An Electrophysiological Cardiac Model Approach to Measuring T-Wave Alternans

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Abstract

The 2008 Computers in Cardiology Challenge is to automatically identify and measure T-wave alternans. The study presented here applies an electrophysiological cardiac model to the problem of characterizing the T-wave variability. Thus, the hypothesis is that the existence and magnitude of T-wave alternans can be identified and measured using a cardiac inverse problem approach, where the magnitude of the alternans are measured in the model space. The dataset used in this study is a collection of records from selected databases in the Physionet databank. Additionally, a simulated ECG dataset is used to study the sensitivity and specificity of the proposed approach under various noise conditions. Results on the simulated ECG data set show that the approach is able to differentiate between 5, 10, 20, and 100 microvolt T-wave alternans in the presence of various noises between -25 and 5dB SNR. The score from the challenge, which is the Kendall rank correlation coefficient, is 0.331.

1. Introduction

The 2008 Physionet/Computers in Cardiology (CinC) challenge [1] is to automatically detect and quantify T-wave alternans (TWA), which is crucial in predicting sudden cardiac death. T-wave alternans are defined as the appearance of periodic beat to beat changes in the T-wave measurements. Although this phenomenon was detected by HE Hering over a hundred years ago, its existence is still not fully explained. However, studies in the past 25 years have shown a correlation between T-wave alternans, the heart rate on which they appear, and the risk of sudden cardiac death.

Many automatic techniques have been presented for the quantification of T-wave alternans. Most of these techniques are based on measurements in the frequency domain [2-4]. Generally, these techniques require parameter tuning in order to be effective. On the other hand, in 2004, Martinez et al. [2] provided a unified framework for the detection of T-wave alternans based on many previous methods, which provides a comparison between several published TWA approaches. The approaches discussed in [2] include spectral, complex demodulation, Karhunen-Loève transform, Capon filtering, Poincaré mapping, periodicity transform, statistical test, modified moving average, and Laplacian likelihood ratio methods.

The approach presented here models the generation of the ECG signal with an inverse problem solution and uses this solution to quantify the T-wave alternan. The modeling approach is based on cardiac electrophysiology, where the ECG signal is generated from models of the SA node, AV node, Bundle branches, Purkinje fibers, and left and right ventricular walls. The electrical activity of each of these components of the heart is estimated by the difference of two sigmoid functions. The model has the ability to characterize the P wave, PR segment changes, QRS complex, ST segment changes, and T-wave.

2. Data sets

We use two datasets, the CinC Challenge dataset and a simulated dataset, to evaluate the hypothesis that model based approach can identify and measure T-wave alternans. The CinC Challenge dataset consists of 100 records of various lengths selected from the following Physionet Databank databases: Long-Term ST Database, PTB Diagnostic ECG Database, MIT-BIH ST Change Database, Sudden Cardiac Death Holter Database, and the BIDMC Congestive Heart Failure Database.

The simulated dataset is generated using the Clifford and McSharry et al. [5] model, where the T-wave magnitude is varied by 5, 10, 20, and 100 microvolt with SNR levels of 5, 0, -5, -10, -20, and -25 db of white, pink, and brown noise. First, the clean T-wave is determined from the model. Second, different noise levels are added to the clean T-wave to generate 40 simulations for each of the noise level. For each of the 40 simulations the T-wave magnitude is varied by 5, 10, 20, and 100 microvolt. The process is repeated for white, pink, and brown noise.

3. Methods

Our TWA measurement method is based on an electric potential heart model during the cardiac cycle. While substantial research has been done on the internal

dynamics of the cardiac cell, our model focuses, for complexity and computational reasons, on characterizing key cardiac regions: the SA node, the AV node, bundle branches (bb), Purkinje fibers (Pf), and left and right ventricles (LV and RV). Individual models are used to represent the electrical activation and conduction of each region. The interaction between regions is also modeled, as well as the net behavior of the whole cardiac model at the body surface.

Each region is modeled as a signal generator. The generated waves propagate from each of the regions to leads present at the body's surface. The signals captured at the leads represent the ECG, which is generated by the potential difference between the waves arriving at the positive and negative electrodes of a lead. Figure 1 illustrates the output of an example cardiac region, which is modeled by the difference of two sigmoids. By summing the potential difference of the waves generated by each cardiac region arriving at the positive and negative terminals of a lead, the ECG signals are generated.

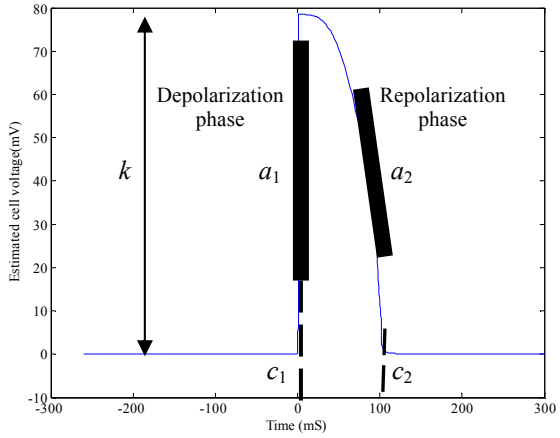

Figure 1: Proposed cardiac region activity

While other mathematical structures, such as polynomials may be used, there is a distinct advantage to the difference of two sigmoids. Only five parameters are needed to model each cardiac region and these parameters correspond well to physiological characteristics of the heart and also to fiduciary points on the ECG. These parameters are the magnitude (k), inflection points (c_1, c_2), and slopes (a_1, a_2) of the difference of two sigmoids. They correspond, respectively, to the magnitude of electrical activity, the inflection points of depolarization and repolarization, and the rate of potential change within the cardiac region.

