Detection of Heart Rate Turbulence Using an Extended IPFM Model

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Abstract

In this study, the IPFM model is extended to account for the presence of ectopic beats and heart rate turbulence (HRT). Based on the model extension, a new approach to characterize HRT is presented based on a set of Karhunen-Loeve (KL) basis functions. The three most significant basis functions possess attractive physiological interpretations which reflect the difference in heart rate prior to the ventricular ectopic beat (VEB) compared to after HRT, an "average" HRT, and a delayed "average" HRT, respectively. HRT detection is based on the IPFM model extension, and involves a test statistic that results from a linear model. The HRT test statistic was studied on patients who underwent hemodialysis treatment. The goal was to distinguish between patients considered to be hypotension-resistant (HtR) and hypotension-prone (HtP). The results show that the test statistic of the two groups formed two non-overlapping clusters. The HtR-cluster exhibited much larger values than did the HtP-cluster (mean values 51 and 2, respectively), suggesting that HRT is mostly present in HtR patients.

1. Introduction

It has recently been demonstrated that HRT is a powerful predictor of mortality after acute myocardial infarction [1, 2], and offers considerable potential in other clinical issues as well [3]. Several parameters for HRT characterization have been presented of which turbulence onset (TO) and turbulence slope (TS) are the most commonly employed. While both these parameters have proven to be useful, they are heuristic in nature and do not relate to recent techniques for analysis of heart rate variability. Therefore, the purpose of the present paper is to develop model-based signal processing techniques for HRT characterization.

Based on an extension of the IPFM model, we present an approach which involves a set of KL basis functions. These functions express HRT as a function of time, as opposed to existing HRT measures which are based on the RR interval tachogram. The KL representation is then used in a HRT detection procedure.

The clinical goal of the present study is to investigate whether HRT can be used to distinguish between hemodialysis patients considered to be HtR and HtP, assuming that HRT is present in HtR patients, but not in HtP patients.

2. Background

2.1. HRT analysis

The short-term fluctuation in heart rate which follow a VEB is referred to as HRT [1, 2]. In normal subjects, the heart rate should increase and then decrease to baseline, immediately after a VEB. The increase in heart rate is probably due to compensation of the sudden local drop in blood pressure induced by the VEB. Once blood pressure is restored, heart rate returns to baseline in order to stabilize blood pressure. Thus, HRT is desirable in normal subjects, and the subjects' ability to recover from a local decrease in blood pressure is reflected by the degree of turbulence.

The degree of turbulence may be characterized with the parameters TO and TS. The former parameter reflects the initial acceleration in heart rate and the latter the deceleration of heart rate back to baseline. In particular, TO is the relative change of RR intervals immediately before and after a VEB. The parameter TS is defined by the steepest slope observed over five consecutive RR intervals in the first 15 RR intervals following the VEB.

2.2. IPFM model and heart timing signal

The IPFM model generates a series of occurrence times for normal sinus beats with known rate variability, and reflects basic electrophysiological properties of the sinoatrial node [4, 5]. The input signal to the IPFM model is the sum of a DC level, accounting for average heart rate, and a modulating signal, $m(t)$, accounting for variability due to

parasympathetic and sympathetic activity. The input signal to the IPFM model is integrated until a threshold, T_0, is reached, representing the mean interval length between successive events. Then, an event is created at time t_k as the output of the model, and the integrator is reset to zero. As a result, the output signal of the IPFM model becomes an event series which represents the beat occurrence times. In mathematical terms, the following equation defines the series of event times,

$$\int_0^{t_k} (1 + m(\tau))d\tau = kT_0 \qquad k = 0, \ldots, K, \quad (1)$$

where k is an integer that indexes the k^{th} beat following the initial event. The initial event is assumed to occur at $t_0 = 0$.

The heart timing signal $d_{HT}(t)$ is at time t_k defined as the difference between the expected occurrence time at the mean heart rate, kT_0, and the event time t_k [6]. The heart timing signal is closely related to the IPFM model and its modulating signal $m(t)$ [5].

3. Methods

3.1. Extended IPFM model

The physiological influence of a VEB may be viewed as a reset of the charging potentials in the sinoatrial node. In order to incorporate such a property in the IPFM model, the integrator is reset at the occurrence time t_l^e corresponding to the l^{th} VEB, see Fig. 1. Hence, this modification accounts for the very presence of VEBs in the generation of occurrence times of normal sinus beats.

