A Mathematical Model of The Atrioventricular Node during Atrial Fibrillation

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Abstract

The atrioventricular (AV) node plays a crucial role during atrial fibrillation (AF). The aim of this study is to present an AV node model which can be fitted to short-term ECG recordings in order to infer certain AV node characteristics. The proposed model is characterized by: i) the arrival rate of atrial impulses; ii) two different refractory periods, corresponding to dual AV nodal paths; iii) the probability of an atrial impulse choosing either of these pathways; iv) a parameter modeling prolongation of the refractory period due to different physiological reasons. The model was tested on atrial fibrillatory ECGs recorded from 33 patients; the average normalized absolute error between the normalized RR histogram and the estimated model probability density function was 0.0023 ± 0.0016*, (20-ms bin size, 0–2 s interval). These preliminary results are encouraging as AV nodal properties can be noninvasively assessed by a set of statistical parameters with a simple electrophysiological interpretation.*

1. Introduction

During atrial fibrillation (AF), a large number of atrial impulses bombard the atrioventricular (AV) node and some of them are blocked. Even if the important role played by the AV node is widely recognized, the relationship between atrial and ventricular frequencies and AV node has not been deeply studied. A number of models of the AV node during AF have been proposed. The first proposed AV node model [1] considers the AV junction as a lumped structure, whose behavior represents the temporal and spatial summation of the electrical activity of the cells in this complex structure. The atria are assumed to bombard the AV node with impulses arriving randomly in time, according to a Poisson distribution. When the AV node is not refractory, its transmembrane potential is assumed to increase, spontaneously as well as by each atrial impulse arriving. When the transmembrane potential reaches a certain threshold a new action potential starts, initiating a ventricular beat. This model is primarily useful for simulations, whereas its use on real data produced parameter estimates which are unphysiological.

Other models [2, 3] need invasive atrial and ventricular recordings to be applied to real data. In [2], given the measured atrial activation times, the times of ventricular activations are computed. The computed activation times are compared to the observed ones, computing a distance based on either the area below the series or the Kolmogorov-Smirnov test, while the parameters describing AV node function are varied. Parameters which give the best agreement between the computed and observed activation times are identified by scanning the parameter space of the model. The model was tested on only two patients' recordings (one during AF and one during atrial flutter): the results were less satisfactory during AF than during flutter, due to the higher irregularity of AF. Finally, simulation models have been proposed, which attempts to explain AV nodal characteristics [4] or the effect of pacing [5]. These models have many parameters that describe the underlying dynamics in more detail than the abovementioned models; however, these models are not suitable for parameter estimation from real data.

The aim of this study is to present an AV node model which can be used on short-term surface ECGs to estimate AV node characteristics. Information contained in the RR series as well as in the atrial activity of the ECG are combined to find the optimal model parameters. Thus, a set of parameters related to the electrophysiological characteristics of the AV node is obtained for each patient. This set could be used to classify patients, to better plan therapy, and to better understand the electrophysiological characteristics of the AV node during AF.

2. Methods

2.1. AV node model

Atrial impulses are assumed to arrive to the AV node according to a Poisson process with a mean arrival rate λ. The AV node is assumed to have two possible nodal pathways. Each atrial impulse arriving at the AV node is suprathreshold, i.e., it results in a ventricular contraction, un-

less the atrial impulse is blocked. The atrial impulses are blocked at the AV node according to the following time-dependent probability:

$$\beta(t) = \begin{cases} 1, & x < \tau \\ 1 - \frac{x-\tau}{\tau_{e_{max}}}, & \tau < t < \tau + \tau_{e_{max}} \\ 0, & t > \tau + \tau_{e_{max}} \end{cases} \quad (1)$$

where τ models the minimum refractory period, and $\tau_{e_{max}}$ the maximal prolongation of the refractory period due to factors such as relative refractory period and concealed conduction. An atrial impulse arriving prior to the end of the AV nodal refractory period is blocked, while one arriving after the end, but close in time to the previous ventricular contraction, is more likely to be blocked. When $t > \tau + \tau_{e_{max}}$, no atrial impulses are blocked. Two different refractory periods (τ_1 and τ_2), corresponding to dual AV nodal paths, are considered, whereas $\tau_{e_{max}}$ is assumed to be equal for the two paths. The probability of an atrial impulse taking the shortest path with refractory period τ_1 is given by α, $0 < \alpha < 1$; the probabilities of an atrial impulse taking either of the two paths sums up to 1, see Fig. 1.

