Effects of Macroscopic Heterogeneity on Propagation in a Computationally Inexpensive 2D model of the Heart

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***Abstract*— We have developed a computationally inexpensive, two-dimensional, bidomain model of the heart to demonstrate the effect of tissue heterogeneity on propagation of cardiac impulses generated by the sino-atrial node (SAN). The geometry consists of a thin sheet of cardiac tissue with designated areas that represent the SAN and atria. The SAN auto-generates continuous impulses that result in waves of normal propagation throughout the tissue. On the introduction of heterogeneous patches with low tissue conductivities, the rhythm of the waveform becomes irregular. The study suggests that simplified and computationally inexpensive models can be insightful tools to better understand the mechanisms that cause atrial fibrillation (AF) and hence more effective treatment methods.**

I. Introduction

Tissue discontinuities in the myocardium affect propagation of cardiac impulses [1]. These discontinuities can be a result of the essentially heterogeneous nature of heart tissue, such as the existence of coronary vasculature or abnormalities, such as atrial fat, fibrosis, scars, and ischemic regions which vary in size and structure [1]. In a healthy heart, these heterogeneities may not have any significant impact on cardiac function and activity; however, on the application of external electric fields or in a diseased condition, heterogeneities can induce ectopic activity and formation of virtual electrodes [2]–[4]. Though it is known that these ectopic foci or virtual electrodes play a significant role in the genesis and termination of arrhythmia [5], the specific mechanisms of the interaction between propagation, tissue heterogeneities and applied external field is yet to be understood.

Infiltrated atrial fat, in recent years, has been considered as a risk factor associated with atrial fibrillation (AF) [6]–[8]. Though previous modeling studies have studied the role of microstructural heterogeneities [9], there is no simple simulation model of the heart that has studied the role of macroscopic heterogeneities, such as infiltrated fat tissue on propagation. As has been demonstrated in earlier studies, simple cardiac models may be sufficient as a first step to understand the electrical mechanisms in the heart [10]–[13].

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The purpose of this study is to determine the effect of macroscopic atrial tissue heterogeneities on propagation and hence conditions such as AF in a simple 2D bidomain model of cardiac tissue.

II. Methods

The electrical activity in the heart was represented by the bidomain model and the modified Fitz-Hugh Nagumo equations in a 2D sheet of cardiac tissue with areas designated to represent the sino-atrial node (SAN) and atria.

A. Model Equations

The bidomain equations are the most widely used system of partial differential equations to represent cellular activation in cardiac tissue [14]. The bidomain model was chosen for this study so that the combined effect of varied anisotropy ratios in the extracellular and intracellular domains and heterogeneous conductivities on propagation can be realized. The bidomain equations were implemented along with the modified FitzHugh-Nagumo equations to represent cellular ion kinetics as in a previous study [11]. The model equations are represented by equations 1, 2 and 3.

$$\frac{\partial V_e}{\partial t} - \frac{\partial V_i}{\partial t} + \nabla \cdot (-\sigma_e \nabla V_e) = i_{ion}$$

$$\frac{\partial V_i}{\partial t} - \frac{\partial V_e}{\partial t} + \nabla \cdot (-\sigma_i \nabla V_i) = -i_{ion} \qquad (1)$$

$$\frac{\partial u}{\partial t} = ke\left[\frac{(V_m - B)}{A} - du - b\right]$$

V_e and V_i are the dependent variables that represent extracellular and intracellular potentials respectively, $V_m = V_i - V_e$ is the transmembrane potential and u is the recovery variable that represents cellular refractoriness. σ_e and σ_i are the extracellular and intracellular conductivities respectively. a, b, c1, c2, c3, d, e, k, A and B are region-specific parameters. i_{ion} is the ionic current, and is defined by different quantities in the SAN and the rest of the tissue to enable sustained and auto-initiated impulses in the SAN. i_{ion} was calculated as

$$i_{ion} = kc_1(V_m - B)\left[a - \frac{(V_m - B)}{A}\right]\left[1 - \frac{(V_m - B)}{A}\right] + kc_2 u \qquad (2)$$

within the SAN, and,

$$i_{ion} = kc_1(V_m - B)\left[a - \frac{(V_m - B)}{A}\right]\left[1 - \frac{(V_m - B)}{A}\right] + kc_2 u(V_m - B) \qquad (3)$$

in the rest of the tissue. The conductivity values and parameters were chosen as in the previous study by Sovilj et al. [11].

