Model-Based Analysis of the Ventricular Response during Atrial Fibrillation

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Abstract

We study a model of the atrioventricular node function during atrial fibrillation (AF), for which the model parameters can be estimated from the ECG. The proposed model is defined by parameters which characterize the arrival rate of atrial impulses, the probability of an impulse choosing either one of the two atrioventricular nodal pathways, the refractory periods of these pathways, and the prolongation of the refractory periods. The parameters are estimated from the RR intervals using maximum likelihood estimation, except for the shorter refractory period which is estimated from the RR interval Poincaré plot, and the mean arrival rate of atrial impulses by the AF frequency estimated from the ECG. The model was evaluated on 30-min ECG segments from 36 AF patients. The results showed that 88% of the segments can be accurately modeled when the estimated probability density function (PDF) and an empirical PDF were at least 80% in agreement.

1. Introduction

During atrial fibrillation (AF), the atrioventricular (AV) node is continuously bombarded with atrial impulses. The ventricular activity during AF is irregular and manifested by shorter RR intervals than during normal sinus rhythm, and is largely determined by AV nodal blocking of the impulses. Electrophysiologic factors such as intrinsic refractoriness of the AV node and concealed conduction influence the ventricular response [1]. The existence of two dominant pathways through the AV node, each with different electrophysiological properties, has been documented [2]. Even though these properties play a prominent role in ventricular rate control, they are not routinely evaluated in clinical practice.

Analysis of the ventricular response during AF has largely been confined to phenomenological exploration to better understand AV nodal electrophysiology, e.g., by using techniques based on RR interval histograms and Poincaré plots [3]. Although parameters extracted using such methods can be useful, they do not come with a physiological interpretation.

An alternative approach to study AV nodal characteristics is through mathematical modeling. A number of models have been proposed, which consider the AV node as a lumped structure whose behavior represents the temporal and spatial summation of the cellular electrical activity [4–8]. However, none of these models are particularly well-suited for parameter estimation from the ECG. Attempts were made to determine the model parameters from the RR series using an ad hoc procedure in [4], but the resulting estimates could assume unphysiological values. In other models, invasive information on atrial activity is crucial for the parameter estimation procedure [5, 6]. The detailed simulation models presented in [7, 8] are unsuitable for estimation since a very large number of parameters are embraced.

The aim of this paper is to study an AV node model which accounts for important electrophysiological properties, but which still lends itself to ECG-based parameter estimation. In contrast to the above-mentioned models, the present one accounts for dual AV nodal conduction and makes use of an AF rate which is inferred from the ECG. The output of the method is a set of parameter estimates which provides an electrophysiological characterization of the AV node.

2. Methods

In the present model, the AV node is treated as a lumped structure which accounts for concealed conduction, relative refractoriness, and dual AV nodal pathways. Atrial impulses are assumed to arrive to the AV node according to a Poisson process with mean arrival rate λ. Each arriving impulse is suprathreshold, i.e., the impulse results in ventricular activation unless blocked by a refractory AV node. The probability of an atrial impulse passing through the AV node depends on the time elapsed since the previous ventricular activation t.

The length of the refractory period is defined by a deterministic part τ and a stochastic part τ_p. The latter part models prolongation due to concealed conduction and/or relative refractoriness, and is assumed to be uniformly distributed in the interval $[0, \tau_p^{\max}]$. Hence, all atrial impulses

arriving at the AV node before the end of the refractory period τ are blocked, no impulses arriving after the end of the maximally prolonged refractory period $\tau + \tau_p^{\max}$ are blocked, and the likelihood of an impulse to pass through the AV node in $[\tau, \tau + \tau_p^{\max}]$ is linearly increasing. The deterministic part of the refractory period can assume two values, τ_1 or $\tau_2 = \tau_1 + \Delta\tau$ ($\Delta\tau \geq 0$), which characterize the two pathways. The maximal prolongation $\tau_p^{\max}$ is assumed to be identical for both pathways.

