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A Cellular Automata Model For Dynamics and Control of Cardiac Arrhythmias

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Introduction

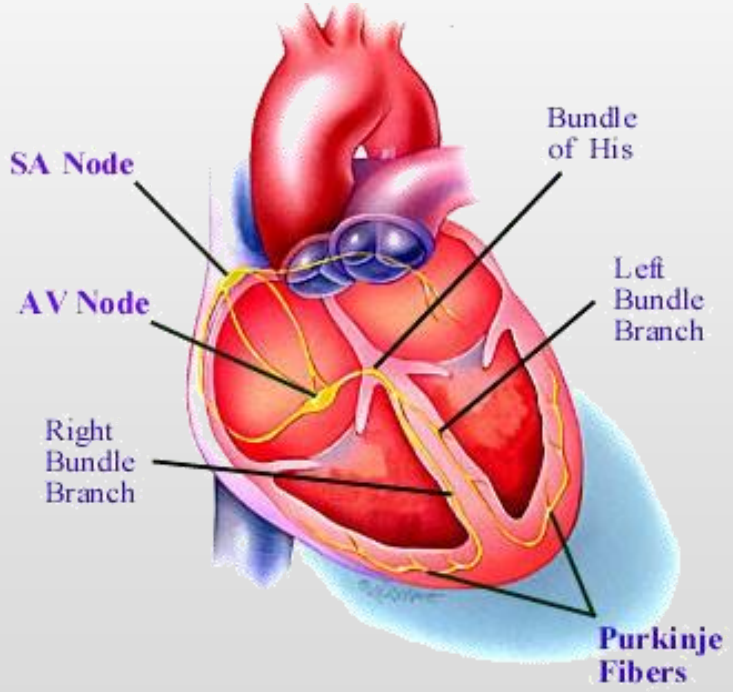
- Sudden cardiac arrest is responsible for 325,000 deaths in the US each year
- Arrhythmias
  - Not being identified in time
  - Their onset is difficult to predict
- Illustration of wave propagation through cellular automata models
  - Two-variable PDEs are computationally expensive and properties are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

Introduction

- 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

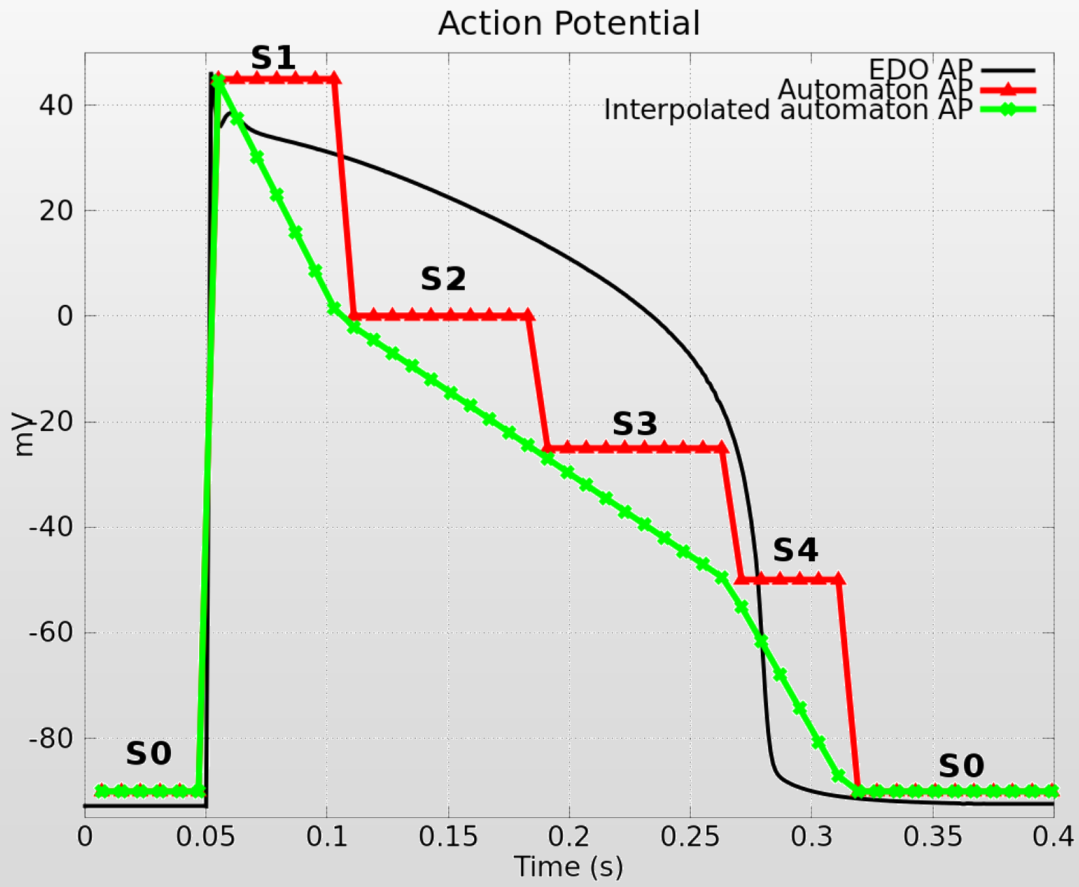
- Four chambers
- Electrical signal propagates through chambers
  - Originates in the sinus node
- As signal passes through each chamber, the heart contracts



