Noise Characteristic

search for a T-wave offset point. The T-wave offset point is identified within the first time window, and the identified...characteristic of the ECG signal in a second time window that includes at least a portion of the T-wave.

29 Claims, 10 Drawing Sheets

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ABSTRACT

A T-wave offset point of an ECG signal is provided. In accordance with various example embodiments, a location of a QR complex in the ECG signal is identified and used to determine a first time window of the ECG signal in which to search for a T-wave offset point. The T-wave offset point is identified within the first time window, and the identified T-wave offset point is provided as an output based upon a noise characteristic of the ECG signal in a second time window that includes at least a portion of the T-wave.
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120 Identify location of QRS complex in ECG signal

130 Determine first time window in ECG signal

140 Identify T-wave offset point within first time window

150 Provide T-wave offset point as output based upon noise characteristic

FIG. 1A
Figure 1B

Input ECG Signal

- Denoise
- Identify Q-wave onset & T-wave offset
- Compute dynamic signal-to-noise ratio (dSNR) & a validity metric

101

102

103

104

dSNR > T1

YES

Trigger sensor failure alarm

NO

Discard QT for this cardiac cycle and classify as uninterpretable

Validity metric > T2

YES

Compute QT parameter by combining valid QT interval measurements

Tally count of cardiac cycles for which QT was discarded

NO

Validity metric > T3

YES

Classify QT and repolarization signal as valid

105

106

107

108

109

110

111

112

113

108

109

110

111

112

113

Output
Figure 3

1. Decompose input ECG signal into subcomponents, identify QRS location
2. Identify subcomponents in time windows in a cardiac cycle as primarily associated with a signal wave or with noise.
3. Compute T-wave subcomponents
4. Compute QRS subcomponents
5. Compute SNR for second time window
6. Compute T-wave emphasis signal from denoised subcomponents
7. Compute QRS emphasis signal from denoised subcomponents
8. Detect R-wave
9. Create search window for T-wave offset
10. Create search window for QRS offset
11. Identify T-wave offset
12. Identify QRS offset
13. Append time period of denoised ECG from QRS offset to T-wave offset to cardiac repolarization time series
14. Characterize rhythm and morphology
15. Compute validity metric
16. Validate Metric > T2
17. Yes: Output
18. No: Exclude T-wave from this cardiac cycle from repolarization time series
Figure 4

Input ECG Signal

Decompose ECG into subcomponents in a second domain of higher dimension

Denoise subcomponents

Combine denoised subcomponents to create emphasis signal

Evaluate emphasis signal to identify peaks, valleys, and baseline points to find T-wave offset

Output
Figure 6

1. Input ECG
2. Identify initial T-wave offset points
3. Compute a T-wave emphasis signal
4. Characterize T-wave morphology by evaluating amplitude and time of peaks, valleys, and zero crossings (fiducial points) of emphasis signal
5. Assign T-waves with common morphology characteristics to a cluster
6. Align T-waves in a cluster using location of a peak or valley in the emphasis signal (alignment point) while preserving the location of initial T-wave offset point relative to the alignment point
7. Compute a composite T-wave offset value for the cluster by combining T-wave offset points of aligned T-waves
8. Adjust T-wave offset for each cardiac cycle in the cluster by matching T-wave offset points to the composite value

Output
Decompose signal from first domain to create a set of subcomponents, D2sub, in a second domain using one of the following transforms:
- Discrete cosine transform
- Wavelet related transform
- Karhunen-Loeve transform
- Fourier transform
- Gabor transform
- Filter bank

Identify subsets, D2n and D2s, of subcomponents associated with noise energy and signal energy, respectively, in set D2sub using at least one of:
- Spatially selective filtering
- Periodic component analysis

Identify sets, D2n and D2s, of subcomponents associated with noise energy and signal energy, respectively, in set D2den, using at least one of:
- Spatially selective filtering (SSF)
- Periodic component analysis (PCA)

Compute noise power (Pn) as the energy contained in subset D2n
Compute signal power (Ps) as the energy in residual subcomponents of D2s.

Compute $dSNR = 10 \log (Ps/Pn)$

Output
Figure 9

Input ECG Signal

- Amplify sensed ECG
- Filter to remove out-of-band noise
- Digitize signal

Identify QRS complex
- Use the QRS complex to define a search window to search for T-wave offset

Remove most energy from the search window that is not T-wave energy. Use MDSP denoising, band-pass filtering, wavelet thresholding, or adaptive filtering.

Denoised T-wave Signal

Identify T-wave offset

Compute noise signal using the residuals of the denoising process

Identify a second time window where signal-to-noise ratio (SNR) can impact the accuracy of T-wave offset detection.

Compute SNR for the ECG signal in the second time window

SNR > Threshold

YES

Identified T-wave offset is accurate

NO

Identified T-wave offset may not be accurate.

NO

SNR < Threshold
EXTRACTION OF CARDIAC SIGNAL DATA

RELATED PATENT DOCUMENTS


FIELD OF INVENTION

The present invention relates to measurement of cardiac interval and extraction of other cardiac repolarization information from an ECG of human or animal subjects.

BACKGROUND

The cardiac repolarization period of the cardiac cycle, primarily consisting of the T-wave, is of interest for a variety of uses, including the analysis of cardiac function. For instance, repolarization abnormalities can be associated with dangerous arrhythmias, which are desirable detected for use in assessing cardiac function, ongoing health monitoring and/or treating cardiac pathologies. The QT interval (the time measured as an indicator of repolarization time with longer-than-normal or shorter-than-normal QT interval associated with possible risk of life-threatening arrhythmias. Evaluation of QT interval as an indicator of risk of life-threatening arrhythmias can involve measurement of average QT interval, QT interval dynamics, or both. Regulatory agencies can require that QT interval be measured in both animal models and human subjects during the course of developing new drugs as a means of assessing potential for drug-induced arrhythmias. QT interval measurements are also used to guide therapies in clinical care. Beyond measurement of QT interval, cardiac repolarization can be evaluated for clinical care and research using other methodologies including T-wave alternans, T-wave complexity, T-wave variability, and T-wave morphology changes.

Accurate measurement of QT interval has been challenging as a result of difficulties in accurately and consistently identifying T-wave offset due to its flat pattern, especially in the presence of noise. The accuracy of results produced by current methods is compromised, however, by noise in the ECG and by difficulty in accurately identifying T-wave offset. Further, approaches to identifying T-wave offset have suffered from an inability to accurately determine whether a particular T-wave offset is accurate, or whether the result may have been compromised due to the presence of noise, certain arrhythmias or difficult repolarization waveform morphology. These and related matters have presented challenges to the measurement of QT interval, assessment of QT interval dynamics, and isolation of the cardiac repolarization signal of an ECG.

SUMMARY

Various aspects of the present invention are directed to devices, methods and systems involving evaluating repolarization activity of the heart as represented in the ECG of a human or animal subject, in a manner that addresses challenges including those discussed above.

In connection with various example embodiments, T-wave offset points for ECG signals are provided as an output, based upon a noise characteristic of an ECG signal in a second time window that includes at least a portion of the T-wave. In certain implementations, the location of a QRS complex in the ECG signal is identified and used for determining a first time window of the ECG signal in which to search for the T-wave offset point, and the T-wave offset point is identified within the first time window.

According to another example embodiment, a T-wave offset point is identified in an ECG. The ECG is decomposed into subcomponents in a second domain in which at least a portion of the subcomponents representing noise are independent of a portion of the subcomponents representing the signal. The noise and signal subcomponents are separated, and which separation is used as a basis upon which the T-wave is provided.

The separation of the signal and noise subcomponents can be accomplished in a variety of manners. In some embodiments, the subcomponents are separated using one or more of spatially selective filtering, principal component analysis, independent component analysis and periodic component analysis. One or more subcomponents associated with the T-wave of the ECG are separated from other signal subcomponents within the second domain and used to evaluate a noise characteristic in the vicinity of the T-wave offset point.

According to another example embodiment, a noise characteristic is computed for a portion of the T-wave where the presence of noise can impact the accuracy of T-wave offset identification. The noise characteristic is computed by separating the T-wave energy and the noise energy in the portion of the T-wave and using the respective energies to compute a signal-to-noise ratio or other measures indicative of the relative levels of signal and noise energy in the portion. T-wave energy and noise energy in the portion can be separated by a number of techniques including band-pass filtering, wavelet thresholding, multidomain signal processing, or adaptive filtering.

According to another example embodiment, an emphasis signal is computed that exaggerates inflections in the signal and transition points of the emphasis and denoised signals, such as peaks, valleys, and baseline points, are detected to identify the T-wave offset point. These transition points may be detected in one or more of a variety of manners, using one or more approaches as described herein, such as via the analysis of subcomponents separated in accordance with the above.

According to another example embodiment, the subcomponents used to compute the emphasis signal are denoised using at least one of spatially selective filtering, principal component analysis, independent component analysis and periodic component analysis to improve consistency and accuracy of detecting transitions within the emphasis signal. In additional embodiments, the denoised subcomponents are used to reconstruct a denoised ECG.

According to another example embodiment, a validity-type metric is computed to assess the validity of a T-wave offset point, which can be used to automatically include the T-wave offset point as an outcome indicative of an accurate ECG characteristic. The validity metric is computed based on noise (e.g., using a dynamic signal-to-noise ratio) computed for a portion of the T-wave of a cardiac cycle as the ratio of energy in said signal subcomponents and noise subcomponents. In some embodiments, the validity metric is computed based upon the presence of ventricular or atrial fibrillation,
ventricular tachycardia, an RR or QT interval outlier, QT dispersion and the degree of T-wave complexity.

