Assessment of AF Capture during Antitachycardia Pacing Using Largest Lyapunov Exponent Estimation. Insights From a Biophysical Model

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Abstract. *The present study investigates the potential of the Largest Lyapunov Exponent (LLE) for the quantification of AF complexity as a marker of antitachycardia pacing (ATP) effectiveness in a biophysical model of the human atria. From ongoing simulated atrial fibrillation, 20 transmembrane potential maps were used as initial conditions for a rapid pacing from the septum area (at pacing cycle length as a percentage of the AF cycle length). The LLE was separately computed during AF and ATP for the transmembrane potential time series recorded at a single site in the right atrial posterior wall. The averaged results over all 20 simulations show that the LLE decreases during ATP relative to AF. These results suggest that LLE may serve as an indicator of AF complexity and also as a discriminating metric in automatic assessment of AF capture during ATP.*

Keywords: atrial fibrillation, largest Lyapunov exponent, pacing therapies, biophysical model of the human atria

1. Introduction

Atrial fibrillation (AF) is the most common type of sustained arrhythmia which affects about 2% of the general population and 8-11% of those older than 65 years and its incidence is increasing. Important clinical issues in AF data processing are the discrimination between AF groups using the electrocardiogram, the efficient monitoring of AF catheter ablation and the quantification of the influence of antitachyarrhythmia pacing in AF termination. In this context, computer modelling has gained importance in the development of therapeutic strategies for atrial fibrillation, overcoming some of the limitations encountered in clinical research. Specifically, a computer model of AF gives access to the global atrial electrical activity, that is, it is possible to record the electrical activity on a grid covering the atrial tissue.

The three previously mentioned issues in AF data processing are in fact closely related: many research works point to a close relationship between the ability to terminate AF and the amount of disorder in atrial electrical activity during AF, revealing thus the potential of chaos theory based approaches for the quantification of atrial activity organisation in the context of AF treatment. Techniques derived from non-linear dynamics analysis have been used to characterize and to gain a deep insight into the behaviour of cardiac electrical activity, [1-4]. In this context, our study considers the Largest Lyapunov Exponent (LLE) for the quantification of the complexity of the atrial electrical activity during AF. The effectiveness of LLE in the assessment of AF capture during rapid atrial septal pacing was tested by using a biophysical model of the human atria [5].

2. Methods

Biophysical Modelling of Atrial Fibrillation

The biophysical model was based on a homogenous tissue in which the Luo-Rudy model was adjusted to mimic electrical remodelling as observed in patients with permanent AF. This was simulated by setting the channel conductance G_{Na}, G_K and G_{si} to 16, 0.423 and 0.55 mS/cm^2 respectively, [6]. A programmed stimulation protocol was used to initiate atrial fibrillation in the biophysical model. The simulated AF (SAF) dynamics revealed multiple wavelets continuously changing in size and duration due to functional or anatomical re-entries. Figure 1(a) illustrates a snapshot of the wavelet dynamics for simulated AF.

Modelling Pacing of Atrial Fibrillation

From 10 minutes of ongoing SAF, 20 instantaneous transmembrane potential maps were selected as initial conditions for the subsequent simulation of ATP. These maps correspond to different states of electrical activity in the atrial tissue. For each initial condition, a rapid pacing was applied from the whole septal area during 60 seconds at a pacing cycle length (PCL) as a percentage of the AF cycle length (AFCL). The AF cycle length computed out of 10 minutes of SAF was AFCL = 72 ms. The rapid pacing was simulated by injecting a stimulus current inside the cells located in the septal area. The pacing strategy (pacing site and PCL) was designed according to the results from [7, 8], in which the computer modelling was used to search for optimal pacing sites and pacing cycle length leading to a local capture of AF. Figures 1(b)-(c) show the snapshots of the dynamics during atrial septal pacing for two situations: PCL equal to 83% of AFCL and PCL equal to 91% of AFCL, respectively.