Electrophysiology of the Heart

Four states

- S0 = Resting
- S1 & S2 = Excited
- S3 = Absolute Refractory
- S4 = Relative Refractory

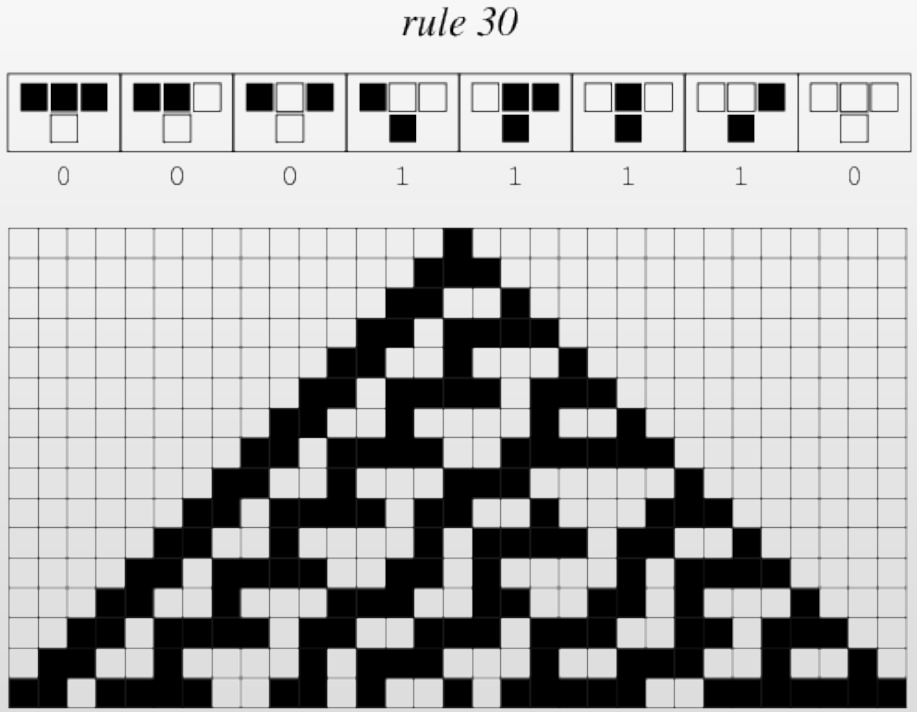


Cardiac Arrhythmias

- 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
- Φ_e (Transmembrane Potential)

Scenarios

Normal Conduction

- 50x50 model
- Basic cycle length (BCL) = 75ms
- Time = 2000ms

Normal Conduction with Scar

- 50x50 model
- Basic cycle length (BCL) = 75ms
- Time = 2000ms
- Scar cells at $x \in [10,15]$ and $y \in [15,20]$
  - Excluding (10,15), (10,20), (15,15), and (15,20)

Spiral Wave with Scar

- 50x50 model
- Basic cycle length (BCL) = 75ms
- Time = 2000ms
- Scar cells at $x \in [10,15]$ and $y \in [5,10]$
  - Excluding (10,5), (10,10), (15,5), and (15,10)