It is assumed that a ventricular activation immediately follows the first non-blocked atrial impulse among those reaching the AV node. Hence, ventricular activations occur according to an inhomogeneous Poisson process and the time intervals between consecutive ventricular activations x_m are independent. An expression for the joint probability of an RR series can be derived [9],

$$\begin{aligned} p_x(x_1, x_2, \ldots, x_M) &= \prod_{m=1}^{M} p_x(x_m) \qquad (1) \\ &= \prod_{m=1}^{M} (\alpha p_{x,1}(x_m) + (1-\alpha) p_{x,2}(x_m)), \end{aligned}$$

where α is the probability of an atrial impulse to take the AV path with shorter refractory period, and $p_{x,1}(x_m)$ and $p_{x,2}(x_m)$ are given by

$$p_{x,i}(x) = \begin{cases} 0, & x < \tau_i \\ \dfrac{\lambda(x-\tau_i)}{\tau_p^{\max}} \exp\left\{\dfrac{\lambda(x-\tau_i)^2}{2\tau_p^{\max}}\right\}, & \tau_i \leq x < \tau_i + \tau_p^{\max} \\ \lambda \exp\left\{\dfrac{\lambda\tau_p^{\max}}{2} - \lambda(x - \tau_i - \tau_p^{\max})\right\}, & x \geq \tau_i + \tau_p^{\max}. \end{cases} \qquad (2)$$

2.1. Model parameter estimation

It is well-known that the property in (1) of statistically independent time intervals is not fully valid for observed RR intervals. In order to better fulfill this assumption, a functional dependence of the refractory periods τ_i on the previous RR interval is considered,

$$\tau_{1,m} = \tau_1^{\min} + s_\tau x'_{m-1}, \qquad (3)$$

where x'_m denotes the m-th observed RR interval. The parameters s_τ and $\tau_1^{\min}$ are estimated from slope and the intercept of the lower envelope of the Poincaré plot, respectively. It is assumed that s_τ is identical for both $\tau_{1,m}$ and $\tau_{2,m}$.

With the availability of $\hat{s}_\tau$, the observed RR intervals are subjected to the following linear transformation,

$$x_m = x'_m - \hat{s}_\tau x'_{m-1}. \qquad (4)$$

The resulting series x_m is a modified version of the observed RR series for which the interdependence of successive RR intervals has been reduced, and thus the model assumption in (1) becomes more valid.

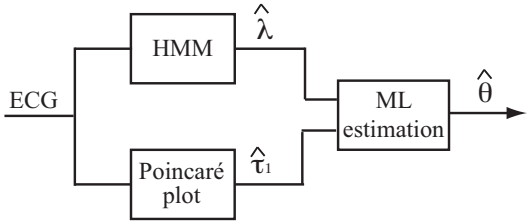

Figure 1. Block diagram of AV node model parameter estimation.

The arrival rate λ is determined by the dominant AF frequency which is derived from the ECG, and thus it is estimated independently of the model parameters which characterize ventricular activity. The atrial activity is extracted from the ECG using spatiotemporal QRST cancellation [10], after which the AF frequency is tracked on a short-term basis using a method based on a hidden Markov model (HMM) [11]. An estimate of λ is given by the median value of the AF frequency estimates computed over the analyzed ECG segment length.

The model parameters $\alpha, \Delta\tau$, and $\tau_p^{\max}$ are estimated by jointly maximizing the log-likelihood function with respect to $\boldsymbol{\theta} = \begin{bmatrix}\alpha & \Delta\tau & \tau_p^{\max}\end{bmatrix}^T$, i.e., the maximum likelihood estimator (ML) is given by

$$\hat{\boldsymbol{\theta}} = \arg\max_{\boldsymbol{\theta}} \log p_x(x_1, x_2, \ldots, x_M | \boldsymbol{\theta}; \hat{\lambda}, \hat{\tau}_1^{\min}), \qquad (5)$$

where p_x is given by (1). Since no closed-form solution could be found for $\hat{\boldsymbol{\theta}}$, combined with the fact that the gradient is discontinuous, simulated annealing [12] is employed to numerically optimize the log-likelihood function. The optimization algorithm was initiated with 10 different randomly chosen values for each estimation, and where the results were found to differ, the $\hat{\boldsymbol{\theta}}$ which yielded the maximum value of $p_x(x_1, x_2, \ldots, x_M | \boldsymbol{\theta}; \hat{\lambda}, \hat{\tau}_1^{\min})$ was chosen.

The block diagram in Fig. 1 illustrates the procedure employed for estimating the model parameters.

2.2. Evaluation

The model was evaluated on 36 Holter recordings from patients with sustained and paroxysmal AF, available from Physiobank [13]. The duration of the AF episodes ranged from approximately 30 min to 25 h. RR intervals preceding and following ectopic beats were excluded from further analysis; ectopic beats were detected based on heartbeat morphology. Whenever possible, the recordings were divided into 30-min segments with 50% overlap, and the model parameters were estimated in each segment.

