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A CELLULAR AUTOMATA MODEL FOR DYNAMICS AND CONTROL OF CARDIAC ARRHYTHMIAS

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ABSTRACT

As a leading cause of death in 325,000 adults per year in the United States, a significant proportion of sudden cardiac arrest (SCA) result from arrhythmias. To better understand the onset of arrhythmias and its potential treatment with more rapid and effective control approaches, a two-dimensional 50×50 cellular automata (CA) model is used in this study to illustrate the propagation of electrical waves across its tissue, and a constant diastolic interval (DI) control mechanism is adopted to help stabilize and prevent cardiac arrhythmias. Simulations of various scenarios including normal conduction and spiral waves in the presence of scar, normal conduction and alternans under control conditions are shown. The results validate that the CA model and constant DI control method are very efficient and effective in the study of dynamics and control of cardiac arrhythmias.

Keywords: CA model; arrhythmias; constant DI control; spiral wave; alternans

1. INTRODUCTION

Sudden cardiac arrest (SCA) and other cardiac arrhythmias are vital topics of interest among scientists because a better understanding of them could help to significantly reduce SCA related death rates in the United States. The prognosis for out-of-hospital sudden cardiac arrest is 7%. Specifically, there is limited understanding in predicting the onset of an arrhythmia. If we can identify arrythmias before they occur, then cardiopulmonary resuscitation and other treatments can be expedited to improve health outcomes [1].

A heartbeat is essentially an electrical signal originating from the sinus node, which is a group of pacemaker cells, and propagates through the heart's chambers from the right atrium to the atrioventricular node, the His-Purkinje system, and then the ventricles. As the electrical signal passing through each chamber, the heart contracts and pumps blood to flow throughout the rest of the body [2].

Cardiac arrhythmias are essentially disruptions in the heart's electrical conduction and manifested as irregular heartbeats. Although most arrhythmias are not life-threatening, some of them predispose people to stroke, heart failure, and even sudden death [3].

In this paper, we will focus on two cardiac disturbances, spiral wave and alternans, which is considered to be a precursor to arrhythmias. Spiral wave is a reentrant arrhythmia where tissue is excited repetitively by waves circulating in the tissue [4] either around a scar, or via solely dynamical mechanisms. Alternans is an unstable rhythm of the heart, which manifests a long-short action potential duration (APD) pattern thus allowing for the APD to alternates with every heartbeat. Alternans is also regarded as a harbinger of cardiac fibrillation such as atrial and ventricular fibrillation. Therefore, if we identify and remedy alternans in time, then we can prevent fibrillation before it happens.

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As a common reentrant arrhythmia, atrial fibrillation (AF) is characterized by an extremely rapid atrial heart rate of 350-600 bpm, and the contraction ability of atria is compromised by continuously circulating waves in the atria during fibrillation. Although AF is not immediately life-threatening because the contraction of atria is not necessary for its main function to fill chambers in the heart, it will increase the risk of heart failure, dementia, and stroke. On the other hand, ventricular fibrillation (VF) is a life-threatening condition in which many small waves circulate through the ventricles, thus preventing synchronized contraction of the ventricles and their ability to pump the blood. Defibrillation is the only way to remedy this, and it must be done within minutes of onset [5] [6].

To study the dynamics of cardiac electrical activity, regular physiological models of cardiac tissue were widely used in past [7]. However, full physiological models are computationally taxing. Aiming at this problem, cellular automata (CA) models are favored to illustrate heartbeat behaviors.

Capable of universal computation, CA models have successful applications in physics, biology, engineering, and so on. CA models utilize simplified approaches to compute complex phenomena with fewer involved calculations, thus they are preferred over full physiological models for fast computation and simulation. In addition to being efficacious, CA models also provide visual descriptions of the states of each cell, allow for analysis of wave propagation in real-time [8] [9].