Alternans

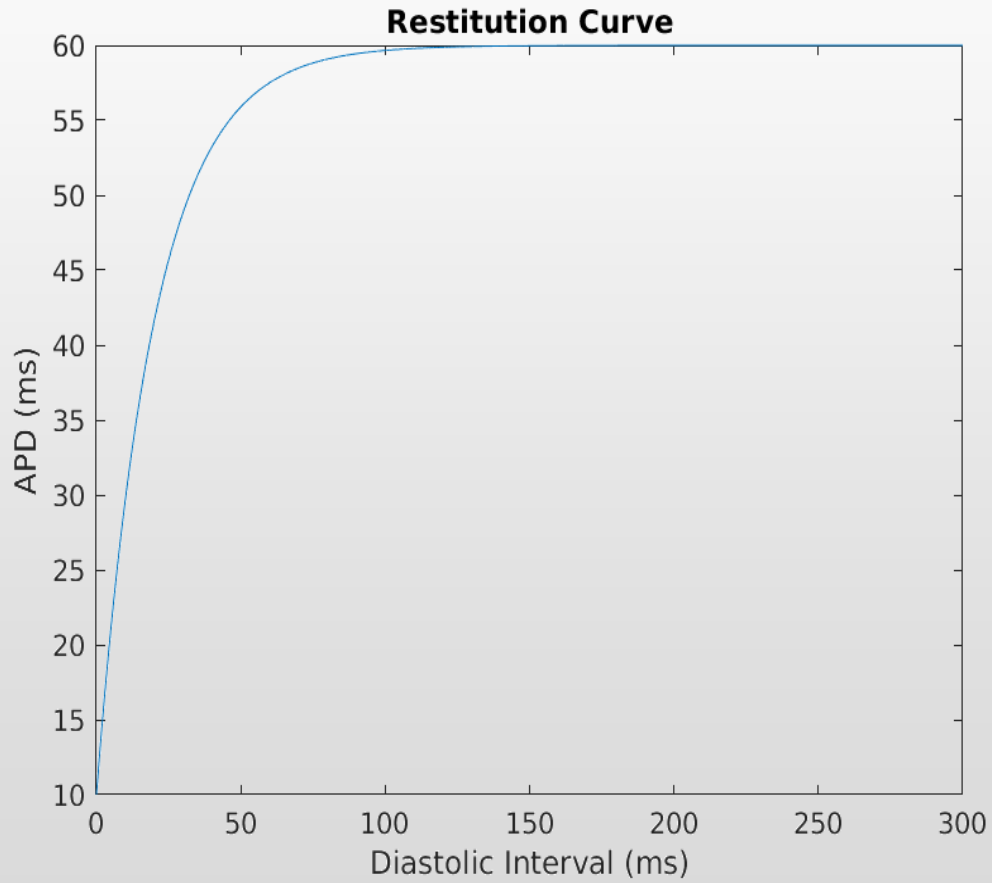
- 25x25 model
- Basic cycle length (BCL) = 54ms
- Time = 2000ms

