Beat-to-beat In Silico Assessment of AV-nodal Conduction Dynamics during AF

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Abstract

The refractory period (RP) and the conduction delay (CD) of the atrioventricular (AV) node play a crucial role in regulating the heart rate during atrial fibrillation (AF). Assessing short-term variations in these conduction properties could provide novel information for improved diagnosis and treatment optimization on an individual basis.

We propose a methodology comprising a network model of the AV node, a particle filter, and a smoothing algorithm to quantify the conduction properties for each heartbeat. The methodology was evaluated using simulated data and applied to endocardial recordings from five patients in the Intracardiac Atrial Fibrillation Database (PhysioNet).

Estimated RP and CD matched the simulated ground truth values with a mean absolute error (± std) for each heartbeat of 181±158 ms for the RP in the fast pathway (FP), 123±109 ms for the CD in FP, 51±53 ms for the RP in the slow pathway (SP), and 153±161 ms for the CD in SP. Furthermore, the resulting RP and CD trends from the endocardial recordings for one patient are shown in Fig 2.

The beat-to-beat assessment of AV node conduction properties offers potential insights for personalized treatment strategies during AF, constitutes a novel research tool in itself, and provides an important step toward ECG-based assessment of short-term variations in AV node conduction.

1. Introduction

Atrial fibrillation, characterized by disorganized electrical activity in the atria, is the most common sustained cardiac arrhythmia and is associated with an increased risk of mortality [1]. Despite extensive research on AF, very little robust evidence exists to inform the best type and intensity of rate control treatment on an individual level [1].

The AV node normally functions as the sole electrical connection between the atria and ventricles, playing a crucial role during AF by protecting the ventricles from impulses originating in the atria. This function is accomplished through two distinct pathways; the FP and the SP, which converge at the Bundle of His [2]. Based on its RP, the AV node can either block an incoming impulse or send it through with a CD. Thus, the RP and CD of the two pathways – denoted RP^{FP}, RP^{SP}, CD^{FP}, and CD^{SP} – are critical determinants of its filtering capability, serving an essential role in regulating heart rate during AF. Accurately tracking changes in these properties over time has the potential to provide patient-specific insights into the dynamics of their AV-nodal conduction during AF, which are assumed to be regulated by the autonomic nervous system (ANS).

We have previously proposed a network model of the AV node including the RP^{FP}, RP^{SP}, CD^{FP}, and CD^{SP} [3], as well as a framework for estimating the model parameters during 24 hours using non-invasive data with a temporal resolution of 5 minutes [4, 5]. However, the ANS is known to affect the heart at a higher rate. In fact, during normal sinus rhythm, spectral analysis of heart rate variability traditionally divides the power spectra into a high-frequency area, between 0.15 and 0.40 Hz, and a low-frequency area between 0.4 and 0.15 Hz. Hence, a temporal resolution greater than 1.25 seconds, corresponding to 0.8 Hz, is needed to capture the ANS activity.

In this work, we aim to estimate beat-to-beat AV node conduction dynamics during AF using the atrial activation times as input to our model and the ventricular activation time as an output. By viewing the RP^{FP}, RP^{SP}, CD^{FP}, and CD^{SP} of the model as states in a dynamical system, and a clinical ventricular activation time series as observations, the posterior distributions of these states are approximated using a particle filter (PF) together with a smoothing algorithm, to solve the so-called smoothing problem [6].

2. Methods

The method for estimating the AV node properties ($\hat{\phi} = [RP^{FP}, RP^{SP}, CD^{FP}, CD^{SP}]$) can be divided into three stages: (1) Signal processing to derive the series of atrial and ventricular activation times from the endocardial and ECG recordings (Sec. 2.1); (2) Computation of the posterior distribution of $\hat{\phi}$ using a PF (Sec. 2.3); (3) Refining the posterior estimate using a smoothing algorithm (Sec. 2.4).

2.1. Data

The data in this study are divided into two categories; simulated and clinical. In both cases, the series of atrial and ventricular activation times are known.

Clinical data from the publicly available intracardiac atrial fibrillation database (iafdb) [7] was used in this study, consisting of endocardial recordings from four separate regions of the right atria with simultaneous three-lead ECG from eight patients with AF or flutter. The recordings at the tip of the tricuspid valve annulus are used in this study, due to its proximity to the AV-node entrance. Five recordings were selected for analysis, containing only AF. The ventricular activation series is detected from the R peaks in the ECG, and the atrial activation series is extracted from the endocardial recordings using an iterative method [8].

