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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 the United States, sudden cardiac arrest (SCA) which caused mainly by arrhythmias brings about 325,000 adult deaths per year. To better understand the onset of arrhythmias and treat arrhythmias with effective control approaches faster, a two-dimensional 50×50 cellular automata (CA) model is used in this study to illustrate the propagation of heart 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, normal conduction with scar, spiral wave with scar, and alternans 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 reduce SCA caused death rate in the United States significantly. Specifically, it is still unknown how to predict the onset of an arrhythmia, and if we can identify arrythmias before they happen, then more life can be saved with timely treatment [1].

To better understand dynamics of cardiac arrhythmias, we should take a look at the basic structure and behavior of heart first. The heart is made up of four chambers: the right atrium, the left atrium, the right ventricle, and the left ventricle. A heartbeat is essentially an electrical signal originates 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 to 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. Variations of heart rates are categorized by tachycardias and bradycardia. Bradycardia is the condition of having a heart rate less than 60 beats per minute. This is usually due to low sinus rhythm, causing a secondary, slower pacemaker to take over. Tachycardia is the condition in which one's heart rate is greater than 100 beats per minute and can typically lead to reduced blood flow to the body's organs and fatigue. In serious cases where blood flow is very low, tachycardia can lead to death [3].

In this paper, we will focus on two cardiac arrhythmias, spiral wave with scar and alternans. Spiral wave with scar is a reentrant arrhythmia where tissue is excited repetitively by waves circulating around a scar in the tissue [4]. Alternans is an unstable non-reentrant arrhythmia which manifests a long-short action potential duration (APD) pattern, which means that the APD alternates with every heartbeat. Alternans is also regarded as a harbinger of cardiac fibrillation such as atrial fibrillation and ventricular fibrillation. As a common reentrant arrhythmia, atrial fibrillation 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 atrial fibrillation 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 is life-threatening right away. Ventricular fibrillation is like atrial fibrillation, except many small waves circulate through the ventricles. This causes the ventricles unable to contract. Ventricular fibrillation is serious because blood cannot be pumped properly, so blood pressure drops to zero. Defibrillation is the only way to remedy this, and it must be done within minutes of onset [5] [6].

So, if we identify and remedy alternans in time, then we can prevent fibrillation before it happens. Thus, the study of spiral wave with scar and alternans is of great meaning for cardiac arrhythmias research.

To study the dynamics of cardiac behaviors, two-variable partial differential equation models (PDEMs) of cardiac tissue with a fast excitatory current and a slow repolarizing current were widely used in many researches. However, PDEMs are computationally taxing, and it is difficult to adjust all the characteristic wave properties of the heart tissue. Aiming at this problem, cellular automata (CA) models are favored to illustrate heartbeat behaviors [7].

As models capable of universal computation, CA models have successful applications in physics, biology, engineering, image processing, and so on. CA models utilize a simple way to compute complex phenomenon with much less calculations than PDEMs, thus they are preferred when fast computation or fast simulation is required. In addition to the efficiency advantages, CA models also provide visual descriptions of the states of each cell, making analysis of wave propagation easier [8] [9].

Based on a two-dimensional CA model, this paper studies the electrophysiologic characteristics of heartbeat waves in different scenarios, including normal conduction, normal conduction with 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 systems of PDEMs. In the following part, 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 and the refractory phase. In this study, we use an excitation threshold of 0.9 V and a refractory threshold of 0.1 V. 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 exciting 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 has some excitability again. Once the action potential reaches 0 V, it returns to the resting phase, and the cycle continues [10].

