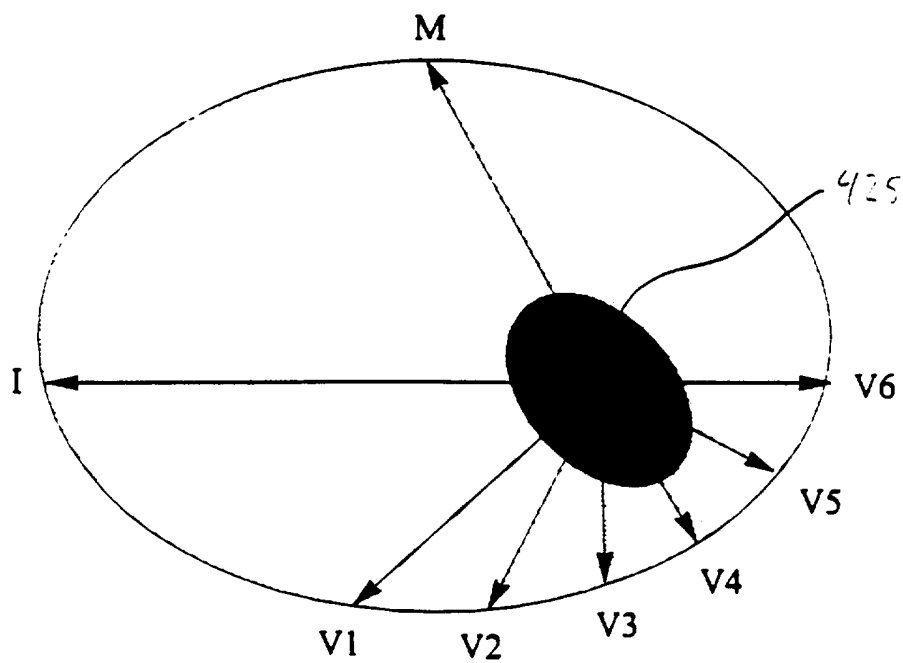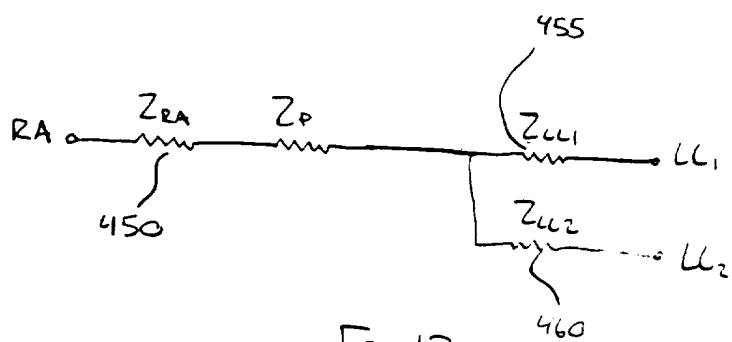