

Tailoring Process for the Regional Personalization of Atrial Fibrillation with a Novel Cardiac Model

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Abstract

The personalization of mathematical models has the goal of helping in the identification of optimal antiarrhythmic therapies for each patient. Nevertheless, their need for high computational resources and long running times move them far away from real-time clinical practice.

In this study, we present a novel cellular mathematical model which includes the main electrophysiological characteristics that allow personalization whereas requires a low number of resources and time. This model incorporates some important dynamics seen in real myocardium tissue. Moreover, we present a tailoring process that allows the regional model personalization.

The simplified-mathematical model and the tailoring procedure have been compared against the simulations obtained from an already validated detailed-mathematical model. The simplified-mathematical model demonstrated its accuracy both during regular rhythms and during Atrial Fibrillation (i.e., similar regional locations of drivers).

This novel simplified-mathematical model and its personalization framework open the door to producing fast and personalized simulations from patients' data. Those individualized models will allow the in-silico evaluation of ablation therapies to improve the current clinical treatment for cardiac arrhythmias.

1. Introduction

In recent years, complex computer models have been used to understand the mechanisms behind arrhythmias and to study the effects of different pharmacological and surgical therapies[1,2,3]. Moreover, efforts have been made toward the personalization of these models through the development of individualized digital twins, which incorporate some of the properties observed in real patients, for a better understanding of the patient's pathology and for the personalization of the treatment [4]. Nevertheless, these complex models have the disadvantage that they require large computational resources and long

simulation times to produce their high-detailed results which move them far away from real-time clinical practice.

Cellular automata (CA) models offer a way to reproduce electrophysiological cardiac behavior, whereas they require low computer resources and time. Different CA models have been proposed which have been shown to be able to capture the main electrophysiological properties observed during diverse cardiac pathologies[5,6].

In this study, we present a new CA that incorporates similar electrophysiological dynamics to those seen in real human myocardium. Moreover, a new tailoring process that allows real-time regional personalization of the CA simulation is presented. This personalization will enable us to produce fast digital twins which can be used in clinical practice to understand the patient's pathology and evaluate the potential efficacy of different treatments.

2. Methods

2.1. The electrophysiology behind the CA model

In the presented CA, the nodes of the cardiac tissue (which are going to be called cells from now on) could have an active or inactive state depending on their potential value. Different rules were applied to the cells depending on their state. When a cell was not active, the potential in each time step depended on their previous potential as well as on the potential of the surrounding neighbors in proportion to the distance between the cell and each one of them. Once the potential reached a certain threshold, an action potential was triggered, and the cell passed to be active. The potential in the active state continued to depend on the previous potential and the neighbors; however, it also depended on a decrease ratio which reduced the potential each time step. Once the cell potential returned to 0, the cell state returned to be inactive.

The rules described above were based on the ones published by Y. T. Lin et al [5]. As in their CA model [5], each cell had its own APD₈₀ restitution curve which depended on the diastolic interval (DI). This restitution curve determined the maximum potential value that the cell

acquired once an AP was triggered. However, in our CA model, the influence of the neighbors over each cell was modeled differently than in the Y.T Lin et al model. Their model considered the neighbors just for activation purposes, whereas in our model the influence of neighbors was considered for active and inactive cells. In our model, the weight of the neighbors was not fixed and depended on three electrophysiological factors: the diffusion coefficient of the tissue (D) and the conduction velocity (CV) of each cell, and the distance to the neighbors. The mentioned CV was modeled through a restitution curve related to the DI , whereas the distance factor increased the relevance of neighbors when they were closer.

2.2. Gold standard model for the personalization

To validate the electrophysiological properties of the CA, its performance was compared against an already validated detailed-mathematical model[1]. This reference model was also used to establish the initial conditions of our CA by introducing the observed potential and state of the cells as the starting point of the CA simulations.

All simulations have been run over a 3D realistic atrium with 284,578 nodes which has been segmented into ten different regions, as seen in Figure 1.

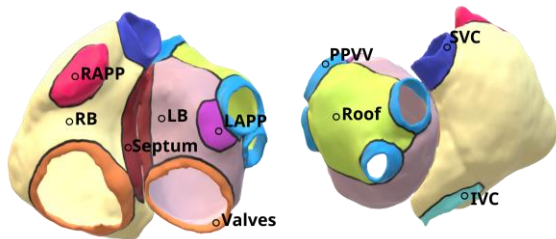


Figure 1. Front and back view of the used atria models where the segmented regions used for the models' comparison and CA personalization is seen. These regions are right atrial body (RB), left atrial body (LB), right appendix (RAPP), left appendix (LAPP), superior vena cava (SVC), inferior vena cava (IVC), pulmonary veins (PPVV), roof of the PPVV, septum, and valves.

From the detailed-mathematical model, the CV s (using the state of the art presented in the doctoral thesis of Ismael Hernández [7]) and the APD_{S80} were measured over the most external layer of cells of the atria along diverse time windows. For each window, the mean value within the 90 percentile for each region was computed.