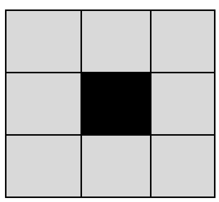


FIGURE 1: NEIGHBORING CELLS IN CA MODEL

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 a fixed basic cycle length (BCL) or other rules. All the cells are in the resting phase at the beginning, and the pacemaker cells stimulate when the simulation starts. Then, after the initial stimulation, time progresses. At each timestep, every heart cell is checked to see whether they will become excited. 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 neighbors of a cell are illustrated in Figure 1. The black cell in the middle is the cell being evaluated to see if it becomes excited. The eight gray cells surrounding the black cell are checked to see if they are excited [11]. A bordering cell has five neighbors, and a corner cell only has three. 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 timestep. 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 signifies the voltage of a cell after it has been stimulated, we define a voltage form function as

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

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

Where t is the duration, and $V(APD,t)$ is the action potential based on the *APD* and *t*. 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.

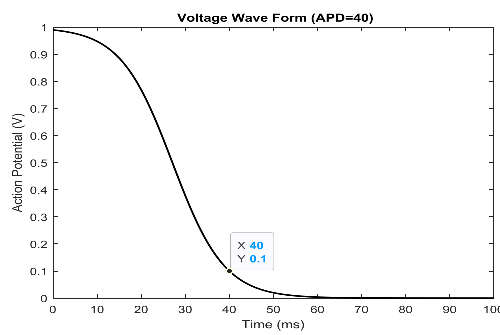


FIGURE 2: VOLTAGE WAVE FORM WHEN APD IS 40

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 last stimulation cycle [12]. The relationship defined in this research 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 is 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.

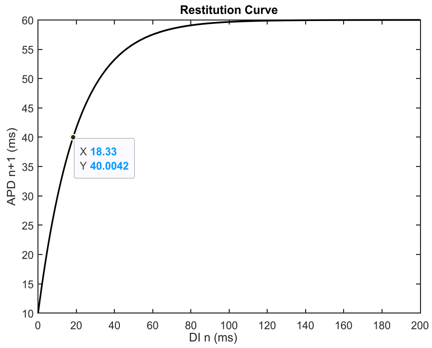


FIGURE 3: RESTITUTION CURVE

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. Conversely, a shorter DI results in a shorter APD at the next beat.

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.