Based on a two-dimensional CA model, this paper studies the electrophysiological characteristics of heartbeat waves in different scenarios, including normal conduction, normal conduction in the presence of scar, spiral wave, and alternans. The rule and structure of the implemented CA model are explained in-depth. Considering that feedback control is only effective for small tissue rather than large tissue, a constant diastolic interval (DI) control approach is implemented to stabilize the heart's electrical patterns, and its effect is verified with electrocardiogram (ECG) analysis.

2. TWO-DIMENSIONAL CA MODEL OF CARDIAC CONDUCTION

2.1 Rule of Wave Propagation in CA Model

A two-dimensional CA model is a grid of cells where each cell has various states. Each cell changes state based on the states of their neighbors and predefined rules governing the CA model. CA models are effective for modeling complex systems consisting of simple units and are much faster computationally than partial differential equation models. In the following section, we present how a CA model can be used to simulate heart wave propagation.

To simulate the various heart scenarios, a 50×50 CA model is constructed in MATLAB. Each cell in the model represents an individual heart cell. The action potential, or voltage, of each cell can be characterized by four unique states: resting, exciting, absolute refractory, and relative refractory. Thresholds are set for the exciting phase (0.9 V in this study) and the refractory phase (0.1 V in this study). When a cell is stimulated, its voltage becomes 1.0 V and will then gradually decrease. Before the cell's action potential drops below 0.9 V, it is in the excitation phase. During this period, the cell is able to excite its neighboring cells. When the cell's action potential is between 0.9 V and 0.1 V, it is in the absolute refractory phase. The cell loses its ability to excite its neighbors, and the cell itself cannot be stimulated. When the action potential drops below 0.1 V, the cell enters the relative refractory phase, where the cell regains excitability. Once the action potential reaches 0 V, it returns to the resting phase, and the cycle continues [10].

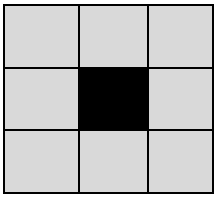


FIGURE 1: NEIGHBORING CELLS OF A SINGLE CELL IN CA MODEL

In the CA model, a 3x3 square in the bottom left of the cardiac tissue acts as the pacemaker cells in the heart and excites according to some rules, for instant, at a fixed basic cycle length (BCL). All the cells are in the resting phase at the beginning, and the pacemaker cells stimulate when the simulation starts. After the initial stimulation, at each time step, every cell is monitored for its potential to undergo excitation. If the action potential of the cell is less than or equal to the refractory threshold, then each neighboring cell of the cell being evaluated is checked to see if it is excited. The eight gray neighbors of a black cell are illustrated in Figure 1 [11]. If at least three neighboring cells have an action potential that is greater than the excitation threshold, then the cell being evaluated becomes excited. If the action potential of the cell being evaluated is greater than the refractory threshold, then duration, i.e., the time elapsed since last excitation increases, and the voltage progresses based on the APD and the current duration.

If scar cells exist in the tissue, the voltage of those cells are set as 0 V at every time step. The entire process repeats for the next time step. In this study, we use 1 ms represent 1 time step in simulation. When the global simulation time reaches the next stimulation time, the pacemaker cells become stimulated again, and the pattern continues.

2.2 Voltage Wave Form Function

As mentioned above, the voltage progresses based on the APD and the current duration. To calculate the voltage of a cell after stimulation, we define a voltage function $V(APD,t)$ as

$$V(APD,t) = \frac{e^{-t/T(APD)}}{\mathrm{c}+\, e^{-t/T(A)}} \quad (1)$$

$$T(APD) = \frac{APD}{\ln(0.9)-\ln(0.1*c)} \quad (2)$$

Here, t is the duration, c is a constant small enough to ensure the action potential is very close to 1.0 V at t=0. In this study, c

is set to be 0.01. For each value of t thereafter, the action potential decreases. Then, the action potential becomes 0.1 V at t=APD, and 0 V as t goes to infinite. When APD is 40, the voltage curve is shown in Fig 2.