According to yet another example embodiment, a cardiac repolarization signal is constructed by identifying T-wave offset and T-wave onset. A portion of an ECG between (or about between) T-wave onset and T-wave offset is isolated from the remainder of the ECG to construct a time series consisting primarily of repolarization activity, which can then be subsequently analyzed to evaluate T-wave alternans, T-wave morphology changes, T-wave complexity, T-wave variability, or other methods of analysis.

The above summary is not intended to describe each embodiment or every implementation of the present disclosure. The figures and detailed description that follow more particularly exemplify various embodiments.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention may be more completely understood in consideration of the following detailed description of various embodiments of the invention in connection with the accompanying drawings, in which:

FIG. 1A is a data flow for an approach to providing a T-wave offset, consistent with one or more example embodiments of the present invention;

FIG. 1B provides an example high-level data flow for computing a QT interval, as may be implemented in connection with FIG. 1A, consistent with one or more example embodiments of the present invention;

FIG. 2 provides an example detailed data flow and decision diagram for computing a QT interval, consistent with one or more example embodiments of the present invention;

FIG. 3 provides an example data flow and decision diagram for creating a cardiac repolarization signal, consistent with one or more example embodiments of the present invention;

FIG. 4 provides an example data flow and decision diagram for identifying T-wave offset using an emphasis signal, consistent with one or more example embodiments of the present invention;

FIG. 5 provides an example data flow and decision diagram for computing a validity metric, consistent with one or more example embodiments of the present invention;

FIG. 6 provides an example data flow block diagram and example waveforms for a technique that provides a systematic adjustment of T-wave offset involving clustering of T-waves with similar morphology followed by alignment of T-waves within the cluster, consistent with one or more example embodiments of the present invention;

FIG. 7 provides an example embodiment of a system that employs a battery or passively powered subject device for collecting ECG in communication with a data collection or review system, consistent with one or more example embodiments of the present invention;

FIG. 8 provides an example data flow diagram for computing a dynamic signal-to-noise ratio, according to another example embodiment of the present invention; and

FIG. 9 shows another flow diagram involving the processing of an ECG signal to provide a T-wave offset, in accordance with another example embodiment of the present invention.

While the invention is amenable to various modifications and alternative forms, specifics thereof have been shown by way of example in the drawings and will be described in detail. It should be understood, however, that the intention is not to limit the invention to the particular embodiments described. On the contrary, the intention is to cover all modifications, equivalents, and alternatives falling within the scope of the invention including aspects defined in the claims.

DETAILED DESCRIPTION

Aspects of the present invention relate to methods and devices for assessing repolarization activity. More particular aspects are directed to identifying accurate, consistent, and valid T-wave offset points within an ECG of human or animal subjects. Identification of accurate, consistent, and valid T-wave offset feature points in an ECG is useful in connection with measurement of QT interval and for creating a cardiac repolarization signal for evaluation of repolarization activity of a heart.

In connection with various embodiments of the present invention, accurate and consistent QT interval measurements are for a variety of applications such as those involving measurement of the QT interval of ambulatory subjects in environments susceptible to noise. The noise contained in these signals can vary in character and composition. For many applications, these signals include in-band noise whereby the spectral content of the noise overlaps with the spectral content of the ECG signal, which can present challenges to the detection/measurement and use of signals as discussed herein. In-band noise can be problematic because, unlike noise with spectral content outside the signal bandwidth, removing in-band noise without introducing distortion in the ECG signal can be particularly challenging. Various embodiments of the present invention are directed to the processing of signals having reduced in-band noise, to facilitate a determination of a validity-type aspect of the signals for evaluation thereof, and related provision of signals (e.g., as an output) with a relatively high degree of confidence in the validity of the signals. Certain embodiments are also directed to the reduction of in-band noise and, in many applications, reducing such in-band noise without significantly distorting the ECG signal. These embodiments may be implemented with the analysis of the portion of the ECG associated with cardiac repolarization, thereby improving the accuracy and consistency of subsequent analysis of repolarization activity.

The T-wave offset point can be selected and provided based upon one or more of a variety of approaches. In connection with one embodiment, a T-wave offset point of an ECG signal is provided as follows. The location of a QRS complex in the ECG signal is identified and used for determining a first time window of the ECG signal in which to search for the T-wave offset point. The T-wave offset point is identified within the first time window, and the identified T-wave offset point is provided as an output based upon a noise characteristic of the ECG signal in a second time window that includes at least a portion of the T-wave.

In other embodiments, the identified T-wave offset point is provided based upon a comparison of the noise characteristic to a threshold. Other embodiments are directed to providing the identified T-wave offset point based upon a presence, in the cardiac cycle, of at least one of: atrial fibrillation, QT dispersion in a multi-lead ECG exceeding a threshold, T-wave morphology complexity exceeding a predefined threshold, ventricular ectopy, a QT interval measurement that falls outside of a user-defined physiologic outlier value or a statistical outlier value. In certain embodiments, the identified T-wave offset point (or a plurality of such identified points) is used to assemble a time series of the provided QT interval values, which can be subjected to analysis of variability.

The second time window can be defined in one or more manners to suit various embodiments and applications, and may include the identified T-wave offset point. In some
embodiments, the duration of the second time window can be set to about 30% of the duration of a nominal QT interval of the ECG signal, and extends beyond the T-wave offset point by about 10% of the nominal QT interval duration. In one example, the second time window may have a duration of about 50 msecs and be centered on about (e.g., within a few milliseconds of) the identified T-wave offset point. In another embodiment, the second time window extends from about the point of a large deflection of the T-wave from an isoelectric line of the ECG signal to (or near) the T-wave offset point. In other embodiments, the second time window includes a time period extending from about a QRS onset point in the ECG signal to about the T-wave offset point. In still other embodiments, the second time window includes a time period extending the full duration of a cardiac cycle in the ECG signal.

5 The noise characteristic may be obtained in one or more of a variety of manners, depending upon the application. In some embodiments, the noise characteristic is computed as follows. The ECG signal is decomposed into subcomponents, and subcomponents in the second time window are identified as primarily associated with either noise or the T-wave of the underlying ECG signal. A denoised signal is computed for the second time window by combining the subcomponents that are primarily associated with the T-wave. A noise signal is computed for the second time window by combining the residual subcomponents not primarily associated with the T-wave (e.g., the residual components being those not combined to form the denoised signal). The noise characteristic is then computed based upon aspects of the noise and/or denoised signal. For example, the noise characteristic can be computed using one or more of energy of the noise signal, standard deviation of the noise signal, zero crossing density of the noise signal, a metric of noise amplitude computed using an envelope of the noise signal, and a metric of energy of the denoised signal relative to energy of the noise signal. Further, metric of energy of the denoised signal relative to energy of the noise signal may be a signal-to-noise ratio of the ECG signal within the second time window.

In other embodiments, the noise characteristic is computed as follows. A denoised signal is computed for the second time window using at least one of a band-pass filter, wavelet thresholding, and an adaptive filter that passes primarily T-wave energy. A residual of the step of computing the denoised signal is captured as the noise signal for the second time window. The noise characteristic is computed based upon one or both of the noise and denoised signals, such as by using one or more of energy of the noise signal, standard deviation of the noise signal, zero crossing density of the noise signal, a metric of noise amplitude computed using an envelope of the noise signal, and a metric of energy of the denoised signal relative to energy of the noise signal.

With respect to the above and other discussion herein, the term envelope, as applied to a noise signal by way of example, refers to a curve joining the successive peaks of the noise signal following smoothing or low-pass filtering. One approach for computing the envelope involves applying a Hilbert transform of the noise signal, computing the absolute value of the transform output, and then low-pass filtering the absolute values.

Another example embodiment is directed to a method for providing a repolarization signal for a cardiac cycle of an ECG signal. The location of a QRS complex in the cardiac cycle is identified and used to further identify T-wave onset and offset points in the signal, which are in turn used to respectively define the start and end of the repolarization signal for the cycle. A noise characteristic of the ECG signal is determined for a time window spanning from about the start to about the end of the repolarization signal, and the repolarization signal is provided as an output, based upon the determined noise characteristic. The noise characteristic can be determined using one or more of a variety of approaches, such as those discussed above.

In some implementations, the repolarization signal is provided as an output based upon a comparison of the noise characteristic to a threshold. In other implementations, the repolarization signal is provided as an output based upon the determined noise characteristic and the presence in the cardiac cycle of at least one of: atrial fibrillation in the ECG signal, a degree of QT dispersion exceeding a threshold when the ECG signal is a multi-lead signal, T-wave morphology complexity of the ECG signal exceeding a threshold, ventricular ectopy, and a QT interval measurement that falls outside of a user-defined physiologic outlier value or a statistical outlier value. In some implementations, the provided repolarization signal is appended to a matrix of repolarization signals in which a dimension of the matrix corresponds to the number of cardiac cycles of the ECG signal.

Another example embodiment is directed to a method for providing a time series of beat-to-beat QT interval values from a digitized ECG signal of an ambulatory subject. The location of a QRS complex and a Q-wave QT onset point of a cardiac cycle of the ECG signal are identified and used for determining a first time window of the cardiac cycle in which to search for a T-wave offset point for a T-wave in the cardiac cycle. The T-wave offset point is identified within the first time window, and a QT interval value is computed using the identified Q-wave onset point of the QRS complex and the identified T-wave offset point. The QT interval value is included in a time series of beat-to-beat QT interval values, based upon a noise characteristic of the ECG signal in a second time window that includes at least a portion of the T-wave. The noise characteristic can be computed in one or more of a variety of manners, such as described above. In various implementations, the series of beat-to-beat QT intervals consists of QT interval values having error due to noise that is less than 2.5% of the mean QT interval of the ECG signal, and generated using the aforementioned inclusion approach. Such an error condition can be achieved, for example, as facilitated by the use of a second time window, which may be limited to a range about the T-wave offset point, and further by the use of denoising approaches as discussed and/or referenced herein or in the above-noted patent documents to which benefit/priority is claimed.