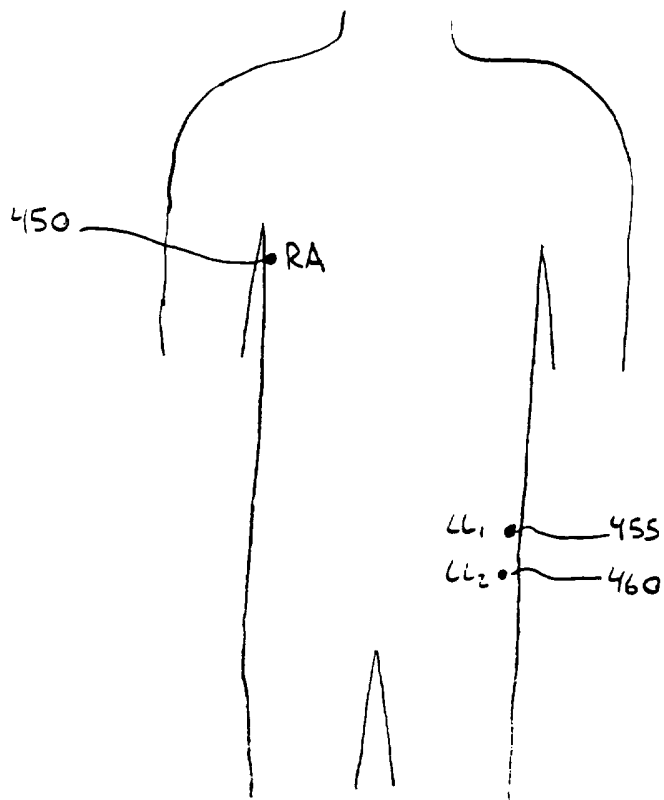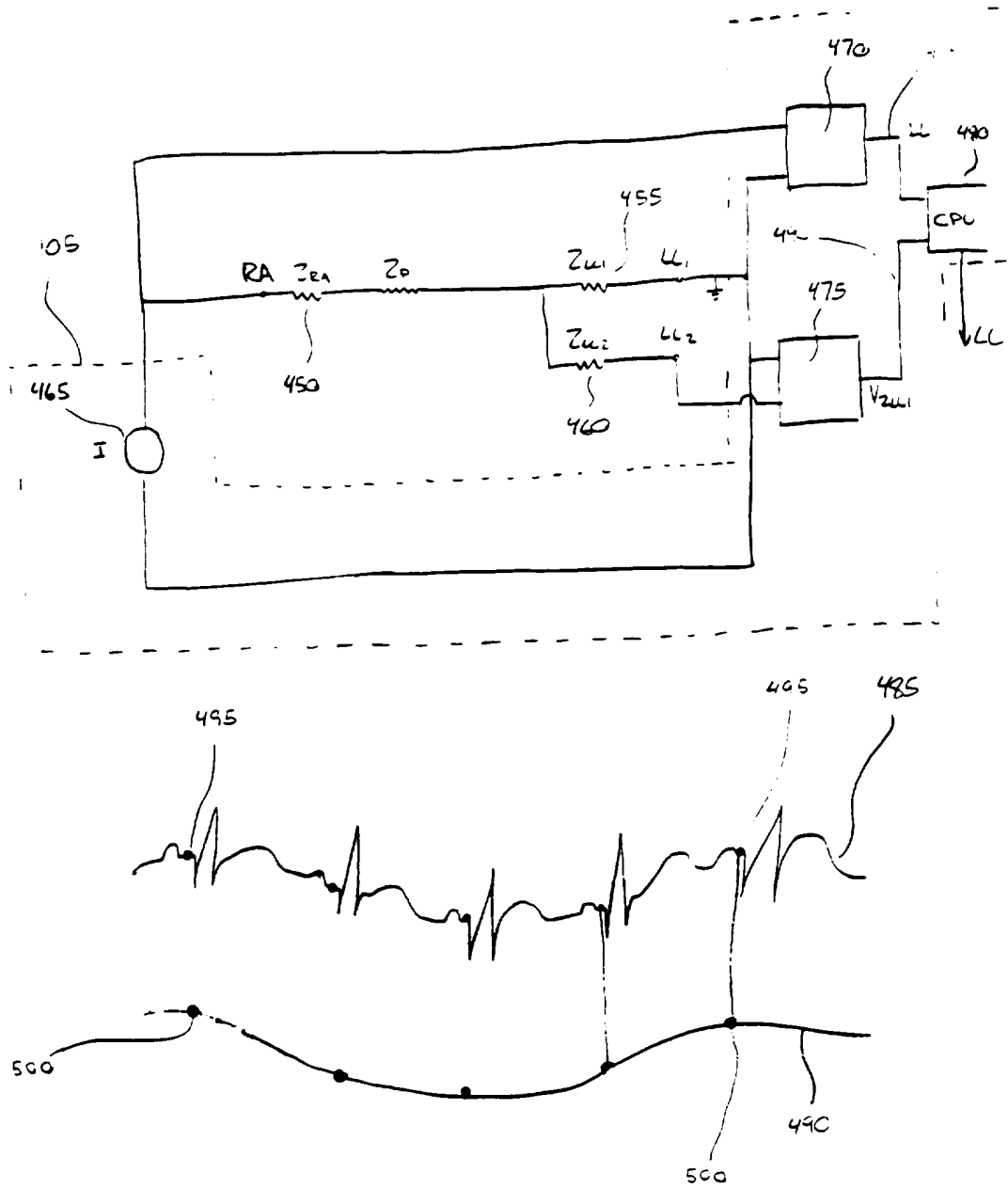
