Electrocardiogram-Based Restitution Curve

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Abstract

This work investigates the relationship between the QT interval and its preceding TQ interval of the electrocardiogram (ECG) recorded under the handgrip isometric exercise. The experimental results at the ECG scale in this work show that the relationship between these intervals is similar to the well established restitution curve observed in isolated cells, between the action potential duration and its preceding diastolic interval. This result opens new perspectives for the analysis of ECG signals.

1. Introduction

The electrocardiogram (ECG) has a great clinical value for diagnostic of disorders in heart rate and anomalies in electric conduction. Each cardiac cycle is characterised by successive waveforms, known as P wave, QRS complex and T wave.

Time intervals defined between onsets and offsets of different waves are significant because they reflect physiological processes of the heart and autonomous nervous system (ANS). One of the most important intervals is the QT interval, which reflects, in an electrical point of view, the ventricular depolarization and repolarisation duration and, in a mechanical point of view, the ventricular systole (contraction). This interval is calculated on the ECG signal as the time distance from the onset of the QRS complex to the end of the T wave.

Although the QT interval reflects the duration of global ventricular electrical activity, its relationship with ventricular cellular action potential duration (APD) in the heart is in general complex [1]. The APD represents the time required for a cardiac cell to achieve the repolarisation following a depolarizing stimulus in the cell, and the QT interval recorded at the body surface is related to the APDs of a large number of cells which vary from site to site in the ventricle [2, 3, 4]. Moreover, many of ECG expressions of electrical systole may be cancelled by the multidirectional nature of the process of activation and recovery [1, 5].

In this paper, we report experimental results revealing the relationship between the QT interval and the preceding TQ interval of the ECG recorded under the handgrip isometric exercise. In an electrical point of view, the TQ interval is a rest period, while in a mechanical point of view it represents the ventricular diastole (ventricular filling period). Such a relationship is similar to the well established restitution curve observed in isolated cells, between the APD and the preceding diastolic interval (DI). Two factors are essential for the success of these experimentations: the isometric handgrip test exercised by the tested subject which ensures a sufficient variation of the QT interval [6], and a reliable algorithm for the detection of T-wave end in non stationary ECG signals [7].

The results show that the curve obtained by plotting QT interval against the preceding TQ interval has a shape similar to that of the cellular restitution curve, despite the difference between the macroscopic measurements based on ECG and the cellular measurements. The curve obtained is referred as the *ECG-based restitution curve* in the sequel. Following this similarity, a parametric restitution curve model, derived from a two-current model of cell membrane action potential, is fitted to the ECG-based restitution curve with a satisfactory accuracy.

The paper is organized as follows. In section 2 the method to obtain the ECG-based restitution curve, including the isometric handgrip test and the parametrical restitution curve derived from an action potential model, is described. In section 3 the experimental results are presented. The concluding remarks and discussion are shown in section 4.

2. Methods

In this section the method to obtain the ECG-based restitution curve is presented. First, the handgrip test is explained followed by the procedure to obtain the curves and the confirmation of the relationship between ECG scale and cellular scale.

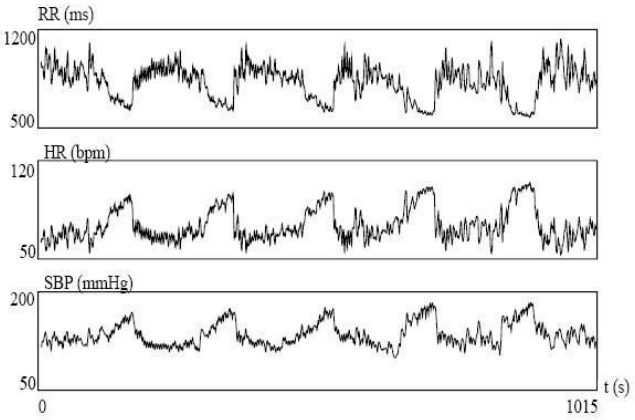

Figure 1. RR interval, heart rate (HR), and systolic blood pressure (SBP) time series during five handgrip bouts which are separated by recovery bouts, in one subject.