In various implementations, energy that is not primarily associated with T-wave energy in the first time window of the digitized ECG signal is suppressed, prior to identifying the T-wave offset point. This suppression can be achieved using, for example, one or more of MDSP denoising, wavelet threshold denoising, band-pass filtering, and adaptive filtering.

The QT interval value is included in the time series of beat-to-beat QT interval values, based upon one or more conditions. In one implementation, the QT interval can be included based upon a comparison of the noise characteristic to a threshold value. In another implementation, the QT interval value is included based upon the noise characteristic and the presence, in the cardiac cycle, of at least one of: atrial fibrillation, ventricular ectopy, QT dispersion in a multi-lead ECG exceeding a threshold, T-wave morphology complexity exceeding a predefined threshold, ventricular ectopy, a QT interval measurement that falls outside of a user-defined physiologic outlier value or a statistical outlier value.
Various embodiments are also directed to implementing one or more approaches as discussed herein, via a computer circuit executing instructions to carry out the various functions. In some embodiments, instructions are executed to repeat the steps as discussed herein to compute a plurality of QT interval values. Each QT interval value is included in a time series of beat-to-beat QT interval values based upon a comparison of a noise characteristic of a corresponding ECG signal in the second window to a predefined threshold.

For general information regarding exemplary aspects including performance aspects, as may be effected and/or realized in connection with various embodiments of this invention for providing beat-to-beat QT intervals, reference may be made to M. Brockway and R. Hamlin, “Evaluation of an algorithm for highly automated measurements of QT intervals,” Journal of Pharmacological and Toxicological Methods, 2011, Article in press, doi:10.1016/j.jvp.2011.05.004, which is fully incorporated herein by reference.

Many embodiments described here are directed to signal processing approaches that may be implemented in accordance with those referred to as Multi-Domain Signal Processing (MDSP), and Multi-Domain Filtering (MDF) that uses MDSP to denoise physiological signals, as exemplified in U.S. patent application Ser. No. 12/938,995, entitled “Physiological Signal Denoising,” which is referenced above and fully incorporated herein by reference. Various embodiments may implement noise filtering and signal denoising using one or more approaches as described herein.

In the following discussion, reference is made (in brackets) to number of references listed in order near the end of this document, which are fully incorporated herein by reference. These references may assist in providing general information regarding a variety of fields that may relate to one or more embodiments of the present invention, and further may provide specific information regarding the application of one or more such embodiments. Accordingly, one or more embodiments as described herein may be implemented in accordance with, or otherwise using, information, approaches, devices and systems as may be described in these references.

Turning now to the figures, and referring to FIG. 1A, a data flow diagram exemplifies approaches for providing a T-wave offset, consistent with one or more example embodiments of the present invention. At block 120 the location of a QRS complex in the ECG signal is identified, and the identified location is used at block 130 for determining a first time window of the ECG signal in which to search for the T-wave offset point. At block 140, the T-wave offset point is identified within the first time window, and the identified T-wave offset point is provided as an output at block 150, based upon a noise characteristic of the ECG signal in a second time window that includes at least a portion of the T-wave. Various embodiments and implementations as discussed above (and otherwise herein) may be implemented in connection with the approach shown in FIG. 1, including those directed to obtaining and using a noise characteristic.

According to example embodiments involving the computation of QT interval, and referring to FIG. 1B, an input ECG signal 101 is denoised and Q-wave onset and T-wave offset points are identified using the denoised ECG in process 102. In many embodiments, ECG signal 101 has been filtered to remove noise energy outside the bandwidth of the sensed electrical activity of the heart and has been digitized using an analog-to-digital converter. Such filtering can be accomplished using a variety of well-known methods and the passband of the filter will vary depending upon the species. As an example, a passband often used for human ECGs is 0.05 to 100 Hz. In some embodiments, a dynamic signal-to-noise ratio (dSNR) and a validity metric (VM) are computed in process 102 and used to assess the validity of the onset and offset points as well as ECG sensor integrity. In some embodiments, dSNR and VM is computed for a portion of the T-wave where the presence of noise can impact the accuracy of T-wave offset detection. In other embodiments, VM can be computed for a complete cardiac cycle. VM is evaluated relative to predetermined thresholds, T1, T2 and T3, in decision processes 103, 107 and 111 where T3>T2>T1. Evaluation of the VM is useful to determine the disposition of the information derived from a cardiac cycle and in particular, can be useful in determining if the information should be retained, discarded, or if there is value in having a human being review the QT interval measurement result provided by the algorithm. In some embodiments, the QT interval is computed if the VM>T2, and is otherwise classified as uninterpretable in process 105 (e.g., the T-wave offset information for that cardiac cycle cannot be determined). Cardiac cycles determined as being uninterpretable may generally refer to signals that have a noise and artifact level that is so high that review by a human being will render no additional useful information. In some embodiments a count of cardiac cycles is tallied, in process 106, that are determined to be uninterpretable (e.g., VM<T2 and/or discarded) as an indicator of signal quality.

If VM for a particular cardiac cycle is greater than T2 but, in decision process 111, is found to be less than T3, then the information for that cardiac cycle is classified as uncertain in process 113 and may be flagged for later review by a human being. If, in decision process 111, VM=T3 then the information for that cardiac cycle is classified as valid in process 112. In some embodiments, QT interval measured for those cardiac cycles classified as valid is considered to be sufficiently accurate and consistent that review by a human being adds no additional value or accuracy improvement, and those QT interval measurements are hence derived in a fully automated manner and without any human intervention.

In some embodiments, cardiac cycles classified as uncertain are recommended for review by a human being. The ECG for cardiac cycles classified as uncertain may be visually displayed to a human being along with the marker location for Q-wave onset and T-wave offset. The human operator can then accept the markers as determined by the algorithm, discard the cardiac cycle computing a QT interval, or move a marker if it is believed to be incorrectly placed by the algorithm.

In some embodiments, a time series of beat-to-beat QT interval values is further analyzed using techniques such as QT interval alternans and QT interval variability as markers of arrhythmic risk. In various embodiments, techniques used to analyze beat-to-beat QT interval measurements include root mean square of successive differences, standard deviation of successive differences, short-term variability using a mean of successive differences, long-term variability computed as the length of the long axis of the ellipsoid of a Poincare plot, and multiscale entropy. In another embodiment, valid QT values are averaged over a predetermined time period (e.g., 30 seconds) to compute a mean QT interval.

In some embodiments a sensor failure alarm is triggered if the ECG is excessively noisy or if the ECG signal is absent. Either of these conditions can lead to a very low dSNR. This may indicate that an electrode has become loose or has fallen off the subject, or it may indicate that a lead connecting the electrode to a monitoring device may have become broken. In these embodiments dSNR is compared to a threshold T1 in decision process 103 and if dSNR is <T1, a sensor failure alarm is triggered in process 104. In some embodiments, the
sensor failure alarm is only triggered after dSNR has remained below threshold T1 for a predetermined period of time in order to reduce the risk of false alarms.

According to other example embodiments, FIG. 2 shows more detailed approaches for computing the QT interval. In an example embodiment, an input ECG signal 201 is present in a first domain and is composed of an underlying ECG signal and a noise signal. For the purposes of this explanation, underlying ECG signal refers to the sensed electrical activity generated by the heart. Noise signal refers to sensed electrical activity generated by noise sources independent of the heart such as muscle EMG and measurement artifact caused by dynamic changes in electrical properties of the tissue-electrode interface of the sensor. Signal 201 is decomposed into subcomponents in a second domain of higher dimension than the first domain in process 202. In some embodiments, decomposition is accomplished using a discrete cosine transform [1], Fourier transform [2], filter bank [3], Gabor transform [4] or Karhunen-Loève transform [5, 6]. In another embodiment, decomposition is accomplished using a wavelet-related transform and the decomposition levels correspond to wavelet scales [7]. In another embodiment, decomposition is achieved by representing the observed signals as a linear combination of basis functions. Signal decomposition embodiments and the use of subcomponents derived from the decomposition for denoising (i.e. removal of at least some of the in-band noise contained in the signal), extraction of information from the signal, and evaluation of the quality of extracted information is referred to as Multi-Domain Signal Processing (MDSP) by way of example, in the discussion herein. Use of MDSP techniques for removal of in-band noise from a signal is referred to as Multi-Domain Filtering (MDF), also by way of example.

Subcomponents are evaluated in process 203 to determine if those contained within a defined time window are primarily associated with noise or primarily associated with the underlying ECG signal. Each ECG signal wave (e.g., R-wave, Q-wave, T-wave, and P-wave) contributes energy to one or more subcomponents. The association of a set of one or more subcomponents with a particular signal wave (e.g., T-wave, QRS-waves, and P-wave) pertains to the representation of energy contained within a signal wave within the associated subcomponents [8]. In some embodiments, spatially selective filtering is employed. In this embodiment the subcomponents associated with the underlying ECG change during the time course of the cardiac cycle. Spatially-dependent selection of subcomponents within the cardiac cycle is determined according to time location of the subcomponents relative to the QRS complex. For example, once a QRS complex is identified, the approximate location of the T-wave is known. Subcomponents primarily associated with T-wave energy are selected as related to the underlying ECG signal during the time spanning the approximate T-wave location, and those subcomponents not associated with T-wave energy during this time span are said to be primarily associated with noise. Subcomponents may contain both energy of the underlying ECG signal and noise energy. For the purposes of this discussion, subcomponents are said to be associated with a particular signal wave of the ECG if more than about 50% of the energy in the subcomponent is energy of the underlying ECG signal wave.

