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Statistical Modeling of the Atrioventricular Node during Atrial Fibrillation: Data Length and Estimator Performance

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Abstract— **The atrioventricular (AV) node plays a central role during atrial fibrillation (AF). We have recently proposed a statistical AV node model defined by parameters characterizing the arrival rate of atrial impulses, the probability of an impulse choosing either one of the dual AV nodal pathways, the refractory periods of the pathways, and the prolongation of refractory periods. All model parameters are estimated from the RR series using maximum likelihood (ML) estimation, except for the mean arrival rate of atrial impulses which is estimated by the AF frequency derived from the f-waves. The aim of this study is to present a unified approach to ML estimation which also involves the shorter refractory period, thus avoiding our previous Poincaré plot analysis which becomes biased. In addition, the number of RR intervals required for accurate parameter estimation is presented. The results show that the shorter refractory period can be accurately estimated, and that the resulting estimates converge to the true values when about 500 RR intervals are available.**

I. 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 rates and AV node has not been thoroughly studied. Various models of the AV node during AF have been proposed, either models for simulation or models for parameter estimation involving observed data. Simulation models aim at explaining AV nodal characteristics [1] or the effect of pacing [2], [3]. Although such models can offer detailed characterization of the underlying electrophysiological dynamics, they are unsuitable for parameter estimation due to problems of uniqueness as a consequence of the large number of parameters which must be subjected to optimization.

Recently, we proposed a statistical model of AV nodal function during AF which lends itself well to ECG-based parameter estimation [4], [5]. The model is defined by a small set of parameters which characterizes the arrival rate of atrial impulses, the probability of an impulse choosing either one of the dual AV nodal pathways, the refractory periods of the pathways, and the prolongation of refractory periods. The parameters were estimated from the RR series using maximum likelihood (ML) estimation, except for the mean arrival rate of atrial impulses which was estimated by the AF frequency derived from the f-waves [6], and the shorter refractory period estimated from Poincaré plot analysis.

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The aim of this study is to present a unified approach to ML estimation which also involves the shorter refractory period of the AV node, thus avoiding the Poincaré-based analysis which may produce unreliable and biased estimates. Another aim is to determine the number of RR intervals required for accurate parameter estimation, simulating different scenarios.

II. METHODS

A. Definition of the AV node model

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 refractory period is defined by both a deterministic part τ and a stochastic part, the latter modeling prolongation due to concealed conduction and/or relative refractoriness and assumed to be uniformly distributed over the interval $[0, \tau_p]$. Hence, all atrial impulses arriving to the AV node before the end of the refractory period τ are blocked. Then follows an interval $[\tau, \tau + \tau_p]$ with linearly increasing likelihood of penetration into the AV node. Finally, no impulses can be blocked if they arrive after the end of the maximally prolonged refractory period $\tau + \tau_p$.

The mathematical characterization of refractoriness of the i:th pathway ($i = 1, 2$) is thus defined by the positive-valued function $\beta_i(t)$,

$$\beta_i(t) = \begin{cases} 0, & 0 < t < \tau_i \\ \frac{t - \tau_i}{\tau_p}, & \tau_i \le t < \tau_i + \tau_p \\ 1, & t \ge \tau_i + \tau_p, \end{cases} \quad (1)$$

where t denotes the time elapsed since the preceding ventricular activation. In (1), the deterministic part of the refractory period is assumed to have a length either of τ_1 or τ_2 ($\tau_1 \le \tau_2$), depending on the penetrating pathway. The probability of an atrial impulse to take the pathway with the shorter refractory period τ_1 is equal to α, and accordingly the other pathway is taken with probability $(1 - \alpha)$.

Hence, non-blocked atrial impulses occur according to an inhomogeneous Poisson process with intensity function $\lambda\beta_i(t)$, where $\beta_i(t)$ characterizes the time-dependent refractoriness and is either equal to $\beta_1(t)$ or $\beta_2(t)$, depending

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on the pathway taken by the atrial impulse. With the assumption that AV conduction time is incorporated into $\beta_i(t)$, ventricular activations immediately occur following a non-blocked atrial impulse. Consequently, ventricular activations also occur according to an inhomogeneous Poisson process with intensity function $\lambda\beta_i(t)$.