2.3. Personalization of CA model

A process to tailor the value of two CA parameters (the D and the decrease ratio) was designed thus the CA could replicate the electrophysiological behavior observed in the reference model. These two parameters have a strong

relationship with the CV s (the D) and the APD_{S80} (the decrease ratio) of CA model. The adjusting of D has been done regionally (defining a specific D for each defined region), whereas a global decrease ratio was determined for the whole atria.

The tailoring process was based on the data collected over two simulation databases during sinus rhythm: Database A (simulations with different values of D and a fixed decrease ratio) and Database B (simulations with a fixed value of D and various decrease ratios). The APD_{S80} and CV s were measured regionally in each of the simulations, leading to the regression curves in Figure 2. Both databases are linked through a simulation run with the fixed decrease ratio used in database A and the fixed D used in database B. This linking simulation and Database B were used to build regression curve c. Curve c was estimated by computing the difference between the regional APD_{S80} for various decrease ratios used in Database B and the regional APD_{S80} of the linking simulation.

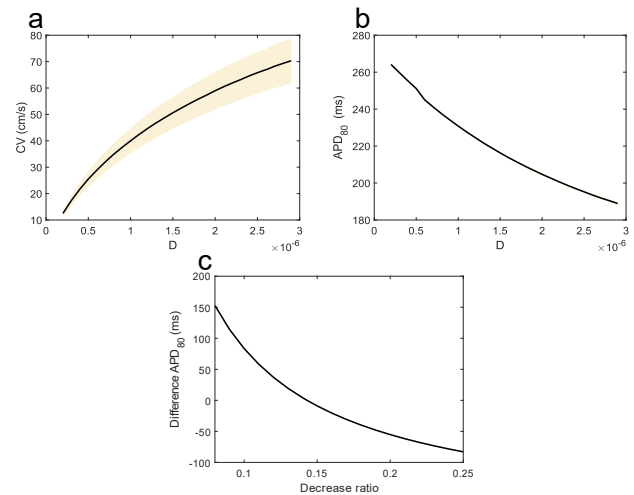


Figure 2. The regression curves used during the tailoring procedure. The mean regression line for all areas and its standard deviation (the dashed orange area) are plotted in all the figures. A: The CV s in database A for different values of D . B: The APD_{S80} in database A for different values of D . C: The difference between the APD_{S80} measured for different decrease ratios in database B and the measured APD_{S80} in the simulation with the fixed decrease ratio of database A and the fixed D for database B.

To use these regression curves, the mean regional CV s and APD_{S80} among time windows that the model should try to replicate were needed. These values were considered our reference for the tailoring process. Based on these reference CV s, an expected value for D for each region was found using regression curve a. With these values of D and regression curve b, the APD_{S80} for each region which should have been obtained if the simulation had been run with those D s and the decrease ratio used in Database A were obtained. From the difference between the reference APD_{S80} and those obtained from regression curve b, the

decrease ratio for each region was found using regression curve c . The final decrease ratio was obtained by computing the weighted mean among the regions (the weight of each region was proportional to the number of nodes in the most external layer of the atria).

2.4. Validation experiments

To prove the CA performance as well as the regional tailoring for its personalization, three different scenarios have been analyzed. Two of them corresponded to regular rhythms (sinus rhythm, Atrial Flutter (AFL)), whereas the third one is a case of Atrial Fibrillation (AF).

To compare the CA and reference simulations, the CVs and APD_{S80} were measured over different time windows using the same techniques as the ones employed for these measurements in the reference model. Then, the errors between their regional CVs and APD_{S80} of both models were computed. The weighted average relative error among the regions (the weight of each one of the regions depended on its number of nodes in the most external layer of the atria) in absolute value for each time window was calculated. Finally, the mean error of the CVs and APD_{S80} between the different windows was obtained.

3. Results

From the regular cases (Figure 3 and Figure 4), the local activation time (LAT) maps for the reference and the CA models have been obtained.

In figure 3, the results for the sinus rhythms simulations are presented which shows a precise match between the activation pattern of both models. This can also be appreciated in the mean absolute relative error which was 1.02% for the APD_{80} and 6.14% for the CV. For AFL, whereas the APD_{S80} were considerably similar (the mean absolute relative error for the APD_{80} 4.76%), the CVs observed in the CA were slower than in the reference leading to a slower activation as seen in the LATs maps of Figure 4 (with mean absolute relative error for the CV of 11.97%). The CA has difficulties capturing the pattern of activation of small, localized areas as the small late activation area in the atrial septum of the reference; however, through the tailoring process, the complete septum was assigned a smaller D reducing the CV of that area. Moreover, although some details were not captured, the global activation pattern was similar to the reference model.

