Inducibility Tests of Atrial Fibrillation by Automata-based Efficient Simulations

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Abstract

This study extends an existing cellular automaton (CA) model to simulate atrial electrophysiology across diverse stages of Atrial Fibrillation (AF) by integrating tissue-specific properties. The CA model, initially developed by the authors, undergoes meticulous training using biophysical simulations across varying degrees of electrical remodeling within a limited atrial tissue domain, accounting for tissue differentiation and anisotropic propagation through pacing simulations.

Validation involved comprehensive comparisons with realistic 3D atrial model to assess pro-arrhythmic behaviors. Results demonstrate remarkable congruence between the extended CA model and the biophysical solver, with CA exhibiting an 80% accuracy rate in predicting AF inducibility and a notable decrease in computing time compared to the conventional biophysical solver: 1.96 sec vs 126.75 sec for a 284.578 nodes geometry.

In conclusion, the extended CA emerges as an efficient and valid alternative for simulating atrial electrophysiology across various stages of AF, providing a valuable tool for personalized therapy planning through digital twin simulations and facilitating more targeted and effective treatment strategies.

1. Introduction

Among cardiac arrhythmias, atrial fibrillation (AF) is the most prevalent, a trend projected to persist in the forthcoming years [1]. The varied clinical presentations of AF render its diagnosis and prognosis arduous, consequently contributing to a considerable portion of heart-rhythm disorder-related hospitalizations [2]. Despite therapeutic options, management of chronic AF (cAF) remains suboptimal [3].

In silico models with advanced computational capabilities are being introduced as promising diagnostic tools focused on personalization. Biophysical models enable precise assessment of patient responses [4]. However, the complexity of those models leads to higher computational costs, impacting diagnostic efficiency [5].

Efforts now concentrate on designing electrophysiological models that balance precision and computational efficiency, with cellular automata (CA) emerging as particularly promising tools. Our group described CA's potential, in the reduction of computational time for atrial simulations [6]. Nonetheless, challenges persist due to the complex nature of atrial conduction, influenced by factors such as fibre orientation and tissue differentiation [7], necessitating further model refinement. Moreover, evaluating the efficacy of these models in predicting the induction of self-sustained arrhythmia is crucial for their practical application.

This paper extends a CA model for atrial electrophysiology [6], including differentiation of different atrial tissue types within complex geometries. Finally, evaluation of this model's efficacy in predicting chronic AF (cAF) instances across varied conditions is presented herein.

2. Materials and Methods

2.1. Fine-tuning of propagation properties

Our CA [6] was validated and trained with the restitution properties of Koivumäki's biophysical model [8]. Briefly, the CA has been trained using hundreds of pacing simulations in reduced slabs (N=2106) of homogeneous left atrial tissue. The simulations encompassed varying degrees of electrical remodelling. Specifically, a 0% remodelled condition denoted a normal condition, whereas a 100% remodelled condition represented cAF. The latter was induced by modifying the sinus rhythm model detailed in reference [8], as elaborated in reference [6]. Additionally, model

parameter values were linearly interpolated to simulate intermediate degrees of remodelling {33%, 66%, 135%}.

Atrial conduction is significantly affected by fibre orientation and tissue differentiation, leading to variations in propagation across atrial regions. To address this, specific biophysical simulations were conducted to adjust the CA model accordingly. This involved establishing tissue-specific conduction velocity (CV) parameters and a scalar parameter to differentiate between longitudinal (CV_L) and transversal (CV_T) components, tailored to each type of atrial tissue and level of electrical remodelling.

The biophysical simulations utilized for refining the CA were executed within a square tissue domain (5 × 5 × 0.3 cm, 63.072 vertices, 340.048 tetrahedra, Figure 1). The properties of longitudinal and transversal diffusion were adjusted in accordance with the findings of [9], aligning them with established literature standards to achieve physiological sinus propagation [10]. This customization process was tailored to various types of atrial tissues, including the left atrium (LA), right atrium (RA), crista terminalis (CT), Bachmann bundles (BB), pectinate muscles (PM), cavo-tricuspid isthmus (ICT), and valves. Ten stimuli, S1 = 500 ms, were delivered from a central point within the square tissue. These simulations were repeated across varying degrees of electrical remodelling {0%, 33%, 66%, 100%, and 135%}, to evaluate and incorporate transversal and longitudinal components of CVs into the CA framework (Figure 1).

The reduction in CV associated with cAF [11], was incorporated into the biophysical model as a diminishing factor in diffusion. This reduction was integrated into the CA as a direct adjustment applied to the CV restitution curve. Indeed, biophysical simulations were conducted within the LA square tissue described above, spanning diffusivity values ranging from 20% to 120% of normal diffusivity conditions. Consequently, the ratio of $CV_{x\%\,diff.}$ diffusivity to $CV_{100\%\,diff.}$ diffusivity was assessed to derive a multiplicative parameter influencing velocity values within the CA framework.

