Whole Heart Modeling – Spatiotemporal Dynamics of Electrical Wave Conduction and Propagation

Hui Yang*, Yun Chen, and Fabio M. Leonelli

***Abstract*—Cardiac electrical activities are varying in both space and time. Human heart consists of a fractal network of muscle cells, Purkinje fibers, arteries and veins. Whole-heart modeling of electrical wave conduction and propagation involves a greater level of complexity. Our previous work developed a computer model of the anatomically realistic heart and simulated the electrical conduction with the use of cellular automata. However, simplistic assumptions and rules limit its ability to provide an accurate approximation of real-world dynamics on the complex heart surface, due to sensitive dependence of nonlinear dynamical systems on initial conditions. In this paper, we propose new reaction-diffusion methods and pattern recognition tools to simulate and model spatiotemporal dynamics of electrical wave conduction and propagation on the complex heart surface, which include (*i*) whole heart model; (*ii*) 2D isometric graphing of 3D heart geometry; (*iii*) reaction-diffusion modeling of electrical waves in 2D graph, and (*iv*) spatiotemporal pattern recognition. Experimental results show that the proposed numerical solution has strong potentials to model the space-time dynamics of electrical wave conduction in the whole heart, thereby achieving a better understanding of disease-altered cardiac mechanisms.**

***Index Terms*—whole heart model, reaction-diffusion dynamics, cardiac conduction, computer simulation.**

I. Introduction

Recently, computer simulation of electrical conduction and propagation on a human heart is receiving increasing attentions, because it overcomes many practical and ethical limitations in real-world biomedical experiments. In addition, computer simulation offers greater flexibility for biomedical scientists to test their hypothesis and develop new hypotheses for cardiovascular research and knowledge discovery. There has been significant development of cardiac models during the past 20 years. For example, the Physiome project [1] is a worldwide umbrella program to build a comprehensive framework for modeling the human body. The OpenCMISS software project [2] provides an example finite-element model of canine heart. In January 2011, Circulation Research published a series of papers [3-6] to review cardiac modeling and envision that "Biophysics-based cardiac modeling has the potential to dramatically change the 21st century cardiovascular research and the field of cardiology."

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However, whole-heart modeling involves a greater level of complexity. Cardiac electrical activity in a single cell involves orchestrated transportation of large amounts of ions through various biological channels. Electrical waves will also propagate from cell to cell through the entire heart to couple excitation with contraction and blood ejection. In the literature, cellular automata and reaction-diffusion models were widely used to model cardiac electrical propagation and conduction processes [7]. A cellular automaton is a discrete model with a regular grid of cells, each is with a finite number of states. Every cell has the same updating rules based on its neighboring states. Because of its simplicity and superior computational speed, cellular automata was popular in whole heart simulation. However, simplistic assumptions and rules are limited in their ability to model cardiac electrical activity, especially in the level of whole heart. Reaction-diffusion models describe how dynamic variables change the distribution in space and time under two processes, i.e., (1) ***Reaction process***: dynamic variables are interacting with each other for conversion, and (2) ***Diffusion process***: dynamic variables spread out in space. Although reaction-diffusion models provide more realistic simulation of electrical activity through the whole heart, they are more difficult to implement on complex geometry and more computationally expensive.

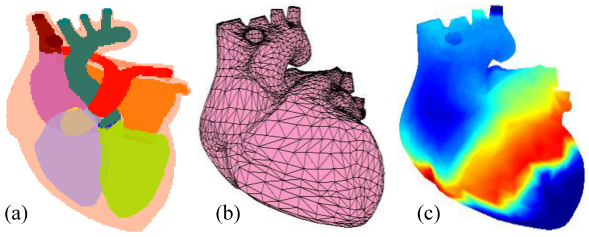


Fig. 1. Whole heart models: (a) Colored components of the human heart, (b) Finite element meshes, (c) Electrical conduction on the human heart (Note: *red region represents electrically activated tissue*).

In addition, a significant challenges resides in the representation of complex geometry of the heart. This representation must not only characterize geometric complexities but also yield sufficient resolution to capture activation wavefronts and cell-to-cell propagation dynamics. As shown in Fig. 1, we utilized an anatomically realistic heart geometry for reaction-diffusion modeling of cardiac electrical activity. However, traditional finite-difference methods (FDM) are effective on regular surfaces with orthogonal and regular grids by discretizing the diffusion tensor in the domain. The complex geometry and high dimensionality of heart (see Fig. 1) pose great challenges for FDMs.

