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Involving Action Potential Morphology on a New Cellular Automata Model of Cardiac Action Potential Propagation

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***Abstract*—**Computer modeling has played a unique role in understanding electrocardiography. Modeling and simulating cardiac action potential propagation is suitable for studying normal and pathological cardiac activation. This paper presents a 2-D Cellular Automata model for simulating action potential propagation in cardiac tissue. We demonstrate a novel algorithm in order to use minimum neighbors. This algorithm uses the summation of the excitability attributes of excited neighboring cells. We try to eliminate flat edges in the result patterns by inserting probability to the model. We also preserve the real shape of action potential by using linear curve fitting of one well known electrophysiological model.

***Keywords*—**Cellular Automata, Action Potential Propagation, cardiac tissue, Isotropic Pattern, accurate shape of cardiac action potential.

I. Introduction

COMPUTATIONAL systems biology is an emerging field that provides tools to model and analyze complex dynamic systems such as the heart [1] Computer models have long been used for the simulation of electrical activity in the heart[2]. The goal of modeling cardiac tissue is to provide a platform to study and understand the features underlying the spread of electric activity through the cardiac tissue [1].

The modeling of electrical propagation in cardiac tissue has been approached using a number of distinct methods, each with different degrees of realism, complexity and computational cost [3]. Cellular Automata (CA) models can be valuable tools to assist in studying the complex process of propagation in the heart [4]. The CA model uses a simple set of rules to represent the complex physiological processes that result in electrical impulse generation, conduction and propagation. The simplicity of the assumptions allows one to simulate wave propagation within a realistic whole heart model [4].

CAs is dynamical systems in which space and time are discrete. The cells are arranged in the form of a regular lattice structure and each must have a finite number of states. These states are updated synchronously according to a specified local rule of interaction. At each step, each cell computes its new state from that of its close neighbors. Thus, the laws of the system are local and uniform [5]

The neighborhood is described by specifying the set of cells that neighbor a given cell. For a square lattice, two types of neighborhood are typically used. The first one, the generalized "Von Neumann" neighborhood (the cells above, below, right and left from a local cell) and the second, the "Moore" neighborhood (the eight cells surrounding a central cell)[5]. In this paper, both "Moore" and "Von Neumann" are studied.

Excitable media exist popularly in nature [6]. The study of excitable media is important in understanding the behavior of complex systems such as mold growth, star formation, and cardiac tissue contraction [7]. The cells in CA model which constitute the cardiac muscle tissue have special properties which allow to consider the cardiac tissue to be the excitable medium, i.e., the medium which have the ability to propagate signals without damping [8]. The properties of nonlinear waves in excitable media have been a focus for studying [6]. As a kind of simple waves, ring waves and spiral waves [9]are studied in this paper (see fig. 1).

The model presented for action potential propagation in excitable media must be able to show these patterns. Ideally waves generated by computer models should be as circular as possible avoiding flat edges.

Whilst CA models are efficient they exert problems such as a lack of curvature in the spiral waves generated. Solutions to create this curvature have been proposed but many of them require complex operations which significantly decrease the performance of the CA models.

(a) (b)

Fig. 1 Wave propagation patterns including (a) ring pattern (b) spiral pattern

The aim of this study is to design a computer model of action potential propagation based on cellular automata theory

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that simulates complex electrophysiological phenomena and does not require a sophisticated computing infrastructure. Our model can produce isotropic patterns from a simple probabilistic rule by using minimum neighbors.

In this paper, we propose a new model for simulating action potential propagation in cardiac tissue using cellular automata concepts, together with accurate action potential morphology for the ventricular cells. We discuss the sensitivity analysis in our presented model. We also find the minimum neighborhood between "Moore" and "Von Neumann" neighborhoods for optimization of our model. We shall show qualitatively that our model reproduces cardiac action potential propagation with less computational time than previous models.

II. Cellular Automata models of propagation in Excitable media

An early CA model for atrial flutter consisting of states and transition rules was the Moe et al. [10]model. He considered five states for his model; consist of one state for resting, one state for being fully excited and three intermediate states for describing different refractory levels (fig. 2 (a)). Six neighbors were assumed for each cell with regard to hexagonal shape cells (fig. 2 (b)). A spiral wave generated by Moe model in cardiac tissue after 184 sec. is shown in fig. 3 below.