2.2. Biophysical simulations for CA validation

To validate the CA model, simulations were conducted using both CA and a biophysical solver mimicking pathological conditions. The simulations utilized highly detailed volumetric bi-atrial geometries derived from magnetic resonance images, with tissue types differentiated, as shown in Figure 2. The geometry comprised 284.578 vertices connected in 1.353.783 tetrahedra, with an average node distance of 0.67338 mm [9].

Specifically, AF inducibility tests were simulated within the bi-atrial geometry [12]. These tests involved evaluating arrhythmia induction using a S1 pacing protocols from four different location within the atria (posterior LA wall, LA roof, superior and inferior cava vena). A total of 192 simulations were conducted using identical node activation and stimulus values in both simulators to ensure comparability.

To assess arrhythmic behavior under various AF conditions, four substrate conditions were considered: 100% remodeling and diffusion, 100% remodeling and 25% diffusion, 135% remodeling and 25% diffusion, and 135% remodeling and 50% diffusion. Inducibility of arrhythmic episodes was tested by applying a series of 20 S1 stimuli {130, . . . , 240} ms The presence of sustained arrhythmia after the pacing protocol was evaluated by observing self-sustained activity beyond 8 seconds of simulation time.

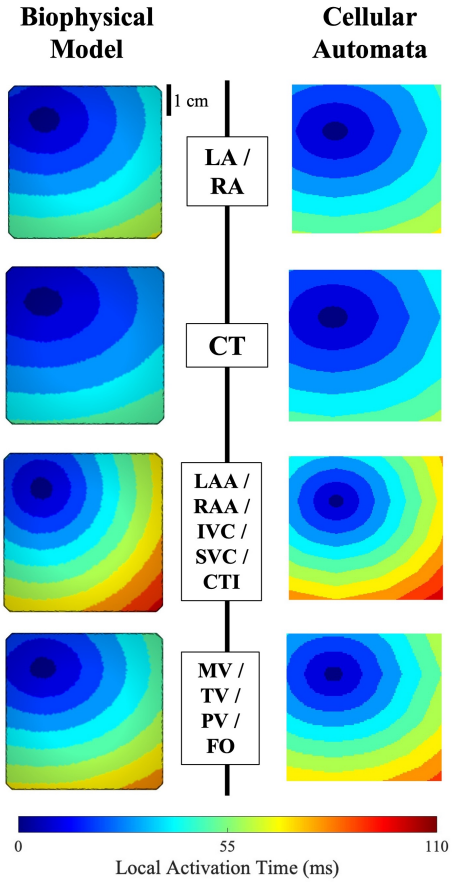

Figure 1 Comparison between biophysical (left) and cellular automata (right) simulations in different atrial tissues. From up to down: left (LA) and right atrium (RA); crista terminalis (CT); left (LAA) and right (RAA) atrial appendage, inferior (IVC) and superior (SVC) vena cava, cavo-tricuspid isthmus (CTI); mitral valve (MV), tricuspid valve (TV), pulmonary veins (PV) and fossa ovalis (FO).

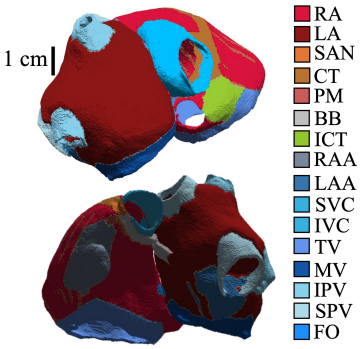

Figure 2. Detailed, 3D volumetric bi-atrial geometry derived from MRI represented with colors according to different tissue types. RA: right atria; LA: left atria; SAN: sinoatrial node; CT: crista terminalis; PM: pectinate muscle; BB: Bachmann bundle; ICT: cavo-tricuspid isthmus; RAA: right atrial appendage; LAA: left atrial appendage; SVC: superior vena cava; IVC: inferior vena cava; TV: tricuspid valve; MV: mitral valve; IPV: inferior pulmonary veins; SPV: superior pulmonary veins; FO: fossa ovalis.

3. Results

3.1. Biophysical model characterization

Regarding the inclusion of anisotropy in the CA model to align with the biophysical model, the tissue-type analysis resulted in adjustments per tissue type concerning conduction velocity (CV) and its longitudinal (CV_L) and transversal (CV_T) components. These adjustments yielded consistent outcomes across varying degrees of electrical remodeling. A visual representation of the propagation variance per tissue type is provided in Figure 1, while the scalar parameters utilized to refine longitudinal tissue-specific CV ($CV_L/CV_{L,LA}$) and the transverse-to-longitudinal ratio (CV_L/CV_T) are summarized in Table 1.

Table 1. CV tissue-specific ($CV_L/CV_{L,LA}$) and transversal-to-longitudinal (CV_L/CV_T) scalar parameters considered for the fine-tuning of the CV properties of the cellular automata.