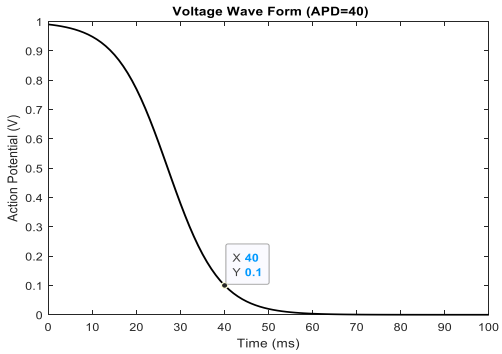


FIGURE 2: VOLTAGE WAVE FORM WHEN APD IS 40

2.3 Restitution Function

In calculation of the action potential of a cell during one stimulation cycle, the t is easy to obtain as it is just the time elapsed since last excitation, and to get the APD, we need the restitution function. The restitution function introduces an approach to calculate the APD of one stimulation cycle based on the DI of the last stimulation cycle [12]. In our work, the relationship can be expressed as

$$APD_{n+1} = 60 - 50e^{-DI_n/20} \quad (3)$$

The initial DI for every cell is 100, which signifies that they are fully rested. In the subsequent cycles, when a cell depolarizes, its DI in the previous heartbeat is determined by taking the time elapsed since the cell's last stimulation and subtracting the calculated last APD. Then, the DI of the previous heartbeat determines the APD in the new cycle according to the restitution function. When a new cycle begins, the action potential of the cell becomes 1.0 V, and the duration is reset upon stimulation.

From the restitution curve shown in Fig 3, we can see that, the longer the DI_n is, the longer the APD is for the next cycle, but it will never increase over 60 ms. Conversely, a shorter DI results in a shorter APD at the next beat.

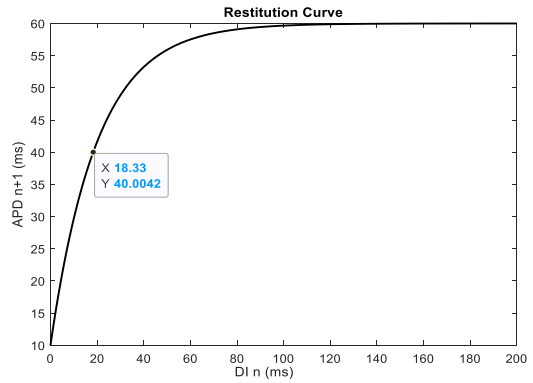


FIGURE 3: RESTITUTION CURVE

In addition, if $d(APD_{n+1})/d(D_n) > 1$, then the cardiac dynamics are unstable and must be remedied. So, in this study, the cardiac conduction will be unstable when DI is less than 18.3300, and the corresponding APD and BCL are 40.0042 and 58.3342, respectively, as pointed out in Figure 3. Later when we refer to different cardiac scenarios, normal conduction is stable, and alternans is unstable.

3 SIMULATION RESULTS

With the two-dimensional 50×50 CA model, four scenarios are simulated in this study. The simulation results are shown and explained as follows.

3.1 Normal Conduction

In this simulation, to illustrate a normal propagation through the cardiac tissue, we initialize the BCL of pacemaker cells as 75 ms, thus the pacemaker cells stimulate at every 75 ms. The DI of pacemaker cells is set as 25 ms at the beginning, and after some oscillation, it will stay around 27.59 ms.

The wave propagation under normal conduction is shown in Figure 4. The wave originates from the stimulus, then travels to the upper right throughout the tissue.

3.2 Normal Conduction in the Presence of Scar

In this scenario, all the settings are the same as normal conduction, but there is a scarred tissue.