The simulated data was created using the network model of the AV node (Sec. 2.2) with parameters obtained from the analysis of clinical data. After the PF and smoothing methodology (Sec. 2.3 and 2.4) was applied to all five patients in the iafdb dataset to estimate the model parameter trends, their estimated modes together with the clinical atrial activation series were used as ground truth to generate a simulated series of ventricular activations. This simulated ventricular activation series together with the corresponding atrial activation series for that patient are used as the simulated data in this work. Because the simulated data is based on the results of the iafdb dataset, the characteristics for the simulated patients are the same as the results for the iafdb dataset, and thus presented in Table 1.

2.2. Network Model of the AV Node

Our network model of the AV node [3] describes it as two pathways (FP and SP), each comprising 10 nodes, interconnected with a coupling node in the end (see Figure 1). Each node corresponds anatomically to a localized section of its respective pathway, while the coupling node represents the Purkinje fibers and Bundle of His [2].

The atrial activation series extracted from data (Sec. 2.1) arrive at the first nodes of the FP and the SP simultaneously. Each node can be refractory (blocking impulses) or non-refractory (transmitting impulses). Transmitted impulses arrive at adjacent nodes with an added CD, and transmitting nodes become refractory. The RP ($R_i(n)$) and CD ($D_i(n)$) for node i are updated for each incoming impulse n according to Equations 1, 2, and 3,

$$R_i(n) = R_{min} + \Delta R(1 - e^{-\tilde{t}_i(n)/\tau_R}) \quad (1)$$

$$D_i(n) = D_{min} + \Delta D e^{-\tilde{t}_i(n)/\tau_D}, \quad (2)$$

$$\tilde{t}_i(n) = t_i(n) - (t_i(n-1) + R_i(n-1)), \quad (3)$$

where, $\tilde{t}_i(n)$ is the diastolic interval preceding impulse n and $t_i(n)$ is the arrival time of impulse n at node i. When $\tilde{t}_i(n) < 0$, the node is in its refractory state and will block incoming impulses. Each pathway has three parameters for the RP and three for the CD (thus all nodes in the same pathway have the same parameter values), totaling 12 model parameters in vector $\boldsymbol{\theta}$. Hence, $\boldsymbol{\theta} = [R^{FP}_{min}, \Delta R^{FP}, \tau^{FP}_R, R^{SP}_{min}, \Delta R^{SP}, \tau^{SP}_R, D^{FP}_{min}, \Delta D^{FP}, \tau^{FP}_D, D^{SP}_{min}, \Delta D^{SP}, \tau^{SP}_D]$. The coupling node's RP is fixed to the shortest RR interval in the data minus 50 ms, and its CD is fixed at 60 ms.

The model is evaluated using a modified version of Dijkstra's algorithm [3]. Impulses are propagated through the network in an event-based fashion where the impulse with the lowest $t_i(n)$ in the queue is propagated next (or blocked depending on $\tilde{t}_i(n)$). Three elements are needed to run the model. First, the parameter vector $\boldsymbol{\theta}$ is necessary, corresponding to the properties of the AV node. Second, a queue ($\boldsymbol{q}$) of impulses is required, where each impulse is represented by a tuple containing $t_i(n)$ and node index i. These impulses can arrive from the atria or from a transmitting node within the AV node. Finally, the repolarization time ($\boldsymbol{RT}$) for each of the 21 nodes in the model is needed, corresponding to the end of the diastolic interval ($\tilde{t}_i(n)$). The model code and a basic user example can be found at `https://github.com/FraunhoferChalmersCentre/AV-node-model`.

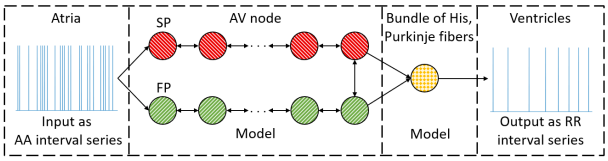

Figure 1: The network model, divided into the SP (red), the FP (green), and the coupling node (yellow). Arrows indicate impulse conduction direction.