Atrial region	$CV_L/CV_{L,LA}$	CV_L/CV_T
RA, LA	1	1.36
SAN	0.99	1
CT	1.25	1.49
PM	1.66	1.63
BB	1.67	1.42
RAA, LAA, IVC, SVC, CTI	0.56	1
MV, TV, PV, FO	0.77	1.38

Subsequently, the relationship between the diffusivity rates of the biophysical model and the adjustment parameters for CV in the CA model was established. The multiplication factors $CV_{x\%\,dif.}/CV_{100\%\,dif.}$, derived from simulation results, were of 0.42 for 25% diffusion, 0.67 for 50% and 0.86 for 75%.

3.2. Validation of CA: arrhythmic case

The comprehensive analysis of the inducibility test, encompassing N=192 S1 pacing protocols across four remodeled/diffusion conditions and four pacing zones as depicted in Figure 3a, is summarized in Figure 3b. The panels, organized by substrate condition and pacing site, illustrate that the CA model reproduced arrhythmic activity in similar scenarios compared to the biophysical model.

Overall, the CA exhibited sustained activity in fewer S1 cases, yet it successfully replicated pacing sites and conditions that exhibited pro-arrhythmic activity in the biophysical model. Conversely, scenarios that did not induce arrhythmia in the biophysical solver did not manifest any activity in the CA. Across all N=192 simulations, the CA demonstrated an 80% accuracy (153/192), 96% specificity (127/132), and 45% sensitivity (27/60). In terms of the N=16 substrate conditions and pacing locations, irrespective of the S1 interval, the CA displayed 100% specificity (3/3) and 62% sensitivity (8/13) compared to the biophysical solver.

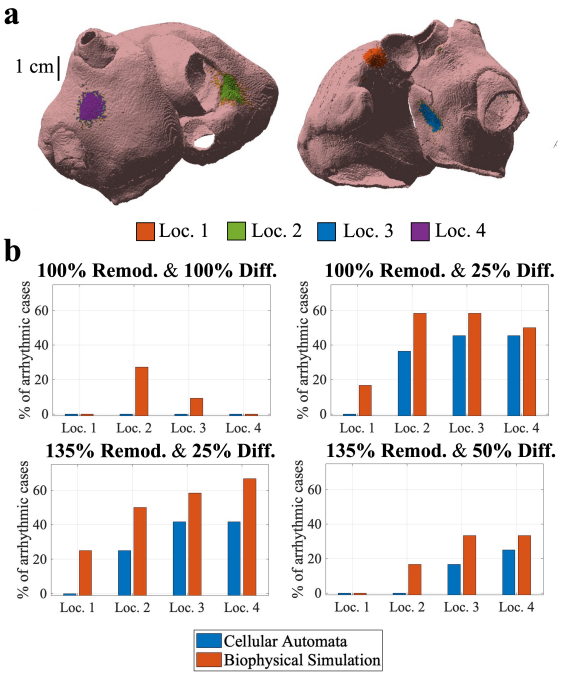

Figure 3. a) Bi-atrial geometry with the four different atrial locations considered to analyze the presence of sustained AF after interrupting a pacing protocol. b) Comparison between biophysical and CA models:

percentage of arrhythmic cases after S1 protocol under four remodeling/diffusivity conditions and 4 pacing locations.

4. Discussion and Conclusion

This study extends a CA model [6] by integrating tissue-specific properties to simulate atrial electrophysiology. A meticulous tissue-dependent analysis using biophysical simulations defined longitudinal and transversal CV components for each tissue type and accounted for CV reduction seen in cAF. Biophysical simulations with regional ionic differences and decreasing diffusion properties informed the CA model, establishing node-specific parameter dependencies based on atrial zone and diffusion reduction levels. Our CA model offers significant advancements in modeling atrial tissue heterogeneity, characterizing changes in longitudinal and transversal CV for each atrial region and diffusion properties.

Pro-arrhythmicity tests between the CA and biophysical solver demonstrated comparable conditions. Concretely, the CA was able to reproduce atrial arrhythmia induction in the same places as the biophysical solver, with high specificity and accuracy measures, validating the CA's potential in evaluating arrhythmic substrates.

The computational cost difference between the two simulators across various models was tested on the same computer setup. The biophysical model was implemented in an in-house solver on Graphics Processing Units (GPUs) used as computing platforms to carry out the simulations, whereas the CA was implemented without the need for parallelization. In this setup, the CA consistently demonstrated shorter computational times compared to the biophysical solution, with notable speed-ups of 4.7 for 2106 nodes and 64.6 for 284578 nodes.

Future work will focus on extending CA behavior in patient-specific anatomies compared to clinical outcomes, aiming to evaluate the clinical utility of simulations under anti-arrhythmic therapies.

This novel approach presents a promising alternative to existing biophysical models, offering faster simulations while maintaining high accuracy and specificity. The study underscores the potential of CA models in simulating atrial electrophysiology and their application in patient-specific simulations for personalized therapies.

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