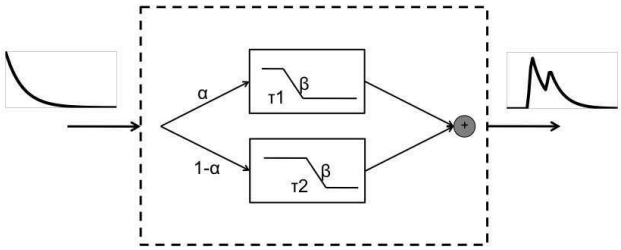

Figure 1. AV node model (see text for details).

The arrival of non-blocked atrial impulses to the AV node is assumed to be an inhomogeneous Poisson process with arrival rate $\lambda(1 - \beta(t))$. Since a ventricular contraction immediately follows the first non-blocked atrial impulse reaching the AV node, the probability density function (PDF) of the time x between two consecutive ventricular contractions is given by

$$p_x(x) = \lambda(1 - \beta(x))e^{-\int_0^x \lambda(1-\beta(\tau))d\tau}, \quad (2)$$

As a consequence of the dual nature of $\beta(x)$, $p_x(x)$ is composed of two different PDFs, so that

$$p_x(x) = \alpha p_{x,1}(x) + (1 - \alpha)p_{x,2}(x), \quad (3)$$

where

$$p_{x,i}(x) = \lambda(1 - \beta_i(x))e^{-\int_0^x \lambda(1-\beta_i(\tau))d\tau} \quad (4)$$

Inserting (1) into (4) and defining $\tau_{i_{max}} = \tau_i + \tau_{e_{max}}$ gives that

$$p_{x,i}(x) = \begin{cases} 0, & x < \tau_i \\ \lambda \frac{x-\tau_i}{\tau_{e_{max}}} e^{\frac{\lambda(x-\tau_i)^2}{2\tau_{e_{max}}}}, & \tau_i < x < \tau_{i_{max}} \\ \lambda e^{\left(\frac{\lambda\tau_{e_{max}}}{2} - \lambda(x-\tau_{i_{max}})\right)}, & x > \tau_{i_{max}}. \end{cases} \quad (5)$$

2.2. Model parameter estimation

The arrival rate λ is estimated by the AF frequency obtained from the atrial activity of the surface ECG. In particular, atrial fibrillatory activity is extracted using spatiotemporal QRST cancellation [6]. The dominant frequency of the resulting atrial signal is tracked using a method based on a hidden Markov Model (HMM) [7], which produces an optimal frequency trend from a sequence of observed frequency estimates using a priori knowledge about the likelihood of frequency changes and the frequency estimation method employed. For each 10-s ECG segment, one frequency estimate is produced by the HMM method; λ is obtained by averaging these estimates.

The functional refractory period τ_1 is obtained from the lower envelope of the Poincaré plot of the RR series; in this plot each RR interval is displayed against the previous one. It has been shown that the lower envelope of the Poincaré plot can be used as a measure of cycle length dependence on the functional refractory period of the AV node [8]. Briefly, the horizontal axis is divided into consecutive bins and, for each bin, the minimal value of subsequent RR interval is determined. Finally, a linear regression of the minimal points is performed, so that the equation for the lower envelope of the Poincaré plot

$$\tau_1(m) = \tau_{1min} + \tau_{slope}x'_{m-1}, \quad (6)$$

is defined, where x'_m denotes the m:th RR interval. The linear dependence τ_{slope} is assumed to be equal for τ_1 and τ_2, thus the difference between the two refractory periods $\Delta\tau$ is constant.

Apart from τ_1, which is independently estimated, the model parameters, $\boldsymbol{\theta} = [\alpha, \Delta\tau, \tau_{e_{max}}]$ are estimated by maximizing the joint probability $p_x(x_1, x_2, \ldots, x_M)$. Since a ventricular contraction is triggered according to a Poisson process, the time intervals between consecutive ventricular contractions are independent. Therefore, the dependences of consecutive RR intervals $(x'_1, x'_2, \ldots, x'_M)$ are eliminated making use of the estimated value of τ_{slope}, so that

$$x_m = x'_m - \tau_{slope}x'_{m-1} \quad (7)$$

Since the model assumes statistical independence of $(x_1, x_2, \ldots, x_M)$, the joint probability is given by

$$p_x(x_1, x_2, \ldots, x_M; \boldsymbol{\theta}) = \prod_{m=1}^{M} p_x(x_m; \boldsymbol{\theta}) = \prod_{m=1}^{M} (\alpha p_{1,x}(x_m; \boldsymbol{\theta}) + (1-\alpha) p_{2,x}(x_m; \boldsymbol{\theta})) \quad (8)$$

where $p_{1,x}(x_m; \boldsymbol{\theta})$ and $p_{2,x}(x_m; \boldsymbol{\theta})$ are given by (4). Maximizing the likelihood function $p_x(x_1, x_2, \ldots, x_M; \boldsymbol{\theta})$ is equivalent to maximizing $\log p_x(x_1, x_2, \ldots, x_M; \boldsymbol{\theta})$; the maximum is found using the Nelder-Mead simplex algorithm [9].