B. Geometry

The geometry consists of a sheet of tissue of dimensions 40 mm x 40 mm as shown in figure 1. The SAN and atrial regions are differentiated from each other in the model by altering model parameters in each of the regions [11] and via expressions (2) and (3). Note that atrial regions R1 and R2 are assigned the same model parameters, and are delineated for purposes of identifying atrial regions with and without heterogeneous patches. The dimensions of the three regions were chosen arbitrarily. In this study we assume the fibers are straight and aligned parallel to Cartesian x-axis. Low conductivity values were assigned to heterogeneous patches, depicted by VE1, VE2 and VE3 in figure 1, which represent cardiac tissue heterogeneities such as infiltrated atrial fat. Several studies have recognized that these heterogeneities act as virtual electrodes or ectopic foci and play an important role in the genesis and termination of cardiac arrhythmia [3], [5], [15], [16].

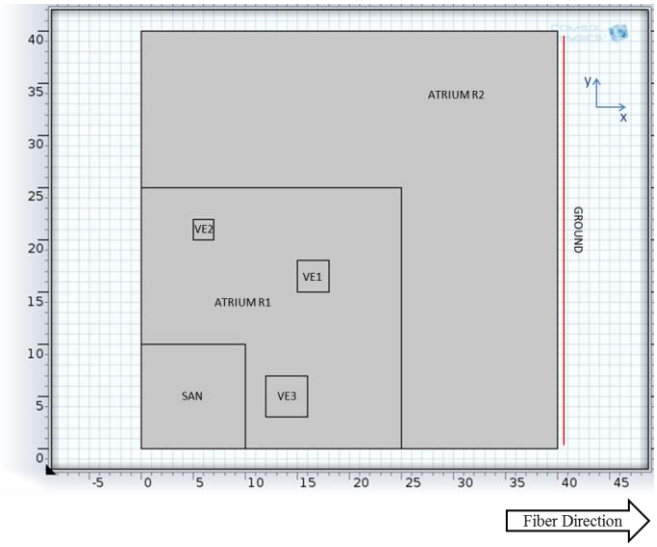

Figure 1. 2D geometry consists of a 40 mm x 40 mm sheet: including areas designated as SAN, atrium R1 and atrium R2. VE1, VE2 and VE3 represent three heterogeneous patches.

C. Model Execution

The purpose of this study is to simulate the effect of atrial heterogeneous patches on propagation. Model parameters were chosen to simulate sustained normal propagation with wave-fronts auto-generated in the SAN and transmitted to the atria continuously without external stimulation, as in a previous study by Sovilj et al. [11].

Though there is no consensus on the actual values of tissue conductivities, previous studies discuss that conductivity ratios in the planes along and across the fiber direction in the two domains are different and this phenomenon affects propagation [17] and hence anisotropic tissue conductivities were used. Table 1 lists the assigned values of tissue conductivities used in the model.

The simulations were carried out using COMSOL Multiphysics v4.3b package for finite element analysis, on an Intel core i7-XPS 8100 PC with a processor speed of 2.93 GHz.

TABLE 1. ANISOTROPIC TISSUE CONDUCTIVITY VALUES

	σ_{ex} (mS/m)[a]	σ_{ey} (mS/m)	σ_{ix} (mS/m)	σ_{iy} (mS/m)
SAN	0.4	0.2	0.5	0.05
Atria (R1 & R2)	6	4	8	0.8
VE1	$3e^{-4}$	$1.5e^{-4}$	$1e^{-4}$	$1e^{-5}$
VE2	$4e^{-7}$	$2e^{-8}$	$1e^{-7}$	$1e^{-8}$
VE3	$8e^{-7}$	$4e^{-8}$	$1e^{-8}$	$1e^{-9}$

a. In the notation for conductivity values, σ_{ex}, σ_{ey}, σ_{ix} and σ_{iy}, the 1st subscript denotes extracellular or intracellular and the 2nd subscript denotes direction; x implies along, and y across the fiber direction, respectively [11].

III. RESULTS AND DISCUSSION

Simulations were carried out using a simplified two-dimensional geometry as shown in figure 1 with areas designated to represent the SAN and atria with and without heterogeneous regions. The model parameters were varied to study the effect of heterogeneity on the rate and rhythm of propagation. Patches of heterogeneous tissue conductivities were introduced to represent regions known to be responsible for the formation of ectopic foci and virtual electrodes in the atria, such as, fatty tissue, scar tissue and coronary vasculature [5], [16], [18], [19].