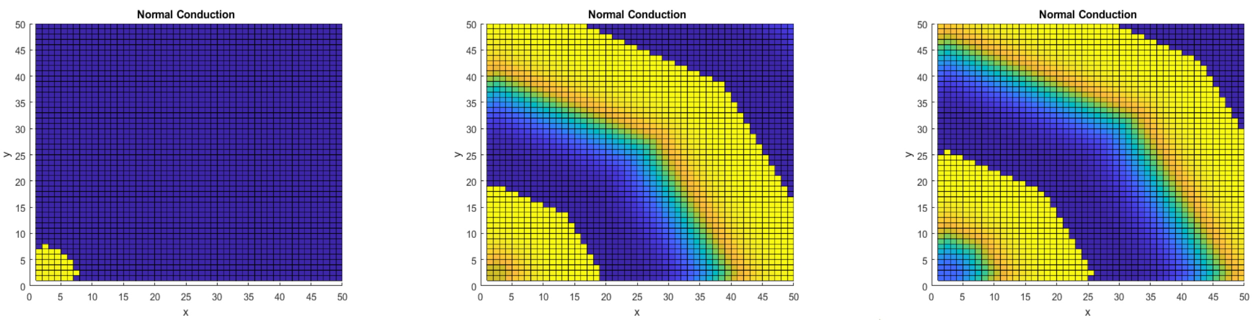


FIGURE 4: SNAPSHOTS OF THE CA MODEL FOR NORMAL CONDUCTION

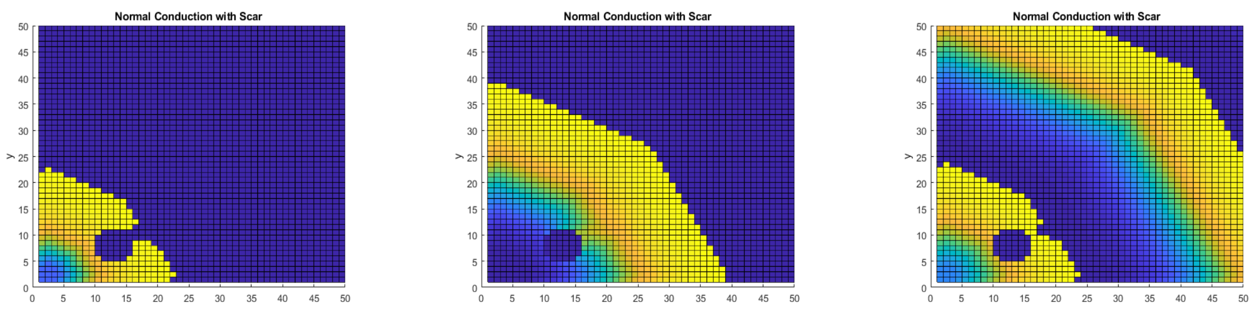


FIGURE 5: SNAPSHOTS OF THE CA MODEL FOR NORMAL CONDUCTION WITH SCAR TISSUE

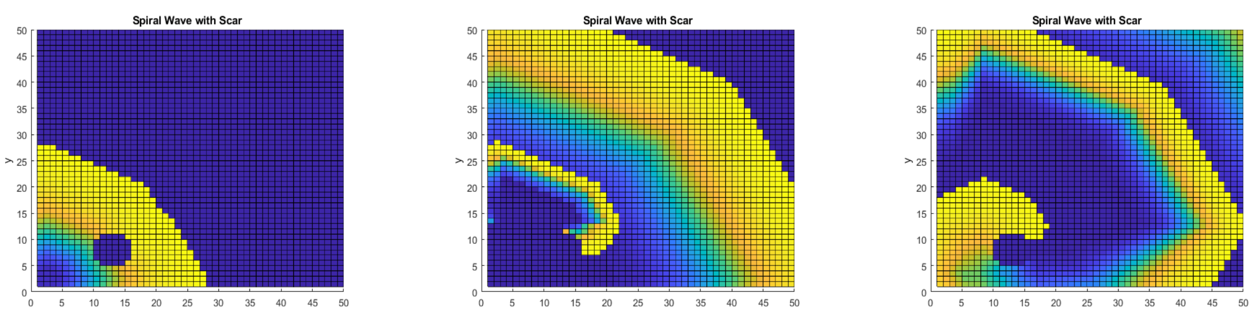


FIGURE 6: SNAPSHOTS OF THE CA MODEL FOR A SPIRAL WAVE AROUND SCARRED TISSUE

3.1 Normal Conduction

In this simulation, to illustrate how a heart typically behaves, first we initialize the BCL of pacemaker cells as 75, thus the pacemaker cells stimulate every 75 timestep. The DI of pacemaker cells is set as 25 at the beginning, and after some oscillation, it will stay around 27.59.

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

3.2 Normal Conduction with Scar

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

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, and the initial DI of pacemaker cells to be 20. 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 change the BCL of pacemaker cells as 54 all the time and remain other settings the same as normal conduction simulation. Because the BCL is less than 58.3342, 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.