2.1. The ECG signal during the Handgrip test

Handgrip test is an isometric exercise, which triggers in a short term strictly autonomic responses. It produces heart rate and arterial pressure increases [6]. This cardiovascular response (alteration of the baroreflex functioning) is thought to be mediated by the voluntary central command, which arises at the onset of any kind of exercise. This command leads to a synchronous activation of the motor and cardiovascular system. Such an activation results in an indirect but very fast stimulation of the cardiovascular system as though the system anticipated the hypothetical oxygen muscle needs. The first minute of a handgrip test is an exceptional physiological condition of pure parasympathetic response, resulting in cardiac acceleration, blood pressure augmentation, and alteration of cardiovascular parameters variability (see Figure 1).

2.2. Experimental restitution curves

In order to obtain the experimental restitution curve from ECG the following steps are required:

- Recording of the ECG during handgrip test.
- Computation of the QT interval and its preceding TQ interval at each cardiac cycle.
- Plot of QT_{n+1} and the preceding TQ_n.

For the computation of QT, instead of directly detecting the onset of QRS, we detect R peaks and shift them to obtain the QRS onset, by considering that the QR interval is constant in an ECG record. This is a usually used method for QT interval computation, because it is easier to detect R peak than the Q wave onset. The T wave end is detected at each cardiac cycle with the algorithm presented in [7].

In the sequel the obtained experimental restitution curve will be called *ECG-based restitution curve*

2.3. Analytic restitution curve

Some analytical models for cellular restitution curve are well known in the literature. By similarity we look for an analytical model for the ECG-based restitution curve. One possibility is to derive such a model from an action potential (AP) model.

A model for electrical activity of cardiac membrane [8], which incorporate an inward and an outward current, is used in this work. The model contains two functions of time, the action potential (AP) $v(t)$ and a gating variable $h(t)$ as shown in equations (1) and (2).

$$\frac{dv}{dt} = J_{in}(v,h) + J_{out}(v) + J_{stim}(t) \quad (1)$$

$$\frac{dh}{dt} = \begin{cases} \frac{1-h}{\tau_{open}} & \text{si } v < v_{gate} \\ \frac{-h}{\tau_{close}} & \text{si } v > v_{gate} \end{cases} \quad (2)$$

where $J_{in}(v) = \frac{hv^2(1-v)}{\tau_{in}}$ represents the enter current and $J_{out} = -\frac{v}{\tau_{out}}$ represents the outward current, τ_{in}, τ_{out}, τ_{open} and τ_{close} are time constants. The stimulus current J_{stim} is an external current applied by the experimenter. Typically, it consists of a periodic train of brief pulses with duration of 1 ms [9],

One of the advantages of this model, that will be exploited later, is that it naturally gives rise to an explicit formula for the restitution curve that can be derived from the model. This restitution curve is qualitatively similar to the commonly used exponential restitution curve [10, 11].

The action potential duration at time instant $n+1$ derived from the model of equations (1) and (2) is defined at follows:

$$APD_{n+1} = \tau_{close} ln\left(\frac{1-(1-h_{min})e^{-\frac{DI_n}{\tau_{open}}}}{h_{min}}\right) \quad (3)$$

where DI_n is the preceding diastolic interval at time instant n, $h_{min} = 4\frac{\tau_{in}}{\tau_{out}}$ corresponds to the minimum of the nullcline $\frac{dv}{dt} = 0$ in equation (1).