This paper presents a practical solution to simulate electrical propagation and conduction through the heart. We proposed reaction-diffusion modeling on the two-dimensional isometric graph that is the reduced-dimension

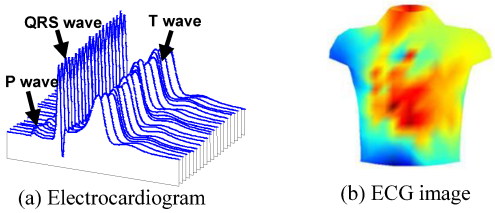
projection of complex heart geometry. Then, 2-D reaction diffusion dynamics on the isometric graph are one-to-one projected back onto the original geometry of a 3D heart.

This paper is organized as follows: Section II presents the research background. Section III introduces the methodology and results of whole-heart modeling. Section IV discusses and concludes this presented research.

II. Research Background

A. Spatiotemporal Cardiac Electrical Dynamics

A correctly beating heart is necessary to ensure adequate circulation of blood throughout the body. Normal heart rhythm is produced by the orchestrated conduction of electrical signals throughout the heart. Aberrant changes (e.g., an occlusion of coronary artery, disease-altered ion channel activity) can influence the propagation of electrical waves and lead to cardiac arrhythmias. Temporal electrocardiogram (ECG) signals (Fig. 2a) are widely used in the clinical practice to monitor cardiac electrical activity for cardiovascular diagnostics. The ECG trace is often segmented into P wave, QRS complex, and T wave in the time domain (Fig. 2a). Each segment represents phases of cardiac electrical activity and functions of heart chambers. For examples, atrial depolarization is represented by the P wave, ventricular depolarization is represented by the QRS complex, and ventricular repolarization is represented by the T wave.



(a) Electrocardiogram (b) ECG image

Fig. 2. Examples of electrical signals from the human heart

While electrical activities are excited and propagated through the heart in both space and time (see electrical conduction in the whole heart model in Fig. 1c), the temporal ECG is a 1-dimensional projection of space-time cardiac electrical activities. Such 1-D temporal projection will hide spatial information generated by cardiac pathologies [8, 9] limiting medical understanding of the process. As such, medical decisions that are made will be significantly influenced by such an information loss. Therefore, ECG imaging (Fig. 2b) uses hundreds of electrodes to record and measure cardiac electrical activities over the body torso. Note that ECG imaging is varying dynamically in both space and time on the body surface, which captures spatiotemporal variations of electrical conduction in the heart. Considering the spatiotemporal cardiac process, we denote the data of electrical conduction in the heart as $\{V(s,t): s \in R \subset \mathbb{R}^d, t \in T\}$, where the dependence of spatial domain R on time T symbolizes the condition where the spatial domain changes over time. Spatiotemporal modeling of electrical conduction in the whole heart has the potential to provide rich information and provide a better understanding of cardiac operations. The extraction of physiopathology knowledge from whole-heart models is critical to improving cardiac care services, from preventive screening to diagnosis to treatment to follow-up monitoring of heart diseases and cardiac arrhythmias.

B. Parallel-computing simulation of electrical excitation and conduction in 3D human heart:

We recently developed a whole-heart simulation model based on modern GPGPU (i.e., General-purpose computing on graphics processing units) architecture [7]. Because of the complex heart geometry, finite-element methods are utilized to address the issues of irregular node spacing, complex boundaries, and regionally dependent conductivities. The anatomically realistic heart geometry is derived based on digital image dataset of human cadavers, available in the Visible Human Project. This whole-heart model is made of 728,321 cells, and is segmented into various components (i.e., 2 atria, 2 ventricles, 3 aortic valves, 2 mitral valves, 5 pulmonary valves, 3 tricuspid valves and others) to facilitate the modeling of regional variations. This geometry can be further discretized to render a fine-grained finite element model using common meshing methods, i.e., tetrahedral or hexahedral elements. Fig. 3 shows the simulated cardiac electrical activity at two time indices (a-b) and cross sections of the 3D whole-heart model (c-d).

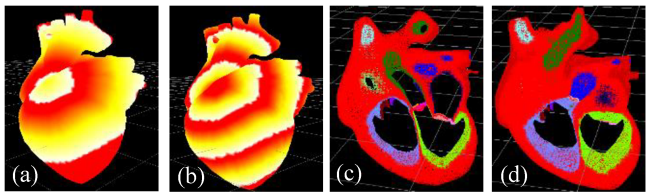


Fig. 3: (a-b) Electrical wave conduction in the whole heart; (c-d) Cross sections of the 3D whole heart model.