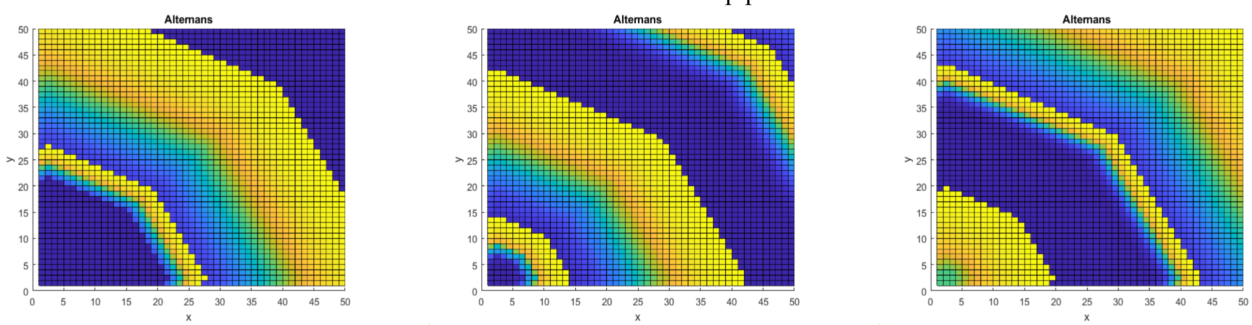


FIGURE 7: SNAPSHOTS OF THE CA MODEL FOR ALTERNANS

4 SIMULATION RESULTS WITH CONSTANT DI CONTROL

To stabilize heart rhythms that are not normal, we will implement a constant DI control mechanism to remedy these abnormal wave conductions.

4.1 Constant DI Control Method

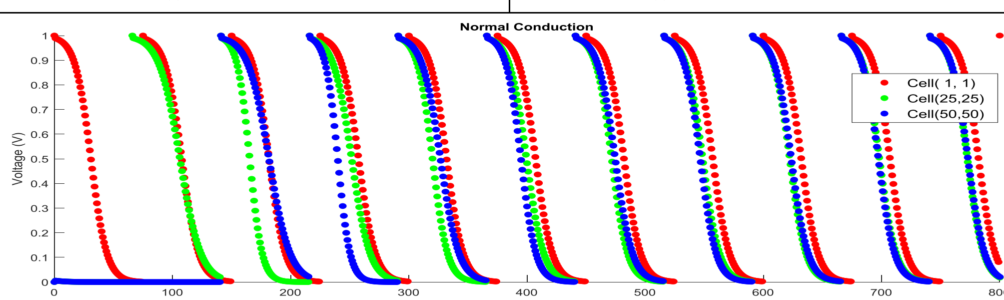
Instead of stimulating the heart based on a predefined constant BCL, the pacemaker heart is stimulated based on a constant DI when the constant DI control method is applied.