Determining whether a subcomponent is primarily associated with noise or ECG signal, or denoising the subcomponents within the second domain, can be accomplished by using one or more of principal component analysis (PCA), independent component analysis (ICA), periodic component analysis (nICA) and spatially selective filtering (SSF). PCA and ICA are applicable to multi-lead ECG, while RCA and SSF can be applied to either multi-lead or single-lead ECG. The PCA technique [9, 10] uses subcomponent covariance information to orthogonally separate subcomponents. The orthogonalized subcomponents with low signal power are often associated with noise and can be removed to achieve denoising. PCA can be used as a preliminary step prior to applying an ICA technique. The ICA technique further separates signal and noise sources [11] as a solution of an optimization problem that maximizes independence between them. The 7/CA technique computes and jointly diagonally and autocorrelation matrices of subcomponents to separate them based on their periodicity or quasi-periodicity. [12, 13] The RCA technique extracts most periodic subcomponents corresponding to ECG rhythm and, since noise is not generally periodic, it is left behind.

SSF techniques [14, 15, and 16] detect signal-related features and pass them across the subcomponents while blocking features inherent to noise, relying upon the differences of noise and signal distributions across decomposition levels. In one embodiment, an SSF approach is used to exploit the fact that most noise subcomponents are confined to decomposition levels that represent high frequencies. In this embodiment, the locations of signal features are identified by examining subcomponents corresponding to lower frequency. The QRS location is identified, and a QRS window surrounding the detected QRS wave is created. The subcomponents associated with high frequencies are preserved within the QRS time window. The remainder of the cardiac cycle is assigned to a second time window where the high-frequency subcomponents are zeroed. QRS wave location for creating the first time window can be identified as high amplitude changes in peaks and valleys that occur simultaneously across multiple decomposition levels associated with lower frequencies. Techniques such a correlation or multiplication of these low-frequency subcomponents can be useful for computing an emphasis signal that provides for improved detection of the QRS complex in a noisy ECG. The subsequent emphasis signal can be passed through a constant or adaptive threshold detector to locate the QRS complex.

In another embodiment, some artifacts can be detected as large peaks present in subcomponents corresponding to high frequency. These artifacts can then be removed by zeroing subcomponents where the large peaks were detected. By zeroing out the subcomponents of time segments within subcomponents associated with noise, and reconstructing the ECG signal using those subcomponents associated with the ECG signal, the in-band noise level in the ECG is substantially reduced, or "denoised", to create a denoised ECG. A denoised signal can be reconstructed by performing the inverse of the transform used to decompose the signal on the denoised subcomponents. For general information regarding example denoising techniques that can be used in this and related embodiments, reference may be made to U.S. patent application Ser. No. 12,938,995, referenced above.

In some embodiments signal energy relative to noise energy in second window 218 is computed as a signal-to-noise ratio (SNR) as in process 204. In one embodiment second window 218 spans from about the T-wave peak to shortly after the T-wave offset point. In other embodiments, the duration of second window 218 is a percentage of the QT interval, 30% for example. In this embodiment ½ of the duration of window 218 spans before T-wave offset and ½ extends after T-wave offset. In another embodiment, window 218 has a fixed duration for a given species. For
example, for human beings window 218 may be about 50 msec in duration and is approximately centered on the T-wave offset point.

In one embodiment, referring to FIG. 8, SNR (dSNR) is computed as the ratio of the energies in signal and noise subcomponents. Input signal 801 in a first domain is decomposed into subcomponents, referred to as set D22a, in a second domain of higher dimension in process 802.

The dimension of the first domain is evaluated in decision process 803. If the dimension of the first domain is larger than 1 then a PCA or ICA technique can be used to identify at least some of the subcomponents primarily associated with noise in process 804. The noise subcomponents extracted at this initial denoising step are discarded and the residual noise and signal subcomponents are evaluated using SSF or PCA in process 805. The noise subcomponents identified in process 805, D22a, are used to compute an estimate of noise energy in process 806. The residual subcomponents, D22a, are used to compute an estimate of signal energy in process 806.

If the dimension of the first domain evaluated in decision process 803 equals 1 (e.g., a single channel ECG signal), then subcomponents primarily associated with noise, referred to as set D22a, are identified using SSF or PCA in process 807. The residual subcomponents, D22a, are those primarily associated with an underlying ECG signal. In these contexts, signals primarily associated with noise are those signals having an energy value of which at least half is from noise components. Similarly, signals primarily associated with an underlying ECG signal are those having an energy value of which at least half is from an underlying ECG signal. In process 808, an estimate of noise energy is computed using subcomponents D22a and an estimate of signal energy is computed using subcomponents D22a.

Once noise energy and (underlying ECG) signal energy are computed in processes 806 and 808, dSNR is then computed in process 809 according to formula:

\[ SNR_{dSNR} = \log_{10}\left(\frac{P_{signal}}{P_{noise}}\right) \]

where \(P_{signal}\) and \(P_{noise}\) are respective signal and noise energy. Using this approach, dSNR can be updated on a sample-by-sample basis, and can likewise be computed for a group of sample points or a time window. In one embodiment dSNR is computed for each cardiac cycle. In other embodiments, dSNR is computed for a time window surrounding the location of a detected feature point (e.g., T-wave offset) and can be used to assess validity of the detected feature point. Alternate embodiments may involve updating dSNR more or less often. For example, it may be useful in some embodiments to compute a value of dSNR for a window of two to ten cardiac cycles and use this value in calculation of the validity metric for all cardiac cycles within the window.

In other embodiments, signal-to-noise ratio is estimated using conventional approaches following denoising of the signal using an MDF-based embodiment as discussed herein, or using conventional approaches in combination with the approach(es) described in FIG. 8. In one embodiment, the noise is measured between signal waves by computing the peak amplitude and density of zero crossings. In other embodiments, a signal-to-noise ratio is estimated by computing a spectral distribution of the denoised ECG signal. In this embodiment, peaks in the spectral distribution are evaluated to determine the relative power in the spectrum that occurs within and outside of the normal range of the QRS complex, T-wave, and P-wave.

In various embodiments, and referring to FIG. 2, subcomponents are used to compute T-wave (process 205), QRS (process 206), and Q-wave (process 207) emphasis signals that exaggerate peaks, valleys, and slopes of an ECG wave for identifying feature points. As an example, R-wave identification is accomplished by generating a QRS emphasis signal that highlights the significant slopes of the R-wave by combining subcomponents associated with the R-wave. Likewise, T-wave offset identification is achieved by computing an emphasis signal from subcomponents associated with the T-wave.

The specific subcomponents associated with the R-wave, Q-wave, or T-wave depend upon the decomposition technique used, sampling rate, frequency content of the signal wave, and the species from which the ECG was recorded. As an example, when decomposition is accomplished using a discrete wavelet-related transform of a human ECG sampled at 250 Hz, the associated R-wave subcomponents correspond to wavelet scales 2^1 through 2^4. The associated T-wave subcomponents for this same scenario correspond to wavelet scales 2^3 to 2^5. In this example, the set of subcomponents associated with R-waves and T-waves overlap and are discriminated based on temporal occurrence by creating a search window relative to the QRS complex in process 210. In one embodiment, all subcomponents associated with a signal wave are combined to create the emphasis signal. In another embodiment, a subset of these subcomponents is used to compute the emphasis signal. In one embodiment, evaluation of the emphasis signal to detect a feature point is accomplished using techniques described by Martinez et al [8] based upon examination of the pattern of significant peaks, valleys, and zero crossings within the emphasis signal. In one embodiment of process 208, the R-wave is detected by applying an adaptive threshold technique [17] to the emphasis signal. In one embodiment of process 213, T-wave offset is identified as the first baseline point after the last significant peak or valley of the T-wave emphasis signal. In another embodiment a combination of the emphasis and denoised signals are used to detect feature points.

To identify Q-wave onset in process 214, a search window is created in process 211 to identify a time window relative to the R-wave where Q-wave onset is expected to occur. The denoised subcomponents associated with the QRS-wave are used to compute an emphasis signal in process 207 that is subsequently evaluated to identify the Q-wave onset point in process 214. In one embodiment, Q-wave onset is identified as the last baseline point prior to the first significant peak or valley of the QRS-wave emphasis signal. To improve the accuracy of identifying T-wave offset and Q-wave onset, search windows are created relative to the location of the R-wave in processes 210 and 211 to limit identification of the offset and onset times to windows in time within the cardiac cycle where it would be reasonable for the respective onset and offset to occur.

Once Q-onset and T-offset are identified in processes 213 and 214, QT interval is computed in process 215. In some embodiments, a determination is made as to whether the QT interval is accurate and valid. This can be accomplished by computing a validity metric (VM) in process 212 and then comparing the validity metric to a threshold T3 in decision process 216. If VM>T3, then the QT interval computed in process 215 is considered valid. If not, then the QT measurement for that cardiac cycle is discarded as in process 217. The validity metric computed in process 212 is a function of
dSNR computed in process 204 and rhythm and morphology characteristics computed in process 209. Rhythm and morphology characteristics may include characteristics indicative of the presence of atrial fibrillation, QT dispersion when the ECG signal is a multilead signal, and complexity of T-wave morphology. In some applications, such as when computing a cardiac repolarization signal, the validity metric is modulated based upon the presence of ventricular ectopy such that a repolarization wave is excluded for a cardiac cycle containing a ventricular ectopy. In some applications where QT interval is computed, including QT measurements from cardiac cycles containing ventricular ectopy may improve the predictive value of QT variability assessments [18]. In this application it would therefore not be desirable to modulate VM as a function of the presence of ventricular ectopy.