For this model, the time intervals x_i between consecutive ventricular activations, i.e., corresponding to the RR intervals, must be independent. It can be shown that the joint PDF is given by [4]

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

where M is the total number of intervals, and $p_{x,i}(x_m), i = 1, 2$, is given by

$$p_{x,i}(x) = \begin{cases} 0, & x < \tau_i \\ \dfrac{\lambda(x-\tau_i)}{\tau_{p,i}} \exp\left\{\dfrac{-\lambda(x-\tau_i)^2}{2\tau_{p,i}}\right\}, & \tau_i \le x < \tau_i + \tau_{p,i} \\ \lambda \exp\left\{\dfrac{-\lambda\tau_{p,i}}{2} - \lambda(x-\tau_i-\tau_{p,i})\right\}, & x \ge \tau_i + \tau_{p,i}. \end{cases} \tag{3}$$

To account for the interdependence between successive RR intervals, the deterministic part of the refractory period is assumed to depend on the preceding RR interval, so that a longer RR interval is followed by a longer refractory period, and vice versa.

B. Model parameter estimation

Since the property of statistical independence is not fully valid for observed RR intervals, preprocessing of the original RR interval series is needed to reduce the interdependence of successive RR intervals. During AF the first lag of the RR interval correlation is significant, whereas it is negligible for larger lags. Hence, to reduce this interdependence between subsequent RR intervals, approximate decorrelation of the RR series is obtained using $x_m = RR_m - aRR_{m-1}$, where a is the smallest value in the interval $[0, 0.5]$ that makes the first lag negative.

All model parameters, except λ, are estimated from the RR intervals using ML estimation.

The atrial impulses are assumed to arrive to the AV node according to a Poisson process with rate λ. An estimate of λ is obtained by [5]

$$\lambda = \frac{\lambda_{\mathrm{AF}}}{1 - \delta\lambda_{\mathrm{AF}}}, \tag{4}$$

where λ_{AF} is the dominant AF frequency estimated from the ECG (independently of the AV node parameters), and δ is minimum time interval between successive impulses arriving to the AV node.

The model parameters $\alpha, \tau_1^{\min}, \tau_2^{\min}, \tau_{p,1}$, and $\tau_{p,2}$ are estimated by jointly maximizing the log-likelihood function with respect to $\boldsymbol{\theta} = \begin{bmatrix}\alpha & \tau_1^{\min} & \tau_2^{\min} & \tau_{p,1} & \tau_{p,2}\end{bmatrix}^T$. The corresponding parameters of a single pathway model, $\begin{bmatrix}\alpha & \tau_1^{\min} & \tau_{p,1}\end{bmatrix}^T$ are also estimated. The Bayes information criterion is used to determine the most appropriate model [5]. Since no closed-form solution could be found for $\hat{\boldsymbol{\theta}}$, combined with the fact that the gradient is discontinuous, the multi-swarm particle swarm optimization (MPSO) is in the present study proposed for optimizing the log-likelihood function. Briefly, a multi-initialization with N concurrent swarms is employed in MPSO [7], [8]. Each swarm is moved within a search area to find the optimal solution. After a certain number of optimization epochs, particles are exchanged between swarms to avoid local maxima.

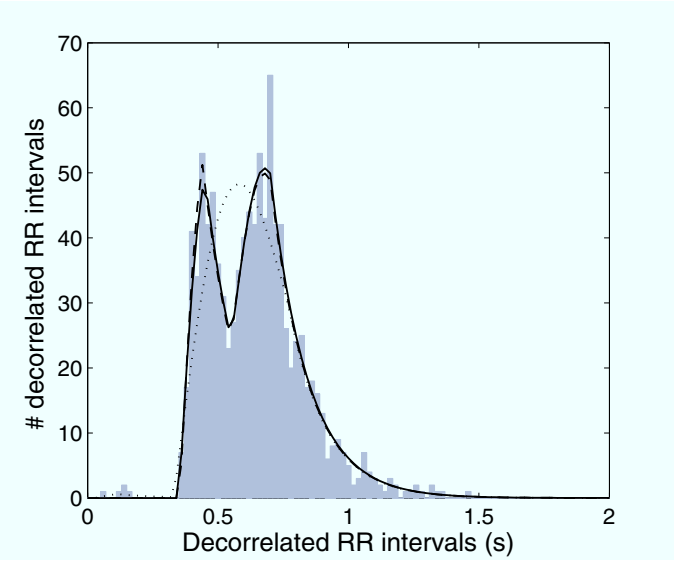

Fig. 1. Histogram of the transformed RR series and superimposed the true (solid line) and estimated PDFs, with (dashed line) and without (dotted line) the iterative procedure for removing incorrect RR intervals. See text for details.

