

A Novel Statistical Model of the Dual Pathway Atrioventricular Node during Atrial Fibrillation

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Abstract

The atrioventricular (AV) node plays an important role during atrial fibrillation (AF). In particular, the refractoriness of its cells influences the conduction of atrial impulses to the ventricles and, thus, the ventricular response. This study introduces a novel statistical model of the AV node, accounting for pathway switching, which can be used for non-invasive assessment of the refractory properties of the slow and the fast AV nodal pathway during AF, using the atrial fibrillatory rate and the series of RR intervals obtained from the ECG. A number of simulated histograms is presented, illustrating that even though only four parameters are used to characterize the AV node, the model is capable of representing a wide range of different RR interval series. Estimation of model parameters is evaluated with simulated RR interval series. It is shown that a signal consisting of 2400 RR intervals is sufficient for accurate parameter estimation, with an average estimation error less than 50 ms in all parameters. It is concluded that the model offers a novel way to obtain information regarding AV nodal refractoriness from the ECG.

1. Introduction

The atrioventricular (AV) node plays a central role during atrial fibrillation (AF) as it conducts impulses from the atria to the ventricles and, therefore, acts as one of the main determinants of the heart rate. Anatomical and electrophysiological studies support the existence of dual AV nodal pathways [1]. These pathways, described by their respective refractory periods, are subject to modelling in order to acquire further understanding of the AV node and its role during AF. Estimation of AV nodal properties during AF is of great interest, for example to evaluate the effect of rate control drugs, representing a common treatment option for AF patients [2].

Assessment of AV nodal properties is typically accomplished by invasive procedures, e.g., atrial pacing [3]. The

usability of these methods is limited since atrial pacing is not possible during AF. It is therefore desirable to develop methods capable of non-invasive estimation of AV nodal properties during AF, suitable for clinical use.

The AV node has previously been modelled as a lumped structure, characterized by refractoriness and automaticity, and used to generate realistic simulations of RR intervals during AF [4, 5].

A more simplified model, intended for estimation of AV nodal properties from the ECG, has recently been presented [6, 7]. The properties of the AV node are assessed by the relationship between the atrial fibrillatory rate, extracted from the f-waves from the ECG, and the ventricular activations. Applying the model to ECG signals from AF patients allows for estimation of parameters characterizing the refractory properties of the slow and the fast pathway of the AV node. The model has been used on clinical data, estimating the effect of rate control drugs on the functional refractory period of the AV nodal pathways [8].

In that model, all subsequent atrial impulses following a ventricular activation were implicitly assumed to arrive at the same pathway until one of them was conducted. In the model presented in this study, being a modification of the previous model, pathway switching is introduced, meaning that atrial impulses arrive at each pathway with a fixed probability, independent of all previous impulses. The probability of an atrial impulse passing through the slow pathway, α , introduced in the reference model, is therefore omitted from the estimation procedure and the number of model parameters defining the AV node is reduced from five to four.

This model, defined by a small set of parameters and based on information attainable from the ECG, provides a non-invasive approach to AV nodal property assessment.

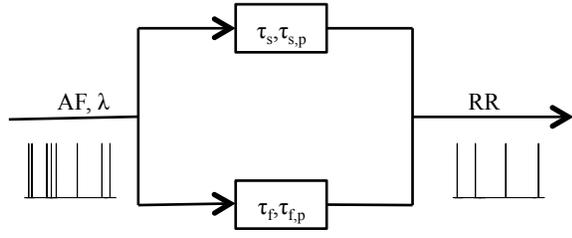


Figure 1. The proposed model of the AV node. Atrial impulses are fired at the node with intensity λ , and attempt conduction through the slow or the fast pathway with equal probability. Conduction is successful if the pathway is not refractory, which is determined by the parameters $[\tau_s, \tau_{s,p}]$ and $[\tau_f, \tau_{f,p}]$ for the slow pathway and the fast pathway, respectively. Successful conduction immediately results in ventricular activation.

2. Methods

2.1. The model

The atrial impulses are assumed to arrive at the AV node according to a Poisson process with intensity λ . The distribution of the interarrival time Δt of two subsequent impulses is therefore given by an exponential distribution, $p_1(\Delta t)$:

$$p_1(\Delta t) = \lambda e^{-\lambda \Delta t}, \quad \Delta t \geq 0. \quad (1)$$

Each impulse attempts to pass through either the fast pathway or the slow pathway, with equal probability.