One problem of this model is its lack of isotropy means the model does not provide precise representation of the shape of cardiac spiral wave. Lacked spatial or temporal information about the model and the parameters that were used was the other disadvantage of this model [4]. Therefore, future models were presented more convenient model for excitable media relying on the principles used in this model.

Gerhardt [11]reproduced wave curvature using a CA by introducing two variable u and v for the excitation and the recovery value for each cell. The variable u can have a value of 0 or 1, while the variable v can have a value between 0 and v_{max} which is determined before by the model. This model presented a near isotropic pattern by using square neighborhood with a radius of 3 (containing 48 neighbor for a central cell), as depicted in fig. 4 (a). Although the model used large number of neighbors for a central cell, flat edges in result patterns were observed over large distances. By using this amount of neighbors, the advantage of applying CA was ignored and the speed of simulation in large scale reduced significantly.

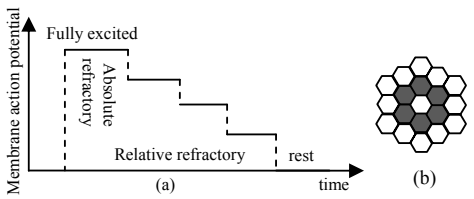


Fig. 2 (a) 6 neighbours of a central cell in Moe method. (b) schematic representation of the five states of activity

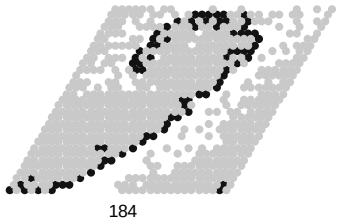
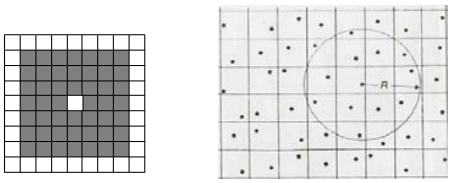


Fig. 3 Spiral wave produced by Moe model in arbitrary time (t=184) in which black colors shows fully excited cells is displayed. It also shows resting and refractory states by White and gray colored cells respectively.

A model of excitable Media to achieve the same goal of isotropy by creating some changes in Gerhardt idea was proposed by Markus [12]. He reduced two variables u and v into one variable S. This new variable can have the value between 0 and N+1. He showed the quiescent state and fully exciting state by S=0 and S=N+1, respectively. Any value of S between 1 and N was the representative of the recovery state of a cell. Each cell had a point placed at a random position inside of it. A cell's neighbors are those which have their random point within a circular radius of the local cell's own random point (fig. 4 (b)). By this method, Markus achieved Isotropy. The achieved spiral pattern was shown in fig. 5 (a). Because of this circular neighborhood, a square root operation was needed for each pair of 2 points and therefore the simulation was taken long time.

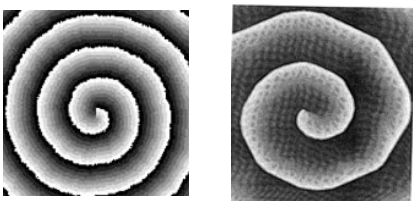
Another models which attempted isotropy was proposed by Weimar [13], [14] containing weighted mask for expressing the premiership of nearer and farther neighbors. These weights were proceeded to 19 or 20 for close neighbors. A square neighborhood with the radius of 7 was used in this model. In these models anisotropy of wave propagation is not completely eliminated, either. This kind of large-scale simulation is only feasible with parallel processing rather than with conventional serial computing [2]. And this is the only problem of these models.

These models recover curvature well; however anisotropy of wave propagation is not completely eliminated.



(a) (b)

Fig. 4 (a) Graphical representation of a cell with a radius of 3, (b) an example of Circular neighborhood of the Markus mode [12]



(a) (b)

Fig. 5 A spiral wave generated (a) by the Markus model (b) by Weimar model on a 686*960 cell domain [14]

III. METHOD

In this section, we describe in detail the cellular automata model used in this paper.

A. The geometry of ventricular action potential

In fig. 6, the ventricular action potential (AP) can be divided into 5 states. A cell's relaxed state is shown by state 4. In this case, quiescent cells are polarized with a transmembrane potential equal to −90 mV. If a cell has a large enough current applied, the cell begins an action potential starting with state 0. This sharp rise is called the upstroke. Once, this upstroke has reached its maximum value, the cell's voltage declines slightly during state 1. Next, the cell reaches state 2 which is a voltage plateau which makes up the majority of the action potential's length (Action Potential Duration[1]). Finally, during state 3 -which is called refractory state- the cell moves back towards the relaxed state of state 4.