Given the definition of $p_{x,i}(x)$ in (3), the estimate of τ_1^{min} is closely related to the shortest RR interval in the series, thus making the handling of artifacts (premature ventricular contractions, misdetected beats, etc.) very important. To reduce the influence of occasional incorrect RR intervals in the series, i.e., RR intervals obtained from artifacts, an iterative procedure is employed. First, 1% of the shortest intervals are removed from the decorrelated RR series $\mathbf{x}$, and ML estimation is performed on the truncated series $\tilde{\mathbf{x}}_0$. Since $\tilde{\mathbf{x}}_0$ is assumed to be free from incorrect RR intervals, the initial estimate $\tilde{\boldsymbol{\theta}} = \begin{bmatrix}\alpha(0) & \tau_1^{\min}(0) & \tau_2^{\min}(0) & \tau_{p,1}(0) & \tau_{p,2}(0)\end{bmatrix}^T$ can serve as a reference. The removed RR intervals are then reversed to the truncated series one by one in order of size, so that $\tilde{\mathbf{x}}_i = [\tilde{\mathbf{x}}_{i-1}\, x(i)]$ where $x(i)$ is the longest interval removed from $\tilde{\mathbf{x}}_{i-1}$; ML estimation is performed for each $\tilde{\mathbf{x}}_i$. The estimates corresponding to the maximum value of the log likelihood function are chosen as the correct ones.

Figure 1 shows the histogram of the transformed RR series and the true and estimated PDFs superimposed, with and without the iterative procedure for removing incorrect RR intervals. It can be noted that when no RR intervals are removed, the estimated PDF is far from the true one.

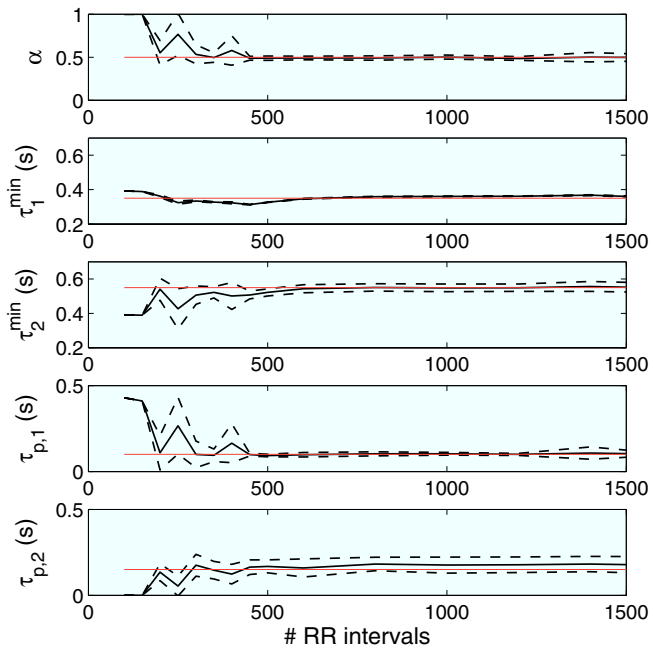

Fig. 2. Mean and standard deviation of estimates (solid and dashed black lines) obtained from simulated RR series with λ = 7 Hz, $\tau_1^{\min}$ = 0.35 s, $\tau_2^{\min}$ = 0.55 s, α = 0.1 s, $\tau_{p,1}$ = 0.1 s, and $\tau_{p,2}$ = 0.15 s. The true values are superimposed (red line).

C. Simulated data

Simulated 30-min RR interval series were generated using the AV node model introduced in [5]. We used 8 different parameter settings (100 runs per setting) for which $\tau_1^{\min}$ spanned from 0.25 to 0.45 s, prolongations of refractory period ($\tau_{p,1}$ and $\tau_{p,2}$) from 0.05 to 0.5 s, λ from 6 to 7 Hz and α from 0.1 to 0.8. As the simulations provided only RR series, λ was supposed to be known. The mean and variance of the parameter estimates were computed. The accuracy of the parameter estimates was tested by applying the estimator to increasing lengths of the RR series.

III. RESULTS

Figure 2 shows the mean and standard deviation of the estimated parameters over one-hundred realizations for a certain parameter setting for different lengths of the RR series. The estimates converge to the true values fast, i.e., for an RR series with about 500 intervals, corresponding to about 6 minutes for this parameter setting.