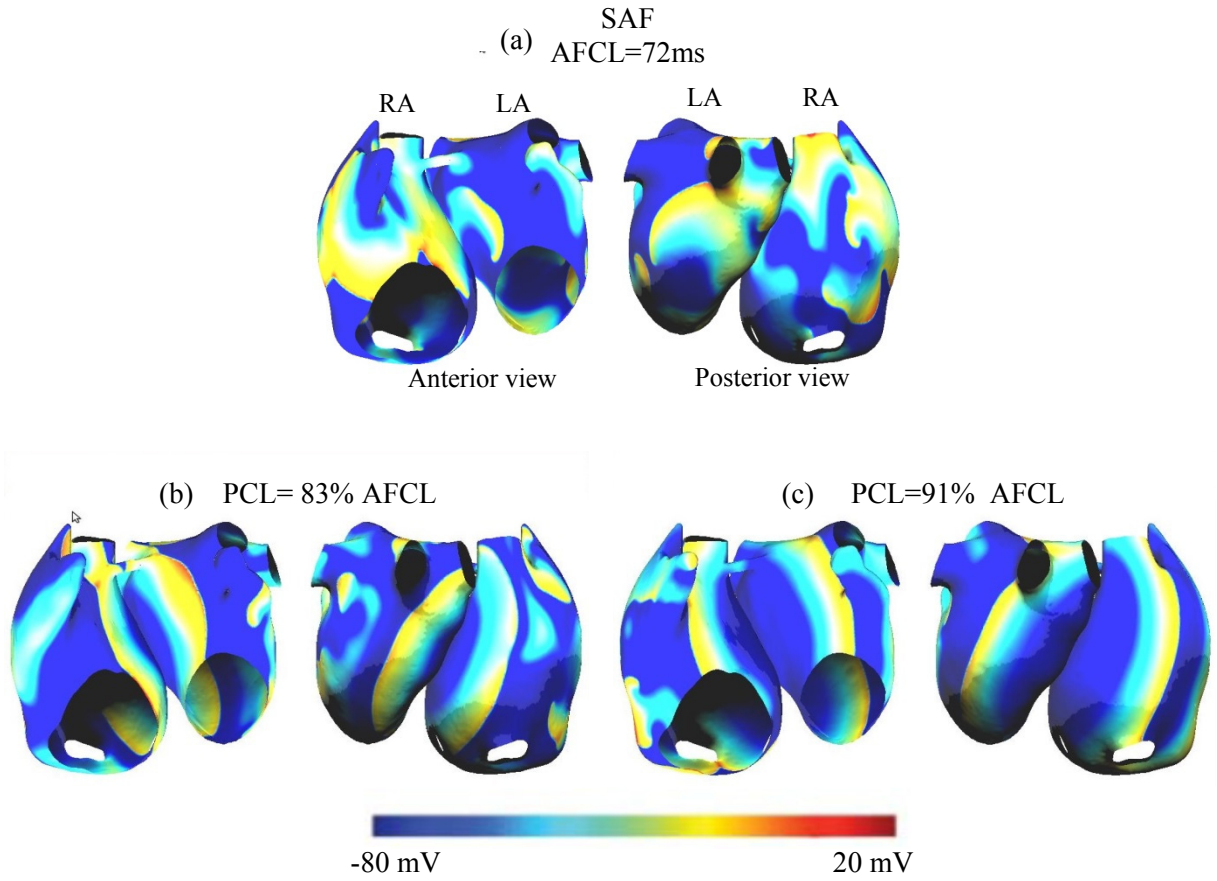

Fig. 1. Snapshots of the dynamics during simulated AF and during pacing for two PCLs. The time of snapshots during the pacing is the 50th second of the simulations.

Assessment of AF capture by using Largest Lyapunov Exponent

20 transmembrane potential time series from a single site in the middle of the right atrial posterior wall were separately recorded during SAF and during pacing. The 20 AF time series consist in non-overlapping segments of 30 seconds length obtained out of 10 minutes of ongoing SAF. The time series during the rapid pacing consist in the last 30 seconds of the pacing simulation. In each situation, the length of the time series was N=30000 samples (the sampling frequency was f=1kHz).

The Lyapunov exponents of a dynamical system are a quantitative measure of the sensitivity of the system to initial conditions (a positive exponent reflects exponential divergence of the trajectories and diagnoses chaos). Furthermore, in many applications it is sufficient to only refer to the largest Lyapunov exponent. The higher LLE is, more complex is the behaviour of the analysed time series (*i.e.* in the present study, a larger LLE means a less organized atrial electrical activity).