In an alternate embodiment, the ECG is denoised using MDL techniques and the feature points of Q-wave onset and T-wave offset can be evaluated using traditional techniques in order to measure QT interval. This approach can be useful in some applications because the accuracy of feature point identification can be improved by using a denoised ECG. In another embodiment, it is possible to compute T-wave offset using an MDSP embodiment described above and compute Q-wave onset from a denoised ECG using traditional techniques. As an example, Q-wave onset can be identified using either threshold, derivative-based, or pattern matching methods applied to the denoised ECG signal. In the threshold model, a region that precedes the first peak or valley associated with R-wave where at least a few samples are below a pre-specified threshold is found. The Q-wave onset is determined as a last point in the identified region. In the derivative-based method an emphasis signal is computed by differentiating the denoised ECG. A region in the emphasis signal is identified preceding the first peak or valley associated with the R-wave emphasis signal where at least a few samples are below a predetermined threshold. The Q-wave onset is identified as the last point in the region.

A pattern or template matching method can also be applied to the denoised ECG. In this approach, a user selected or signal averaged template of the ECG of a representative cardiac cycle is created and subsequently cross-correlated with the ECG to be analyzed. In another embodiment a template can be automatically generated by signal-averaging cardiac cycles for which VM>73. The QRS onset is identified in the template either manually by the user, by using threshold techniques or by derivative based method applied to the template. Once Q-wave onset is identified in the template, the template is cross-correlated with cardiac cycles of the ECG to be analyzed. The template is shifted in time to maximize the cross-correlation function of the full cardiac cycle. In some embodiments, the template can be further shifted to improve the cross correlation between Q-waves of the cardiac cycle under evaluation and the template. The QRS onset is identified from the matched template.

Various embodiments are directed to creating a cardiac repolarization signal. In an example embodiment, and referring to FIG. 3, a cardiac repolarization signal is constructed by isolating the portion of the ECG signal corresponding to the T-wave and suppressing (actively or passively) all other signal waves (e.g., QRS complex, P-wave) and noise. In some embodiments, all or most of the activity in a plurality of cardiac cycles is suppressed except for the T-wave, or repolarization wave, and T-waves from multiple cardiac cycles are aligned sequentially to form a time series representing a cardiac repolarization signal. In another embodiment, the isolated T-waves are joined together to form a time series representing a cardiac repolarization signal. In another embodiment a cardiac repolarization signal consists of organizing the isolated T-waves into a matrix. The length of rows in the matrix is determined by the sampling rate and the length of the longest T-wave and the number of rows is determined by the number of valid T-waves in the ECG segment for which repolarization activity is to be analyzed. The matrix rows containing T-waves can then be added with zero or the isoelectric ECG value to match the longest T-wave in the segment. The T-waves in the matrix can then be aligned by their peak. In some implementations, a signal that consists primarily of ventricular repolarization activity is created using these approaches to facilitate analysis of the repolarization activity of the heart independent of atrial activity and ventricular depolarization activity and mitigate potential issues with the high level of spectral energy in the QRS complex leaking into the bandwidth of the T-wave and biasing the result.

In connection with other embodiments, a denoised cardiac repolarization signal is created to facilitate the use of several analysis methods that can identify and evaluate repolarization abnormalities and can potentially improve the accuracy of results provided by these methods of analysis. These analysis methods include T-wave alternans, T-wave variability, T-wave morphology changes, and T-wave complexity. Various embodiments, beat-to-beat variability of T wave parameters is measured using one or more of the following metrics [18, 19, and 20]:

- Standard Deviation of T wave parameter from N consecutive beats—SD
- Root mean square of N successive differences of the T wave parameter—RMSSD
- Standard deviation of N successive differences of the T wave parameter SDS
- Beat-to-beat variability of successive differences measured as 2*SD−1/2*SDSD
- Short-term variability of the T wave parameter,

\[ STV = \frac{1}{N} \sum_{i=1}^{N} |D_{n-1} - D_{n}| / [N \sqrt{2}] \]

where \( D_{n-1} \) is a T wave parameter from n\(^{th} \) beat

- Long-term variability of the T wave parameter:

\[ LTV = \frac{1}{N} \sum_{i=1}^{N} |D_{n-1} + D_{n} - 2D_{mean}| / [N \sqrt{2}] \]

where \( D_{n-1} \) is a T wave parameter from n\(^{th} \) beat

In another embodiment nonlinear measures of complexity of repolarization dynamics such as multiscale entropy [21] are computed to measure variability beyond a single beat lag.

In one embodiment a denoised cardiac repolarization signal is created by isolating the T-wave in a series of cardiac cycles that have been denoised using MDE. T-wave isolation is accomplished by identifying the onset of the T-wave (T-wave onset), the offset of the T-wave (T-wave offset), and then removing those portions of the ECG that fall outside the time between T-wave onset and offset of a cardiac cycle (or otherwise using the portions of an ECG signal lying within a time window generally extending from the T-wave onset to offset). One or more of the steps employed for isolating the repolarization wave for a cardiac cycle can be accomplished in a manner consistent with the embodiments described for measuring QT interval for a cardiac cycle. In one embry-
As consistent with other embodiments described herein, a denoised cardiac repolarization signal is used to assess repolarization abnormality using one or more of T-wave alternans, T-wave variability, T-wave morphology changes, and T-wave complexity. T-wave alternans (TWA) are defined as beat-to-beat fluctuations in amplitude, polarity, or shape of a T-wave. In one embodiment, T-wave alternans can be measured as spectral energy at one-half the heart rate. In another embodiment, a time-based metric is calculated by separating the cardiac cycles into even and odd beats. A weighted average of odd and even beats can then be calculated and TWA is quantified as the difference between the averaged odd and even beats. In another embodiment, a time-frequency based metric of TWA is calculated by performing a stationary wavelet periodogram of the repolarization signal. The TWA are quantified as a ratio of power at adjacent wavelet scales.

In other embodiments, repolarization abnormalities are characterized by evaluating aspects of T-wave variability. In one embodiment, feature points of valid denoised T-waves are identified using the emphasis signal and variance of the T-wave or T-wave emphasis signal at these feature points is computed. These feature points may include the positive peak amplitude, negative peak amplitude, amplitude approximately midway in time between onset and peak, and amplitude approximately midway in time between peak and offset. In another embodiment, variability and trends in time of the feature points relative to, for example T-wave onset, is analyzed as a means of characterizing repolarization abnormalities and changes. In another embodiment, valid denoised T-waves are segmented into equal intervals (e.g., first one-fourth, second one-fourth, etc.) and area or amplitude variability of each segment is computed for an ECG segment consisting of several (e.g., 10 to 500) cardiac cycles.

Changes in T-wave morphology can be indicative of reduced repolarization reserve leading to a proarrhythmic scenario. In one embodiment, T-wave morphology is quantified using extracted feature points of the emphasis signal, as described above, and changes in T-wave morphology metric are tracked over time (e.g., hours, days, weeks, or months). In one embodiment, at least one of beat-to-beat variability metrics and multiscale entropy of T-wave parameters can be computed and trended in time. Unusual patterns in T-wave morphology can be used as a marker of impending arrhythmia. In one embodiment, these patterns can be detected as changes in a T-wave complexity metric, with the metric computed as described later.

Various embodiments are directed to computing and evaluating an emphasis signal for detecting Q-wave onset and T-wave offset points. In an example embodiment, and referring to FIG. 4, an ECG signal is decomposed into subcomponents in a second domain of higher dimension than the first domain. The subcomponents are denoised by identifying and excluding those subcomponents that are primarily associated with noise at a particular point in time. An emphasis signal for a signal wave is computed by combining one or more subcomponents that are primarily associated with the signal wave and the emphasis signal is evaluated for identifying transitions and features within the ECG. Identifying Q-wave onset and T-wave offset, for example, involves creating an emphasis signal for each signal wave by combining the associated subcomponents and then identifying appropriate peaks, valleys, and baseline points of the emphasis signal.

In connection with various embodiments, the specific subcomponents associated with each signal wave (e.g., T-wave and Q-wave) are used in accordance with the species, sampling rate, and decomposition method used. For example, if decomposition is achieved using a discrete wavelet-related
transform, the species is a human being, and the ECG is sampled at 250 Hz, the T-wave associated subcomponents correspond to wavelet scales 2^4 and 2^5. The emphasis signal that is computed from one or two of these scales is proportional to the derivative of the filtered version of the T-wave. Referring to the right side of FIG. 4, two different T-wave morphologies and the corresponding T-wave emphasis signals are shown with T-wave offset marked by a vertical dashed line on both the ECGs and the emphasis signals. The T-wave emphasis signal is evaluated to identify T-wave offset based upon an evaluation of the pattern of peaks, valleys, and zero crossings. As can be seen in FIG. 4, T-wave offset is identified as the first baseline point following the last significant peak or valley in the T-wave emphasis signal.

The Q-wave emphasis signal is evaluated using similar techniques. In one embodiment, decomposition subcomponents associated with the Q-wave correspond to wavelet scales 2^2 through 2^4 assuming a human ECG sampled at 250 Hz and decomposed using a discrete wavelet-related transform. These subcomponents are combined to create an emphasis signal that is evaluated beginning at the peak of the R-wave, going backward in time. Referring to the left side of FIG. 4, two different QRS morphologies and the corresponding Q-wave emphasis signals are shown. As can be seen in FIG. 4, Q-wave onset is identified (as shown by the vertical dashed line) as the first baseline point prior to the first significant peak or valley of the emphasis signal prior to the location of the R-wave peak.

In some embodiments, noise is removed from the subcomponents in order to create a less noisy emphasis signal. Reduction of noise in the emphasis signal facilitates more accurate and consistent detection of peaks, valleys, and baseline points during the process of identifying T-wave offset, T-wave onset, Q-wave onset, and the R-wave. One denoising approach involves identifying subcomponents that are primarily associated with noise so that they can be eliminated during reconstruction of the signal. This is accomplished by using one or a combination of principal component analysis (PCA), independent component analysis (ICA), periodic component analysis (ACA) and spatially selective filtering (SSF).