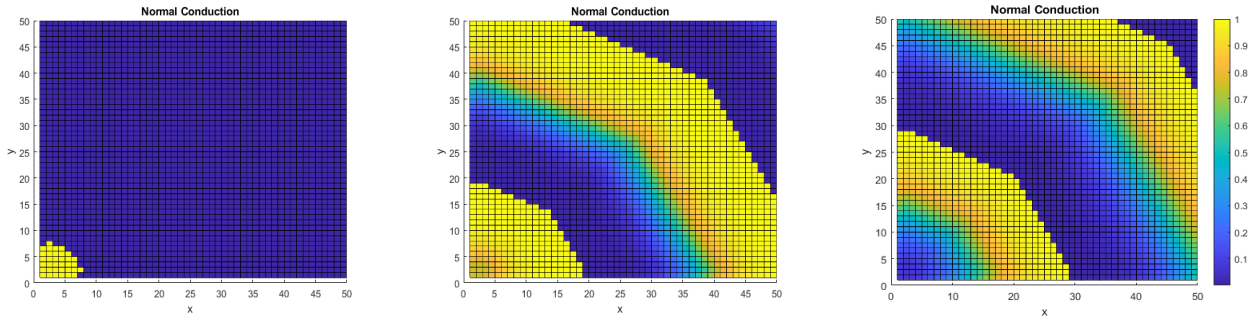


FIGURE 4: SNAPSHOTS OF THE CA MODEL FOR NORMAL CONDUCTION

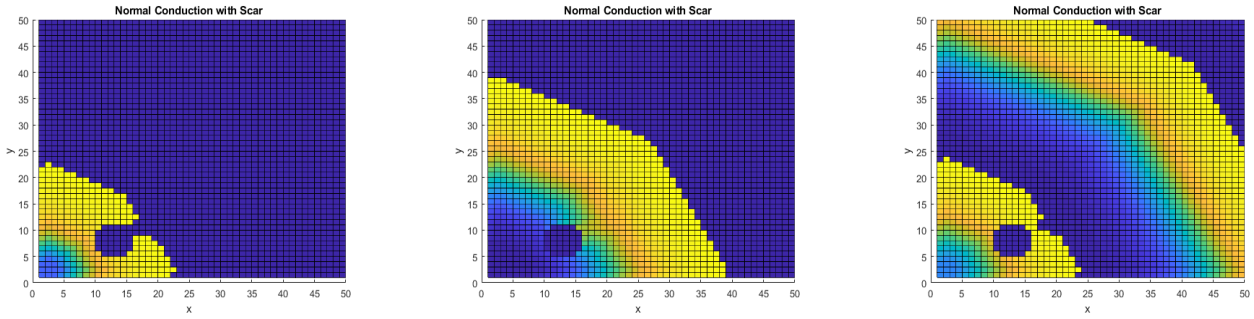


FIGURE 5: SNAPSHOTS OF THE CA MODEL FOR NORMAL CONDUCTION IN THE PRESENCE OF SCAR TISSUE

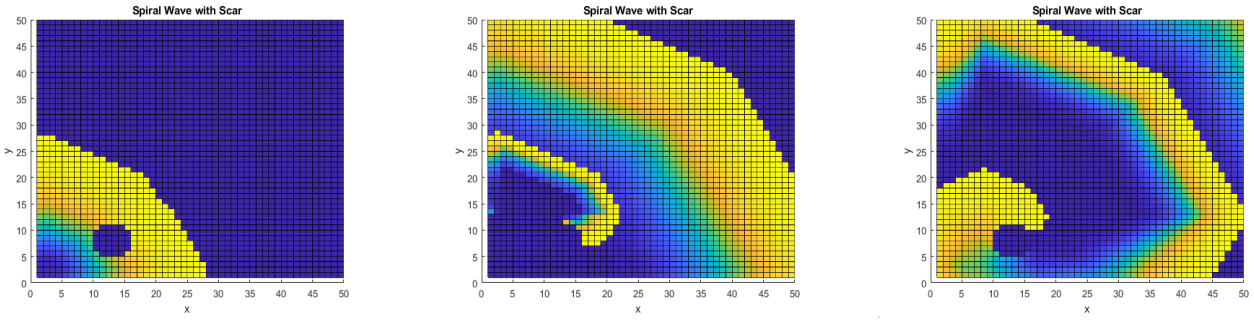


FIGURE 6: SNAPSHOTS OF THE CA MODEL FOR A SPIRAL WAVE AROUND SCARRED TISSUE

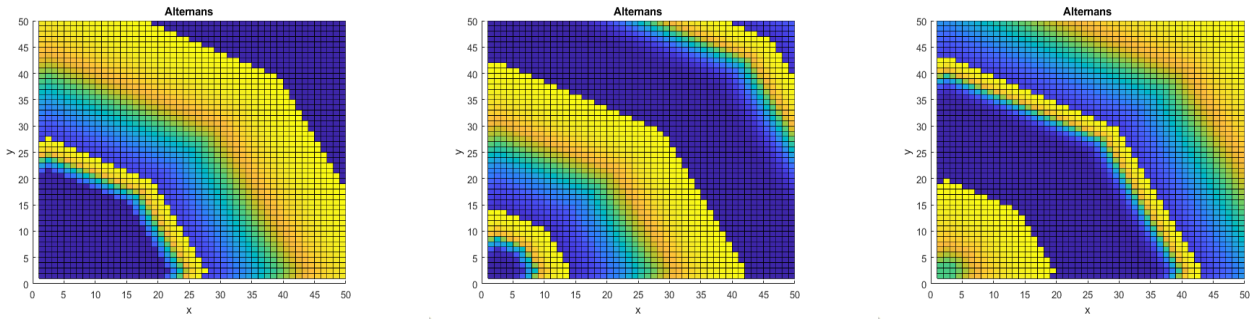


FIGURE 7: SNAPSHOTS OF THE CA MODEL FOR ALTERNANS

As shown in Figure 5, although the scar can never be stimulated, the wave can still propagate to the upper right throughout the tissue. The waves work around the inactive tissue, making some heart cells around the scar spend more time in the refractory period. This causes the subsequent waves to work around those cells in addition to the scar cells, leading to micro irregular wave activity in the tissue.

3.3 Spiral Wave

Then, change the first BCL to be 50 ms, and the initial DI of pacemaker cells to be 20 ms. The simulation result is shown in Figure 6. The wave begins to spiral around the scar, and it would propagate continuously even without the help of stimulation from pacemaker cells.

3.4 Alternans

In this case, we set the BCL of pacemaker cells as 54 ms throughout the simulation and continue with normal conduction simulations otherwise. Because the BCL is less than 58.3342 ms, the cardiac conduction becomes unstable.

As shown in Figure 7. The heart's rhythm alternates between long waves and short waves. As a typical precursor to ventricular fibrillation, alternans must be remedied immediately to help prevent fibrillation.