Fig. 17
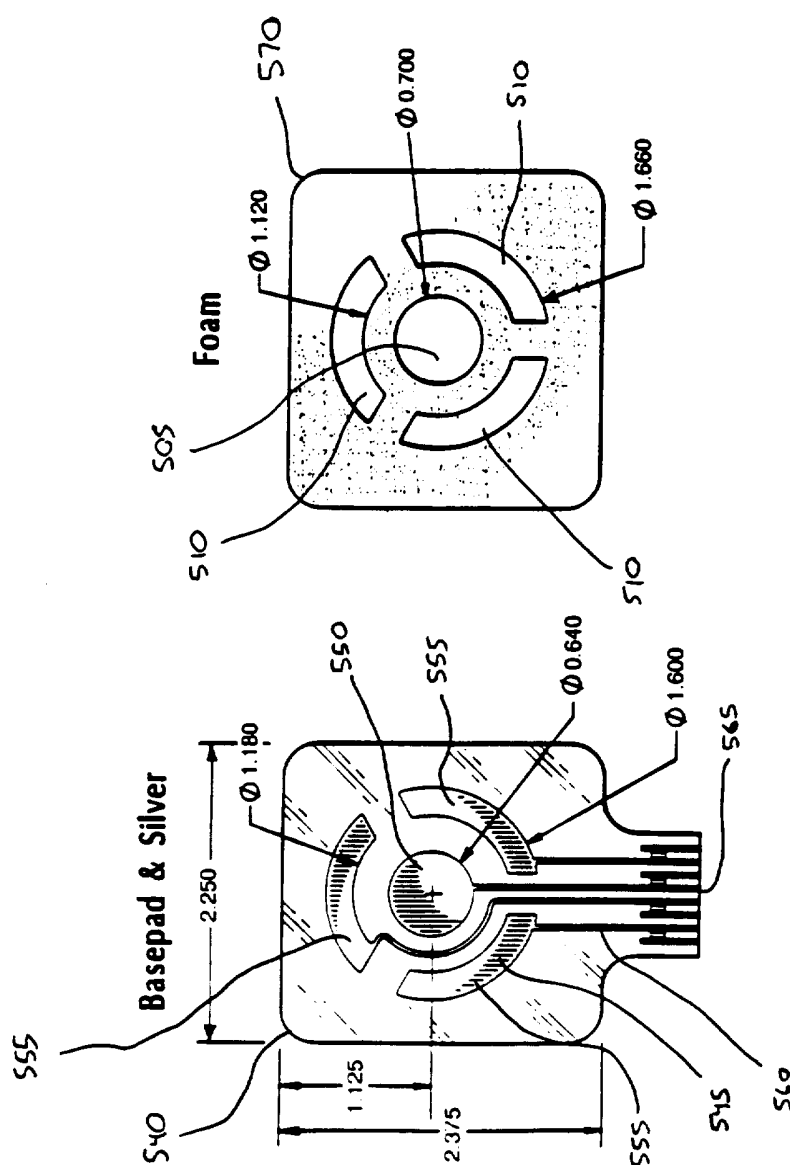
Fig. 18B