The first step in computing the LLE is the reconstruction of the attractor dynamic starting from a particular single time series. One can reconstruct the attractor from a single scalar time series $\{x_k\}$, $k = 1,2,\dots,\mathrm{N}$, using the time delay vectors $(x_k, x_{k+\tau}, \dots, x_{k+(m-1)\tau})$. For an infinite noise free data series one can almost find an embedding dimension *m* (and any delay time τ) for which the delay vectors yields a phase space that has the same properties as the one formed by the original variables of the system. As in practice we do not deal with infinite noise free data series, various methods have been suggested to estimate *m* and τ, but decisions are still often subjective and related to the investigated signals. In the present study, the time delay τ was taken as the time for the autocorrelation function dropped to (1-1/e) of its initial value and the embedding dimension *m* was chosen using Cao's method, [9].

The LLE was separately computed for all time series recorded during AF and during pacing for different PCL values. Based on Rosenstein's algorithm, [10], the LLE was calculated as the slope of the linear regression line defined by:

$$y(i) = \frac{1}{\Delta t} < ln[d_j(i)] >$$

where Δt is the sampling period of the time series, $d_j(i)$ is the distance between the j^{th} pair of nearest neighbours (neighbours from time delay embedding space) after *i* discrete-time steps, i.e. $i \cdot \Delta t$ seconds and $< \cdots >$ denotes the average over all values of *j*.

3. Results

Figure 2 shows the box-plot of LLE estimates during AF and during rapid pacing for two values of PCL (83% of AFCL and 93% of AFCL, respectively). Averaged over all 20 AF initial conditions, the LLE was 0.108±0.002 ms^{-1} (during AF), 0.105±0.003 ms^{-1} (PCL=83% of AFCL) and 0.078±0.009 ms^{-1} (PCL=91% of AFCL).

It can be observed that LLE decreases during pacing relative to AF ($p < 10^{-5}$, Kruskal-Wallis test). Also, the significant difference between LLE for the two values of PCL ($p < 10^{-7}$) indicates that LLE can guide the choice of PCL leading to appropriate AF capture (a smaller LLE means a more regular atrial activity, *i.e.* here a good AF capture by pacing).

4. Conclusions

As we move from AF to ATP, the decrease in the LLE is an evidence of the possibility to use LLE as a non-invasive discriminating metric in automatic assessment of AF capture during ATP. The results obtained in the present model-based study suggest that LLE can quantify the organisation of atrial activity during atrial fibrillation using, noteworthy, measurements from

a single site. These preliminary results motivate further applications of LLE to specific problems in the context of AF treatment, which will permit us to investigate the correlation of the LLE values with AF organization and termination.

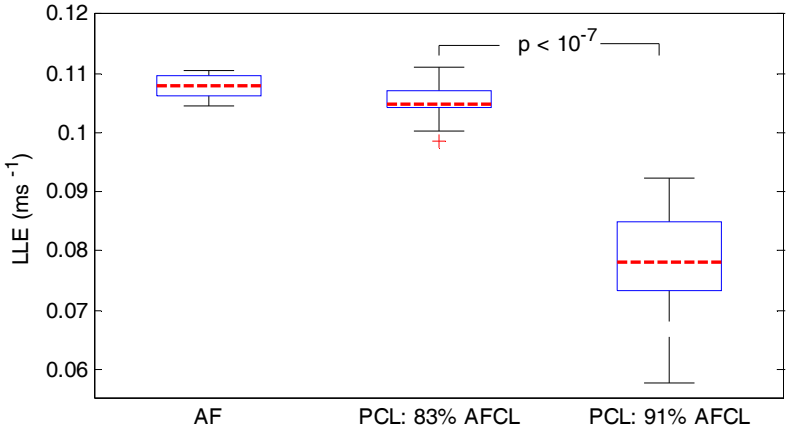

Fig. 2. Box-plot of Largest Lyapunov Exponent during AF and rapid septal pacing for two PCLs

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