Since the underlying PDF is unknown for ECG-derived RR intervals, an empirical PDF, denoted $\tilde{p}_x(x)$, was de-

termined by wavelet-based density estimation [14]. The capability to model different RR series was evaluated in terms of a percentage measure of fit $\mathcal{U}$, defined by

$$\mathcal{U} = 100 \cdot \left(1 - \int_0^2 \left| p_x(x|\hat{\boldsymbol{\theta}}; \hat{\lambda}, \hat{\tau}_1) - \tilde{p}_x(x) \right| dx \right), \quad (6)$$

where the upper integration limit reflects the fact that very few RR intervals are longer than 2 s during AF. In this study $\mathcal{U} > 80\%$ is considered to be a sufficiently accurate model fit. In addition to the Physiobank signals, ECGs recorded before and during head-up tilt test (10 and 8 min duration, respectively) were analyzed.

3. Results

Figure 2 shows the distribution of $\mathcal{U}$ among all 30-min ECG segments; its mean value is 84.6±4.8 %. The predefined threshold for an accurate model fit is fulfilled for 88% of the analyzed 30-min segments, i.e., 1754 out of 2004.

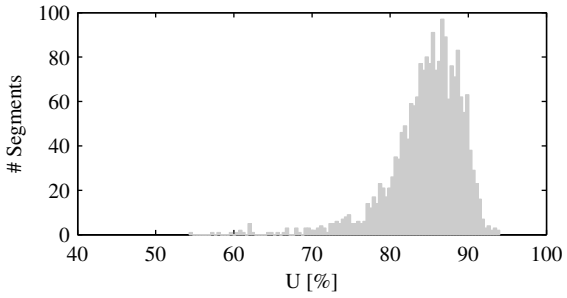

Figure 2. Distribution of the measure of fit $\mathcal{U}$ for 2004 different 30-min ECG segments.

The trends of the estimated model parameters over 24 h are displayed in Fig. 3(a)-(e), starting at time 21:00. For this patient, the parameter trends are relatively stable over the day. However, the α-trend exhibits a gradual increase in the morning, reaching a peak value of 0.78 at time 10:15. This increase is reflected by a transition from longer to shorter RR intervals to become more frequent. The PDFs of two different 30-min segments are displayed in Figs. 3(g) and (h).

Figures 4 and 5 display RR interval histograms and estimated PDFs, obtained from two patients before and during head-up tilt. These patients exhibit similar changes in atrial activity and ventricular response when tilted: the atrial rate λ increases, and the RR intervals are shortened due to an increase in α and decreases in $\Delta\tau$ and $\tau_1^{\min}$. This finding suggests that the refractory period of both AV nodal pathways decreases during tilt, the longer one more than the shorter one. It also suggests that the probability for impulses passing through the pathway with the shorter refractory period increases.

4. Conclusions

A statistical model of AV nodal function during AF is proposed, with parameters that characterize dual AV nodal pathways, concealed conduction, and relative refractoriness. A maximum likelihood approach is devised for estimating the model parameters from an RR interval series. The results from 36 Holter ECG recordings suggest that a wide variety of RR interval distributions can be accurately modeled; 88% of all 30-min segments were judged as accurate. The resulting parameter estimates are potentially useful for noninvasively assessing the influence of antiarrhythmic drugs on patients with AF.

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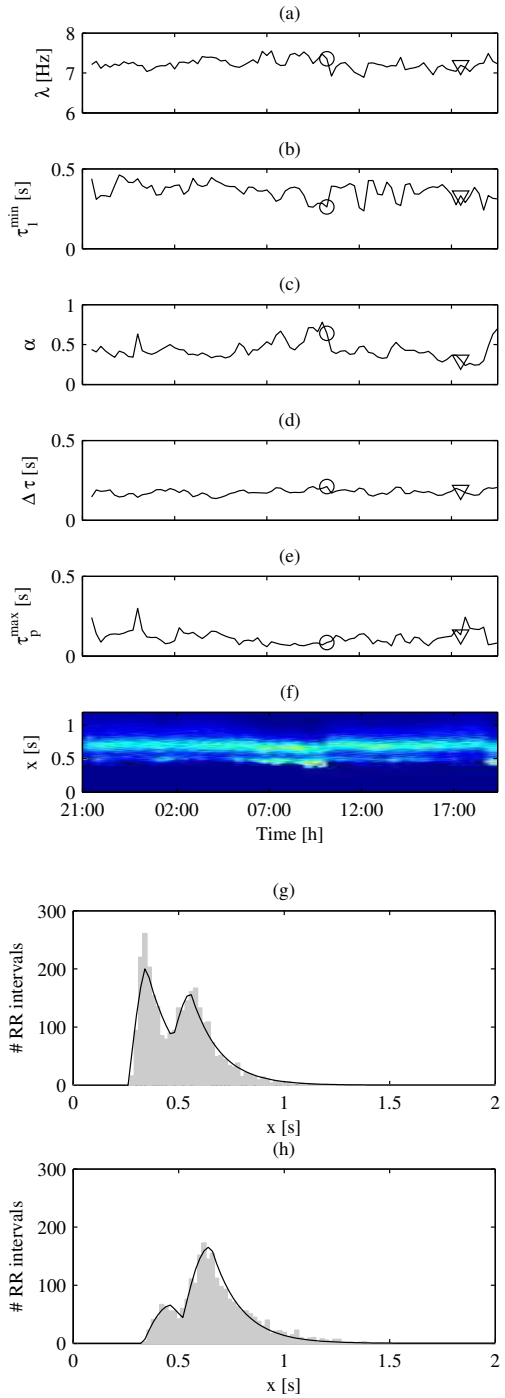

