Cardiac Model Based Approach to QT Estimation

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Abstract

Because the direction of regulatory agencies requires the study of potential proarrhythmic side effects of drugs be conducted by skilled readers, the 2006 Physionet/Computers in Cardiology Challenge focuses on the need for clinically acceptable automatic measurement of the QT duration. This entry to the challenge approaches the problem from an inverse ECG perspective. The model parameters are estimated through the minimization of the squared error between the generated ECG signal from the activity of the AV node, endocardium and epicardium, and the recorded ECG. The PQ junction and the end of the T wave are determined from the activation and deactivation of the ventricular activity. This approach is tested on the PTB Diagnostic ECG Database, which contains 549 records from 294 subjects. The final score for this method was substantially improved from 130.70ms to 51.69ms as compared to the best score of 17.33ms for automatic methods.

1. Introduction

Recent regulatory direction is to require the study of potential proarrhythmic side effects of drugs during clinical trials. Specifically, QT studies are anticipated to be required because of the relationship between QT prolongation and torsade de pointes (TdP), which can devolve into ventricular fibrillation. Because of this regulatory direction and the current requirement that such studies be conducted by skilled readers, the 2006 Physionet/Computers in Cardiology Challenge focuses on the need for clinically acceptable automatic estimation of the QT duration.

The challenge is to automatically estimate the onset and termination of electrical activity in the ventricles as represented on the ECG recording, which correspond to the Q point and the end of the T wave, respectively. This is to be done for at least 95% of the records in the PTB Diagnostic ECG Database and the annotation is to be made for the first "good" beat.

To this end, this entry to the 2006 challenge approaches the problem of automatic QT duration estimation from an inverse ECG perspective. Our proposed approach is based on a simple physiological model of the electrical cycle of depolarization and repolarization of the ventricles, the duration of which is estimated by the QT duration. The endocardium and epicardium of the right and left ventricles are modeled as signal generators. The ECG is generated by the difference in signal amplitudes arriving at the positive and negative terminals of an ECG lead. The model parameters are estimated through the minimization of the squared error between the generated signal and the recorded ECG. The PQ junction and the end of the T wave are determined from the earliest activation and latest deactivation of the signal generators, respectively.

The rest of the paper is organized in the following sections: Background, Data Set, Method, Results, Discussion and conclusion.

2. Background

Prior works has been involved in the estimation QT interval. Meij et al presented an iterative approach for the beat to beat measurement of QT interval [1]. Moreover, McLaughlin et al compared three techniques which considered the T end as the crossing with a 5% line, the tangent from the peak of the T wave to the signal and the tangent from the peak to the derivative of the T wave [2]. Additionally, Sahambi et al presented a wavelet based approach for the determination of the onset and end of the ECG features [3].

Several techniques have been employed for generating a model that characterizes ECG signal or solving the inverse problem. Some of the drawbacks that these techniques have are computational complexity or the difficulty to relate to the heart cell activity. Some of these techniques apply the solution of green's theorem (Method of Moments) or multipole technique in order to determine the scattering of the electric waves over the heart. These methods are considered accurate; however, they require high computational time [4].

Another dynamic ECG model incorporates the ECG features as a combination of Gaussian models. Although this model is easy to build, it cannot be related to the heart cell activity [5]. Moreover, this modeling approach was extended to include beat to beat estimation of the ECG signal, and adaptive estimation using Kalman filter [6].

3. PTB Diagnostic ECG Database

The proposed approach is tested on the PTB Diagnostic ECG Database, which contains 549 records from 294 subjects ranging in lengths from 30 to 120 seconds and sampled at 1kHz. This data set provides 15 ECG leads, including the standard 12 leads and 3 Frank leads. The data includes 54 healthy controls, 148 cases of myocardial infarction, and 92 other diagnoses.

4. Methods

4.1. Concept behind method

The motivation for the proposed approach is that of the inverse ECG problem. However, the models used in standard inverse ECG approaches [4] are computationally intensive and not well suited for analyzing long ECG recordings. The essential quantity that is sought in measuring the QT interval is the duration of the ventricular depolarization and repolarization. So, a model that adequately captures the ventricular depolarization and repolarization process can generate the observed ECG recording, and is computational tractable would be useful. It is exactly this sort of model that we propose and although the performance of the method in the challenge was not all that we expected, we feel that this approach is an interesting avenue for further refinement and study.

4.2. Overview of method

The method is divided in four parts. The first part is a set of preprocessing steps that perform baseline removal, identify potential good beats and perform temporal filtering. The second step is construction and initialization of the model. The third step is an optimization process which estimates the parameters of the model. The final step extracts the onset of the ventricular depolarization and termination of the ventricular repolarization from the model and registering them on the ECG recording.