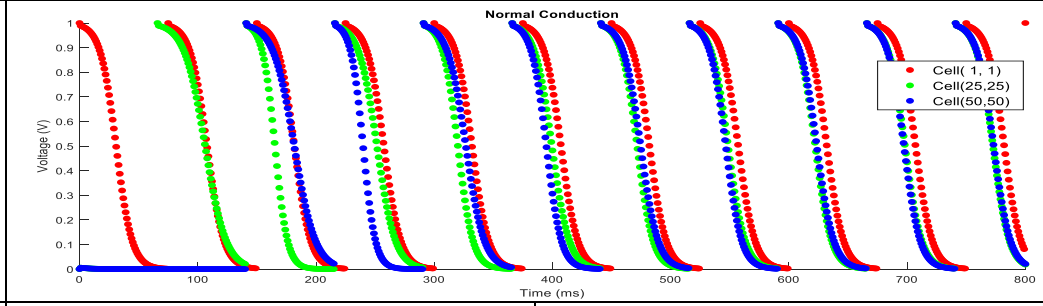
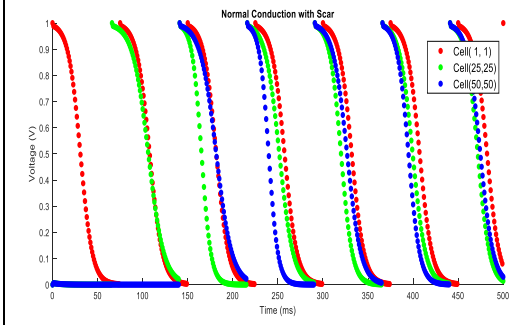
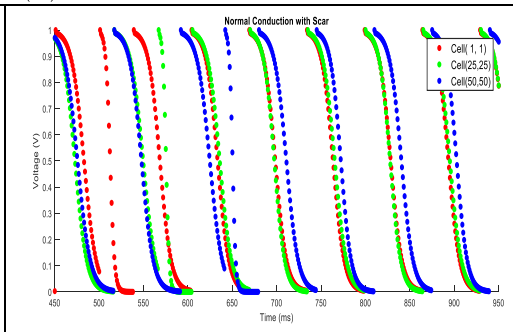
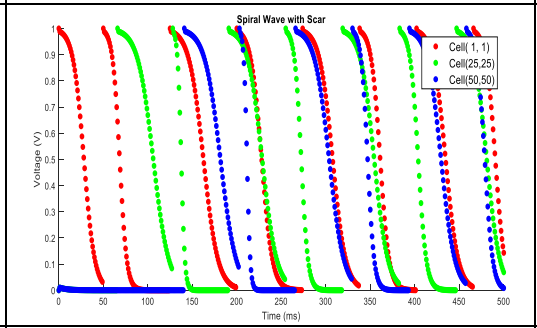
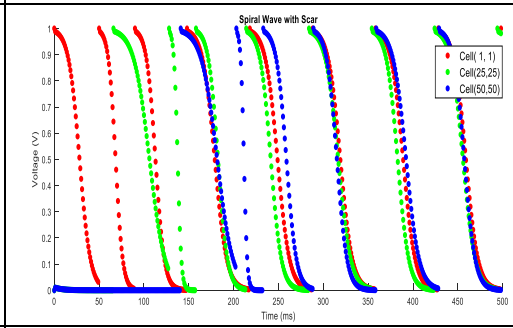
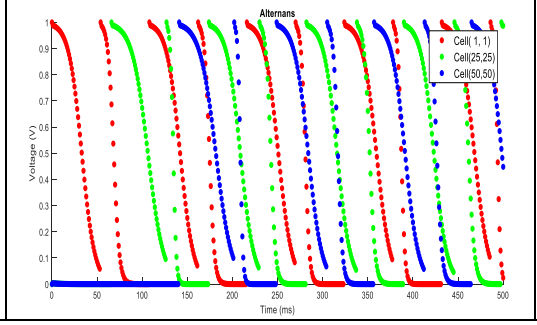
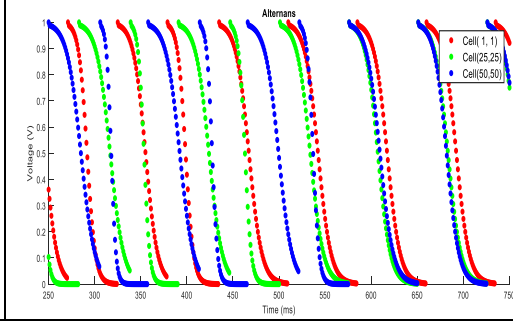
4 SIMULATION RESULTS WITH CONSTANT DI CONTROL

To stabilize abnormal heart rhythms, we will implement a constant DI control mechanism.

4.1 Constant DI Control Method

When the constant DI control method is applied, the pacemaker cells are stimulated based on a constant DI instead of a constant BCL. BCL is the sum of APD and DI, and the APD of the current heartbeat is determined by the last DI.

Table 1: SINGLE CELL BEHAVIOR COMPARISON

	Without control	With constant DI control
Normal conduction		
Normal conduction in the presence of scar		
Spiral wave		
Alternans		

So, when the stimulations of pacemaker cells are controlled by a constant DI, we can get a desired constant BCL along with a stable wave propagation, thus some abnormal wave conductions can be remedied [13] [14].

4.2 ECG

In addition to the snapshots of the CA model, we will examine the heart's electrical activity through analysis of ECG.