A. Effect of heterogeneity on propagation

Figure 2 displays the case of normal propagation with no heterogeneous patches. Figures 2(A) and 2(B) show the spatial distribution of Vm at times, 0.6 s and 0.68 s, respectively. The wave front initiated in the SAN is propagated uniformly to the atria. Figure 2(C) shows the transmembrane potential, V_m, over a span of 10 seconds in the case of homogeneous tissue throughout the atria. The cycle length (CL) is ~ 700-800 ms and the rhythm is regular. The impulses generated in the SAN (solid blue tracing, measured at (5,5) mm) are propagated to the atrium R1 (dashed red tracing, measured at (20,20) mm) and atrium R2 (dotted black tracing, measured at (35,35) mm) in a regular manner.

Figure 3 demonstrates the effect of patchy heterogeneities on propagation. The regions of heterogeneity in atrium R1 act as ectopic foci (figure 3(A)) and result in the formation of a spiral wave (figure 3(B)). In figure 3(C) we note that the average CL is lowered to ~450 ms and the rhythm is irregular as an effect of the heterogeneous patches.

Furthermore, while every pulse propagating through the geometry is initiated in the SAN in the homogeneous atrial tissue (figure 2(C)), there were 8 out of 22 pulses that were initiated in the heterogeneous atria and propagated to the non-heterogeneous atria (figure 3(C)) as a result of ectopic activity. For example, in the 1-2 ms time interval in figure

3(C), while the first impulse was generated in the SAN, the second was generated in the atria. There is no SAN generated impulse (solid blue) corresponding to the impulse generated in the heterogeneous atria (dashed red) and propagating to the non-heterogeneous atria (dotted black).

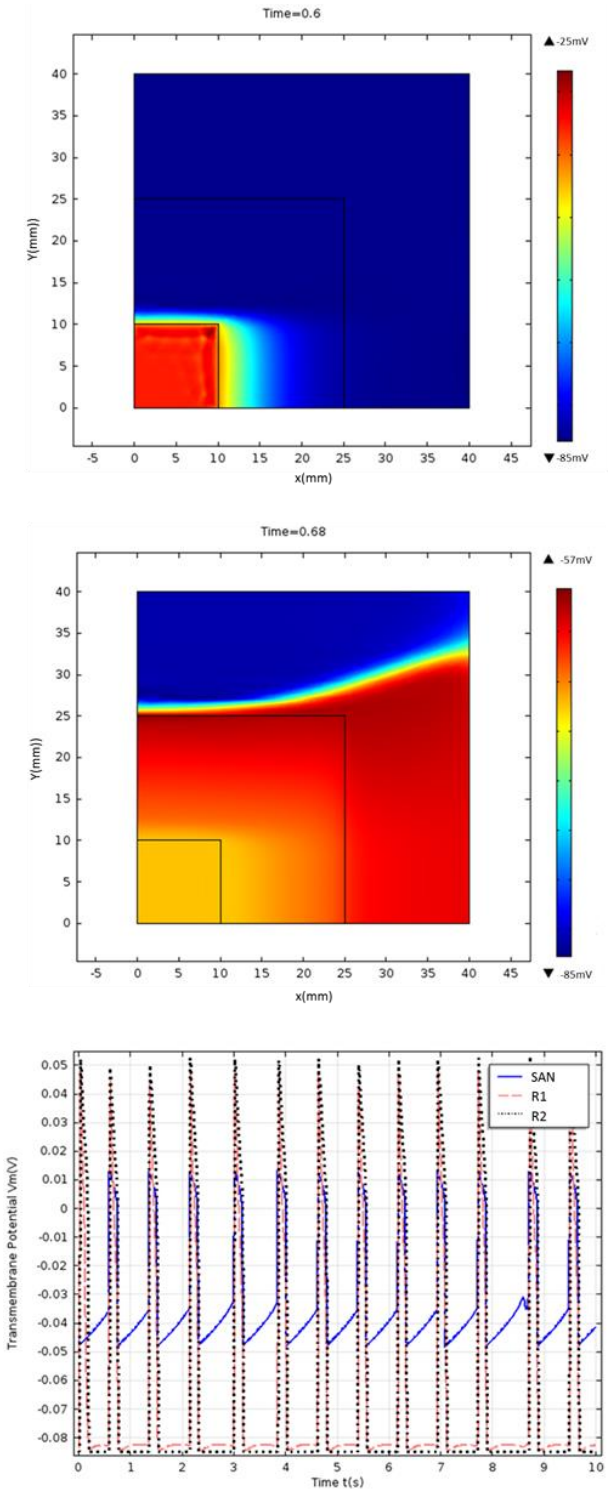

Figure 2. Normal propagation without heterogeneous patches. (A) & (B) Spatial distribution of transmembrane potential (V_m) at t= 0.6 and 0.68 s, respectively; (C) Measurement of V_m at spatial coordinates (5,5), (20,20) and (35,35) mm in the geometry representative of electrical activity in the SAN, atrium R1 and atrium R2, respectively; CL = ~700-800 ms.

