A Cellular Automata Model For Dynamics and Control of Cardiac Arrhythmias

DANNY GALLENBERGER (CARROLL UNIVERSITY)
XIAOPENG ZHAO (UTK)
KWAI WONG (UTK)
Introduction

- Sudden cardiac arrest is responsible for 325,000 deaths in the US each year
- Arrhythmias
  - Not being identified in time
  - Their onset is difficult to predict
- Illustration of wave propagation through cellular automata models
  - Two-variable PDEs are computationally expensive and properties are difficult to adjust
- Control mechanisms
  - Feedback control – only effective for smaller tissue
  - Constant DI?
In this study, we will look at:

- The electrophysiological properties of the heart
- Cardiac arrhythmias
- How a cellular automata model can be used to analyze various scenarios
- The functions used to simulate heart activity
- Constant DI control through the use of electrocardiogram (ECG) data
Electrophysiology of the Heart

- Four chambers
- Electrical signal propagates through chambers
  - Originates in the sinus node
- As signal passes through each chamber, the heart contracts
Electrophysiology of the Heart

Four states

- $S_0$ = Resting
- $S_1$ & $S_2$ = Excited
- $S_3$ = Absolute Refractory
- $S_4$ = Relative Refractory
Cardiac Arrhythmias

▪ A disruption in the heart’s normal rhythm

▪ Variable Heart Rate
  ▪ Bradycardia
  ▪ Tachycardia

▪ Reentrant Arrhythmias – tissue is excited repetitively by free waves
  ▪ Atrial Fibrillation
  ▪ Ventricular Fibrillation

▪ Non-reentrant Arrhythmias
  ▪ Alternans
  ▪ AV Heart Block
Cellular Automata

- Two-dimensional grid of cells
- Each cell has multiple possible states
- Predefined rules based on neighbor states
- Effective for modeling complex systems consisting of simple units
- Faster than solving PDEs
Methods

Steps taken:

▪ Analyze Mathematica simulations that run many heart scenarios
▪ Recreate simulation in MATLAB
▪ Generate action potential graphs and cellular automata models
▪ Generate action potential duration and ECG data
▪ Implement constant DI control on scenarios
Methods

- Two-dimensional cellular automata model
- Each square represents a heart cell
- Excitation threshold = 0.9 V
- Refractory threshold = 0.1 V
- Action potential (V) of a heart cell:
  - (0.9, 1] = excited phase
  - (0.1, 0.9] = absolute refractory phase
  - (0, 0.1] = relative refractory phase
  - 0 = resting phase
- Action potential duration (APD) = time spent in excited and absolute refractory phases
- Diastolic interval (DI) = time spend in relative refractory and resting phases
MATLAB Functions & Scripts

- Simulation
  - Stimulation
  - Propagation
  - Depolarization
  - Evolution
- Parameters
- Restitution
- Action Potential
- Action Potential Plots
- Cellular Automata
- ECG Plots
- $\Phi_e$ (Transmembrane Potential)
<table>
<thead>
<tr>
<th>Scenario</th>
<th>Model Size</th>
<th>Basic Cycle Length (BCL)</th>
<th>Time</th>
<th>Scar Cells at x ∈ [10, 15] and y ∈ [5, 10]</th>
<th>Excluding Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Conduction</td>
<td>50x50</td>
<td>75ms</td>
<td>2000ms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal Conduction with Scar</td>
<td>50x50</td>
<td>75ms</td>
<td>2000ms</td>
<td>x ∈ [10, 15] and y ∈ [15, 20]</td>
<td>(10, 15), (10, 20), (15, 15), and (15, 20)</td>
</tr>
<tr>
<td>Spiral Wave with Scar</td>
<td>50x50</td>
<td>75ms</td>
<td>2000ms</td>
<td>x ∈ [10, 15] and y ∈ [5, 10]</td>
<td>(10, 5), (10, 10), (15, 5), and (15, 10)</td>
</tr>
<tr>
<td>Alternans</td>
<td>25x25</td>
<td>54ms</td>
<td>2000ms</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Other Variables

- **Stimulation Times**
  - Array of \( t \)-values at which the pacemaker cells stimulate

- **Voltage\((x,y,t)\)**
  - Action potential of a heart cell at a given time

- **APD\((x,y)\)**
  - Action potential duration of a heart cell

- **DI\((x,y)\)**
  - Diastolic interval of a heart cell

- **Duration\((x,y)\)**
  - Time elapsed since the cell’s last excitation
Restitution

- Defines the relationship between the DI and the APD
  - $APD_n = f(D_{n-1})$
  - $f(D_n) = A_{max} - A_0 e^{-D_n/\tau}$
  - $f(D_n) = 60 - 50 e^{-D_n/20}$
  - As $D_n \to \infty$, $f(D_n) \to A_{max}$
  - Cardiac dynamics unstable for $f'(D_n) > |1|$
Action Potential

- Signifies what happens to a cell after it has been stimulated as time progresses.