2.3. Particle filter

A PF uses a set of particles to represent the posterior distribution of a stochastic process and can be used to find an approximate solution for the filtering problem – estimating the current state of a system based on current and past observations. A basic particle filter can be described by its four phases: initialization, weighting, resampling, and propagation. These phases all affect the particles in the PF. In this work, each particle corresponds to a model parameter vector, denoted $\hat{\boldsymbol{\theta}}^{PF}_{k,j}$, where k denotes the ventricular activation index and j the particle index. The PF starts with initialization, where all $N = 1000000$ particles in the PF are individually drawn from a uniform distribution. Initialization is followed by running the model with the known atrial activation series for all $\hat{\boldsymbol{\theta}}^{PF}_{k,j}$ until each particle has generated a new ventricular activation ($\hat{V}_{k,j}$). In addition, the current queue ($\boldsymbol{q}_j$) and the current repolarization times ($\boldsymbol{RT}_j$) at the time of the new ventricular activation are saved. After all N particles in the filter have been used to simulate ventricular activation times, each $\hat{V}_{k,j}$ is used together with the true ventricular activation time (V_k) to calculate the weight $w_{k,j}$ according to Equation 4,

$$w_{k,j} = \mathcal{N}(\ (\hat{V}_{k,j} - V_k)\ |0, \sigma_w^2), \tag{4}$$

where σ_w was set to 20 ms to account for uncertainties in R wave detection. In the resampling phase, new particles ($\hat{\boldsymbol{\theta}}_{k+1,j}^{PF}$) with corresponding $\boldsymbol{q}_j$ and $\boldsymbol{RT}_j$ are drawn with replacement from $\hat{\boldsymbol{\theta}}_{k,j}^{PF}$ based on their weights, thereby approximating the posterior distribution. Each particle is then propagated one time step k forward by adding a normally distributed noise drawn from $\mathcal{N}(\hat{\boldsymbol{\theta}}_{k,j}^{PF}, \Sigma)$, where the covariance matrix Σ is calculated from all estimated parameter sets in Karlsson, et al. [4]. The weighting, resampling, and propagation are repeated sequentially for each ventricular activation, from $k = 1$ to $k = K$. The pseudo-code for the PF is shown in Algorithm 1.

Conveniently, each time a ventricular activation is simulated with the model, the RP and CD for each node activation are calculated using Equation 1 and 2, respectively. Thus, a vector of RP:s and CD:s is generated for the FP and the SP. The median of these RP and CD vectors are used as the estimates of the four AV node properties in $\hat{\boldsymbol{\phi}}$ for each particle $\boldsymbol{\theta}$. Additionally, the values for CD^{FP} and CD^{SP} are multiplied by ten to account for the average CD from the ten nodes in either pathway. Each $\hat{\boldsymbol{\theta}}_{k,j}^{PF}$ is therefor associated with a $\hat{\boldsymbol{\phi}}_{k,j}^{PF}$.

Algorithm 1 Particle filter

Initialization (k = 1):
Sample $\hat{\boldsymbol{\theta}}_{1,j}^{PF} \sim U$.
Compute $\hat{V}_{1,j}$ by running the model with $\hat{\boldsymbol{\theta}}_{1,j}^{PF}$.
Save $\boldsymbol{q}_j$ and $\boldsymbol{RT}_j$ at ventricle activation for each particle.
Compute $w_{1,j} = \mathcal{N}(\ (\hat{V}_{1,j} - V_1)\ |0, \sigma_w)$ (Eq. 4).
Normalize $w_{1,j} \leftarrow w_{1,j} / \sum_j w_{1,j}$.
for $k = 2$ to K **do**
Resampling: Generate $\hat{\boldsymbol{\theta}}_{k,j}^{PF}$ by resampling $\hat{\boldsymbol{\theta}}_{k-1}^{PF}$ using w_{k-1}.
Propagation: Sample $\hat{\boldsymbol{\theta}}_{k,j}^{PF} \sim \mathcal{N}(\hat{\boldsymbol{\theta}}_{k-1}^{PF}, \Sigma)$.
Weighting: Compute $\hat{V}_{k,j}$ by running the model with $\hat{\boldsymbol{\theta}}_{k,j}^{PF}$, $\boldsymbol{q}_j$, and $\boldsymbol{RT}_j$.
Compute $w_{k,j} = \mathcal{N}(\ (\hat{V}_{k,j} - V_k)\ |0, \sigma_w)$ (Eq. 4).
Normalize $w_{k,j} \leftarrow w_{k,j} / \sum_j w_{k,j}$.
end

2.4. Smoothing algorithm

The solution of the filtering problem can subsequently be used together with a backward sampling step to solve the smoothing problem [6]. The solution of the filtering problem only takes past and present observations into account for estimating the state at a given time step. By solving the smoothing problem, the estimate is augmented with information from future observations.