3.1. Mathematical description

As discussed above our cardiac model is composed of models of six key electrical components of the heart. Each component is modeled as the difference of two sigmoids.

$$f\left(t,a_1,c_1,a_2,c_2,k\right)=k\left(\frac{1}{1-e^{a_1(t-c_1)}}-\frac{1}{1-e^{a_2(t-c_2)}}\right), \quad (1)$$

where t is time, k represent the magnitude of the electrical activity, a_1 and a_2 determine the slopes, and c_1 and c_2 determine the translation in the direction of the x-axis.

By accounting for the time delays of the depolarization and repolarization signals at the positive and negative electrodes of a lead, the model of the signal at the positive and negative electrodes can be represented by

$$f^{+}=f\left(t,a_1,c_1+\delta_d^{+},a_2,c_2+\delta_r^{+},k\right) \text{ and} \quad (2)$$

$$f^{-}=f\left(t,a_1,c_1+\delta_d^{-},a_2,c_2+\delta_r^{-},k\right), \quad (3)$$

where δ_d^{+}, δ_d^{-}, δ_r^{+}, and δ_r^{-} represent the delay of the depolarization at the positive and negative electrodes and the delay of the repolarization at the positive and negative electrodes, respectively.

The ECG signal are computed by summing the potential difference of the signals generated by the major six cardiac regions arriving at the positive and negative electrodes of a lead as shown in (4).

$$\hat{f}_{ECG}=\sum_{i\in[SA,\ AV,\ bb,\ Pf,\ LV,\ RV]}\left(f_i^{+}-f_i^{-}\right). \quad (4)$$

In order to apply the proposed ECG model, the parameters of (2) and (3) are determined by minimizing the sum squared error between an ECG signal and the model generated signal. However, in this study the aim is to determine the parameters for the T-wave. Thus, the error is minimized using the partially separable nonlinear least squares method presented in [6], where the ventricular activity is divided into the QRS waves, the ST segment, and the T-wave; which are represented in this case by the bundle branches, Purkinje fibers and left and right ventricles. Thus, the T-wave is fit by the repolarization phase of the left and right ventricles as shown in (5).

$$error_{vent}=\sum_{i\in[LV,RV]}\left(T_{wave}-\left(f_i^{+}-f_i^{-}\right)\right)^2. \quad (5)$$

Thus, the estimated T-wave signal is the sum of the ventricular repolarization activity, and the model is represented by the parameters corresponding to the left and right ventricular repolarization.

3.2. Preprocessing and initial condition

We apply our approach sequentially to each T-wave, which requires the use of ECGPUWAVE [1] to identify the T-wave beginning and end. The T-wave amplitude is normalized such that the initial sample is zero, and the signal is zero padded for 30 ms.

We analyze only T-waves in a record that are considered to have common or good morphology in order to avoid signal artifacts. This is done by computing a time average of all T-waves in a record. T-waves whose cross-correlation with the time average greater than 0.7 are kept for further analysis.

Initial model conditions, prior to error minimization, are determined using a template signal with known parameters. The point of the highest cross-correlation between the template signal and the first good T-wave determine the initial model conditions. Subsequent initial conditions are determined using the prior T-wave's estimated model parameters. This results in accurate and rapid estimation of the model parameters for consecutive T-waves.

3.3. Parameter estimation

Least squares minimization of (5) using lsqcurvefit [7] yields the model parameters. A set of constraints applied to the parameter estimation process improve optimization convergence and avoid unrealistic models. In this work, we set the activation phase of the LV and RV zero because they do not contribute to the T-wave generation. Right ventricular repolarization is constrained to start before left ventricular repolarization. Additionally, the slopes and magnitudes of (1) during the depolarization phase are constrained to be greater than zero [8].

3.4. TWA measurement

Our approach estimates model parameters for each T-wave with good morphology in a record. The distance between consecutive T-wave models is calculated in the parameter space.

$$TWA_i = \left\| m_{i+1} - m_i \right\|, \qquad (6)$$

where m_i is the vector of model parameters for the i^{th} T-wave. The TWA magnitude of a record is the standard deviation of the sequence of $TWA_1, TWA_2, ..., TWA_n$.

4. Results

The proposed TWA measurement method is applied to the 2008 Physionet/Computers in Cardiology challenge dataset. Additionally, the method is applied to simulated signals with added white, brown and pink noises. The simulated signals provide a quantitative measure of the method's accuracy.