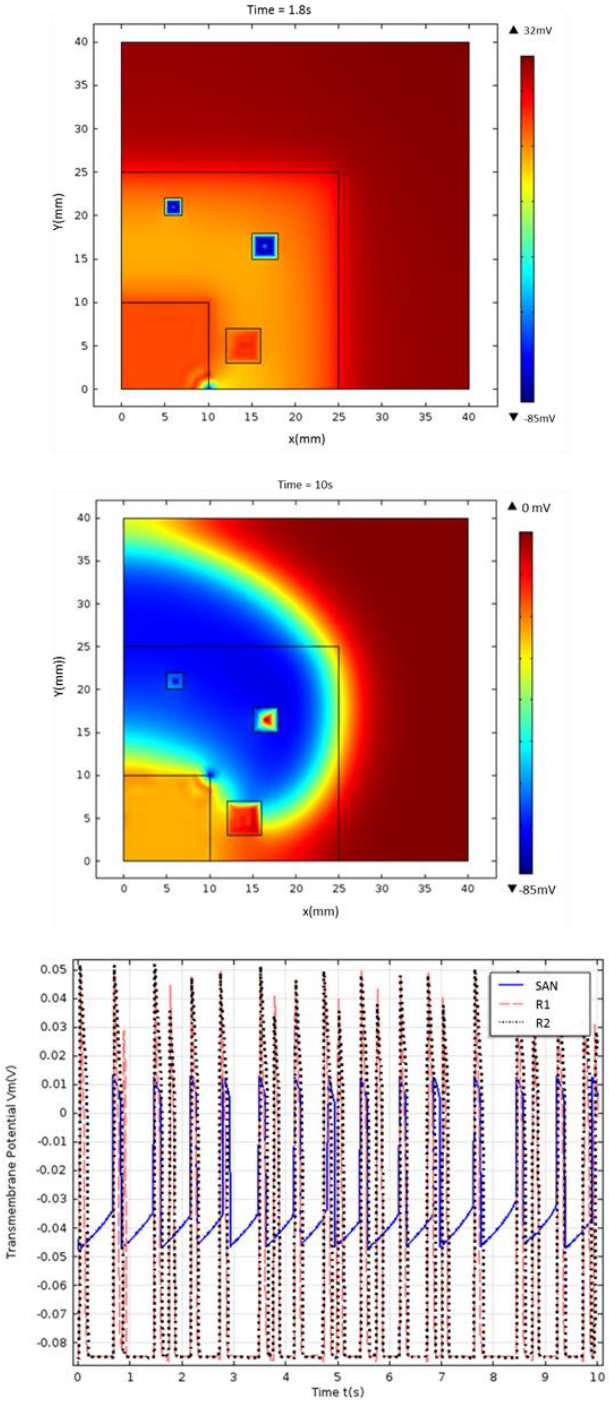

Figure 3. Effect of heterogeneity on propagation. (A) Spatial distribution of V_m at t=1.8 s; Formation of ectopic foci in the region of the heterogeneity patches. (B) Spatial distribution of V_m at t=10 s. A heterogeneous patch located at (15,5) mm acts as an ectopic focus and results in the formation of a spiral wave. (C) Measurement of Vm at spatial coordinates (5,5), (20,20) and (35,35) mm in the geometry representative of electrical activity in the SAN, atrium R1 and atrium R2, respectively; Irregular and faster paced propagation with the introduction of heterogeneous patches; CL = ~ 450 ms.

The novelty of this simulation model is the demonstration of ectopic activity in a simple model, even without the use of realistic ionic currents, thus making it computationally inexpensive and a basis for further studies. The model demonstrates the effects of tissue heterogeneity on the rhythm of propagation. We observe that the rhythm becomes irregular with the introduction of patches of low tissue conductivity in the atrial tissue, resulting in ectopic activity.

The scope of this study was to develop a simple model not inclusive of geometric complexities in order to understand the basic effects of heterogeneous patches on propagation. Hence anatomical and structural details of the heart were not considered. Our next steps will be to enhance this model to further understand the effects of macroscopic heterogeneous patches on the genesis and termination of AF. In future studies we plan to incorporate more realistic geometries and intrinsic microstructure.

IV. References

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