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A dynamic model to characterize beat-to-beat adaptation of repolarization to heart rate changes

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Abstract

An adaptive approach is presented to investigate, on a beat-to-beat basis, the response to heart rate variations of the QT interval and the T wave amplitude (T_a). The relationship between each repolarization index and the RR interval is modeled using a time-variant system composed of a linear filter followed by a memoryless nonlinearity approximated by a Taylor expansion. The linear portion describes the influence of previous RR intervals on the repolarization index and the nonlinear portion expresses how the index evolves as a function of the averaged RR measurement ($\overline{\mathrm{RR}}$) at the output of the linear filter. For the identification of the unknown system, two procedures that simultaneously estimate all of the system parameters are proposed. The first procedure converts the total input–output relationship into one being linear in its parameters and uses a Kalman-based technique to estimate these parameters. The second procedure uses the Unscented Kalman Filter to solve the nonlinear identification directly. Those procedures were tested on artificially generated data and showed very good agreement between estimated and theoretical parameter values. The application to electrocardiographic recordings showed that both repolarization indices lag behind the RR interval, being the effect more noticeable for the QT interval and more strongly manifested in episodes of sustained changes in heart rate, with QT lags after large RR variations of nearly 1 min in mean over recordings. The time variant $\mathrm{QT}/\overline{\mathrm{RR}}$ relationship was found to be adequately modeled by a first-order Taylor expansion, while the $T_a/\overline{\mathrm{RR}}$ relationship was better modeled using a second-order nonlinearity.

Keywords: QT adaptation; QT/RR relationship; Nonlinear models

1. Introduction

Since the extensive reports showing that impaired adaptation of the QT interval to changes in heart rate (HR) might be associated with the risk of cardiac arrhythmias [1–3], the QT interval, which expresses the overall duration of ventricular depolarization plus repolarization, is one of the most well-studied indices of the surface electrocardiogram (ECG). Many of the studies that analyzed the relationship between QT and RR (the inverse of heart rate) were restricted to episodes in which the RR signal was stable [4], when the QT interval is affected mainly by the preceding RR interval. In situations where there is a large variation in cardiac rhythm, the influence of the history of preceding RR intervals on each QT measurement needs to be considered to account for the well-known hysteresis effect present in the QT/RR relationship [5–8]. In [5] a method was proposed to assess the QT interval response to changes in heart rate on ambulatory recordings and characteristics of the adaptation in terms of duration and profile were provided for individual recordings and for selected segments of the recording that showed abrupt changes in heart rate. Those characteristics were used to discriminate between post-myocardial infarction patients at high and low risk of arrhythmic death while on treatment with amiodarone. With that type of method, however, it is not possible to evaluate the QT dynamic behaviour on a beat-to-beat basis, which can be very useful in identifying instances when disturbances in the adaptation occur and which, on the other hand, can be masked by the static analysis performed in [5] if the overall adaptation is not modified. In this study, we develop and test a full beat-to-beat adaptation analysis that can describe changes in the QT

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interval dynamically and relate them to variations in heart rate. Also, the index T_a measuring the T wave amplitude is examined, which has been shown to have a strong heart rate dependence [9]. Since recent works published in the literature have documented that assessment of T wave morphology changes in relation to heart rate can provide more insight into repolarization abnormalities [9,10], we have also investigated in this study the beat-to-beat adaptation of T_a in response to rate variations, using the same methodology as for the QT interval.

To perform the investigation, we propose a general model that, when applied to ECG data, takes the RR series, after interpolation, as the input signal $x_{RR}(n)$ and the corresponding interpolated QT series as the output signal $y_{QT}(n)$, where n is the discrete time index. Analogously, the analysis is performed taking as output signal the interpolated T_a series, $y_{T_a}(n)$. In the description of the methods, the output signal will be generically denoted by $y_{QT}(n)$ to simplify the reading. The system proposed in this study to relate the input and output signals $x_{RR}(n)$ and $y_{QT}(n)$ is assumed to be composed of a linear time-variant FIR filter followed by a zero-memory nonlinear function represented by a Pth-order Taylor polynomial ($P > 0$) whose coefficients are permitted to vary over time. Since the underlying system is time-varying and the stochastic process that supplies the tap inputs can be nonstationary (e.g., in the analysis of the QT/RR or T_a/RR relationship in ambulatory recordings), the adaptive filter proposed for system identification has to deal with nonstationary environments. This led us to formulate the problem using state-space models and apply Kalman-based filters to solve it.