For inserting the geometry of ventricular action potential to our model, the action potential is defined by means of a piece-wise linear function fitting as shown in fig. 7, where each linear segment is associated to a different state of AP.

In our case, we used a prototype action potential obtained from the model called Noble 2000. This model was found in COR[2] software [15]. We choose our appropriate action potential by fitting the states of AP according to fig. 8.

According to fig. 8, the gradient of fitted action potential in state 1 is 65.39. This value in state 2 is -0.42. And -2.49 in state 3 is discovered.

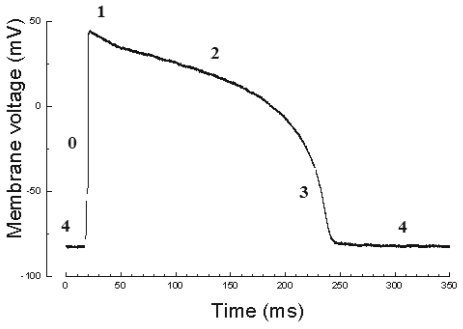


Fig. 6 An example of Ventricular Muscle Action Potential [16]

1 APD
2 Cellular Open Resource

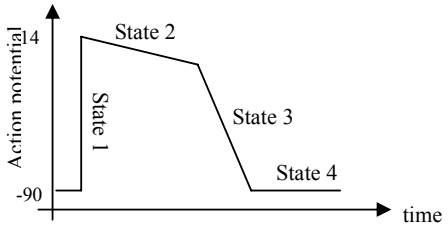


Fig. 7 An approximate action potential used in this research

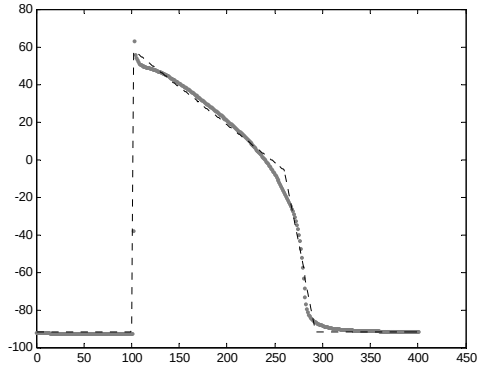


Fig. 8 Noble 2000 action potential model (black line) with its fitting curve (gray dash line) with a proportion of 1/2.8

B. Action potential propagation model

In this section, we describe the rule of CA model which reproduces isotropic patterns for cardiac action potential propagation.

The basic rules for our model are an extension of the 2-D cellular automaton model first described by Markus with fewer neighbors. In this paper, we use both "Moore" and "Von Neumann" neighborhoods and introduce S^t_{mn} like the one proposed by Markus. Where m, n and t denote the row number, column number, and the time step, respectively, when the situation will be studied.

Here S^t_{mn} is defined by the sum of values of the states u^t_{mn} at the time t over the neighboring cells. In fact, we use this method to eliminate flat edges in result patterns. The state variables u^t_{mn} and v^t_{mn} are introduced like Gerhard's ones. But in our model, each of the state variables can take values from 0 up to N-1. N is a parameter of the model which shows the number of discrete states between resting and fully excited in excitability (u^t_{mn}) and recovery (v^t_{mn}) variables.

All cells in the CA network are governed by the uniform rule. Schematic representation of the model is shown in fig. 9.

The cell first increases its excitability value by u_{up} at each time step (t) until u=N-1. Then; the refractory value rises by v_{up} at each time step until v=N-1. And u decreases by u_2, simultaneously. Next; u decreases by u_{Down} at each time step until u=0. Finally; v begins decreasing by v_{Down} at each time step until v=0. At this point; u=0 and v=0, and the cell is back at its relaxed state.

In other words; the transition rule is as follows:

1) If S^t_{mn} is greater than the threshold of excitation (Δ) and $v^t_{mn} = u^t_{mn} = 0$, the cell will be excited in next time step. In this case, $u^{t+1}_{mn} = u_{up}$ and $v^{t+1}_{mn} = 0$.