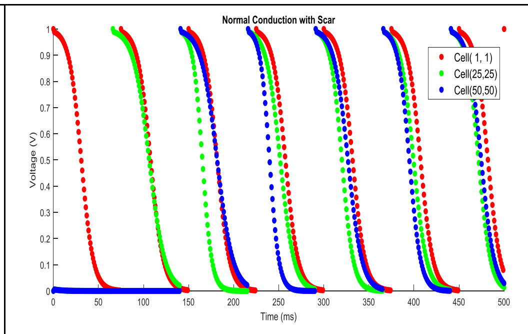
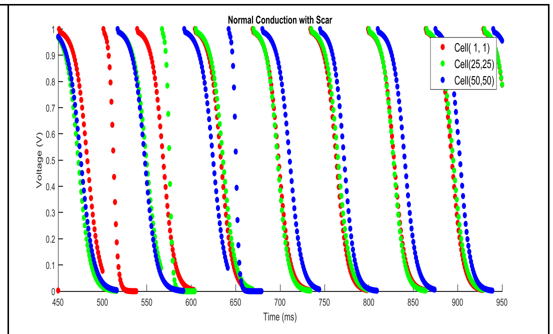
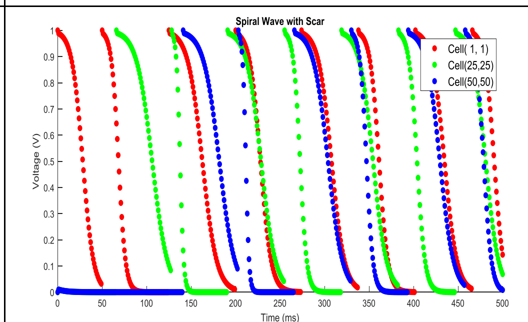
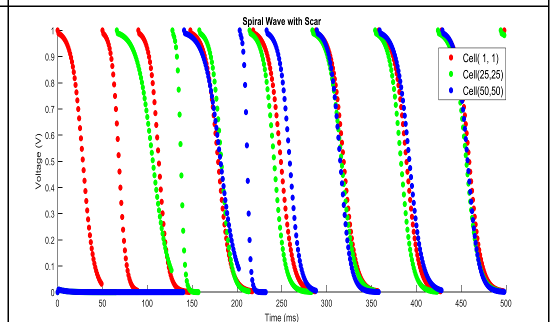
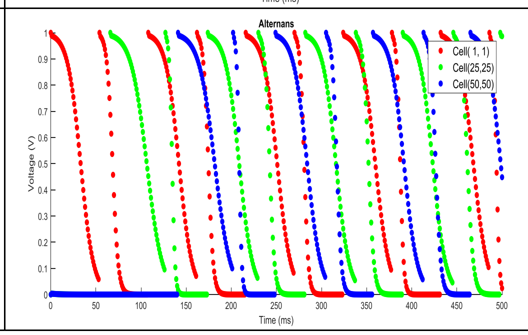
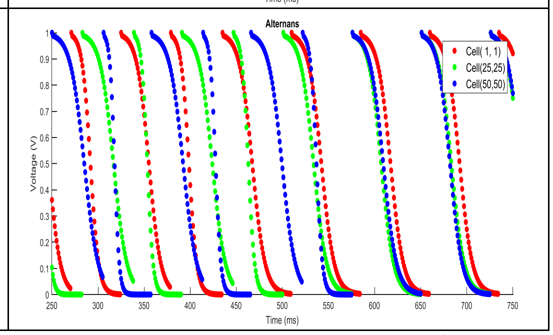
Because the APD of the current heartbeat is determined by the last DI, and BCL is the sum of APD and DI. When the stimulation of pacemaker heart is controlled according to a constant DI, we can get a desired constant BCL along with a stable wave propagation, thus some abnormal wave conductions can be remedied [13] [14].