4.3. Preprocessing, baseline removal, and temporal filtering

Preprocessing of the signal in this approach was performed to combine multiple single beats in order to minimize the power line noise and temporal artifacts in the signal. Moreover, the baseline wandering was removed using a median filter of order N=200.

The temporal artifacts were removed by averaging all good beats. Four steps were applied to perform temporal removal filter. First, the beats were detected using the ECGPUWAVE [8]. Second, one beat is fixed while another is shifted until a high cross-correlation between the detected good beats is reached. Third, the best match is saved and the process is applied for all detected beats. Fourth, the matching beats are averaged.

4.4. Model of heart and generated signals

The proposed modeling technique is adopted from wave propagation of the electric waves over the cardiac tissue. As noted in [7], at first the electric wave is initialized by the sinoartrial (SA) node where it propagates toward the atrioventricular (AV) node. Next, the wave propagates toward the ventricles, which causes them to activate, leading to the appearance of the QRS complex. The T wave is generated during the recovery of the ventricles.

Since the conduction of a single cardiac cell is negligible [7], we model the activation, excitation and depolarization of each of the myocardial tissue as a whole. Before presenting the model for the P wave, the cellular electric representation is presented.

Cell Electric Activity Representation

The electric activity of the myocardial cells is caused by the variation of the positively and negatively charged ions of the cells.

Generally, the conduction activity of the heart is given in figure 2; moreover, we hypothesize that this curve can be approximated by a difference of two sigmoid (diffsig) functions with the right parameters as follows:

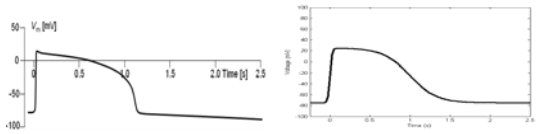

Figure 1. (a) Conduction activity of the heart.
(b) Proposed heart cell activity

The equation describing the diffsig myocardial cell activity is given as follows:

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

where k represent the translation of the wave in the direction of the y-axis, a_1 and a_2 control the rising slope, and c_1 and c_2 control the translation in the direction of the x axis.

We hypothesize that the cumulative ECG signal is generated from the Atrial and Ventricular conduction activity. In this work, the P wave is assumed to be generated from the right atrial activity; while, the QRS complex and T wave are generated from the right and left ventricular endocardium and epicardium.

P Wave Generation

The P wave is generated from the potential difference between the electric conduction activity measured at the atrial cells at the positive and negative probes. In this approach, the atrial conduction activity at a single probe is estimated by equation (1). Moreover, we are to assume

that the P wave can be generated from the right atria conduction activity.

QRS complex and T wave generation

The QRS complex and T wave denote the interval for the beginning and end of the ventricular activation. When modeling the QRS complex, the activity of endocardium and epicardium are accounted for during the ventricle cycle. The representation of the model for the QRS complex and T wave in an ECG signal is dependent on the difference between the positive and negative probes of the left and right epicardium and endocardium.

The combining function used for the representation of the ECG signal is given below:

$$\hat{f}_{ECG}(t) = \sum_{i=RA,Rvep,Rven,Lven,Lvep} (f_{i+} - f_{i-}) \qquad (2)$$

where RA is the activity of the right atria, R_{vep} and L_{vep} is the activity of the right and left ventricular epicardium respectively, R_{ven} and L_{ven} is the activity of the Left and right ventricular endocardium, and *f* is the diffsig function presented in (1).

4.5. Parameter estimation

The parameter estimation of the proposed model function (2) was performed using the minimization of the least squares with the preprocessed ECG signal. This process was performed with the help of the FMINCON function which finds a constrained minimum of a function for several variables. The function being minimized is given in (3).

$$Error = \sum \left(ECG - \hat{f}_{ECG} \right)^2 \qquad (3)$$

The constraints applied to the function are that the atrial activity occurs prior to that of the ventricular. Moreover, the activation of the cell activity is constrained to occur prior to that of the deactivation. Additionally, the slopes of the activation and deactivation curves are constrained to non-zero.

5. Results

The proposed model based approach is applied to the PTB diagnosis database for the estimation of the QT interval. The QT interval is determined from the intersection between the corresponding electrical activity functions with the minimum activation to the maximum activation following that of the activity generating the P wave.

5.1. Method for scoring

The method for scoring the PhysioNet/CinC Challenge 2006 is determined by averaging the RMS difference between the result under consideration and the reference measurement for all records. Since there is no gold standard for QT measurement, the reference measurement was chosen to be the median of submitted records.