The PCA technique can be applied to multi-lead ECG and uses information on subcomponent covariance to orthogonalize subcomponents. The orthogonalized subcomponents with low signal power are often associated with noise and can be removed to achieve denoising. PCA can be used as a preliminary step prior to applying an ICA technique to multi-lead ECG. The ICA technique can further be used to separate signal and noise sources as a solution of an optimization problem that maximizes independence between them. The ICA technique can be applied to both single lead and multi-lead ECG and computes and jointly diagonalizes covariance and autocorrelation matrices of subcomponents to separate them based on their periodicity or quasi-periodicity [12, 13]. The ICA technique extracts most periodic subcomponents corresponding to ECG rhythm and, since noise is not generally periodic, it is left behind.

SSF techniques can be used on either multi-lead or single lead ECG and detect signal-related features and pass them across the subcomponents while blocking features inherent to noise. The technique is based upon the differences in noise and signal distributions across decomposition levels. In one embodiment, spatially selective filtering is facilitated by a decomposition whereby signal energy is concentrated in a small number of large subcomponent coefficients while noise is spread out across many decomposition levels and is represented by small coefficients. In another embodiment, spatially selective filtering exploits the fact that most noise subcomponents are confined to levels that represent high frequencies. In this embodiment the locations of signal features are identified by examining subcomponents corresponding to lower frequency. The subcomponents associated with high frequency are then zeroed except those locations where the signal features were identified.

Computed QT intervals can be used to calculate metrics associated with reduced repolarization reserve and potential proarrhythmic scenario. Such metrics include:

Mean prolongation or reduction of QT interval
Standard Deviation of QT from N consecutive beats (SD)
Root mean square of N successive differences of QT intervals (RMSSD)
Standard deviation of N successive differences of QT intervals (SDSD)
Beat-to-beat variability of successive differences measured as 2*SD2−1/2*SDSD2
Short-term variability of QT interval, where $D_{n}$ is a QT interval from n-th beat
Long-term variability of QT interval:

\[ STV_{n} = \sum_{i=1}^{N} |D_{i+1} - D_{i}| / [N \sqrt{2}] \]

where $D_{n}$ is a QT interval from n-th beat

In another embodiment nonlinear measures of complexity of repolarization dynamic such as multiscale entropy [21] are computed to measure variability beyond a single beat lag. In another embodiment, changes in QT/RR hysteresis [22] are trended over time.

In another example embodiment, and referring to FIG. 5, a validity metric (VM) is computed for assessing the validity of a QT interval measurement or a repolarization wave identified in a cardiac cycle. In one embodiment, and referring to FIG. 5, VM is computed on a cardiac cycle-by-cycle basis. FIG. 5 shows several inputs that can be useful in computing VM. These inputs include: a) a signal 502 indicating whether atrial fibrillation (AF) is present in the cardiac cycle, b) QT interval 503 for the cardiac cycle, c) whether the cardiac cycle is an ectopic beat such as a premature ventricular contraction (PVC), d) degree of complexity of the T-wave morphology, and e) signal-to-noise ratio (SNR) for the second time window. When the ECG being evaluated is a multi-lead ECG, it can also be useful to employ a measure of the degree of dispersion of QT (QTD) measurements between leads [23] when computing validity. In one embodiment, each of these inputs can be selectively enabled in control input 501. For example, in some embodiments the flag is disabled for ectopic beats such that QT values obtained from such cardiac cycles are considered valid. This can be useful when QT variability is computed as an indicator of proarrhythmogenicity [18]. In other embodiments, such as when a repolarization wave is being isolated to construct a repolarization signal time series, the PVC flag is enabled so that ectopic beats are excluded from the repolarization time series.

Inputs 502, 503, 504, and 505 are each processed in a manner that if one of these input signals meets certain criteria
and the flag corresponding to the input is enabled, the multiplier Mx is set to 0 in process 520. The absence of one of the input signals 502 to 505 forces Mx=0, Mx=1 for the cardiac cycle. Mx is passed from process 520 to process 521 and is used as a multiplicative in the computation of VM. Hence if Mx=0, then VM=0 for that cardiac cycle. Hence, if Mx=0 a QT interval measurement or repolarization waveform for a cardiac cycle would be deemed invalid regardless of input SNR 507.

In some embodiments, input 502 contains information as to whether the cardiac cycle is part of an AF episode. If the cardiac cycle is determined to be part of an AF episode in decision process 508, the flag AF is set to a value True in process 515. Otherwise flag AF=False. If the AF Flag is enabled by input 501 and the AF Flag is True, then process 520 will set Mx=0. Modulating the value of VM according to the presence or absence of AF can be useful because, during AF, P (or F) waves may occur during the T-wave resulting in blurring T-wave offset or onset and distorted T-wave morphology.

In some embodiments, the value of QF for the cardiac cycle is contained in input 503. In decision process 509, the QT value is compared to a predetermined range corresponding to the outer borders of the physiological limits of the subject species. If the QT value is outside this range, then the QTo Flag is set to True. If the QT value is within physiological range, then it is evaluated in decision process 512 to determine if it is a statistical outlier (e.g., outside of a statistical range). In process 512, the QT value is compared to a range defining normal and outlier values. In one embodiment, an outlier is defined as mean or median +/-3 standard deviations of QT interval for beats in a predefined time window. In some embodiments a QT interval is evaluated relative to a predefined limit to avoid discarding valid QT interval values when variability is low.

In some embodiments, in which the ECG signal is from a multi-lead ECG, QT measurements for the cardiac cycle from each of the various leads are input in 504. QT dispersion is computed in process 510 (e.g., using methods described in reference 31 below). A high value of QTD can indicate that there are errors in computing QT interval in one or more leads due to noise, artifact, or algorithm error [23] and hence the validity of the QT measurement may be questionable. In decision process 513, QTD is compared to a threshold Tqd. If QTD exceeds Tqd, the flag QTDom is set to True. If QTD is <Tqd, then the flag QTDom is set to False. If the flag QTDom is enabled and is True, then the multiplier Mx is set to 0 in process 520.

In some embodiments, input 505 contains information as to the character of the cardiac cycle. This information is evaluated in decision process 511 and, if the cardiac cycle is identified as containing an ectopic beat, the flag PVC is set to True in process 519. If the beat is determined not to be an ectopic beat in decision process 511, then flag PVC is set to False. If flag PVC is enabled and is True, then Mx is set to 0 in process 520.

In some embodiments the T-wave and emphasis signal for the cardiac cycle are input in process 506. A measure of the complexity of T-wave morphology (CTWM) is computed in process 514. In one embodiment CTWM is computed as the number of significant peaks and valleys in the T-wave emphasis signal during the time from T-wave onset to T-wave offset. In another embodiment relative locations of the emphasis signal peaks and valleys are included in the computation of the CTWM metric. If the T-wave is highly complex, as is the case for a multiphasic T-wave, then the validity metric is reduced to reflect that a U-wave may be present and thus accuracy of identification of the T-wave offset point may be compromised.

In some embodiments, a metric of signal energy relative to noise energy for the second time window (218 for T-wave offset VM and 317 for repolarization VM) is input in 507 for use in computing VM. In some embodiments this metric is SNR and is computed as described previously. In one embodiment, SNR for the second time window is computed in processes 218 and 304 as the energy contained in the subcomponents primarily associated with the T-wave and noise energy is computed from the energy contained in the residual subcomponents. In some embodiments, process 521 computes VM as a function of SNR and CTWM multiplied by Mx, where Mx is computed in process 520 and Mx=0 or 1. In some embodiments VM is maintained at zero for a predetermined number of subsequent beats to account for hysteresis effects in QT interval that can occur following an arrhythmic beat. In some embodiments VM is evaluated and, if found to be below a predetermined threshold Td, the QT measurement for that cardiac cycle is considered invalid and is discarded. Likewise, if VM is >than a predetermined threshold Tg then the QT measurement is considered valid. In some embodiments, if VM has a value between Tg and Td it is considered uncertain. QT measurements for cardiac cycles where VM>Tg or VM<Td may be reviewed by a trained person to manually assign a T-wave offset point.

In some embodiments QRS duration is measured using the Q-onset and QRS offset fiducial points detected as described herein. As part of measuring QRS duration, the signal energy relative to noise energy may be measured in one or more windows within which the presence of noise can impact the accuracy of Q-onset and QRS offset detection in a manner similar to that described for T-wave offset.

Various embodiments are directed to adjusting QT measurements to facilitate and/or improve the accuracy of resulting data. In accordance with an example embodiment, and referring to FIG. 6, measurements of T-wave offset are adjusted using a technique that employs an evaluation of T-wave morphology in order to further improve the accuracy and consistency of T-wave offset detection results. Improved consistency in T-wave offset measurement can be useful because it leads to reduced measurement variability which can translate into a reduction in sample size in various research studies, including those that employ QT measurements to investigate proarrhythmic potential of drugs under development [24]. The embodiments described here may be useful for improving the accuracy and consistency of identifying T-wave offset for computing a QT interval parameter or for improving the accuracy and consistency of identifying T-wave offset and T-wave onset for extracting a repolarization signal. A similar approach may also be useful for improving the accuracy of other feature points such as Q-wave and P-wave onset.