2) If $S^t_{mn} < \Delta$ and $v^t_{mn} = u^t_{mn} = 0$, the cell stays at its previous state. We should remind that the parameter Δ must be in the range of $0<\Delta<2N$ and $0<\Delta<N$ in the case of "Moore" and "Von Neumann" neighborhoods, respectively.

3) Once $v^t_{mn} + u^t_{mn} \neq 0$ and a cell has enough excited neighbors to meet its excitability variable, the cell moves through the transitions given in fig. 9.

If $u_2 = u_{Down}$; the atrial action potential (triangular shape) can be seen that can be used for studying the arrhythmias in atrial for future researches.

After discussing the model with constant parameter Δ, two different threshold Δ_1 and Δ_2 with probability of P will be used in fallowing section. We can achieve the isotropy to the model by using Δ_1 and Δ_2 added randomly over the cells as shown in fig. 10.

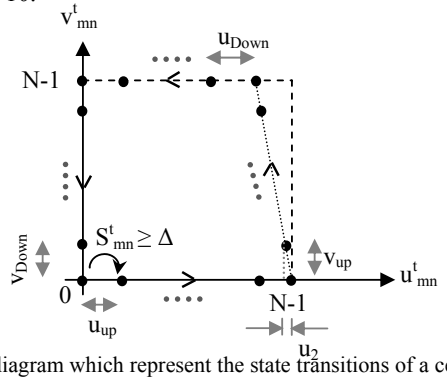


Fig. 9 The diagram which represent the state transitions of a cell

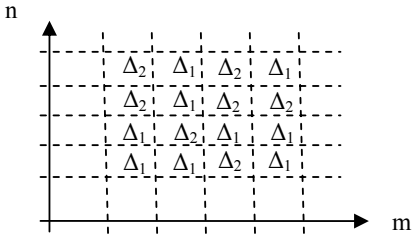


Fig. 10 two different thresholds (Δ_1 and Δ_2) are distributed randomly over the lattice

IV. RESULT

The simulation code was done using both dev-c++ the Matlab® computational software package (The MathWorks Inc.) The source code is available to interested parties as per request to the author.

The cellular automata model comprises a grid of $N_i \times N_j$ rectangular cells. Firstly, the effect of variables N, Δ, two different threshold Δ_1 and Δ_2 with probability of P and different neighborhoods are tested in network with 50×50 and 150×150 cells. We discuss the nature of the patterns and obtain some important results regarding the construction of an isotropic pattern. Secondly, the action potential geometry added to the model by means of a piece-wise linear function fitting of Noble 2000 action potential geometry as mentioned before. Then, action potential propagation is simulated by our CA model.

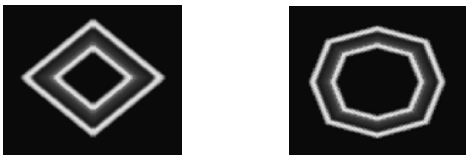
a) The effect of Δ on producing or eliminating flat edges in result patterns is studied in this section. Fig. 11 shows the action potential propagation simulated with the N value of 10, $u_{up} = 1$, $u_{Down} = 1$, $u_2 = 0.2$, $\Delta=2$ and $\Delta=3$. It can be observed that the threshold value of 3 gets octagonal pattern. And a Quadrilateral pattern is obtained for $\Delta=2$ and a dodecagonal pattern for $\Delta=6$. As a result, by greater Δ, the obtained pattern is more isotropic. It has less flat edges and it is more similar to ideal ring pattern shown in fig. 1 (a).

b) The effect of N on result patterns is depicted in fig. 12. It is obvious that the result do not impress by various values of N. By greater N, the thickness of pattern is increased.

According to figures 11 and 12, we can control the shape and propagation speed of the generated patterns by choosing an appropriate value of the threshold.

c) The effect of different neighborhoods on producing or eliminating flat edges in result patterns is studied in this section. In fig. 13 and fig. 14, the comparison of two different neighborhoods used in this paper is mentioned. It can be seen that using "Moore" neighborhood has appropriate result in generating isotropy. In fact, eliminating flat edges by reducing the neighbors from "Moore" up to "Von Neumann" proved less successful. So we will continue to use a "Moore" neighborhood for the remainder of our work.

d) Action potential propagation in a network of 10000 cells with $\Delta=3$ is shown in fig. 15 (a). However, using two different threshold values Δ_1 and Δ_2 is depicted in Fig. 15 (b) for comparison. Using these two distinct threshold value inserted randomly in the lattice, can generate isotropic patterns as shown in fig. 15 (b). As a result, using this method has appropriate effect on eliminating flat edges.