3. Data

Simulated 30-minute RR series were generated using the AV node model as described in Section 2.1. Various AV model parameter settings were used and for each setting 100 different RR series were generated. The AV model parameters $\tau_{1_{min}}$, τ_{slope}, α, $\Delta\tau$ and $\tau_{e_{max}}$ are estimated from the simulated RR series as described in Section 2.2, while λ is assumed to be known. The mean and the variance of the estimates, as well as the average estimation error ϵ, defined as the average absolute difference between each estimate and the actual parameter value, are computed. Convergence of the estimates are tested by applying the estimator to simulated RR series of different lengths; if $\epsilon < 0.05$, the estimation is considered to have converged.

The model was evaluated on 33 Holter recordings of patients with paroxysmal or persistent AF from Physiobank [10]. AF episode duration ranged between 30 minutes and 24 hours: episodes longer than 30 minutes were divided into 50% overlapping segments of 30 minutes. A total of 1282 segments were analyzed.

4. Results

The model parameters were correctly estimated from the simulated RR series, and the estimation was found to converge quite fast (about 500 RR intervals), for most simulations with physiological settings of model parameters. An example of convergence is shown in Fig. 2: all parameter estimates converge to their true values.

Examples of unimodal and bimodal normalized RR histograms, displaying the true PDF and the PDF obtained from maximum likelihood estimation, are shown in Fig. 3.

Analyzing real data, a 97.4% of the ECG recordings could be accurately represented by the AV model; the average normalized absolute error between the normalized RR histogram and the estimated PDF, computed for bins of 20 ms size spaced between 0 and 2 s, was 0.0023 ± 0.0016.

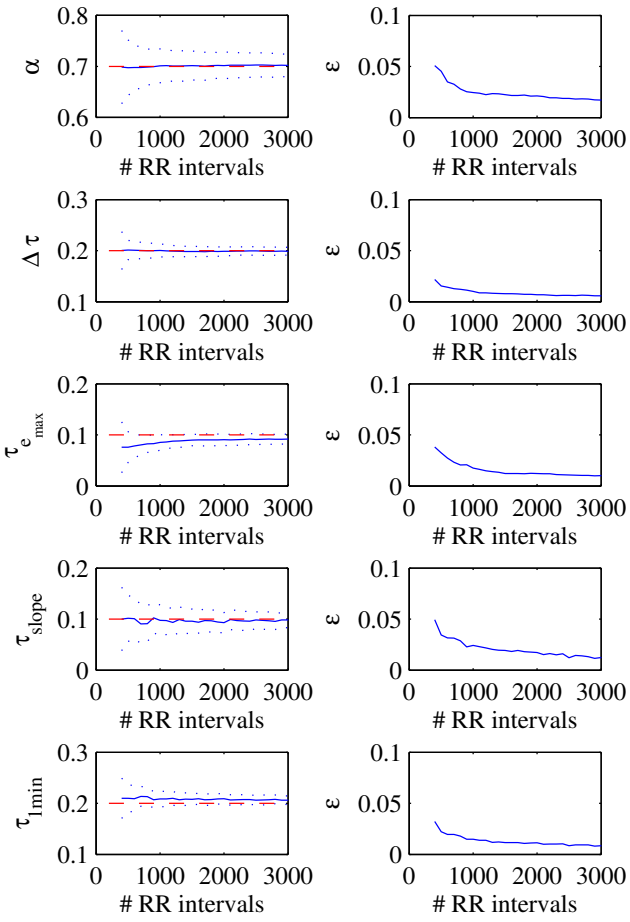

Figure 2. (left) Mean value (solid line) $\pm$ std (dotted line) of parameter estimates of 100 simulated RR series when using actual parameter values (dashed line) of $\tau_{1min} = 0.2$ s, $\tau_{slope} = 0.1$, $\lambda = 7$ Hz, $\alpha = 0.7$, $\Delta\tau = 0.2$ s, and $\tau_{e_{max}} = 0.1$ s, and (right) average absolute error of estimates.

An error of < 0.005 was considered to reflect a sufficient model fit.