We implemented three versions of the whole-heart model. One is the CPU version and the other two are GPU versions on the Nvidia CUDA platform. OpenGL was used for fast rendering and visualization of simulation data. Our results show that GPU versions outperform the conventional CPU approach and significantly improve the speed of computing by approximately 30-fold [7]. With the power of modern massive parallel computing, we also investigated the formation of nonlinear spiral waves and turbulent patterns in the whole-heart model. These preliminary studies established the feasibility to further investigate real-time, multi-scale, and comprehensive simulation of a 3D human heart with unprecedented details and accuracy. However, simplistic assumptions and rules of cellular automata models limit the ability to accurately describe cardiac electrical activity, especially in the level of whole heart. Therefore, we further investigate reaction-diffusion modeling of space-time cardiac electrical activity in this present paper.

III. Whole-Heart Modeling

This paper presents a numerical reaction-diffusion modeling approach to simulate the spatiotemporal dynamics of electrical wave conduction and propagation in the whole heart. This present approach involves four key steps, namely, (i) whole heart model; (ii) 2D isometric graphing of 3D heart geometry; (iii) reaction-diffusion modeling of electrical waves in 2D graph, and (iv) spatiotemporal pattern

recognition. All four components are eventually integrated together to develop better simulation models of electrical wave conduction in the whole heart, thereby achieving better understanding of disease-altered cardiac electrical activity.

A. *Whole-heart Model*

Cardiac electrical activity varies across a fractal network of muscle cells, Purkinje fibers, arteries and veins. An anatomically realistic model of human heart involves irregular node spacing, complex boundaries, and regionally dependent conductivity. As such, electrical excitation and conduction in the human heart exhibit complex spatiotemporal dynamics. Spatiotemporal simulation provides a better understanding of disease-altered cardiac electrical activity and further leads to significant economic and societal impacts. For example, simulation-based optimization of cardiac treatments will help improve the quality of healthcare services, reduce healthcare costs and promote the health of our society. On the basis of our previously developed whole-heart model, we have further investigated the reaction-diffusion modeling of electrical wave conduction on an anatomically realistic heart. In this investigation, we will present the simulation and comparison of the propagation and conduction of electrical activity between a healthy heart and a heart with arrhythmia.

B. *Isometric Graphing*

First, we introduce the isometric graphing approach [10] to extract inherent geodesic properties of the 3-dimensional heart geometry. Note that geodesic distance is the true distance for the reaction-diffusion dynamics (or electrical conduction) to travel between two locations instead of the Euclidean distance. As such, it is imperative to characterize and quantify the intrinsic geometry for reaction-diffusion modeling on the heart surface. We obtain nonlinear and nonstationary characteristics of the whole-heart surface asymptotically by capturing geodesic manifold distances between all the locations. These geodesic distances are further utilized to construct the low-dimensional embedding of heart surface. The key steps of the isometric graphing algorithm include: (1) Build the graph of k nearest neighbours, (2) Compute the shortest path between two locations on the heart surface, (3) Construct low-dimensional embedding. The proposed approach not only captures nonlinear degrees of freedom of heart surface, but also efficiently yields globally optimal solutions for dimensionality reduction. This greatly facilitates the simulation modeling of reaction-diffusion dynamics in the reduced dimension.

C. *Reaction-diffusion modeling in the isometric graph*

Next, we simulate and model reaction-diffusion dynamics on the 2D isometric graph. The two-component reaction-diffusion model on a bounded domain Ω (i.e., isometric graph) with concentration variables u, v and nonlinear reaction expressions f, g as

$$\begin{aligned} \frac{\partial u}{\partial t} &= f(u,v) + \mathcal{D}_1 \nabla^2 u \\ \frac{\partial v}{\partial t} &= g(u,v) + \mathcal{D}_2 \nabla^2 v \end{aligned} \tag{1}$$

where $\mathcal{D}_1$ and $\mathcal{D}_2$ are the diffusion constants of concentration variables u and v, $\nabla^2 \equiv \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2}$ is the Laplacian operator in the two-dimensional space. We discretize the reaction-diffusion model at the time index $t = 1,2,\dots,T$ and locations $i = 1,2,\dots,N$ as:

$$\begin{aligned} (1 - \mathcal{D}_1 \delta t \cdot \nabla^2) u_i^t &= u_i^{t-1} + \delta t \cdot f(u_i^{t-1}, v_i^{t-1}) \\ (1 - \mathcal{D}_2 \delta t \cdot \nabla^2) v_i^t &= v_i^{t-1} + \delta t \cdot g(u_i^{t-1}, v_i^{t-1}) \end{aligned} \tag{2}$$