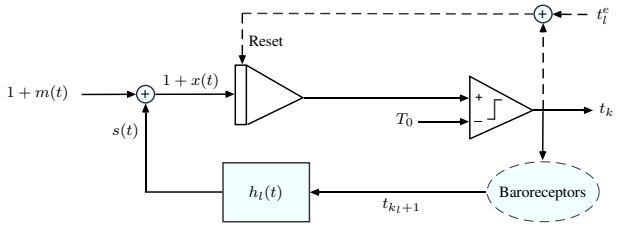

Figure 1. An overview of the extended IPFM model.

In order to account for the related HRT phenomenon, an additional feedback is introduced in the model. Physiologically, the HRT is triggered by the local diastolic blood pressure drop at t_{k_l+1} induced by the VEB. The occurrence time of the first normal sinus beat that follows the l^{th} VEB is denoted t_{k_l+1}. Thus, HRT is incorporated in the IPFM model, with feedback from the output of the IPFM model (the occurrence time of normal sinus beats, t_k) to the baroreceptors, see Fig. 1. When an HRT is triggered, the baroreceptors generate an impulse at t_{k_l+1} to a linear system with impulse response $h_l(t)$, where $h_l(t)$ is the HRT associated with the l^{th} VEB, see Fig. 1. The summation, $s(t)$, of all different HRTs caused by different VEBs

$$s(t) = \sum_{l=1}^{N_e} h_l(t - t_{k_l+1}), \quad (2)$$

is then added to the input of the integrator of the IPFM model, see Fig. 1; N_e denotes the number of VEBs.

The impulse response $h_l(t)$ is causal and reaches zero when the turbulence effect has vanished. It is assumed that $h_{l-1}(t - t_{k_{l-1}+1})$ reaches zero prior to the onset of the next HRT $h_l(t - t_{k_l+1})$. One way to represent different HRTs is as a linear combination of basis functions,

$$h_l(t) = \mathbf{b}^T(t)\boldsymbol{\theta}_l, \quad (3)$$

where $\mathbf{b}(t) = [b_1(t), b_2(t), \ldots, b_p(t)]^T$ contains p basis functions and $\boldsymbol{\theta}_l$ is a $p \times 1$ weight vector associated with the l^{th} VEB.

3.2. Karhunen-Loeve basis functions

In this study, data-dependent basis functions were considered and, in particular, the KL basis functions which are optimal for a given set of data. The KL basis functions are obtained from the eigenvalues and eigenvectors of the data covariance matrix $\mathbf{R_x}$ that results from subjects with HRT. Before calculation of $\mathbf{R_x}$, each subject's HRT is scaled in time with respect to mean heart rate. Thus, it is assumed that the duration of the HRT depends on heart rate. For each subject, the mean RR interval, $\tilde{T}_0$, is estimated from the 10 RR intervals that precede a VEB,

$$\tilde{T}_0 = \frac{1}{N_e} \sum_{l=1}^{N_e} \frac{t_{k_l} - t_{k_l-10}}{10}, \quad (4)$$

where t_{k_l} is the occurrence time of the normal sinus beat immediately prior to the l^{th} VEB. For all subjects, the overall mean $\tilde{T}_0$, denoted $\overline{T}_0$, is determined.

For each subject, $\mathbf{R_x}$ is determined from the available HRTs. In order to obtain an HRT estimate, an estimate of the zero mean input $x(t)$ to the IPFM model is derived from the first order difference of $d_{HT}(t)$ according to

$$\frac{d}{dt} d_{HT}(t_k) = x(t_k) = \frac{\tilde{T}_0}{t_k - t_{k-1}} - 1 \qquad k = k_l + 2, \ldots. \quad (5)$$

where $x(t_{k_l+1}) = 0$, with t_{k_l+1} being the trigger time of the HRT. From $x(t)$, N_e different input signals to the IPFM model, $x_l(t)$, associated with the l^{th} VEB, may be obtained according to

$$x_l\left(\frac{\overline{T}_0}{\tilde{T}_0} t_k\right) = \begin{cases} 0 & k = 0, \ldots, k_l \\ x(t_k) & k = k_l + 1, \ldots, \end{cases} \quad (6)$$

where each subject's time vector is scaled with $\overline{T}_0/\tilde{T}_0$ in order to allow comparison of HRTs from different subjects.