Two different examples of normalized RR histograms with corresponding estimated PDFs, from patients with paroxysmal and persistent AF, respectively, are shown in Fig. 4. The estimated AV model parameters from the paroxysmal AF recording were $\hat{\tau}_{1min} = 0.42$ s, $\hat{\tau}_{slope} = 0.061$, $\hat{\lambda} = 5.13$ Hz, $\hat{\alpha} = 0.71$, $\hat{\Delta\tau} = 0.17$ s, and $\hat{\tau}_{e_{max}} = 0.067$ s, while the estimated AV parameters from the persistent AF recording were $\hat{\tau}_{1min} = 0.62$ s, $\hat{\tau}_{slope} = 0.026$, $\hat{\lambda} = 6.34$ Hz, $\hat{\alpha} = 0.62$, $\hat{\Delta\tau} = 0.26$ s, and $\tau_{e_{max}} = 0.117$ s. The differences in the parameters λ, $\tau_{e_{max}}$, and α between segments of paroxysmal and persistent AF are consistent throughout the set of recordings, see Tab 1.

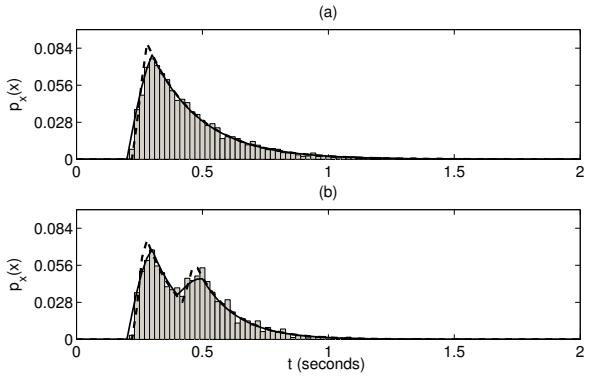

Figure 3. Simulated data. True and estimated PDFs (solid line and dashed line, respectively) for the RR series $(x_1, x_2, \ldots, x_M)$, using the model parameter values: (a) $\tau_{1min} = 0.2$ s, $\tau_{slope} = 0.1$, $\lambda = 7$ Hz, $\alpha = 1$, $\Delta\tau = 0$ s, and $\tau_{e_{max}} = 0.1$ s and (b) $\tau_{1min} = 0.2$ s, $\tau_{slope} = 0.1$, $\lambda = 7$ Hz, $\alpha = 0.7$, $\Delta\tau = 0.2$ s, and $\tau_{e_{max}} = 0.1$ s. The normalized histograms of the data is also displayed.

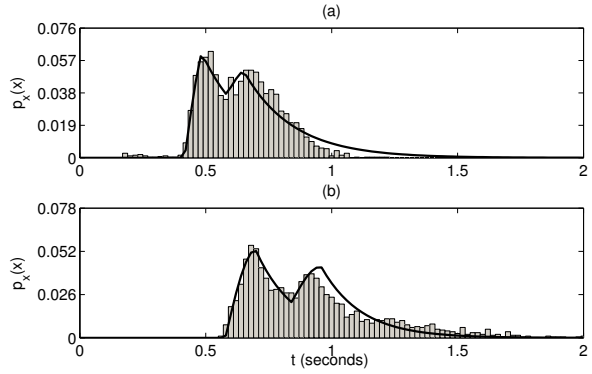

Figure 4. Real RR data. Estimated PDFs (solid line) for the RR series $(x_1, x_2, \ldots, x_M)$ obtained from 30 minutes of (a) paroxysmal and (b) persistent AF. The normalized histograms of the data is also displayed.

5. Conclusion

These preliminary results are encouraging, as, ideally, for each patient a set of parameters related to the electrophysiological characteristics of the AV node is obtained noninvasively. This set could be used to classify AF episodes and to better plan therapy, and obviously to better understand electrophysiological characteristics of the AV node during AF.

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Table 1. Estimated model parameters from segments of paroxysmal and persistent AF (mean $\pm$ sd).

Parameter	Paroxysmal AF	Persistent AF
λ	4.79 ± 0.60 Hz	6.66 ± 0.61 Hz *
$\tau_{1_{min}}$	0.35 ± 0.07 s	0.37 ± 0.11 s
τ_{slope}	0.09 ± 0.04	0.11 ± 0.08
α	0.85 ± 0.17	0.68 ± 0.29 *
$\Delta\tau$	0.13 ± 0.14 s	0.11 ± 0.10 s
$\tau_{e_{max}}$	0.08 ± 0.04 s	0.17 ± 0.14 s *

$^*p < 0.0001$

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