- \[ f(A, t) = \frac{e^{-t/T(A)}}{c + e^{-t/T(A)}} \]

- \[ T(A) = \frac{A}{\ln(0.9) - \ln(0.1*c)} \]

- As \( t \to \infty \), \( f(A, t) \to 0 \)

- The greater \( A \) is, the slower the cell depolarizes.

- \[ f(t) = \frac{e^{-t/9.7025}}{0.01 + e^{-t/9.7025}} \]

- \( T(66) \approx 9.7025 \)
Stimulation & Wave Propagation

- **Stimulation**
  - If voltage $\leq 0.1$, the cell depolarizes (voltage becomes 1 V)

- **Wave Propagation**
  - If voltage $\leq 0.1$, the cell’s neighbors are checked
  - If at least 3 neighbors are excited, the evaluated cell becomes excited
  - Otherwise, the cell evolves

- **Depolarization**
  - DI of previous heartbeat is calculated
  - APD of next beat is determined
  - Voltage becomes 1 V
  - Duration resets

- **Evolution**
  - Duration increments
  - Voltage changes based on APD and duration
Simulation

- 3x3 group of pacemaker cells stimulate at t = 0
- At every time step, the propagation function is called at each cell
- If scar cells exist, they are set to 0 V
- When t reaches a stimulation time, the pacemaker cells become excited
- Process repeats until the entire interval is covered
Constant DI

- Used as a control mechanism
- Heartbeats are regulated by DI rather than BCL
- Stimulation times are not necessarily equally spaced throughout
Electrocardiogram (ECG)

- Diagram used to illustrate electrical activity in the heart
- Measures voltage difference between two points outside the tissue
- \[ \text{ECG} = \Phi_e(B) - \Phi_e(A) \]
- \[ \Phi_e(x', y') = \int (-\nabla V_m) \cdot \left( \nabla \frac{1}{r} \right) \, dx \, dy \]
- \[ r = \left[ (x - x')^2 + (y - y')^2 \right]^{1/2} \]
Results

- Normal Conduction
- Normal Conduction with Scar
Results

- Spiral Wave with Scar
- Alternans
### Normal Conduction

<table>
<thead>
<tr>
<th></th>
<th>Single Cell</th>
<th>Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal Conduction</strong></td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
</tr>
</tbody>
</table>

**Single Cell**
- Voltage (V) vs. Time (ms)

**Tissue**
- Voltage (V) vs. Time (ms)
- 50x50
- 100x100
No Control vs Constant DI Control

- **No Control**
  - $t_{start} = t$
  - $t_{end} = t_{start} + BCL$

- **Constant DI**
  - $t_{start} = t$
  - $t_{end} = t_{start} + APD(1,1) + DI_{target}$

- $DI_{target} = BCL - APD(1,1)$
- $APD(1,1) = 56.5466\text{ms}$
- Normal Conduction with Scar & Spiral Wave with Scar
  - $BCL = 75\text{ms}$
  - $DI_{target} \approx 19$
- Alternans
  - $BCL = 54\text{ms}$
  - $DI_{target} \approx -2$
No Control vs Constant DI Control

<table>
<thead>
<tr>
<th>Normal Conduction with Scar</th>
<th>Normal Conduction with Scar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Cell</td>
<td>Tissue</td>
</tr>
<tr>
<td>50x50</td>
<td>50x50</td>
</tr>
<tr>
<td>100x100</td>
<td>100x100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Spiral Wave with Scar</th>
<th>Spiral Wave with Scar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Cell</td>
<td>Tissue</td>
</tr>
<tr>
<td>50x50</td>
<td>50x50</td>
</tr>
<tr>
<td>100x100</td>
<td>100x100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Alternans</th>
<th>Alternans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Cell</td>
<td>Tissue</td>
</tr>
<tr>
<td>50x50</td>
<td>50x50</td>
</tr>
<tr>
<td>100x100</td>
<td>100x100</td>
</tr>
</tbody>
</table>
Conclusion

▪ Constant DI effectively controlled alternans in smaller tissue
▪ Benefits of cellular automata
▪ Future work
  ▪ 3D simulation
  ▪ GPU implementation
  ▪ Controlling other heart scenarios
  ▪ Constant RT control
  ▪ Other control mechanisms?
References

- **Electrocardiogram – ECG. myDr.**