Starting at $k = K$, one of the j particles is selected based on $w_{K,j}$ and denoted $\boldsymbol{B}(K)$. The algorithm then continues iteratively from time step $k = K - 1$ to $k = 1$, where the weights are updated based on the likelihood that $\hat{\boldsymbol{\theta}}_{k,j}^{PF}$ originated from the selected particle at the time step of the previous iteration $\hat{\boldsymbol{\theta}}_{k+1,\boldsymbol{B}(k+1)}^{PF}$, according to Equation 5.

$$\hat{w}_{k,j} = w_{k,j}\mathcal{N}(\hat{\boldsymbol{\theta}}_{k+1,\boldsymbol{B}(k+1)}^{PF} | \hat{\boldsymbol{\theta}}_{k,j}^{PF}, \Sigma). \tag{5}$$

A new particle j is selected based on $\hat{w}_{k,j}$ and assigned to $\boldsymbol{B}(k)$. After completion, the vector $\boldsymbol{B}$ contains one trajectory of indexes for $\hat{\boldsymbol{\theta}}^{PF}$ sampled from the smoothing probability density function. Running the smoothing algorithm $M = 10000$ times hence generates M trajectories ($\boldsymbol{B}_m$) of $\hat{\boldsymbol{\theta}}^{PF}$ sampled from the smoothing probability density function. Since each $\hat{\boldsymbol{\theta}}^{PF}$ is associated with a $\hat{\boldsymbol{\phi}}^{PF}$, the M trajectories $B_m(k)$ for $m \in \{1, M\}$ also yield M trajectories of $\hat{\boldsymbol{\phi}}^{PF}$ sampled from the smoothing probability density function. These are used as estimates of the posterior distribution of the AV node properties and denoted $\hat{\boldsymbol{\phi}}_m^{sm}(k)$. The pseudo-code for the smoothing algorithm is shown in Algorithm 2.

Algorithm 2 Smoothing algorithm

Initialization (k = K):
Sample $\boldsymbol{B}(K) \sim w_{K,j}$
for $k = K - 1$ to 1 **do**
for $j = 1$ to N **do**
Update weights: $\hat{w}_{k,j} \leftarrow w_{k,j}\mathcal{N}(\hat{\boldsymbol{\theta}}_{k+1,\boldsymbol{B}(k+1)}^{PF} | \hat{\boldsymbol{\theta}}_{k,j}^{PF}, \Sigma)$ (Eq. 5)
end
Sample: $\boldsymbol{B}(k) \sim \hat{w}_{k,j}$
end

3. Results

Running the smoothing algorithm yields one $\hat{\boldsymbol{\phi}}_m^{sm}(k)$ for each patient, containing M samples from the posterior of the RP^{FP}, RP^{SP}, CD^{FP}, and CD^{SP} for each ventricular activation k. The mode of the posterior distribution is calculated for the four AV node properties individually by sorting the M values of $\hat{\boldsymbol{\phi}}_m^{sm}(k)$ into histogram bins with 10 ms width before identifying the bin in the histogram with the highest count. The mean $\pm$ std of these modes for each patient are presented in Table 1. In addition, the $\hat{\boldsymbol{\phi}}_m^{sm}(k)$ for one patient is shown in Figure 2, where beat-to-beat variability can be seen for all four conduction properties.

The mean absolute error (MAE) is calculated by running the framework on the simulated data and calculating the absolute difference between the estimated modes and the ground truth parameters. Additionally, the percentage of ventricular activations for which the 95% credibility region covered the ground truth (C_{95}) is calculated by finding the values at the 2.5th and 97.5th percentiles of $\hat{\boldsymbol{\phi}}_m^{sm}(k)$ and evaluating how often the ground truth lies in between. The average MAE and C_{95} for each ventricular activation for the five simulated patients is presented in Table 1.