Fig. 18A

Fig. 19

Fig. 20

600

605 ⟶ | Preprocess
Signals

⟶

610 ⟶ | Perform electrode
optimization
(procedure 200)

⟶

615 ⟶ | Perform lead
optimization
(procedure 200)

⟶

620 ⟶ | Generate
Alternans
Measure

Fig. 21

Fig. 22

- Anti-alias filter
- Sample at 1Khz
- Align beats
- Select epoch of N beats

$b(n)$

- Filter & decimate to 250 Hz
- Create beat matrices $B(n)$
- Replace bad beats

$B(n)$
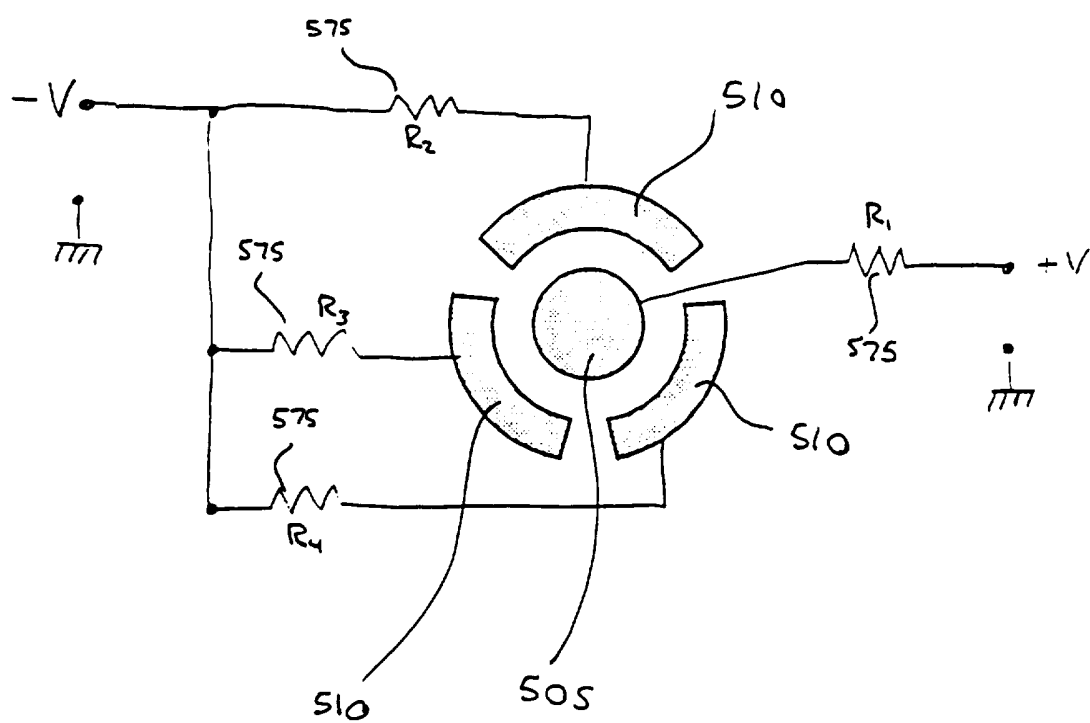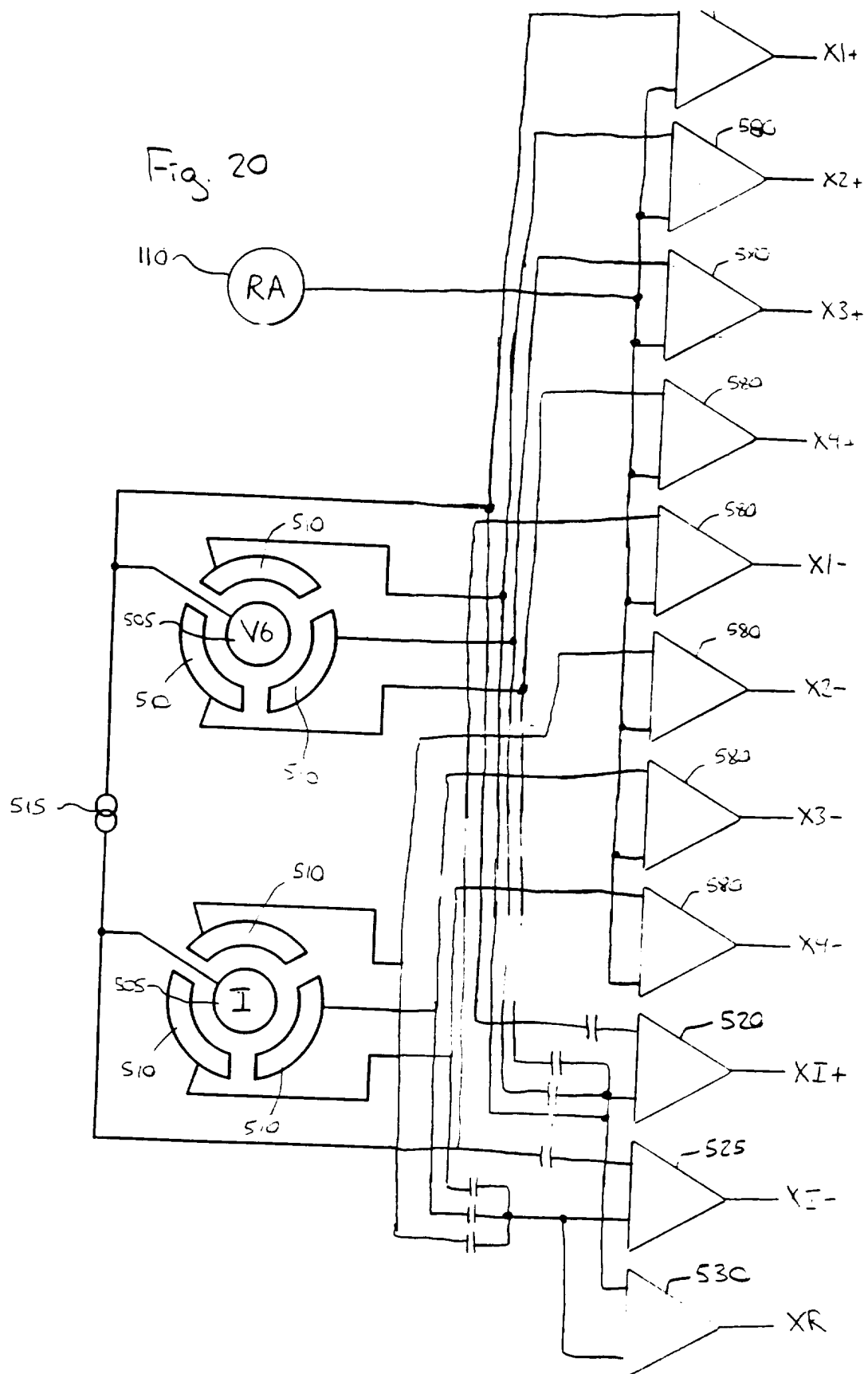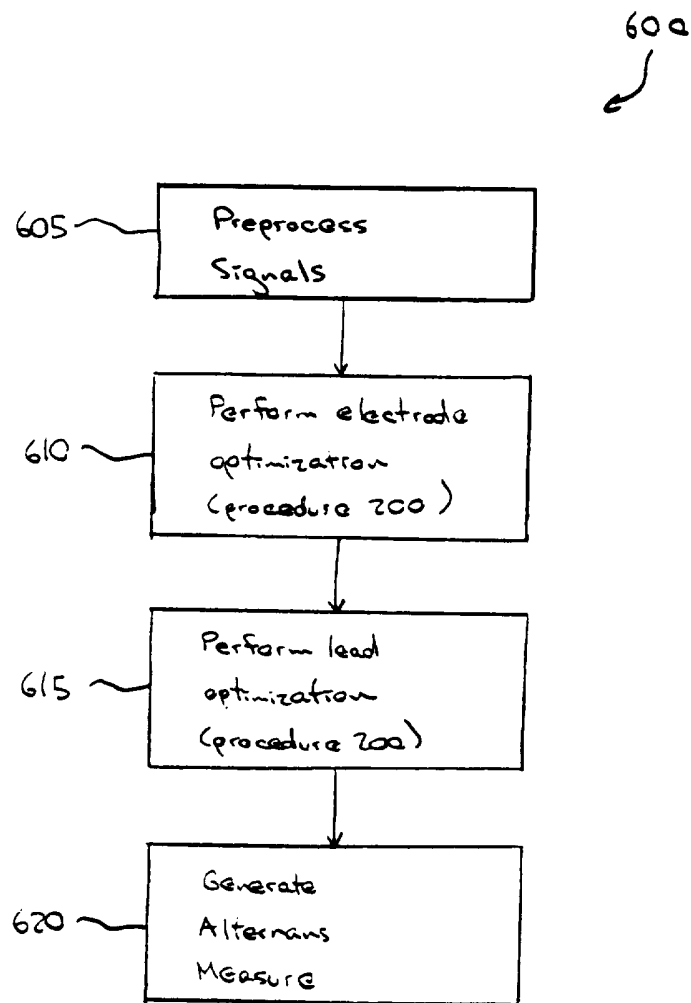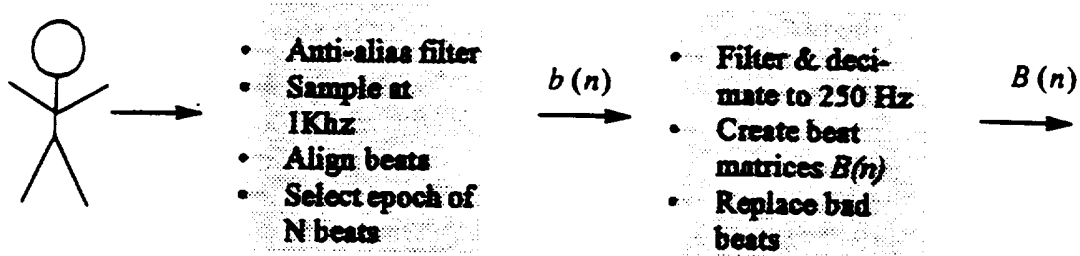
Fig. 23