Figure 3. Trends of model parameter estimates from a patient with sustained AF: (a) λ, (b) $\tau_1^{\min}$, (c) α, (d) $\Delta\tau$, (e) $\tau_p^{\max}$, and (f) intensity plot of sequential RR interval histograms. The histogram and the estimated PDF are displayed at the times indicated by (g) a circle ($\mathcal{U} = 86.8\%$. $\hat{\lambda} = 7.4$ Hz, $\hat{\tau}_1^{\min} = 0.26$ s, $\hat{\alpha} = 0.64$, $\hat{\Delta\tau} = 0.21$ s, $\hat{\tau}_p^{\max}$=0.08 s), and (h) a triangle, respectively ($\mathcal{U} = 89.5\%$, $\hat{\lambda} = 7.2$ Hz, $\hat{\tau}_1^{\min} = 0.33$ s, $\hat{\alpha} = 0.31$, $\hat{\Delta\tau} = 0.19$ s, $\hat{\tau}_p^{\max}$=0.14 s).

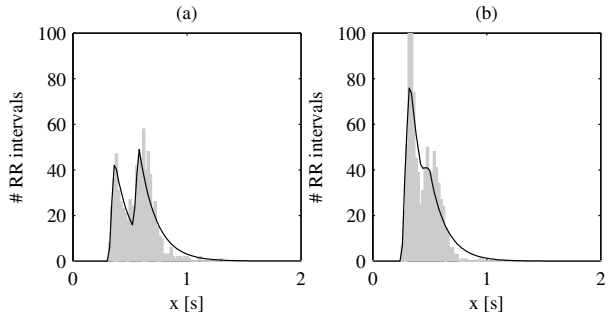

Figure 4. Histogram of transformed RR intervals x and the estimated model PDF from the same patient during (a) rest ($\mathcal{U} = 84.8\%$, $\hat{\lambda} = 6.6$ Hz, $\hat{\tau}_1^{\min} = 0.31$ s, $\hat{\alpha} = 0.54$, $\hat{\Delta\tau} = 0.22$ s, $\hat{\tau}_p^{\max}$=0.05 s), and (b) head-up tilt ($\mathcal{U} = 82.3\%$, $\hat{\lambda} = 6.9$ Hz, $\hat{\tau}_1^{\min} = 0.26$ s, $\hat{\alpha} = 0.84$, $\hat{\Delta\tau} = 0.17$ s, $\hat{\tau}_p^{\max} = 0.07$ s).

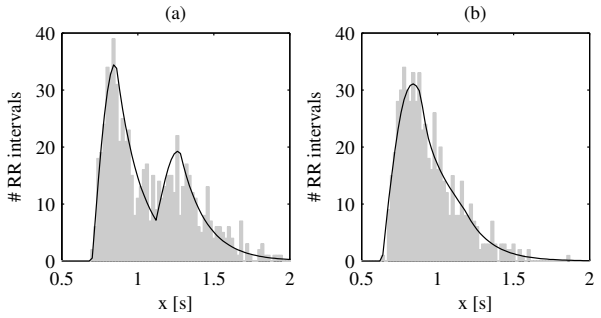

Figure 5. Histogram of transformed RR intervals x and the estimated model PDF from the same patient during (a) rest ($\mathcal{U} = 88.8\%$, $\hat{\lambda} = 6.0$ Hz, $\hat{\tau}_1^{\min} = 0.70$ s, $\hat{\alpha} = 0.68$, $\hat{\Delta\tau} = 0.42$ s, $\hat{\tau}_p^{\max}$=0.15 s), and (b) head-up tilt ($\mathcal{U} = 93.2\%$, $\hat{\lambda} = 6.1$ Hz, $\hat{\tau}_1^{\min} = 0.64$ s, $\hat{\alpha} = 0.88$, $\hat{\Delta\tau} = 0.30$ s, $\hat{\tau}_p^{\max} = 0.25$ s).

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