The matrix form of differential equations will become

$$\begin{pmatrix} \boldsymbol{B_1} & \mathbf{0} \\ \mathbf{0} & \boldsymbol{B_2} \end{pmatrix} \begin{pmatrix} \boldsymbol{U}^t \\ \boldsymbol{V}^t \end{pmatrix} = \begin{pmatrix} \boldsymbol{U}^{t-1} + \delta t \cdot \boldsymbol{F} \\ \boldsymbol{V}^{t-1} + \delta t \cdot \boldsymbol{G} \end{pmatrix} \tag{3}$$

where $\boldsymbol{U}^t = [u_1^t, \dots, u_N^t]^T$ and $\boldsymbol{V}^t = [v_1^t, \dots, v_N^t]^T$, $\{\boldsymbol{F}\}_i = f(u_i^{t-1}, v_i^{t-1})$ and $\{\boldsymbol{G}\}_i = g(u_i^{t-1}, v_i^{t-1})$ for $i = 1,2,\dots,N$, δt is the time step, $\boldsymbol{B_1}$ and $\boldsymbol{B_2}$ are the matrices of constant coefficients pertinent to the domain Ω and diffusion constants $\mathcal{D}_1, \mathcal{D}_2$. Hence, concentration variables $\boldsymbol{U}^t$ and $\boldsymbol{V}^t$ at time step t can be solved through the linear equations $\mathbf{A} \cdot \mathbf{x} = \mathbf{b}$, where $\mathbf{A} = \begin{pmatrix} \boldsymbol{B_1} & \mathbf{0} \\ \mathbf{0} & \boldsymbol{B_2} \end{pmatrix}$ is a constant matrix and $\mathbf{b} = \begin{pmatrix} \boldsymbol{U}^{t-1} + \delta t \cdot \boldsymbol{F} \\ \boldsymbol{V}^{t-1} + \delta t \cdot \boldsymbol{G} \end{pmatrix}$ that are from the concentration variables $\boldsymbol{U}^{t-1}$ and $\boldsymbol{V}^{t-1}$ at the previous time step $\mathrm{t} - 1$.

As shown in Fig. 4, we simulated and compared the propagation and conduction of electrical waves between a healthy heart (see Fig. 4a-f) and a heart with arrhythmia (see Fig. 4g-l). It may be noted that the healthy heart yields regular

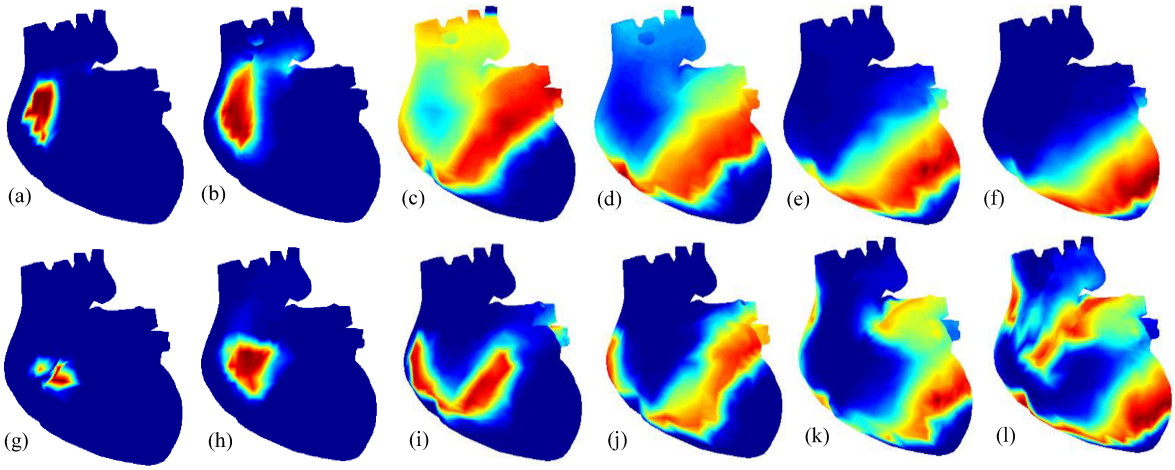


Fig. 4. Spatiotemporal dynamics of electrical conduction at different time indices on the 3-D heart that is healthy (a)-(f), or cardiac arrhythmia (g)-(l).

and periodic electrical impulses. In the healthy heart, electrical activity is near-periodically paced by the sinoatrial node in the right atrium in each cardiac cycle (see Fig. 4a). Cardiac electric activity propagates throughout the whole heart (see Fig. 4b-e) and eventually vanishes (see Fig. 4f), then the next cycle starts.