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

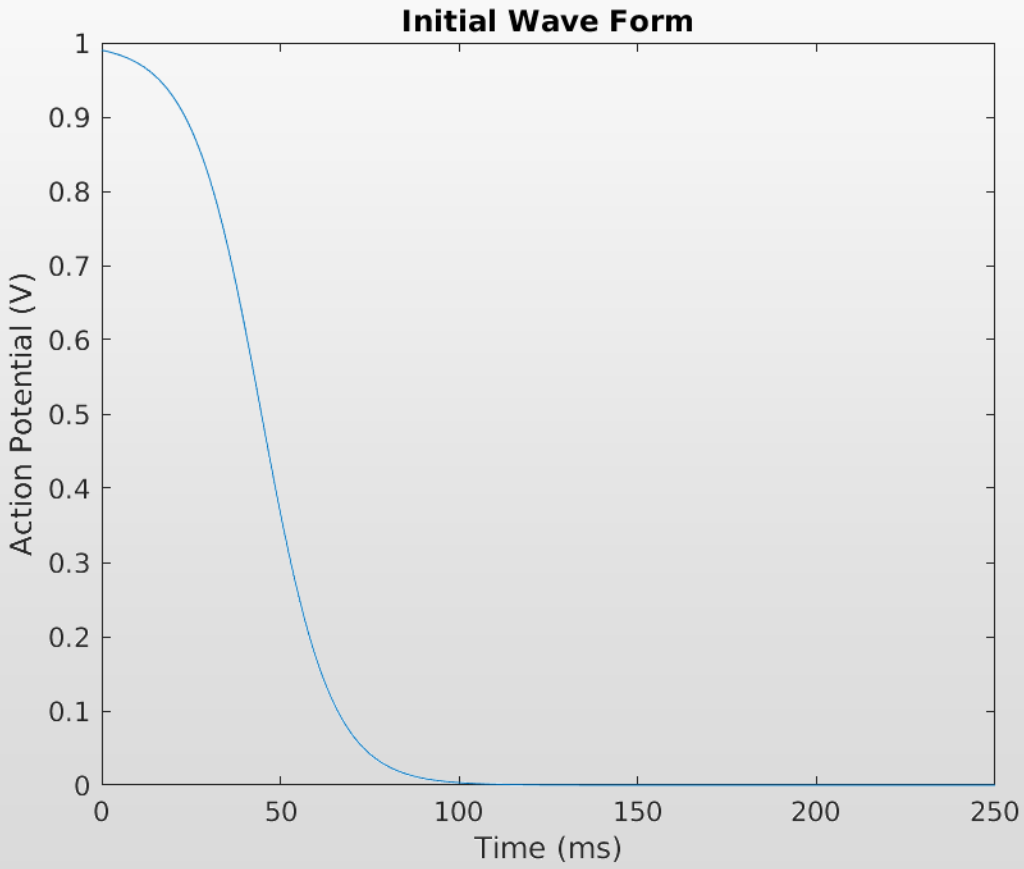
Restitution

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



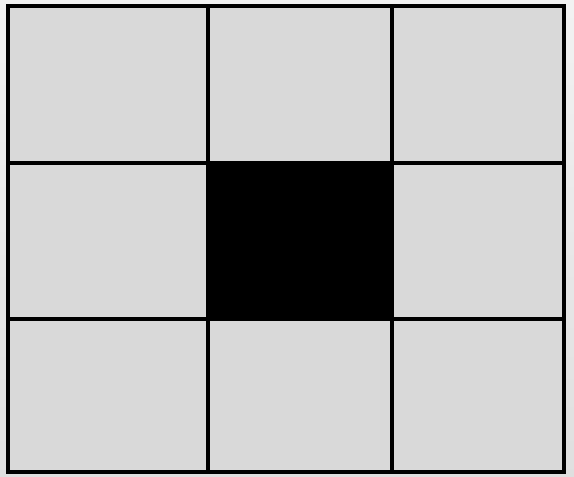
Action Potential

- Signifies what happens to a cell after it has been stimulated as time progresses
- $f(A,t) = \frac{e^{-t/T(A)}}{\mathrm{c} + e^{-t/T(A)}}$
- $T(A) = \frac{\mathrm{A}}{\ln(0.9) - \ln(0.1 * c)}$
- As $t \rightarrow \infty$, $f(A,t) \rightarrow 0$
- 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 ≤ 0.1, the cell depolarizes (voltage becomes 1 V)
- Wave Propagation
  - If voltage ≤ 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