The pathways are defined by two parameters each, $[\tau_s, \tau_{s,p}]$ and $[\tau_f, \tau_{f,p}]$, for the slow pathway and the fast pathway, respectively. The parameters τ_s and τ_f describe the functional refractory period of the slow and the fast pathway, respectively. Thus, by definition, $\tau_s \leq \tau_f$. The parameters $\tau_{s,p}$ and $\tau_{f,p}$ define the maximal prolongation of each refractory period, caused by different electrophysiological phenomena, such as concealed conduction and/or relative refractoriness. The probability that the slow pathway is no longer refractory at time t , t being the time in seconds since the last ventricular activation, is given by the function $\beta_s(t)$:

$$\beta_s(t) = \begin{cases} 0, & 0 \leq t \leq \tau_s \\ \frac{t - \tau_s}{\tau_{s,p}}, & \tau_s \leq t \leq \tau_s + \tau_{s,p} \\ 1, & \tau_s + \tau_{s,p} \leq t. \end{cases} \quad (2)$$

The function describing the refractory period of the fast pathway, $\beta_f(t)$, is defined in a similar way, τ_s and $\tau_{s,p}$ are replaced with τ_f and $\tau_{f,p}$ in (2). Ventricular activations are assumed to occur immediately following conduction of atrial impulses. An illustrative overview of the model is shown in Figure 1.

The probability density function (PDF) of the arrival times t of conducted atrial impulses, $p_c(t)$, is acquired by computing the functions $p_{n,c}(t)$, $p_{n,b}(t)$ and $p_n(t)$,

$$p_{n,c}(t) = \frac{1}{2}(\beta_s(t) + \beta_f(t))p_n(t), \quad (3)$$

$$p_{n,b}(t) = p_n(t) - p_{n,c}(t), \quad (4)$$

$$p_{n+1}(t) = \int_0^\infty p_1(t - \rho)p_{n,b}(\rho)d\rho, \quad (5)$$

for $n = 1, 2, \dots$. The PDF $p_n(t)$ characterizes the arrival time of the n :th consequent atrial impulse following a ventricular activation, where the first atrial impulse, $p_1(t)$, is given by the exponential distribution in (1). The PDFs $p_{n,c}(t)$ and $p_{n,b}(t)$ describe the arrival time of a conducted and blocked n :th atrial impulse, respectively. The PDF $p_c(t)$ is then given by the sum of all $p_{n,c}(t)$,

$$p_c(t; n_{\max}) = \sum_{n=1}^{n_{\max}} p_{n,c}(t), \quad (6)$$

where n_{\max} denotes the longest chain of subsequently blocked atrial impulses considered. All the results presented in this paper are obtained for $n_{\max} = 15$.

2.2. The estimation

The intensity λ is proportional to the atrial fibrillatory rate, estimated from the f-waves from the ECG. In this study, only simulated RR intervals are used, and, therefore, the value of λ is assumed to be known.

The estimation of τ_s , τ_f , $\tau_{s,p}$ and $\tau_{f,p}$ is performed from the RR series using the maximum likelihood technique, accomplished by maximization of the log-likelihood function of the PDF $p_c(t)$,

$$\begin{bmatrix} \hat{\tau}_s \\ \hat{\tau}_f \\ \hat{\tau}_{s,p} \\ \hat{\tau}_{f,p} \end{bmatrix} = \arg \max_{\tau_s, \tau_f, \tau_{s,p}, \tau_{f,p}} \sum_{m=1}^M \log(p_c(x_m; \tau_s, \tau_f, \tau_{s,p}, \tau_{f,p}, \lambda)), \quad (7)$$

where x_m is the m :th RR interval and M is the number of RR intervals included in the segment subject to analysis. The maximization is performed using a gradient-based optimization algorithm.