ECG is a graphical representation illustrating the electrical activity of the heart at each beat. It measures the voltage difference between two points outside the heart tissue, using electrodes placed on the surface of the body [15]. The ECG of heart is calculated as follows

$$\mathrm{ECG} = \Phi_e(\mathrm{B}) - \Phi_e(\mathrm{A}) \tag{4}$$

$$\Phi_e(x', y') = \int (-\nabla \mathrm{V}) \cdot \left(\nabla \frac{1}{\mathrm{r}}\right) dx\, dy \tag{5}$$

$$r = [(x - x')^2 + (y - y')^2]^{1/2} \tag{6}$$

Where $\Phi_e(A)$ and $\Phi_e(B)$ are the transmembrane potentials at points A and B located outside the heart tissue. Points are not chosen inside the tissue because the denominator r will result in zero at some point. Specifically, A is the point (0,0), and B is

the point (51,51). We use (x', y') to represent point A or point B, and (x, y) to represent any point in the heart tissue. r is the distance between (x', y') and point (x, y). $\nabla\frac{1}{r}$ is the gradient of $\frac{1}{r}$. ∇V is the gradient of voltage and results in a vector of the slopes of the action potential at each heart cell. We use ECG to identify abnormalities in the heart's rhythm and use the constant DI control mechanisms to resolve them.

4.3 Simulation Results Comparison

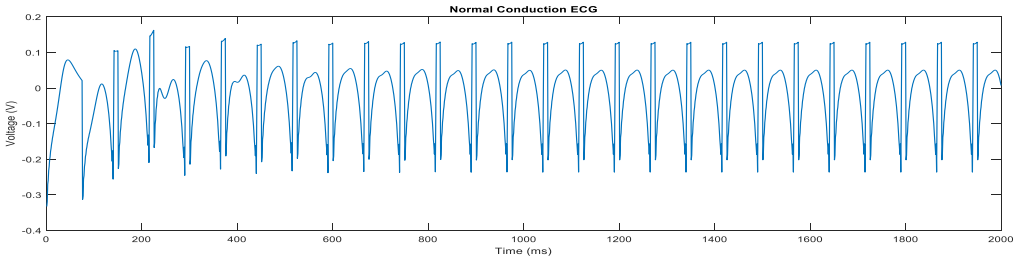
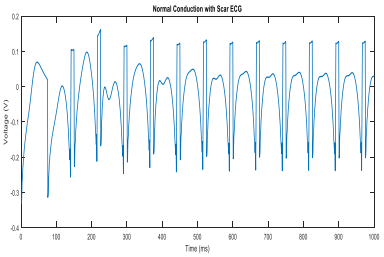
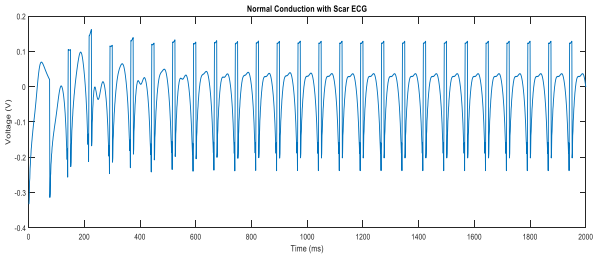
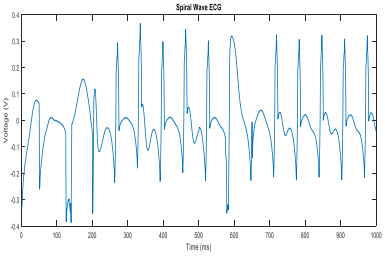
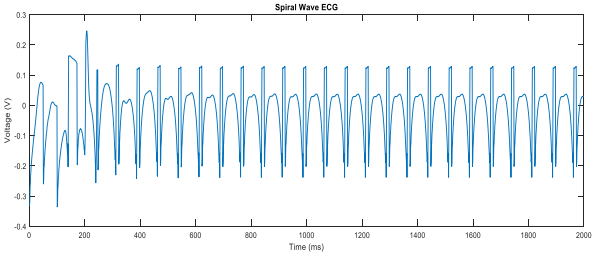
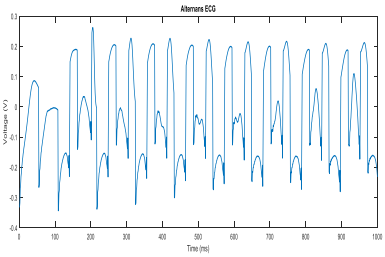
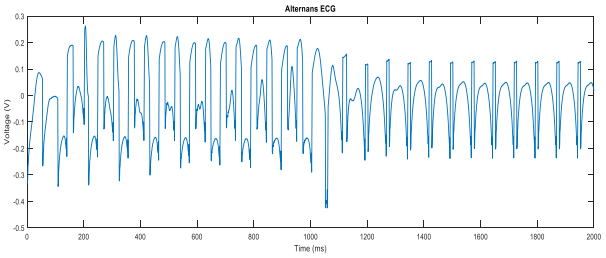
To verify the effectiveness of the constant DI control approach, the simulation results with and without constant DI control are compared in this section.