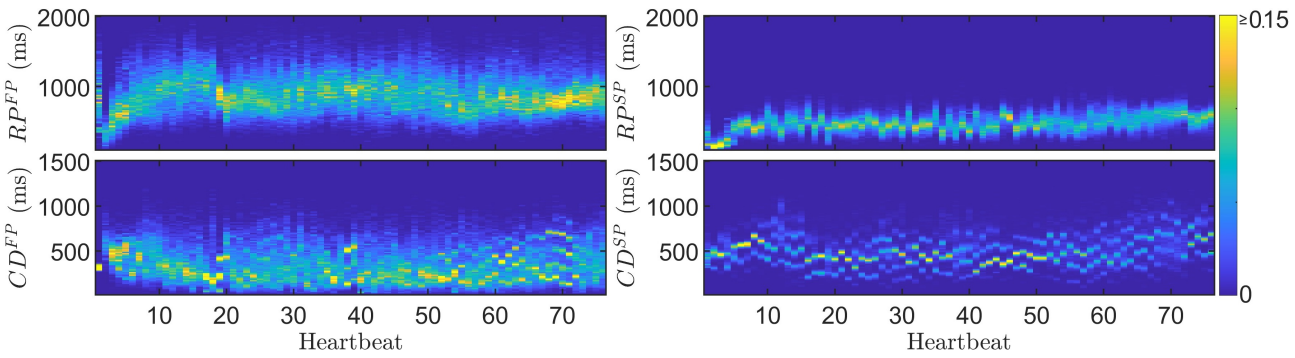

Figure 2: Estimated $\hat{\phi}_m^{sm}(k)$ for patient 1, where values ≥ 0.15 are presented with the brightest color for ease of visualization.

Table 1: Mean $\pm$ std of the mode of $\hat{\phi}_m^{sm}(k)$, as well as the average MAE and C_{95} for the five simulated patients.

Patient	RP^{FP} (ms)	RP^{SP} (ms)	CD^{FP} (ms)	CD^{SP} (ms)
1	895 ± 104	474 ± 90	363 ± 57	507 ± 77
2	851 ± 139	407 ± 66	299 ± 95	569 ± 135
3	1026 ± 107	675 ± 62	401 ± 107	740 ± 124
4	1248 ± 60	774 ± 23	505 ± 80	1017 ± 73
6	1024 ± 267	571 ± 174	203 ± 47	385 ± 80
Average MAE	181 ± 158	51 ± 53	123 ± 109	153 ± 161
$C_{95}(\%)$	98.7	98.2	94	81.3

4. Discussion

We have presented a novel methodology for estimating the beat-to-beat RP and CD within the AV node during AF. This approach utilizes a network model of the AV node in conjunction with a PF and a smoothing algorithm. Preliminary results from the analysis of simulated data indicated that it is feasible to estimate the beat-to-beat AV node conduction dynamics during AF, as evidenced by the MAE and good coverage of the 95% credibility region shown in Table 1. Furthermore, the method was applied to endocardial recordings from patients with AF, as shown in Figure 2.

Our approach estimates the posterior distribution of the AV node conduction properties for each pathway. This is particularly valuable compared to solely providing point estimates. The posterior distribution offers richer information, including the most likely values (modes used here) and the uncertainty associated with the estimates. This allows for a more nuanced understanding of the properties' variability.

While this study utilizes endocardial recordings, a key strength lies in its potential for future adaptation to non-invasive data, such as the ECG. The AV node model has previously been used with only ECG data, where the average atrial fibrillatory rate was extracted from the ECG and used together with a Poisson process to generate the atrial activation series [3]. This approach is still feasible with the PF and smoothing algorithm. However, future work is needed to handle the added uncertainty arising from not knowing the incoming atrial activation series and how best to model it from the ECG.

5. Conclusion

A method for estimating the beat-to-beat RP and CD in the AV node comprising a network model, a particle filter, and a smoothing algorithm has been developed and evaluated using simulated data and applied to endocardial recordings.

These estimated AV node properties offer insights into the conduction dynamics of the AV node during AF, and possibly its ANS regulations. This constitutes a novel research tool in itself and provides an important step toward ECG-based short-term AV node conduction assessment.

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