The analytical restitution curve of equation (3) is used to fit the ECG-based restitution curve obtained in paragraph 2.2. In order to fit this curve, the non linear least squared method is used to minimize the error between $f(TQ_n)$ of the equation (3) and the QT interval at cardiac cycle $n+1$ of the ECG signal. This is defined as

$$\min_{\underline{\theta}} \sum_{n=1}^{N} (f(TQ_n, \underline{\theta}) - QT_{n+1})^2 \quad (4)$$

where $f(QT_n, \underline{\theta})$ correspond to the equation (3), $\underline{\theta} = [\tau_{close}\ h_{min}\ \tau_{open}]$ correspond to the parameter vector of

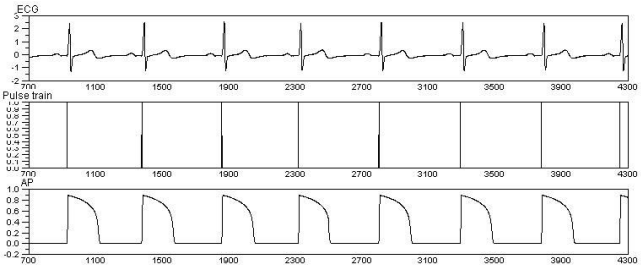

Figure 2. AP model stimulated by a train of pulses of frequency similar to the heart rate.

equation (3) that we desire to estimate, and N is the number of cardiac cycles.

In order to confirm this analytic model, the parameters estimated by solving the minimization problem (4) are used to simulate action potentials with equations (1) and (2). To do this, the AP model is stimulated with a sequence of brief pulses. After QT computing in the same ECG record used to find the ECG-based restitution curve, we use the Q wave onset instants as the instants of impulse occurrences as shown in Figure 2. To simulate the AP model we need the four time constants of equations (1) and (2), however, from the minimization problem (4) only two time constants, τ_{close} and τ_{open} can be estimated. For τ_{in} and τ_{out} it is sufficient to estimate only one of these time constants because they are related with the third estimated parameter, $\widehat{h}_{min}$, by the equation $\widehat{h}_{min} = 4\frac{\tau_{in}}{\tau_{out}}$. To do this, the minimization of the mean square error (MSE) between the QT interval of the ECG and the APD issue from the stimulated AP model has been carried as follows.

$$\min_{\tau_{out}} \frac{1}{N} \sum_{n=1}^{N} \left(QT_n - APD_n(\tau_{out})\right)^2 \qquad (5)$$

3. Results

3.1. ECG-based restitution curve

In this section the results concerning the obtained ECG-based restitution curve during handgrip test and the parametric restitution curve that fits this curve are shown.

In figure 3 at the left, two RR and QT time series for two ECG record during handgrip are shown. At the beginning of the handgrip test the heart rate increases while the QT interval decreases. At the time that handgrip test stops, the heart rate recovers very quickly while the QT interval takes more time to recover.

At the right of the figure 3 (crosses), two ECG-based restitution curves obtained during acceleration of the heart rate (between time instants T_1 and T_2 on the figure) are shown. These obtained curves have similar shape to the rstitution curve between APD and its preceding DI ob-

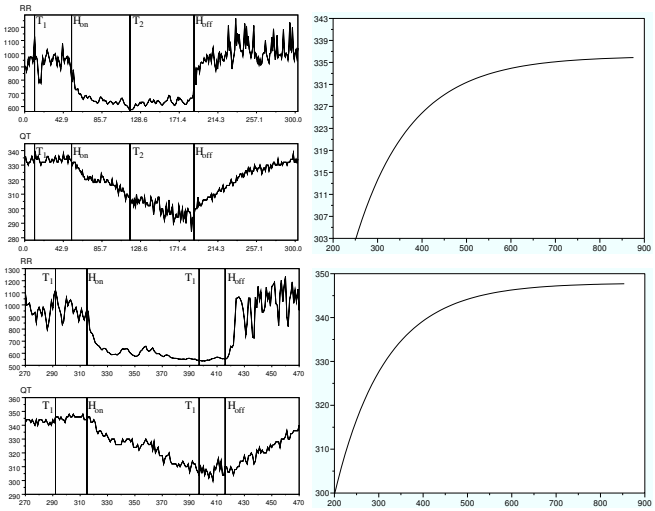

Figure 3. At the left are shown the RR and QT variation, the time instant of onset and offset of the handgrip (H_{on} and H_{off}), and the time intervals taken to plot the ECG-based restitution curve (T_1 and T_2) during acceleration of heart rate for two ECG records. At the right are shown the respectively ECG based restitution curves (crosses) and the parametric restitution curve of equation (3) (solid line).

tained on an isolated cell [12, 13]. In the same figure is shown as well (in solid line) the parametric restitution curve of equation (3) using the estimated parameters of equation (4) that fits the ECG-based restitution curve. The results show that the parametric restitution curve fits the ECG based restitution curve satisfactorily.