An $N \times 1$ vector $\mathbf{x}_l$ is then obtained from interpolation of (6) followed by resampling of $x_l(t)$ starting at the time $\frac{\overline{T}_0}{\tilde{T}_0} t_{k_l+1}$, using a sampling rate of F_s Hz, in order to assure that $\mathbf{x}_l$ contains the HRT from the very first sample. The sample covariance matrix $\mathbf{R}_\mathbf{x}$ of one subject is obtained by

$$\mathbf{R}_\mathbf{x} = \frac{1}{N_e} \sum_{l=1}^{N_e} \mathbf{x}_l \mathbf{x}_l^T. \tag{7}$$

Finally, the mean covariance matrix $\overline{\mathbf{R}}_\mathbf{x}$ is determined from the different $\mathbf{R}_\mathbf{x}$:s.

The p most significant eigenvectors of $\overline{\mathbf{R}}_\mathbf{x}$ are chosen as the discrete representation of the p different basis functions contained in $\mathbf{b}(t)$. Thus, the discrete representation of (3) becomes

$$\mathbf{h}_l = \mathbf{B}\boldsymbol{\theta}_l, \tag{8}$$

where $\mathbf{h}_l$ is an $N \times 1$ vector with the discrete representation of the HRT associated with the l^{th} VEB, and $\mathbf{B}$ is an $N \times p$ matrix with the p most significant eigenvectors given by the columns,

$$\mathbf{B} = \begin{bmatrix} \mathbf{b}^T(0) \\ \mathbf{b}^T(\frac{1}{F_s}) \\ \vdots \\ \mathbf{b}^T(\frac{N-1}{F_s}) \end{bmatrix}. \tag{9}$$

Note that the first sample is associated with $t = 0$.

3.3. HRT detection

Our approach to detect and characterize HRT is based on the extended IPFM model and, in particular, the HRT response is modeled by $\mathbf{B}\boldsymbol{\theta}$. The detection procedure is formulated as one in which the HRT is either absent (hypothesis $\mathcal{H}_0$) or present (hypothesis $\mathcal{H}_1$),

$$\begin{aligned} \mathcal{H}_0 &: \quad \mathbf{x} = \mathbf{m} \\ \mathcal{H}_1 &: \quad \mathbf{x} = \mathbf{B}\boldsymbol{\theta} + \mathbf{m}. \end{aligned} \tag{10}$$

Furthermore, $\mathbf{x}$ is an $N \times 1$ vector with the observed data, $\mathbf{m}$ is an $N \times 1$ vector with random white noise with Gaussian PDF $\mathcal{N}(\mathbf{0}, \sigma^2\mathbf{I})$, where σ^2 is unknown, $\mathbf{B}$ is a known $N \times p$ $(N > p)$ orthogonal matrix, and $\boldsymbol{\theta}$ is a $p \times 1$ vector with unknown weights. The test statistic, $T(\mathbf{x})$, from the generalized likelihood ratio test (GLRT) of a linear model, assuming that the noise variance is unknown, is used for the detection of HRT [7, 8]. Thus, $\mathcal{H}_1$ is decided if

$$T(\mathbf{x}) = \frac{N-p}{p} \frac{\hat{\boldsymbol{\theta}}_{\mathcal{H}_1}^T \hat{\boldsymbol{\theta}}_{\mathcal{H}_1}}{\mathbf{x}^T(\mathbf{I} - \mathbf{B}\mathbf{B}^T)\mathbf{x}} > \gamma', \tag{11}$$

where $\hat{\boldsymbol{\theta}}_{\mathcal{H}_1} = \mathbf{B}^T\mathbf{x}$ is the maximum likelihood estimate (MLE) of $\boldsymbol{\theta}$ under $\mathcal{H}_1$, and γ' is a threshold found from a given probability of false alarm.

3.4. HRT averaging

In contrast to existing HRT studies, this study does not assume that the HRT is averaged, i.e., $\boldsymbol{\theta}_l$ is estimated from a single VEB, viz., the l^{th} VEB. However, averaging is usually adopted in HRT detection in order to improve performance, so that $\mathbf{x}$ in (11) instead is given by

$$\mathbf{x} = \frac{1}{N_e} \sum_{l=1}^{N_e} \mathbf{x}_l. \tag{12}$$

4. Data sets

From the European ST-T database thirty-one patients with myocardial ischemia and isolated VEBs were used as learning set for the KL basis functions. A total of 84 VEBs were selected from the 31 patients considered. The vector $\mathbf{x}_l$ resulted from resampling of $x_l(t)$ with $F_s = 2$ Hz during a time interval of 10 seconds, i.e., $N = 21$. The three most significant KL basis functions were chosen as columns in $\mathbf{B}$, i.e., $p = 3$.