Figure 3 compares the results of estimation for two different parameter settings, differing only in prolongation of $\tau_{p,1}$ and $\tau_{p,2}$. The probability of choosing the slow pathway (α) is very low (equal to 0.1). In the first setting (left panels), $\tau_{p,1}$ does not converge, however, its relevance for the estimation of the true PDF is obviously small because of the low number of atrial impulses going through the slow pathway. In the bottom part, the histogram of the transformed RR series and superimposed the true (solid line) and estimated PDFs (dashed line) are shown. It can be noted that the true and the estimated PDFs are almost identical. It can also be noted

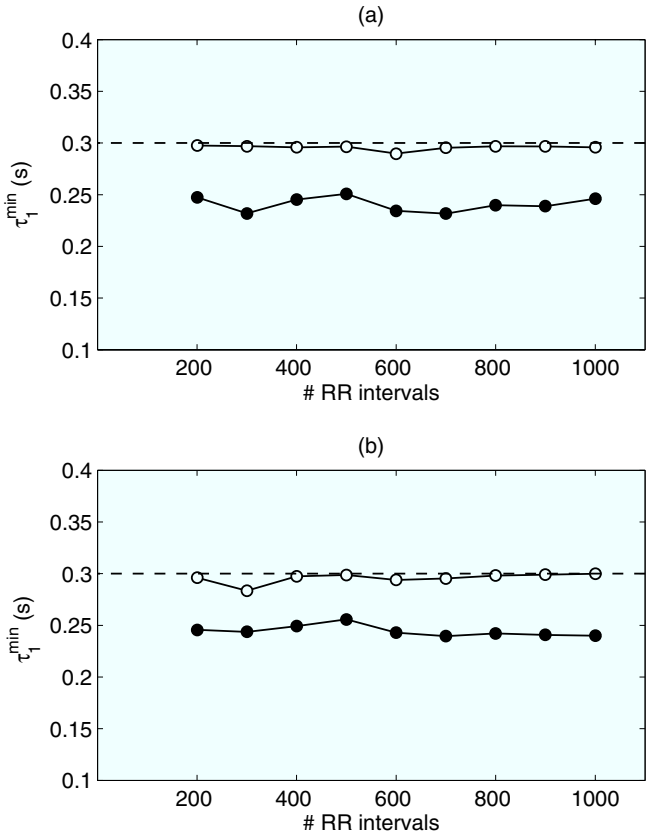

Fig. 4. Comparison of $\hat{\tau}_1^{\min}$ obtained with either the Poincaré-based analysis (empty circles) or ML estimation (full circles). The median of $\hat{\tau}_1^{\min}$, obtained from 10 realizations, is shown as a function of analyzed RR intervals, (a) without any artifacts and (b) with artifacts inserted. The true value of $\tau_1^{\min}$ is indicated by the dashed line.

that the estimate of $\tau_1^{\min}$ converges in a few hundreds RR intervals even if α is close to zero.

Figure 4 shows the median of $\hat{\tau}_1^{\min}$ obtained with Poincaré-based analysis [5] (empty circles) or ML estimation as proposed in this paper. It is obvious from Fig. 4 that the performance of ML estimation is superior since the resulting estimates are much closer to the true value, irrespective of if artifacts are present in the RR series or not. The procedure to simulate artifacts is described in [5].

Figure 5 shows the normalized error between the true PDF and the estimated one, averaged over all studied parameter settings. The error drops below 0.1 when the RR series is longer than 500 samples.

IV. DISCUSSION AND CONCLUSIONS

In this study, a unified approach to ML estimation for our recently proposed AV node model is presented, i.e., all model parameters, except the arrival rate of atrial impulses, are estimated from the RR intervals using ML estimation. The simulations indicate that about 500 RR intervals are generally needed for the parameter estimates to converge to their true values. A comparison of ML estimation of $\tau_1^{\min}$ to Poincaré-based analysis showed that the former approach performs better.