4.2 ECG

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

Table 1: SINGLE CELL BEHAVIOR COMPARISON

	Without control	With constant DI control
Normal conduction		

Normal conduction with scar		
Spiral wave with scar		
Alternans		

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

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

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

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

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). $\nabla \frac{1}{\mathrm{r}}$ is the gradient of $\frac{1}{\mathrm{r}}$. ∇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

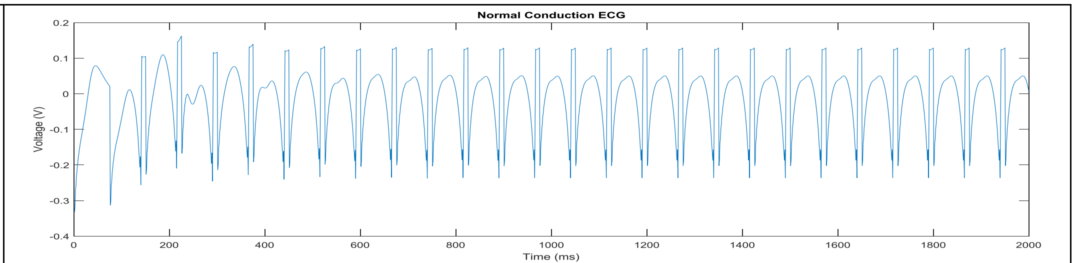
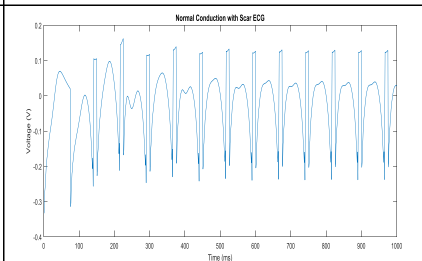
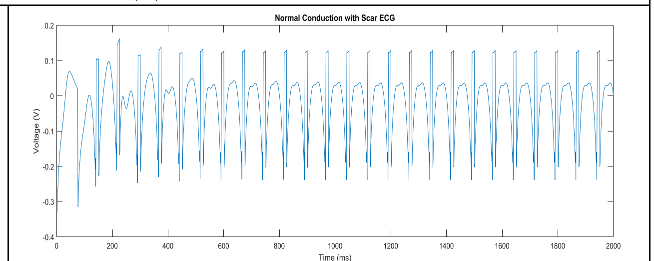
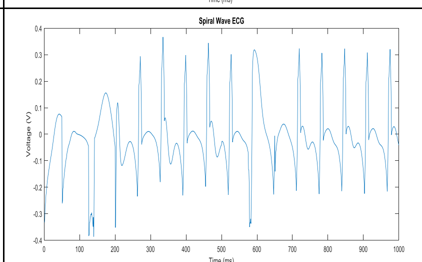
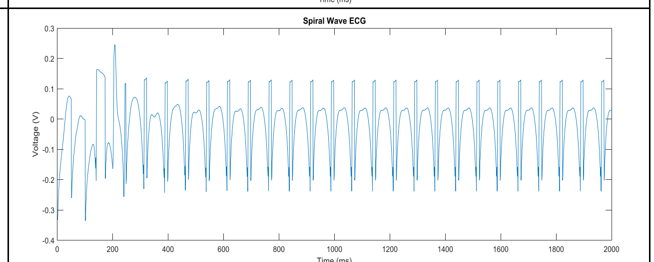
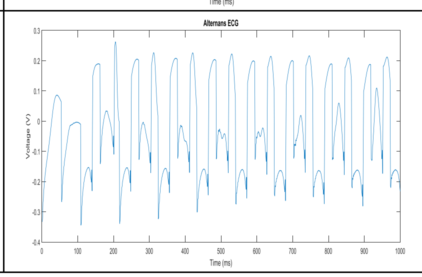
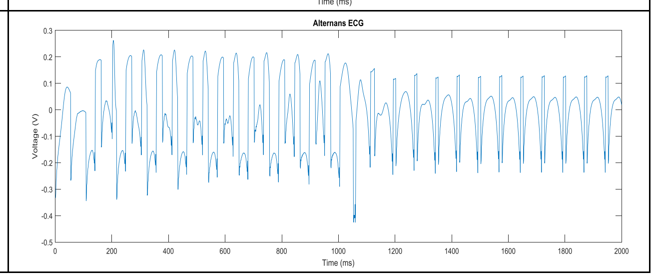
To verify the effectiveness of the constant DI control approach, the simulations results without and with constant DI control are compared in this section.

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.

Table 2: ECG SIMULATION RESULTS COMPARISON

	Without control	With constant DI control

<table>
<tr><td>Normal conduction</td><td colspan="2"></td></tr>
<tr><td>Normal conduction with scar</td><td></td><td></td></tr>
<tr><td>Spiral wave with scar</td><td></td><td></td></tr>
<tr><td>Alternans</td><td></td><td></td></tr>
</table>

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 equals 25 is set for constant DI control here.

From Table 1, we conclude that: (1) In normal conduction scenario, the wave become stable after some oscillation. (2) In normal conduction with 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 is in a mess. Implementing constant DI control at *100 ms* prevents spiral wave and makes the wave stable after short oscillation. In addition, it is very hard to eliminate spiral wave after *125 ms*, because the spiral wave is mature after this time. (4) In alternans scenario, the wave alternates between long and short APD. After implementing constant DI control at *400 ms*, the wave becomes stable.

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 to control the stimulation of pacemaker heart for all abnormal scenarios. In this simulation, constant DI control is applied at *100 ms* for spiral wave, and *1000 ms* for normal conduction with scar and alternans.

From Table 2, we can see that: (1) In normal conduction scenario, the ECG produces a consistent wave pattern after oscillation. (2) In normal conduction with scar scenario, although the ECG is very similar to the normal conduction ECG, there are abnormal flaws in the waveform. Also, constant DI control cannot eliminate waveform flaws brought by scar. (3) Constant DI control could prevent spiral wave before its generation. (4) Constant DI control is effective to eliminate alternans. (5) Recall the single cell results, it is obvious that the effectiveness of constant DI control does not depend on the value of DI.