This approach is based upon the assumption that normal physiologic variability in T-wave offset relative to cardiac depolarization is small over a period of a few respiratory cycles, providing that T-wave morphology is consistent over that time period. However, residual noise, inappropriate high pass filter settings [25] or baseline fluctuations can bias detection of T-wave offset. Such biases can accumulate, resulting in variability of QT interval measurements that is much greater than normal physiologic variability. This embodiment is useful in reducing the impact of these biases on T-wave offset identification.
In this embodiment, and referring to FIG. 6, input ECG 601 is evaluated in process 602 to identify T-wave offset as described previously. The emphasis signal is computed in process 603, also using techniques described previously, and is evaluated in process 604 to identify T-waves with similar morphology characteristics. Morphology characteristics of each T-wave are evaluated and T-waves with common morphology characteristics are assigned to a cluster in process 605. In process 606, T-waves assigned to a cluster are aligned in time around a common feature point of the T-wave emphasis signal, referred to as an alignment point. In one embodiment, the alignment of T-waves in process 606 is performed in a manner that preserves the time difference between the alignment point and the initially derived T-wave offset point. Because QT variability can be caused by changes in the QRS duration (e.g., as often occurs as a result of respiratory modulation), it can be useful to make any adjustment to T-wave offset relative to a reference point within the T-wave. In one embodiment, a composite value for T-wave offset is computed following alignment of T-waves within a cluster. The composite value can be computed as the median, mean, or weighted mean of the T-wave offset points of the aligned T-waves in the cluster. The initially derived T-wave offset points for T-waves in the cluster are then adjusted to match the composite value. In another embodiment, T-wave offset points in the cluster are adjusted to match the computed mean value. In another embodiment, computing the composite value for the cluster involves removing statistical outliers (e.g., T-wave offset times a predefined multiple of S.D. of mean) prior to computing a mean, following alignment of T-waves in process 606, a composite T-wave offset value is computed in process 607 by combining the offset points of the aligned T-waves. In process 608, T-wave offset values for each cardiac cycle in the cluster are adjusted by matching T-wave offset points to the composite values computed in 608.

In another embodiment the T-waves in a cluster can be averaged to compute a template automatically. Template matching techniques, such as cross-correlation, can then be used to correct computed T-wave onset and offset. In one embodiment, T-wave morphology is evaluated by analyzing the time and amplitude of significant peaks, valleys, and zero crossings (e.g., fiducial points) of the emphasis and the denoised signals. In one embodiment, T-waves having the same number and similar amplitude of fiducial points as well as similar time between the fiducial points are assigned to a common cluster. In another embodiment the number and, or and/or the amplitude of the fiducial points are used for morphology classification.

In another embodiment, the time scale of a T-wave is compressed or expanded in order to allow it to match the criteria of a morphology cluster for reducing the number of clusters. Creating this modified T-wave facilitates clustering based upon shape of the T-wave rather than time scale. The T-wave offset point correction for the modified T-wave is adjusted back in time in proportion to the change in time scale made when creating the modified T-wave.

Referring to FIG. 6, relative to respective embodiments, examples are presented for noisy human T-waves in 609 and derived emphasis signals in 610 and for canine T-waves and derived emphasis signals 611 through 614. The rhombus symbols denote the point of detection of T-wave offset for each of the T-waves shown. In 609, T-waves of similar morphology have been identified as belonging to a particular classification by examining peaks and valleys of the emphasis signal. The emphasis signals shown in 610, computed from denoised subcomponents as described earlier, provides a useful tool for evaluating the classification of a T-wave since it contains less noise and provides for a more precise and consistent location of features. The T-waves in a cluster can be aligned by the location of the first significant peak or valley of the emphasis signal. The alignment points computed from the emphasis signals of this cluster are shown as a vertical dashed line in 610.

An example, shown in 609 and 610, reveals that one of the T-wave offset points (indicated by the right-bottom rhombus in T-wave cluster in 609) is displaced from the others in the cluster by about two sample points due to residual noise. The identified wave offset can be repositioned to match mean or median T-wave offsets in the cluster. The examples of 611 (T-waves) and 612 (derived emphasis signals) demonstrate this embodiment as applied to a canine ECG. In 611 and 612 the T-waves and emphasis signals are shown aligned around the first significant peak or valley of the emphasis signal (indicated by the vertical dashed line in 612). As for 611, the majority of T-wave offset points coincide, but one T-wave offset (left-most rhombus) differs from the others by about 5 sample points due to noise. This T-wave offset can be repositioned to match the mean or median of the cluster to ensure consistency of T-wave offset measurement. Alternatively, this initially derived T-wave offset point would be identified as an outlier and removed from computation of the composite value.

Some embodiments may use more or less stringent criteria to evaluate the morphology characteristics for assigning a T-wave to a cluster. An example of a modified embodiment is provided in 613 and 614 whereby a more relaxed definition of the morphology cluster is used. The criteria used to determine if a T-wave is assigned to a cluster has been relaxed to allow a +/-1 sample point difference in the distance between the fiducial points of the emphasis signal, whereas the examples of 609 to 612 require that fiducial points match exactly. The relaxed inclusion criteria results in a smaller number of clusters used for T-wave offset correction, with a larger number of T-waves in each cluster. As is seen from 613 (T-waves) and 614 (emphasis signals) the T-wave offset points are more scattered in time. In one embodiment the initially derived T-wave offsets are replaced by a mean or median of T-wave offsets in the cluster. In an alternate embodiment, statistical outliers are eliminated from computation of the T-wave offset point.

The embodiments described here for measuring and analyzing QT interval and other metrics of cardiac repolarization activity may be implemented in a variety of platforms, such as those including a computer, processor and/or related circuitry. In one embodiment, a microprocessor (such as an Intel Pentium or Core microprocessors) or microcontroller (such as the Texas Instruments MSP 430 microcontroller) is configured (e.g., programmed) to implement one or more embodiments, such as those shown in and/or described in connection with the figures. In other embodiments a mainframe computer or a state machine such as may be implemented on silicon using a hardware description language such as VHDL is used to implement one or more embodiments. Still other embodiments are directed to the implementation of different aspects of the embodiments described herein, such as certain computing steps and/or the computation of certain values (e.g., a denoised signal), whereas other aspects are implemented using different steps using other processors/machines and/or at disparate locations, with resulting data communicated appropriately (e.g., via the Internet). Accordingly, some embodiments are directed to certain post-processing in which certain computations have been made, as may be relevant, for example, to the computa-
tion of a QT interval and related characteristics using a provided denoised signal. Certain embodiments involve combining the measurement of QT interval and other metrics of repolarization activity with other ECG analysis functions such as detection of atrial and ventricular arrhythmias and measurement of characteristics such as QRS duration and PR interval.

Some embodiments of the present invention are implemented in a battery or passively powered device that is worn by or implanted within a human or animal subject. Referring to FIG. 7, aspects of the present invention can be implemented within subject device 704A and 704B while others can be implemented in data review system 707. In FIG. 7, it is anticipated that multiple subjects are monitored and hence there are multiple subject devices (704A and 704B) and multiple base stations (705A and 705B). In one embodiment, input ECG 701 is amplified and filtered to remove out-of-band noise in 702. The conditioned signal from 702 is digitized by microcontroller 703. Microcontroller 703 and related functional elements contains a processor, memory, communications module, and other functions necessary to acquire, process, and control operation of subject devices 704A and 704B. In some embodiments, microcontroller (embedded system 703) processes the conditioned ECG signal to derive QT interval measurements and repolarization signals and transmits the information received from the ECG via a communication module. Information is received by base stations 705A and 705B and is forwarded to data review system 707 via telecon or data network 706.

The computer instructions required to perform the computing operations of the present invention are programmed (e.g., optimized) using integer or fixed point arithmetic and lifting or B-spline implementation [26, 27] of the signal decomposition transform in order to minimize the number of clock cycles or machine states required and hence minimize power consumption. The resulting code can then be implemented, for example, in an embedded system 703 capable of operating for an extended period of time on power supplied by a small battery. In such an embodiment, a portion of the computations required to analyze repolarization activity and extract other information on heart rhythms may be implemented within subject device 704A and 704B while others may be implemented in data review system 707. In another embodiment, the subject device only records the ECG of the subject and the ECG recording is processed off line on data review system 707. Data review system 707 may include a review function that facilitates human review of ECGs that were classified as uncertain by the algorithm.

In another example embodiment, and referring to FIG. 9, a sensed ECG signal 901 is received and processed to provide a T-wave offset. The received signal is amplified and filtered in 902 to remove signal content that is outside the bandwidth of the ECG. The filter employed in 902 may include one of a number of filters, such as a multi-pole Butterworth filter. For human ECGs, the lower and upper (-3 dB) filter cutoff points can be 0.05 and 100 Hz, respectively. The amplified and filtered signal is also digitized in 902 for processing by a computing element such as a microprocessor, signal processing element, or data machine where steps 903 through 912 are implemented via software, firmware, or hardware description language. In step 903, the QRS complex is identified and the location of the QRS complex is used to define a search window within which to search for T-wave offset, using one or more approaches such as those described herein.

The ECG signal is then filtered and/or denoised in step 905 to remove the energy outside the frequency components of the T-wave. Step 905 is accomplished by one of MDSP denois-
tion, and for specific information regarding the application of one or more such embodiments, reference may be made to the following documents, which are fully incorporated herein by reference. Various ones of these references are further cited above via corresponding numerals, and may be implemented as such.


Based upon the above discussion and illustrations, those skilled in the art will readily recognize that various modifications and changes may be made to the present invention without strictly following the exemplary embodiments and applications illustrated and described herein. For example, various thresholds as discussed herein may be used in an inverse sense, with embodiments described as involving a determination of a value exceeding the threshold can be implemented via values that fall below a threshold. In addition, the various manners in which to denote signals, filter signals, combine or otherwise process signals as discussed in connection with certain embodiments, may also be implemented with other embodiments. Similarly, aspects discussed in connection with and/or shown in the figures may be implemented with other figures or otherwise discussed herein. Such modifications do not depart from the true spirit and scope of the present invention, including that set forth in the following claims.