$b(n) =$

Row	Signal	Row	Signal
1	LA	17	V6i
2	LL	18	I
3	LLa	19	Ia
4	LLb	20	Ib
5	LLc	21	Ii
6	LLi	22	H
7	V1	23	Ha
8	V2	24	Hi
9	V3	25	E
10	V4	26	Ea
11	V4a	27	Ei
12	V4i	28	M
13	V5	29	Ma
14	V6	30	Mb
15	V6a	31	Mi
16	V6b	32	Resp

Fig. 24

$$B(n) = \begin{bmatrix} & & & & \\ & & & & \\ & & & & \\ & & & & \end{bmatrix}$$
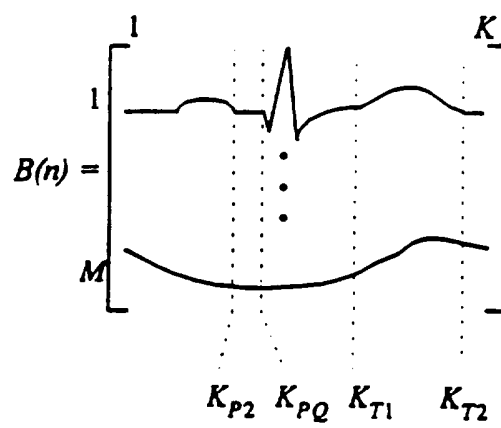
K_{P2}　K_{PQ}　K_{T1}　K_{T2}

Fig. 25

$$F_{xyz} = \begin{bmatrix} F_x \\ F_y \\ F_z \end{bmatrix}$$

$$S_{xyz}(n) = F_{XYZ}B(n)$$
$$D_{V4}(n) = F_{V4}B(n)$$

Col	Signal	F_X	F_Y	F_Z	F_{V4}
1	LA				
2	LL		0.655		
3	LLa				
4	LLb				
5	LLc				
6	LLi				
7	V1				
8	V2				
9	V3				
10	V4	0.171		-0.231	1.000
11	V4a				
12	V4i				
13	V5				
14	V6	0.610		0.133	
15	V6a				
16	V6b				
17	V6i				
18	I	-0.781		-0.264	
19	Ia				
20	Ib				
21	Ii				
22	H		-1.00		
23	Ha				
24	Hi				
25	E			-0.734	
26	Ea				
27	Ei				
28	M		0.345	0.736	
29	Ma				
30	Mb				
31	Mi				
32	Resp				
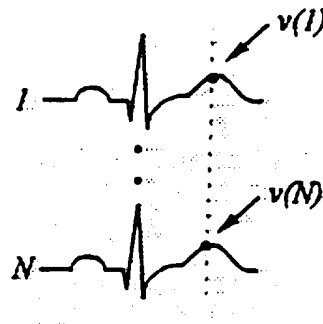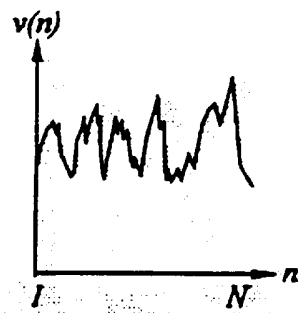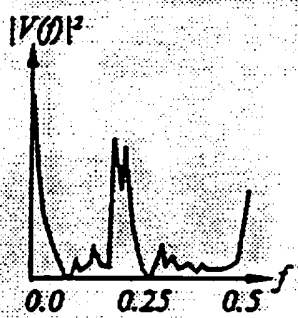
Fig. 26A

Fig. 26B

Fig. 26C

INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 5/0402
US CL :128/696

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/696, 698-700, 707, 733, 734; 364/413.05, 413.06

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US, A, 5,209,237 (ROSENTHAL) 11 May 1993, see column 5 line 30 to column 7 line 19.	1-5, 11, 12, 17, 18, 26, 29-40
X	US, A, 5,020,538 (MORGAN ET AL.) 04 June 1991, see column 4 line 23 to column 7 line 28.	1-5, 11, 31-35, 38, 40

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

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be part of particular relevance		
"E"	earlier document published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed	"&"	document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 FEBRUARY 1996	0 4 MAR 1996
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer JEFFREY R. JASTRZAB Telephone No. (703) 308-2097

Form PCT/ISA/210 (second sheet)(July 1992)*