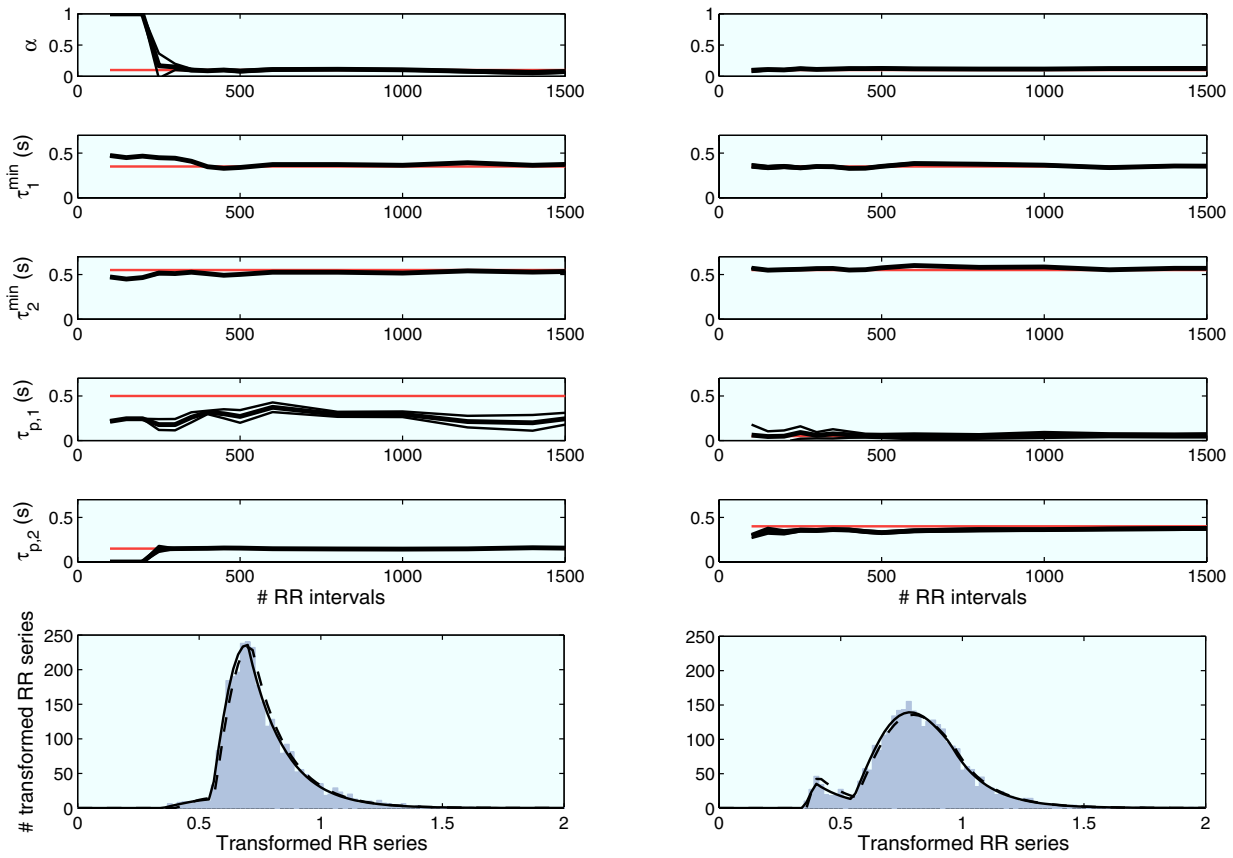

Fig. 3. Mean and standard deviation of estimates (solid and dashed black lines) obtained from two parameter settings, differing only in the refractory period prolongations, being for the left column $\tau_{p,1}$ = 0.5 s, and $\tau_{p,2}$ = 0.15 s, whereas for the right column $\tau_{p,1}$ = 0.05 s, and $\tau_{p,2}$ = 0.4 s, see text for details. The bottom panels show the histogram of the transformed RR series, with the true (solid line) and estimated PDFs (dashed line) superimposed.

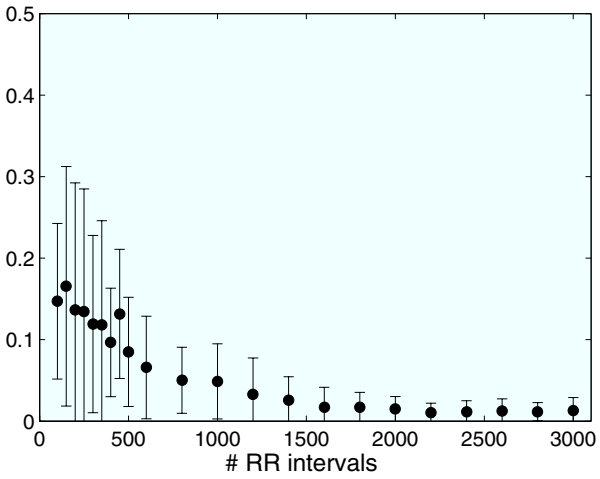

Fig. 5. Mean and standard deviation of the normalized error computed between the true PDF and the estimated one, averaged for all the parameter settings.

Finally, it deserves to be pointed out that the proposed model provides non-invasive characterization of the AV node—a useful property when assessing antiarrhythmic drugs, i.e., to assess their efficacy in the single patient, and for AV node ablation treatment.

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