2.3. Evaluation

Estimation of model parameters is evaluated with simulated RR intervals generated by the present model. Us-

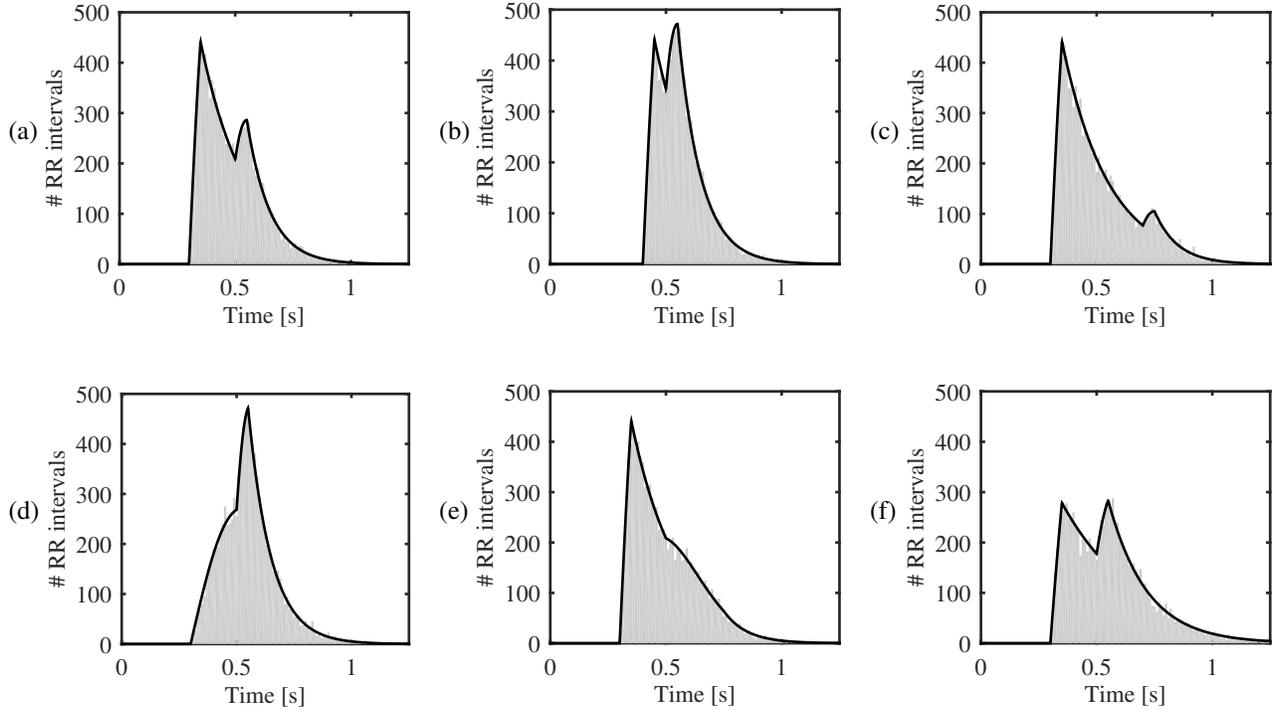


Figure 2. The PDF (solid line) and the histogram obtained from simulated RR intervals, using the following parameter setups (a) $\tau_s = 300$ ms, $\tau_f = 500$ ms, $\tau_{s,p} = 50$ ms, $\tau_{f,p} = 50$ ms, $\lambda = 10$ Hz. (b) $\tau_s = 400$ ms, $\tau_f = 500$ ms, $\tau_{s,p} = 50$ ms, $\tau_{f,p} = 50$ ms, $\lambda = 10$ Hz. (c) $\tau_s = 300$ ms, $\tau_f = 700$ ms, $\tau_{s,p} = 50$ ms, $\tau_{f,p} = 50$ ms, $\lambda = 10$ Hz. (d) $\tau_s = 300$ ms, $\tau_f = 500$ ms, $\tau_{s,p} = 250$ ms, $\tau_{f,p} = 50$ ms, $\lambda = 10$ Hz. (e) $\tau_s = 300$ ms, $\tau_f = 500$ ms, $\tau_{s,p} = 50$ ms, $\tau_{f,p} = 250$ ms, $\lambda = 10$ Hz. (f) $\tau_s = 300$ ms, $\tau_f = 500$ ms, $\tau_{s,p} = 50$ ms, $\tau_{f,p} = 50$ ms, $\lambda = 6$ Hz.

ing 9000 realizations of sets of RR intervals, ranging in length from 200 to 3000 intervals, and generated from different sets of parameters within the intervals $300 \text{ ms} \leq \tau_s \leq 500 \text{ ms}$, $400 \text{ ms} \leq \tau_f \leq 900 \text{ ms}$, $0 \text{ ms} \leq \tau_{s,p} \leq 600 \text{ ms}$, $0 \text{ ms} \leq \tau_{f,p} \leq 600 \text{ ms}$ and $7 \text{ Hz} \leq \lambda \leq 9 \text{ Hz}$, the estimation accuracy's dependence on RR interval length is evaluated. This is done by computation of the average absolute error, defined for $\hat{\tau}_s$ as:

$$\epsilon(\hat{\tau}_s) = \frac{1}{K} \sum_{i=1}^K \left| \hat{\tau}_s^{(i)} - \tau_s^{(i)} \right|, \quad (8)$$

where K is the number of realizations. The average absolute errors $\epsilon(\hat{\tau}_f)$, $\epsilon(\hat{\tau}_{s,p})$ and $\epsilon(\hat{\tau}_{f,p})$ are computed correspondingly.