Black cell is being evaluated
Gray cells are the neighbors being checked

Simulation

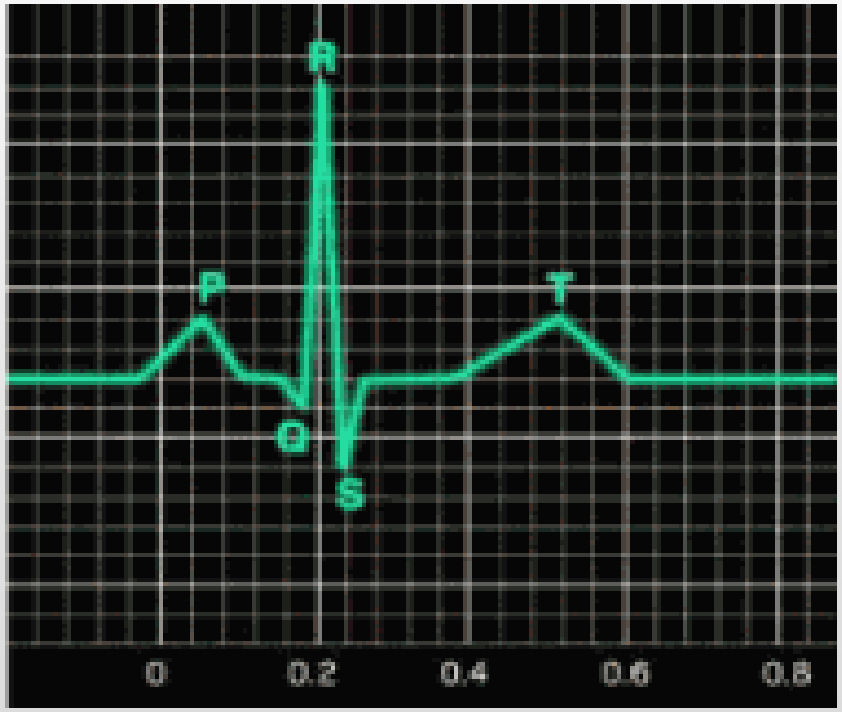
- 3x3 group of pacemaker cells stimulate at t = 0
- At every time step, the propagation function is called at each cell
- If scar cells exist, they are set to 0 V
- When t reaches a stimulation time, the pacemaker cells become excited
- Process repeats until the entire interval is covered

Constant DI

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

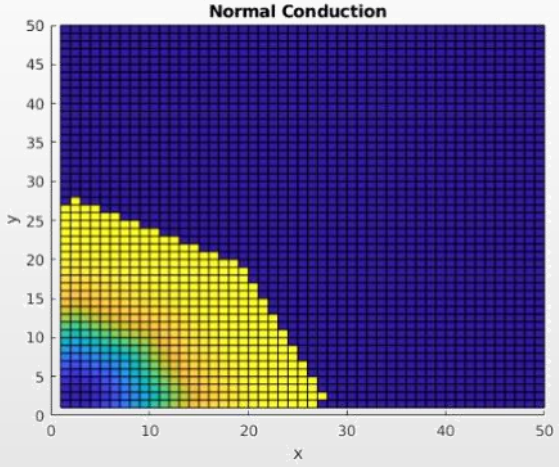
Electrocardiogram (ECG)

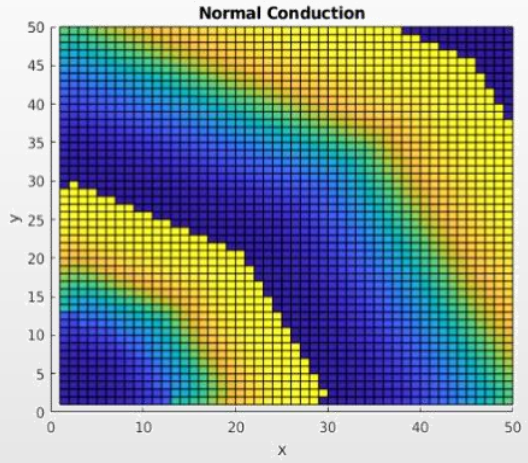
- Diagram used to illustrate electrical activity in the heart
- Measures voltage difference between two points outside the tissue
- $\mathrm{ECG} = \Phi_e(\mathrm{B}) - \Phi_e(\mathrm{A})$
- $\Phi_e(x', y') = \int(-\nabla \mathrm{V_m}) \cdot \left(\nabla \frac{1}{\mathrm{r}}\right) dx\, dy$
- $r = [(x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