5.2. First pass

The initial score for this method was 130.70, which is substantially inferior to the first pass best score of 15.24 for automatic methods. However, it is expected that this method will substantially improve as the number of leads incorporated in the model is increased, atrial activation models are included, the model parameters are estimated from multiple beats, and the parameter estimation routines are improved.

5.3. Second pass

In the second pass we targeted the problem by increasing the number of iterations from 10 to 30 per convergence. These iterations are performed to avoid local minimums. However, the score for this pass was 115.49ms compared to the second pass best score which was 25.56ms for the automatic method.

5.4. Third pass

The third and final pass for the challenge resulted in a score of 51.69ms compared to the third pass best score of 17.33ms for automatic methods. This function estimation was based on the preprocessing approach presented earlier, including multiple leads when a solution is not reached. It's to be noted that the number of iterations was kept the same as that of the second pass. Moreover, Figure 2 and Figure 3 show the estimated electric activity functions and a comparison between the original ECG signal and the estimated signal for a sample data record.

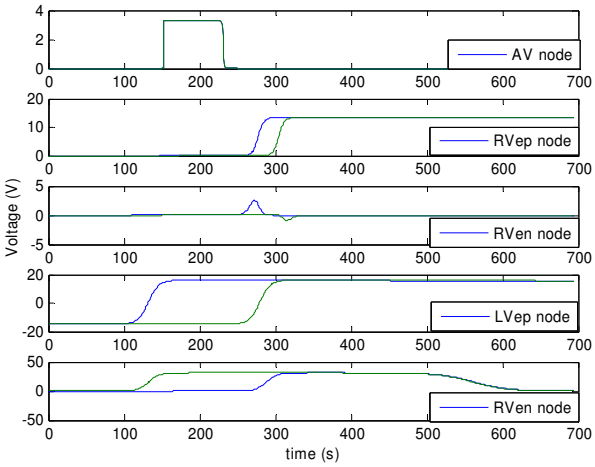

Figure 2. Estimated electrical activity functions

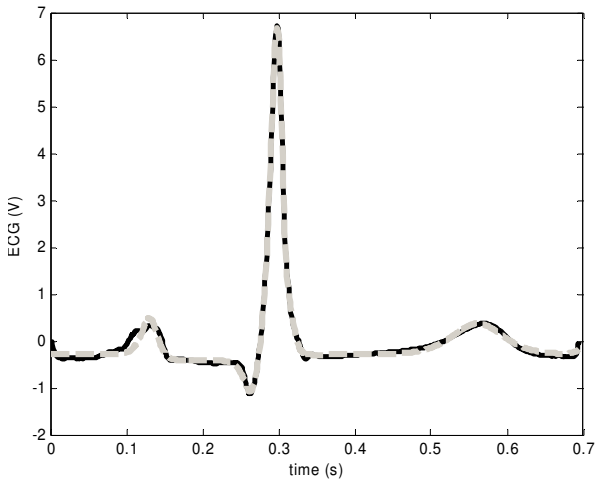

Figure 3. Estimated signal Vs original signal

6. Discussion and conclusions

This article presented a model based approach for the estimation of the QT interval. The advantage of this approach is the ability to relate between the ECG signal and the heart cell electric activity. Although the score of the model based approach was much higher for phase 1 and 2, it was substantially decreased from 130.70 to 51.79ms in the third phase of submitted records.

6.1. Open issues

Two main problems were faced during this optimization process. The first is the problems caused by the preprocessing. The second problem is caused by the constraints which were used to specify the respective position and duration of the atrial and ventricular activation.

6.2. Problems with preprocessing

One of the main reasons that the score for final stage of this work did not reach a lower score is due to some of the pre-processed single beats. For some instances, these beats contained additional artefacts such as another uncompleted beat following the good beat. This was due to the beat detections algorithm used. This caused the optimization problem to fail to estimate the parameters. The second pre-processing problem faced is that some records were corrupted which caused the averaging algorithm to fail.

6.3. Problems with optimization

The main problem faced during the optimization phase was setting up the constraints. The linear constrains of the heart cell functions were setup according to the atrial and ventricular activation. However, when we tried forcing specific duration ranges the ventricular functions tend to push that of the atrial activity to zero. Additionally, the nonlinear constraints were used to set the maximum difference between the activation and deactivation of the electric cell activity. Moreover, it can be noticed that the activation of the AV did not contribute in the ECG signal; this is hypothesized to be modified by enforcing additional constrains on the signals.

6.4. Conclusion

A cardiac based model approach was presented in this work for the determination of the QT interval. Although the score for the challenge is not as good as we hoped for, this approach presents set the bases toward the estimation of the ECG signal and conduction activity of the atria and ventricles simultaneously.

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