The HRT test statistic in (11) was studied on a target data set which consisted of patients with end-stage renal failure who underwent regular hemodialysis treatment three times a week. The goal was to distinguish between patients considered HtR and HtP (five patients in each group). Before the ECG was recorded, a physician classified each patient into one of the two groups. The physicians decision was based on the patient's clinical history, such as the number of hypotension episodes per month. The ECG were acquired during clinical treatment at Park Dialys (Lund, Sweden) and Helsingborg Hospital (Sweden), lasting from 3 to 5 hours; all patients in the target set had isolated VEBs.

5. Results

In order to assure that the ischemic patients exhibit HRT, an averaged RR interval tachogram from the 84 VEBs was determined. The parameters TO and TS were determined, resulting in -0.4% and 3.2 ms/RR interval respectively.

The three most significant KL basis functions accounted together for 91% of the total energy. These three functions possess attractive physiological interpretations: the most significant basis function have the shape of a step function, the second reflects the "average" HRT, and the third reflects a delayed "average" HRT, see Fig. 2. It is common that the heart rate prior to a VEB and after the HRT differ. This offset in heart rate is reflected by the first basis function, e.g., a positive weight indicate a higher heart rate after the HRT than prior to the VEB. The significance of the first basis function is obscured when the

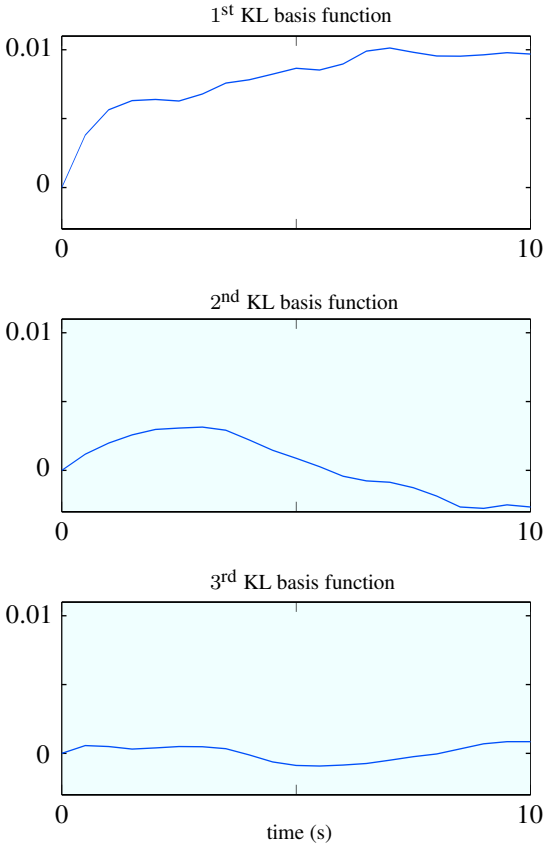

Figure 2. The three most significant KL basis functions, weighted with their respective eigenvalues. The 1st KL basis functions is the most significant, and so forth.

averaged HRT is obtained from several VEBs, since the offset tends to by cancelled out by averaging.

The HRT test statistic in (11) was calculated for the ten hemodialysis patients in order to evaluate its performance. The averaged HRT from each patient obtained according to (12) was used in the calculation of the test statistic. Finally, an asymptotic p-value from the Kolmogorov–Smirnov test between the $T(\mathbf{x})$-values from HtR and HtP patients were determined. The results show that the HRT test statistics of the two groups formed two non-overlapping clusters. The HtR-cluster exhibited much larger values than did the HtP-cluster: mean values 51 and 2, respectively, see Table. 1, indicating that HRT is present in HtR patients only. There was a significant difference between the two clusters (p-value: 0.0038), suggesting that the test statistic can be used to distinguish between HtR and HtP patients.

Table 1. HRT test statistics for HtR and HtP patients with their asymptotic p-value. Values are given in mean $\pm$ std.

	HtR	*HtP*	*p-value*
$T(\mathbf{x})$	51 ± 53	2 ± 1	0.0038

6. Conclusions

This paper presents new model-based signal processing techniques for HRT characterization, based on an extended IPFM model and a set of KL basis functions. The presented HRT procedure does not only provide further insights on the HRT phenomenon, but also relates to heart rate variability through the IPFM model and the heart timing signal. The results show that HRT is present in hemodialysis patients considered to be HtR but not in HtP.

Acknowledgements

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