4.1. Physionet/CinC challenge database

The modelling approach is applied to the challenge's dataset. Figures 2 and 3 show original T-waves, the results from their corresponding models, and their respective error. The error is less than 5% between the original signals and the results of the models. After generating all parameter vectors for a record, the TWA magnitude is measured using the method described earlier.

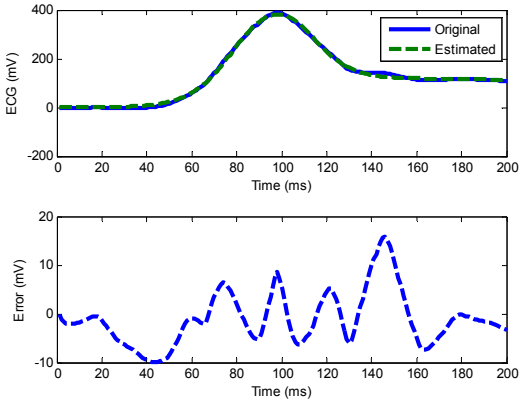

Figure 2: The top figure shows the original and estimated T-waves for the first T-wave in a record. The bottom figure shows the error between the two signals.

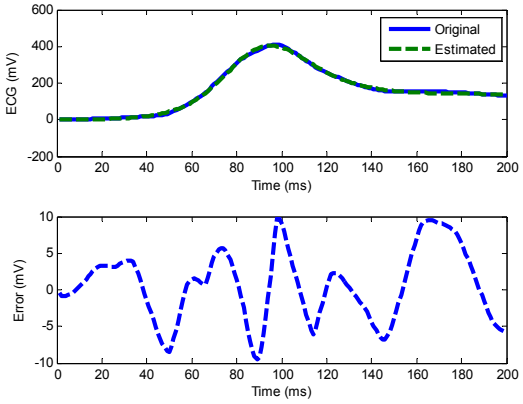

Figure 3: The top figure shows the original and estimated T-waves for the second T-wave in a record. The bottom figure shows the error between the two signals.

The Kendall rank correlation coefficient for the proposed method is 0.331. The challenge's score is determined by sorting the TWA magnitude of each entry. Then, the median of all the rankings is determined and is used as the reference signal. Finally, the score is determined as the Kendal rank correlation coefficient between the sorted magnitudes and the reference ranking.

4.2. Simulated signals

The simulated signals are generated from the model developed in [9]. The T-wave magnitude is varied by 5 to 100 µV. Additionally, white, brown, and pink noise are added to the signal at an SNR level ranging from -25 to 5 dB measured at the ST segment [10]. The process is repeated for 40 trials, and the average error of the T-wave

variation is measured. Figure 4 shows the noisy signal under 5 µV with -25dB additive noise. The error between the original signal and the estimated signal is less than 1%.

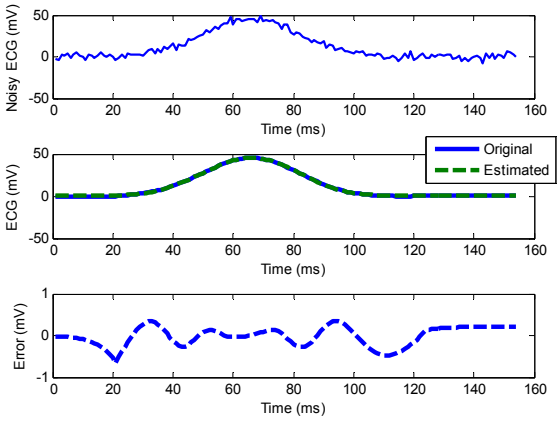

Figure 4: The top, middle, and bottom figures are, respectively, the noisy signal, the original and estimated signals, and error between the two signals.

Table 1 presents the percentage error between original and estimated TWA magnitudes. The reference TWA is the variation of the distance between consecutive modeled parameters of the clean signal with different alternans. After the model parameters are estimated for the noisy signals, the TWAs are calculated. The error between the clean and the noisy TWAs is calculated. The average error is less than 1%.

Noise Type	TWA error ± 1std
White noise	0.44% ± 0.57%
Pink Noise	0.60% ± 0.49%
Brown Noise	0.20% ± 0.40%

Table 1: Error of TWA magnitude with added noise and known T-wave magnitude variations

5. Discussion and conclusion

We present a model based approach for the measurement of T-wave alternans. The model is based on the electrophysiological activity of the ventricles and solves the inverse problem for the ventricular repolarization. The approach measures the TWA in the inverse solution space. The results showed high accuracy in measuring TWAs for simulated signals.

The proposed method is a new way of analyzing TWAs and can be enhanced by accurately identifying the T-waves. The main issue this approach faces is that of the beat detection, baseline wandering, and the lack of alignment of the detected T-waves. These effects can alter the measurement of the TWA.

The cardiac electrophysiological model presented in this paper for the measurement of the T-wave alternan shows high accuracy for detecting the T-wave variations in simulated signals, under various noise conditions and T-wave magnitude variations. The advantage this approach has, in addition to the minimal error compared to the original T-wave signal, is the ability to maintain clinical information such as the beginning and end of the T-wave, which can be relevant in clinical diagnostics.

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