(a) (b)

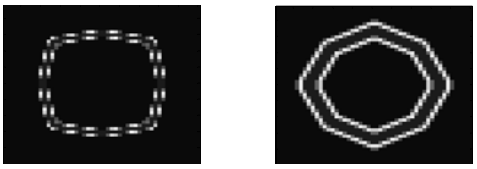
Fig. 11 ring pattern obtained by above method with N=10, $u_{up} = u_{Down} = 1$, $u_2 = 0.2$ and (a) $\Delta=2$ (b) $\Delta=3$. Part b in this figure is more similar to fig. 1 (a) which is shown ideal ring pattern.

(a) (b)

Fig. 12 effect of N on presented model at a network of 10000 cells with $\Delta=3$ and (a) N=7 (b) N=10

(a) (b)

Fig. 13 spiral wave generated by using (a) Moore neighborhood (b) Von Neumann neighborhood.



(a) (b)

Fig. 14 ring pattern obtained by using (a) Von Neumann neighborhood (b) Moore neighborhood.

(a) (b)

Fig. 15 a network of 22500 cells with N=10 and (a) Δ=3 (b) Δ_1=3 and Δ_2=7

e) In this section, the geometry of action potential is inserted to the model as described before. We show propagation of AP on a 2-D square lattice with the above simple rule, using "Moore" neighborhood as a minimum neighborhood described before.

Normal ventricular action potential propagation is simulated in a 2-D cardiac tissue by using Noble 2000 AP geometry, as shown in fig. 16. The membrane potential is represented depolarized and hyperpolarized tissue by white and black colors, respectively.

Abnormal action potential in 2-D cardiac tissue based on Noble 2000 geometry is shown in fig. 17. As it can be seen, the spiral wave is more isotropic and is similar to ideal one shown in fig. 1 (b). Meanwhile, the shape of action potential in our proposed model is more compatible with real APs.

It is obvious that this model is faster than Markus model as it needs no complex operations such as square root calculations. The Markus model used circular neighborhoods but the calculation of distances using square root calculations proved extremely slow. However, in our model the transition rule depend on the sum of the excitability attributes of excited neighboring cells.

V. CONCLUSION

In this paper we discussed new computational aspects of modeling excitable media using cellular automata. Then, we developed the model of excitable media in order to simulate cardiac electrical activity. In this paper, a new cellular automata model for action potential propagation was presented with fewer neighbors compared to previous studies.

The effect of model parameters (Δ and N) on the isotropy and speed of run time was survived in this research. By inserting probability in threshold value of our CA lattice, we avoided flat edges in result patterns. We also find Moore neighborhood as the minimum neighborhood of the presented model.

By means of a piece-wise linear function fitting Noble 2000 action potential shape, an accurate AP was achieved. By applying this model to a square network, the AP propagation was simulated and an isotropic spiral wave was obtained.

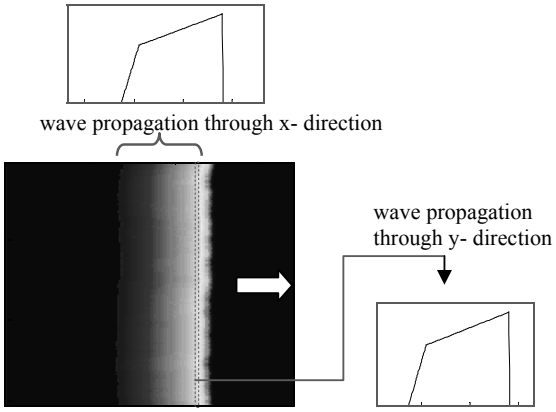


Fig. 16 Linear wavefront propagation in 2-D cardiac tissue.

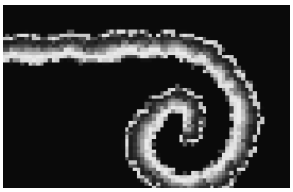


Fig. 17 Spiral wave generated by presented model with Noble 2000 AP geometry.

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