However, electrical excitation does not begin from the sinoatrial node in the simulation of cardiac arrhythmia. Instead, cardiac cycle initiates from another site of the right atrium or muscle cells in the nearby pulmonary veins (see Fig. 4g). As such, the rapid and disorganized electrical impulses occur around atria (see Fig. 4g-l). As shown in Fig. 4, electrical conduction is different between the healthy heart and the arrhythmia one. The snapshots in Fig. 4g-l are taken at the same time indices as Fig. 4a-f. However, traveling patterns of spatiotemporal electrical activity are different. It may be noted that space-time patterns in the arrhythmia heart are more disorganized than the healthy heart. In addition, electrical waves can rotate and self-circulate in the arrhythmia heart without the second stimulus. As such, this causes the heart to fibrillate (commonly known as atrial fibrillations) (see Fig. 4l). Next section will further details the pattern recognition of space-time electrical activities in the whole heart between healthy control and cardiac arrhythmia.

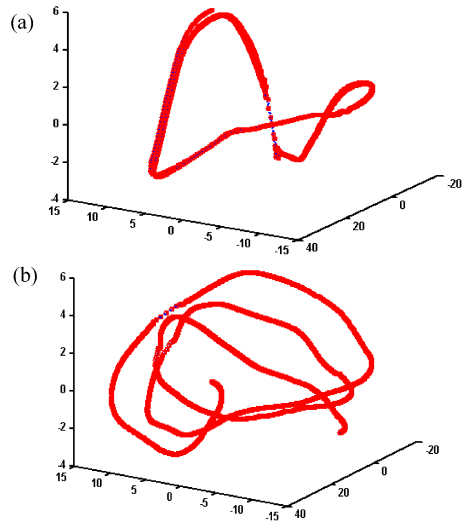


Fig. 5. Self-organizing topology of low-dimensional networks derived from spatiotemporal electrical conduction and propagation of (a) a healthy heart and (b) a heart with arrhythmia.

D. Spatiotemporal Pattern Recognition

Next, it is imperative to characterize and quantify such spatiotemporal patterns for better understanding of disease-altered cardiac electrical activity. Therefore, we proposed a hyper-distance matrix D_T to quantify the frame-to-frame dissimilarity between different time indices.

$$\mathrm{D}_T(l,m) = \left[\sum_{i=1}^{N} \left(\mathrm{Y}(\boldsymbol{s}_i, t_l) - \mathrm{Y}(\boldsymbol{s}_i, t_m)\right)^2\right]^{1/2} \qquad (4)$$

where $\mathrm{D}_T(l,m)$ is a hyper-distance denoting the spatial dissimilarity between two snapshots $\mathrm{Y}(\boldsymbol{s}_i, t_l)$, $\mathrm{Y}(\boldsymbol{s}_i, t_m)$ with time indexes t_l, t_m, respectively. Each frame, e.g., $\mathrm{Y}(\boldsymbol{s}, t_l)$, is treated as nodes in a network and D_T as the edge weight between nodes (i.e., adjacency matrix). Then, a self-organizing approach is used to derive the network topology by minimizing the energy [11]. Fig. 5 shows geometric structures of low-dimensional networks derived from spatiotemporal dynamics of the healthy heart (Fig. 4a-f) and a heart with arrhythmia (Fig. 4g-l).

As shown in Fig. 5a, network structure of the healthy heart shows a regular and periodic pattern. However, network topology of the arrhythmia heart is disorganized and irregular (see Fig. 5b). As such, the proposed approach provides a new means to visualize spatiotemporal dynamics in low-dimensional networks, thereby facilitating the characterization and quantification of dynamical properties of the underlying complex processes.

IV. CONCLUSIONS

In this present investigation, we developed the whole-heart simulation model to investigate the excitation and propagation of cardiac electrical activity between a healthy heart and a heart with arrhythmia. The proposed simulation methodology effectively addresses the complexity of heart geometry such as irregular node spacing, complex boundaries, and regionally dependent conductivities. Experimental results showed that spatiotemporal patterns in the arrhythmia heart are more disorganized than the healthy heart. In addition, spiral waves emerge and self-circulate in the arrhythmia heart without the second pacing. The proposed methodology outperforms traditional modeling approaches based on the Euclidean geometry, and provide effective tools to model and characterize space-time dynamics on the complex heart surface.

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