What is claimed is:

1. A method for providing a T-wave offset point of an ECG signal, the method comprising:
   identifying the location of a QRS complex in the ECG signal;
   using the identified location of the QRS complex, determining a first time window of the ECG signal in which to search for the T-wave offset point; and
in a computer circuit,
identifying the T-wave offset point within the first time window, and
providing the identified T-wave offset point as an output based upon a noise characteristic of the ECG signal in a second time window that includes at least a portion of the T-wave of the ECG signal.

2. The method of claim 1, wherein the second time window includes the identified T-wave offset point.

3. The method of claim 1, wherein the second time window includes the identified T-wave offset point, the duration of said second time window is about 30% of the duration of a nominal QT interval of the ECG signal, and the second time window extends beyond the T-wave offset point by about 10% of the nominal QT interval duration.

4. The method of claim 1, wherein the second time window has a duration of about 50 msec and is centered about the identified T-wave offset point.

5. The method of claim 1, wherein the second time window extends from about the point of the largest deflection of the T-wave from an isoelectric line of the ECG signal to about the T-wave offset point.

6. The method of claim 1, wherein the second time window includes a time period extending from about a QRS offset point in the ECG signal to about the T-wave offset point.

7. The method of claim 1, wherein the second time window includes a time period extending the full duration of a cardiac cycle in the ECG signal.

8. The method of claim 1, further comprising computing the noise characteristic by:
   decomposing the ECG signal into subcomponents,
   identifying said subcomponents in the second time window as either primarily associated with noise or primarily associated with the T-wave of the underlying ECG signal,
   computing a noise signal for the second time window using at least one subcomponent not primarily associated with the T-wave, and
   computing said noise characteristic based upon at least one of: energy of the noise signal, standard deviation of the noise signal, zero crossing density of the noise signal, a metric of noise amplitude computed using an envelope of the noise signal, and a metric of energy of the ECG signal relative to energy of the noise signal.

9. The method of claim 8, further including computing a denoised signal by combining at least two of the subcomponents that are primarily associated with the T-wave, wherein the metric of energy of the ECG signal relative to energy of the noise signal is a signal-to-noise ratio of the ECG signal within the second time window computed as the ratio of respective energies of the denoised and noise signals.

10. The method of claim 1, further comprising computing the noise characteristic by:
    computing a denoised signal for the second time window using at least one of a band-pass filter, wavelet thresholding, and an adaptive filter that passes primarily T-wave energy,
    capturing a residual of the step of computing the denoised signal as a noise signal for the second time window, and
    computing said noise characteristic based upon at least one of: energy of the noise signal, standard deviation of the noise signal, zero crossing density of the noise signal, a metric of noise amplitude computed using an envelope of the noise signal, and a metric of energy of the denoised signal relative to energy of the noise signal.

11. The method of claim 1, wherein providing the identified T-wave offset point as an output based upon a noise characteristic of the ECG signal in the second time window includes comparing the noise characteristic to a threshold and providing the identified T-wave offset point based upon the comparison.

12. The method of claim 1, wherein providing the identified T-wave offset point as an output includes providing the identified T-wave offset point based upon a presence, in a cardiac cycle within the ECG, of at least one of: atrial fibrillation, QT dispersion in a multi-lead ECG exceeding a threshold, T-wave morphology complexity exceeding a predetermined threshold, ventricular ectopy, a QT interval measurement that falls outside of a user-defined physiologic outlier value or a statistical outlier value.

13. The method of claim 1, further including using the provided identified T-wave offset point to assemble a time series of provided QT interval values for analysis of variability.

14. A method for providing a repolarization signal for a cardiac cycle of an ECG signal, the method comprising:
   identifying the location of a QRS complex in the cardiac cycle;
   using the identified location of the QRS complex, identifying T-wave onset and offset points;
   using the T-wave onset and offset points to respectively define the start and end of the repolarization signal for the cycle; and
   in a computer circuit, determining a noise characteristic of the ECG signal in a time window spanning from about the start to about the end of the repolarization signal, and providing the repolarization signal as an output, based upon the determined noise characteristic.

15. The method of claim 14, wherein determining the noise characteristic includes:
    decomposing the ECG signal into subcomponents,
    identifying ones of said subcomponents of the ECG signal within the time window as primarily associated with the T-wave of the underlying ECG signal,
    computing a noise signal for the time window using at least one of the subcomponents not primarily associated with the T-wave, and
    computing said noise characteristic based upon at least one of: energy of the noise signal, standard deviation of the noise signal, zero crossing density of the noise signal, a metric of noise amplitude computed using an envelope of the noise signal, and a metric of energy of the ECG signal relative to energy of the noise signal.

16. The method of claim 15, further including computing a denoised signal by combining at least two of the subcomponents that are primarily associated with the T-wave, wherein the metric of energy of the ECG signal relative to energy of the noise signal is a signal-to-noise ratio of the ECG signal within the second time window computed as the ratio of respective energies of the denoised and noise signals.

17. The method of claim 14, wherein determining a noise characteristic includes computing the noise characteristic by:
    computing a denoised signal for the time window using at least one of a band-pass filter, wavelet thresholding, and an adaptive filter that passes primarily T-wave energy,
    computing a noise signal for the time window using a residual of the step of computing the denoised signal, and
    computing said noise characteristic based upon at least one of: energy of the noise signal, standard deviation of the noise signal, zero crossing density of the noise signal, a metric of noise amplitude computed using an envelope of the noise signal, and a metric of energy of the denoised signal relative to energy of the noise signal.
18. The method of claim 14, wherein providing the repolarization signal as an output, based upon the determined noise characteristic includes comparing the noise characteristic to a threshold and providing the repolarization signal as an output based upon the comparison.

19. The method of claim 14, wherein providing a repolarization signal as an output includes providing the repolarization signal as an output based upon the determined noise characteristic and the presence in the cardiac cycle of at least one of: atrial fibrillation in the ECG signal, a degree of QT dispersion exceeding a threshold when the ECG signal is a multi-lead signal, T-wave morphology complexity of the ECG signal exceeding a threshold, ventricular ectopy, and a QT interval measurement that falls outside of a user-defined physiologic outlier value or a statistical outlier value.

20. The method of claim 14, further including appending the provided repolarization signal to a matrix of repolarization signals in which a dimension of the matrix corresponds to the number of cardiac cycles of the ECG signal.

21. A method for providing a time series of beat-to-beat QT interval values from a digitized ECG signal of an ambulatory subject, the method comprising:
identifying the location of a QRS complex and a Q-wave onset point of a cardiac cycle of the ECG signal;
using the identified location of the QRS complex, determining a first time window of the cardiac cycle in which to search for a T-wave offset point for a T-wave in the cardiac cycle;
identifying the T-wave offset point within the first time window; and
in a computer circuit, computing a QT interval value using the identified Q-wave onset point of the QRS complex and the identified T-wave offset point, and including the QT interval value in a time series of beat-to-beat QT interval values, based upon a noise characteristic of the ECG signal in a second time window that includes at least a portion of the T-wave.

22. The method of claim 21, further including suppressing energy that is not primarily associated with T-wave energy in the first time window of the digitized ECG signal, prior to identifying the T-wave offset point, using at least one of MDSP denoising, wavelet threshold denoising, band-pass filtering, and adaptive filtering.

23. The method of claim 21, further including computing the noise characteristic by:
developing the ECG signal into subcomponents, identifying said subcomponents as primarily associated with either noise or a T-wave of an underlying ECG signal,
computing a noise signal by combining the subcomponents within the second time window that are primarily associated with noise, computing a denoised signal by combining the subcomponents within the second time window that are primarily associated with the T-wave of the underlying ECG signal, and
computing said noise characteristic based upon at least one of: energy of the noise signal, standard deviation of the noise signal, zero crossing density of the noise signal, a metric of noise amplitude based upon an envelope of the noise signal, and a metric of energy of the denoised signal relative to energy of the noise signal.

24. The method of claim 23, wherein the metric of energy of the denoised signal relative to energy of the noise signal is a signal-to-noise ratio.

25. The method of claim 21, further including computing the noise characteristic by:
computing a denoised signal for the second time window using at least one of a band-pass filter, wavelet thresholding, and an adaptive filter, and computing a noise signal as a difference between the digitized ECG and the denoised signal, and
computing said noise characteristic based upon at least one of: energy of the noise signal, standard deviation of the noise signal, zero crossing density of the noise signal, a metric of noise amplitude computed using an envelope of the noise signal, and a metric of energy of the denoised signal relative to energy of the noise signal.

26. The method of claim 21, wherein including the QT interval value in the time series of beat-to-beat QT interval values includes including the QT interval value based upon a comparison of the noise characteristic to a threshold value.

27. The method of claim 21, wherein including the QT interval value in the time series of beat-to-beat QT interval values includes including the QT interval based upon the noise characteristic and the presence, in the cardiac cycle, of at least one of: atrial fibrillation, ventricular ectopy, QT dispersion in a multi-lead ECG exceeding a threshold, T-wave morphology complexity exceeding a predefined threshold, ventricular ectopy, a QT interval measurement that falls outside of a user-defined physiologic outlier value or a statistical outlier value.

28. The method of claim 21, wherein the steps are carried out in the computer circuit executing instructions to carry out the various functions, further including, in the computer circuit, executing instructions to repeat the steps to compute a plurality of the QT interval values, and
wherein including the QT interval value in a time series of beat-to-beat QT interval values includes, in the computer circuit, including ones of the QT interval values in the time series of beat-to-beat QT interval values based upon a comparison of a noise characteristic of a corresponding ECG signal in the second window to a predefined threshold.

29. The method of claim 21, wherein the time series of beat-to-beat QT intervals consists of QT interval values having error due to noise that is less than 2.5% of the mean QT interval of the ECG signal.