3. Results

Different PDFs along with corresponding simulated RR intervals are displayed in Fig. 2. Just as the model described in [6, 7], the present model is capable of modelling RR interval histograms with both uni- and bimodal shapes,

though the number of parameters is one less.

The estimation errors $\epsilon(\hat{\tau}_s)$, $\epsilon(\hat{\tau}_f)$, $\epsilon(\hat{\tau}_{s,p})$ and $\epsilon(\hat{\tau}_{f,p})$ are displayed in Fig. 3. In order for the estimate to be considered reliable, a maximal average estimation error of 50 ms is accepted, 50 ms being the minimum difference in conduction time used to distinguish between the slow and the fast pathway during atrial pacing procedures [3]. This is accomplished for all estimates when 2400 RR intervals are used, reflecting a typical number of RR intervals in a 30-min ECG signal from an AF patient. The error differs significantly between the different parameter estimates, where $\epsilon(\hat{\tau}_s)$ always is well below 50 ms, while $\epsilon(\hat{\tau}_f)$ and $\epsilon(\hat{\tau}_{s,p})$ are below 50 ms for signal lengths of 500 and 1000 RR intervals, respectively.

4. Discussion and Conclusion

A statistical model of the dual pathway AV nodal function during AF is introduced. While only defining the AV nodal refractoriness by four different parameters, a wide selection of RR series histograms can be modelled, as illustrated in Fig. 2.

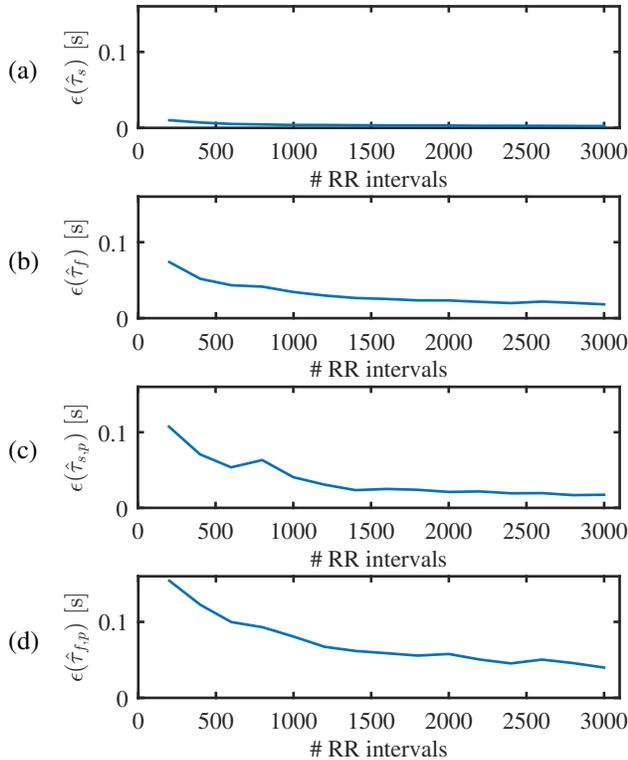


Figure 3. The estimation error ϵ as a function of the number of RR intervals for (a) $\hat{\tau}_s$, (b) $\hat{\tau}_f$, (c) $\hat{\tau}_{s,p}$, (d) $\hat{\tau}_{f,p}$.

The parameter α in the previously presented model [6,7] exhibited significant short-term variation when estimated during 24 hours. Certain covariation between α and the other parameters were observed, suggesting overfitting. Such a problem is evaded with the present model since α no longer is a model parameter.

Acceptable estimation accuracy is achieved when estimating the parameters from 2400 RR intervals, reflecting the approximate number of ventricular activations during a 30-minute session for an AF patient. Evaluation on real data remains to be done, to further evaluate the model's ability to capture the shapes of RR histogram and produce reliable estimates.

Acknowledgements

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