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) Arrhythmias including spiral wave, and alternans can be resolved by controlling the heart's electrical rhythms using the constant DI control approach. In addition, constant DI control cannot eliminate the micro abnormality caused by scar.

(3) This study can be extended further to simulation models in three dimensions to give a full illustration of how waves propagate throughout the heart. Also, other scenarios such as wave break, ectopic, combination of different scenarios and other control mechanism such as constant RT method can be explored in future study.

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REFERENCES

[1] Mehra, R., 2007. Global public health problem of sudden cardiac death. Journal of electrocardiology, 40(6), pp. S118-S122.

[2] Benchimol, A. and LIGGETT, M.S., 1966. Cardiac hemodynamics during stimulation of the right atrium, right ventricle, and left ventricle in normal and abnormal hearts. Circulation, 33(6), pp.933-944.

[3] Delorme, M. and Mazoyer, J. eds., 2013. Cellular Automata: a parallel model (Vol. 460). Springer Science & Business Media.

[4] Spector, P., 2013. Principles of cardiac electric propagation and their implications for re-entrant arrhythmias. Circulation: Arrhythmia and Electrophysiology, 6(3), pp.655-661.

[5] Zheng, Y., Wei, D., Zhu, X., Chen, W., Fukuda, K. and Shimokawa, H., 2015. Ventricular fibrillation mechanisms and cardiac restitutions: An investigation by simulation study on whole-heart model. Computers in biology and medicine, 63, pp.261-268.

[6] Atkins, D.L., Hartley, L.L. and York, D.K., 1998. Accurate recognition and effective treatment of ventricular fibrillation by automated external defibrillators in adolescents. Pediatrics, 101(3), pp.393-397.

[7] Avdeev, S.A. and Bogatov, N.M., 2014. Simulation of electrochemical processes in cardiac tissue based on cellular automaton. In IOP Conference Series: Materials Science and Engineering (Vol. 66, No. 1, p. 012019). IOP Publishing.

[8] Feldman, A.B., Chernyak, Y.B. and Cohen, R.J., 1999. Cellular automata model of cardiac excitation waves. Herzschrittmachertherapie und Elektrophysiologie, 10(2), pp.92-104.

[9] Mitchell, R.H., Bailey, A.H. and Anderson, J., 1992. Cellular automaton model of ventricular fibrillation. IEEE transactions on biomedical engineering, 39(3), pp.253-259.

[10] Campos, R.S., Amorim, R.M., de Oliveira, B.L., Rocha, B.M., Sundnes, J., da Silva Barra, L.P., Lobosco, M. and dos Santos, R.W., 2013, September. 3D heart modeling with cellular automata, mass-spring system and CUDA. In International Conference on Parallel Computing Technologies (pp. 296-309). Springer, Berlin, Heidelberg.

[11] Pourhasanzade, F. and Sabzpoushan, S.H., 2010. A new cellular automata model of cardiac action potential propagation based on summation of excited neighbors. World Academy of Science, Engineering and Technology, 44, pp.917-921.

[12] Lipsius, S.L., Fozzard, H.A. and Gibbons, W.R., 1982. Voltage and time dependence of restitution in heart. American Journal of Physiology-Heart and Circulatory Physiology, 243(1), pp.H68-H76.

[13] Zlochiver, S., Johnson, C. and Tolkacheva, E.G., 2017. Constant DI pacing suppresses cardiac alternans formation in numerical cable models. Chaos: An Interdisciplinary Journal of Nonlinear Science, 27(9), p.093903.

[14] Otani, N.F., 2017. Theory of the development of alternans in the heart during controlled diastolic interval pacing. Chaos: An Interdisciplinary Journal of Nonlinear Science, 27(9), p.093935.

[15] Geselowitz, D.B., 1989. On the theory of the electrocardiogram. Proceedings of the IEEE, 77(6), pp.857-876.