In Figure 5, the results for the AF model are depicted. Activation maps are not useful during AF due to the irregular propagation pattern. To summarize AF activity, histograms of rotors and dominant frequencies have been proposed in the literature as clinically relevant parameters [8].

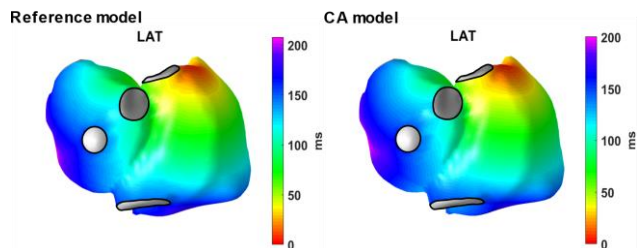


Figure 3. The local activation time maps of the reference model and the cellular automata model for a sinus rhythm simulation.

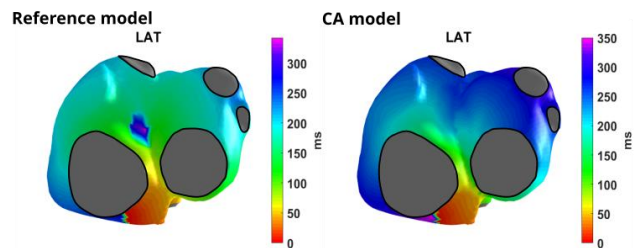


Figure 4. The local activation time maps of the reference model and the cellular automata model for an Atrial Flutter simulation.

As visible in Figure 5, rotor histograms obtained from the CA have similar distribution as the one obtained in the detailed model. The areas with more singularity points continue to congregate around the same regions in the CA than in the reference model (the roof of the pulmonary veins). Notice that the AF simulation in the CA only had just as inputs the initial potential and state of the cells apart from the selected regional Ds and decrease ratio whereas the propagation process was independent of the detailed process. Regarding the mean absolute relative error, it was higher for the CV (30.44%) than for the APD_{S80} (10.36%).

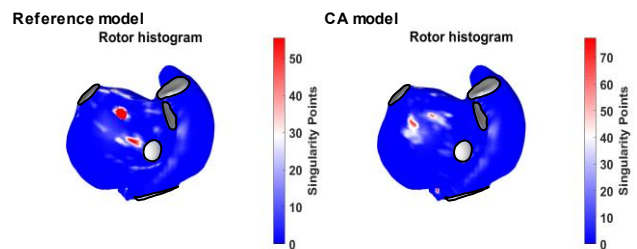


Figure 5. The rotor histogram maps of the reference model and the cellular automata model for an Atrial Fibrillation simulation.

A systematic comparison between the detailed model and the CA indicates that the mean absolute relative error of CV were 6.14%, 11.97%, and 30.44 % for the sinus rhythm, AFL, and AF models, respectively. Regarding the mean absolute relative error of APD_{80} , errors were 1.02% for sinus rhythm, 4.76% for AFL, and 10.36% for AF.

4. Discussion

In this study, a fast CA has been developed which incorporates relevant properties related to the myocardium cell dynamics. Moreover, we have designed a process that allows us to tailor the value of CA parameters thus it can mimic the electrophysiological properties observed in a detailed-mathematical model allowing us to produce personalized CA simulations.

The presented CA model was based on the one published by Y. T. Lin et al [5]; however, new electrophysiological properties were included as a CV restitution curve for each cell and a modulation of the effects of neighbors over the cells proportional to distance.

Using the CA model and the tailoring process, CA simulations have shown to have similar dynamics to the ones displayed by our reference model with a low computational cost. The results show that described tailoring process works considerably better for regular rhythms (sinus rhythms and AFL) than for AF. This may be caused because the regression curves used to estimate the regional Ds and the decrease ratio have been obtained from regular rhythm simulations. In the future, a similar database with irregular rhythms will be generated to improve the performance of the tailoring process in these cases.

The estimation offered by the tailoring procedure has shown to provide a good initial guess for the CA parameters, but the value of these parameters could be further improved through an optimization process which will be developed during the next steps. Also, the parameter optimization could be expanded to a higher number of CA parameters and efforts will be made to try to optimize their value locally instead of regionally. This will increase the faithfulness of our CA simulations.

In the future, instead of mimicking a detailed-mathematical model, we will try to reproduce the patients' behavior will be reproducing in the CA from the patients' recordings over their individualized geometry. This personalized framework will allow us to produce digital twins in a similar way as other already published papers [4] but replacing the detailed model with a fast CA model. Over this personalized CA model, different surgical procedures will be simulated to try to define the best ablation strategy for each patient.

5. Conclusions

The presented mathematical model and its personalization process have shown their capacity to emulate the dynamics displayed by already validated detailed-mathematical models during simulations of various heart rhythms. This opens the door to obtaining personalized CA simulations from patient recordings which can be used during clinical practice.

Acknowledgments

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Conflict of interests

AMC, MSG and IHR are co-founders and shareholders of Corify Care SL.

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