3.2. AP model simulation

Some results concerning the APD variability obtained from the model of equations (1) and (2) as explained in section 2 are shown.

In figure 4 at left are shown, for two ECG records, the variability of the QT interval (dot line) of the ECG-based restitution curve and the APD variability (solid line) calculated from the model of equations (1) and (2) after stimulation of the AP model and optimization of τ_{out} (τ_{in}). At the right of the same figure, the respective restitution curve plotting DI_n versus APD_{n+1} (crosses), both calculated from the model, and the ECG-based restitution curve plotting TQ_n versus QT_{n+1} (triangles) are shown.

The results show that the time course of the model's APD follows in a very good way the time course of the the QT interval of the ECG during Handgrip, moreover, both restitution curves have similar shapes.

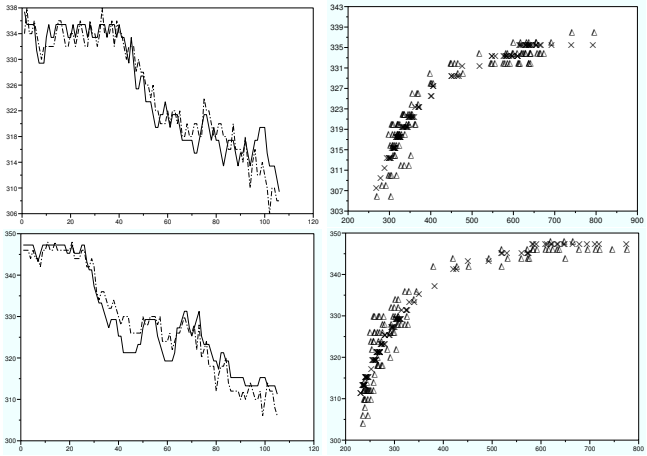

Figure 4. Results for two ECG registers. At the left, the QT time course (dot line) and the APD time course (solid line) issue from the AP model. At the right, the respective ECG restitution curve (triangles) and AP model restitution curve (crosses).

4. Discussion and conclusions

In this paper, experimental results revealing the relationship between the QT interval and its preceding TQ interval have been presented. This relationship is similar to the restitution curve observed in isolated cells. Despite of the difference between macroscopic measurements of the ECG during the handgrip test and cellular measurements, we obtain satisfactory results reflecting the relationship between ECG scale and cell scale. Following this similarity a parametric model of a restitution curve has been developed. This model is derived from a two current based cardiac cellular action potential model. In addition, the action potential model has been stimulated using a train of impulse with frequency equal to the heart rate frequency. This simulation indicates that APD model variation time course track the QT interval variation time course confirming the relationship between ECG scale and cell scale.

ECG-based restitution curves have been observed under the isometric handgrip test in most of situations. However, the ECG-based restitution curve is not always observed. In acceleration phase the results show that the restitution curves, similar to that seen on isolated cells, are obtained if a large QT variability is observed during handgrip test. Otherwise, no restitution curve is observed if an increase in heart rate is not followed by persistently increasing QT intervals. In the recover phase, when the handgrip test stops and the heart rate decreases, the results show a correlation between TQ_n and QT_{n+1}. However, in contrast to the heart rate acceleration stage, these curves have not a shape similar to that seen on isolated cells in most of the cases. This difference of shapes can be explained by the rapidity of the recover phase resulting in small quantity of data to analyze. Despite that, in certain cases at the recovery phase restitution curves are observed.

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