The proposed methodology was evaluated using simulated data and, subsequently, applied to the analysis of real ECG recordings to assess the QT/RR and T_a/RR adaptation on a beat-to-beat basis. ECG data were obtained from healthy subjects as they changed their posture in a prescribed way, which caused substantial and, frequently, very abrupt changes in heart rate. In this study, we investigated the mode of adaptation of the two repolarization indices to those changes in rate and we explored interindividual differences. Also, we examined differences in the adaptation to accelerating and decelerating heart rates.

The paper is organized as follows: Section 2 contains the procedures of the study, and the data are described in Section 3. Section 4 proposes a number of performance measures for assessing the procedure. Section 5 presents the results, which are discussed in Section 6.

2. Methods

2.1. Model composition

A nonlinear system with memory is used to model the relationship between scalar and real input and output signals, $x_{RR}(n)$ and $y_{QT}(n)$, respectively. The input signal $x_{RR}(n)$ is the realization of a stochastic process that can be nonstationary and for which no a priori probability density function distribution is assumed. In the ECG application, the input $x_{RR}(n)$ represents an RR interval series interpolated to a sampling rate of 1 Hz, while the output $y_{QT}(n)$ corresponds to a 1 Hz-interpolated QT interval series. The system to be identified (Fig. 1) is assumed to be composed of a linear time-variant FIR filter of order N:

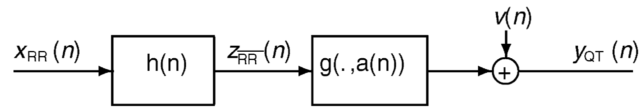

Fig. 1. Block structure of the system used in the study, which is composed of a linear FIR time-variant filter h(n) followed by a time-varying nonlinear function $g(\cdot, \mathbf{a}(n))$. The output of the system is corrupted by additive noise $v(n)$.

$$\mathbf{h}(n) = [h_0(n), \ldots, h_{N-1}(n)]^{\mathrm{T}} \in \mathbb{R}^{N\times 1}, \tag{1}$$

whose output is denoted by $z_{\overline{RR}}(n)$, followed by a time-varying zero-memory nonlinearity $g(\cdot)$ that is expandable as a Pth-order Taylor series around a bias point:

$$g(z_{\overline{RR}}(n), \mathbf{a}(n)) = \sum_{k=0}^{P} a_k(n) z_{\overline{RR}}^k(n), \tag{2}$$

with $\mathbf{a}(n) = [a_0(n), \ldots, a_P(n)]^{\mathrm{T}} \in \mathbb{R}^{(P+1)\times 1}$. The Taylor expansion for the nonlinearity $g(\cdot)$ is valid in a neighbourhood of a bias point different from 0 and the original Taylor series was subsequently reformulated as in Eq. (2), with the bias point integrated in the coefficients. The orders N and P of the subsystems are defined a priori based on the characteristics of the input and output signals to be processed. In the case of the QT/RR relationship, it is sufficient to consider polynomial nonlinearities up to order $P = 2$ and filter lengths up to $N = 50$ (which corresponds to 50 s due to series interpolation to 1 Hz) because even a larger number of preceding RR intervals can influence each QT, the initial 40–50 s are the most clinically relevant [5].

An important remark about the identification of the proposed system is that its linear and nonlinear portions can only be determined up to a scale factor, because the multiplication of each filter weight by a factor η (i.e., $\eta h_i(n)$, $i = 0, \ldots, N-1$) and the division of the nonlinearity coefficients by η^k (i.e., $a_k(n)/\eta^k$, $k = 0, \ldots, P$) does not alter the output of the overall system. If a restriction is imposed on the linear filter, such as $\mathbf{h}^T(n)\mathbf{1} = 1, \forall n$, with $\mathbf{1}$ denoting the $N \times 1$ vector of ones, uniqueness in the estimation of the filter weights and nonlinearity coefficients is guaranteed. Other constraints are imposed in the identification procedure with the objective of providing a meaningful physiological interpretation of the ventricular repolarization adaptation. The constraints are such that all of the filter weights in $\mathbf{h}(n)$ are positive, which permits the interpretation of the relative contribution of previous RR intervals to each QT measurement.

With such restrictions, the output of the linear portion,

$$z_{\overline{RR}}(n) = \mathbf{h}^{\mathrm{T}}(n)\mathbf{x}_{RR}(n), \tag{3}$$

where

$$\mathbf{x}_{RR}(n) = [x_{RR}(n)\, x_{RR}(n-1) \ldots x_{RR}(n-N+1)]^{\mathrm{T}}, \tag{4}$$

can be interpreted in the ECG application as a running weighted-averaged RR measurement with weights specifically defined at each instant n. The nonlinear subsystem is representative of how