4.3.1 Single Cell Behavior Comparison

Before using the ECG, we describe how single cells behave in heart tissue in each scenario in Table 1. This is a quick way to observe abnormalities in the heart's rhythm.

In each single cell plot, the red, green, blue line represents the heart cell at location (1,1), (25,25), and (50,50) in the CA model, respectively. A constant DI is set 25 ms here for control. From Table 1, we conclude that: (1) In the normal conduction scenario, the wave becomes stable after a short oscillation. (2) In the normal conduction in the presence of scar scenario, the wave before and after the implementation of constant DI control at 500 ms are both stable, although they have different BCLs. (3) In spiral wave scenario, the wave pattern varies widely. It is very hard to eliminate spiral wave pattern after 125 ms, because the spiral wave becomes persistent after this time. (4) Implementing constant DI control at 100 ms prevents spiral wave and stabilizes the spiral wave after a short oscillation. (5) In the alternans scenario, the wave alternates between long and short APD. After implementing constant DI control at 400 ms, the wave becomes stable.

Table 2: ECG SIMULATION RESULTS COMPARISON

	Without control	With constant DI control
Normal conduction		
Normal conduction in the presence of scar		
Spiral wave		
Alternans		

4.3.2 ECG Simulation Results Comparison

The ECG results obtained from simulations with and without constant DI control are shown in Table 2. Here we implement a constant DI equals 28 ms to control the stimulation of pacemaker cells for all abnormal scenarios. In this simulation, constant DI control is applied at *100 ms* for spiral wave, and *1000 ms* for normal conduction in the presence of scar and alternans.

From Table 2, we can see that: (1) In the normal conduction scenario, the ECG produces a consistent wave pattern after oscillation. (2) In the normal conduction in the presence of scar scenario, although the ECG is very similar to that of normal conduction, there are waveform abnormalities. Also, constant DI control cannot eliminate waveform anomalies resulting from cardiac scars. (3) Constant DI control could prevent spiral wave formation. (4) Constant DI control is effective in eliminating alternans. (5) From the single cell results, the effectiveness of constant DI is not dependent on its specific value.

5 CONCLUSION

A CA model is established to illustrate the propagation of heart waves, and a constant DI control mechanism is adopted to help stabilize and prevent cardiac arrhythmias in this paper. Simulation experiments validate that:

(1) CA is an excellent model to illustrate the wave propagation and electrical activity in the heart with high efficiency. They can help medical professionals identify arrhythmias and treat them before they become life-threatening, thus lowering the mortality rate due to SCA.

(2) Cardiac disturbances including spiral wave and alternans can be resolved by controlling the heart's electrical rhythms using the constant DI control approach. However, constant DI control cannot eliminate the micro-abnormality caused by scar.

(3) This study can be extended further to 3-dimensional simulation models to fully illustrate wave propagation throughout the heart. Also, other scenarios such as wave break, ectopic, combinations of different disturbances and other control mechanisms such as constant RT method can be further explored in future studies.

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