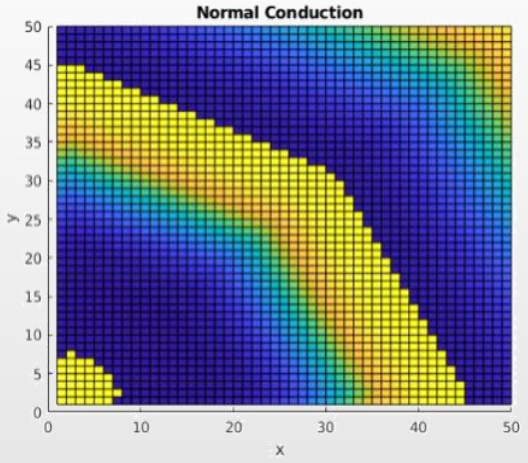


Results

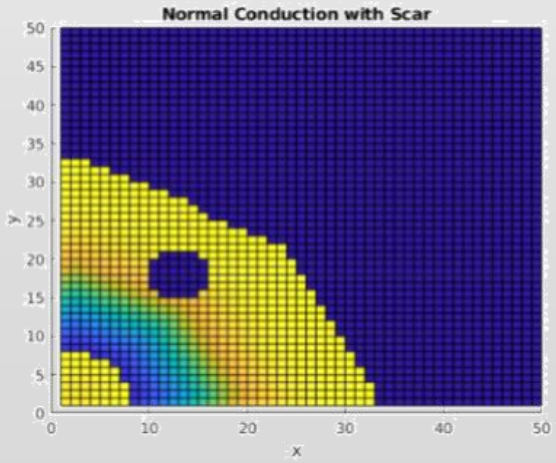
- Normal Conduction

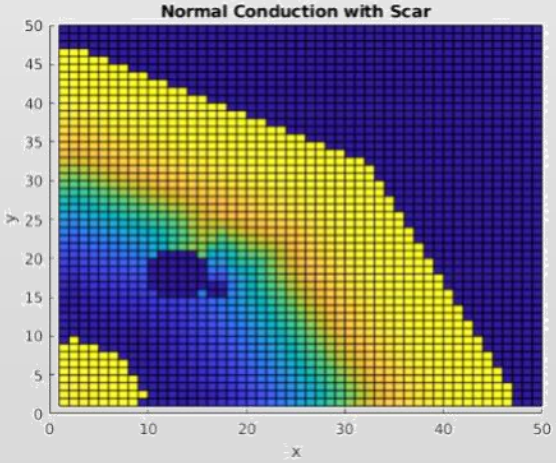


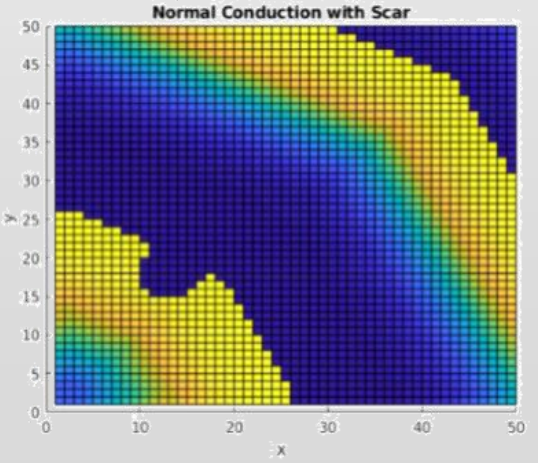




- Normal Conduction with Scar

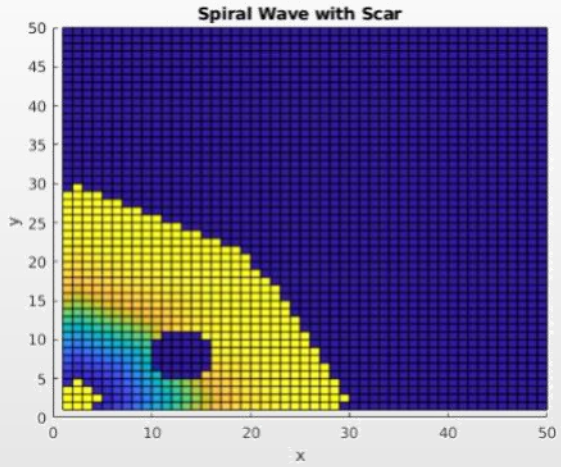


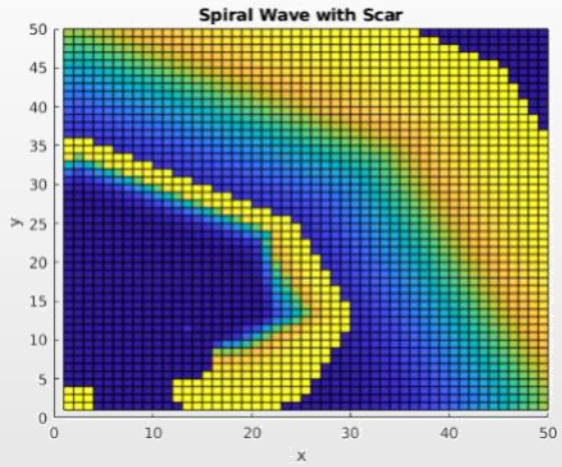


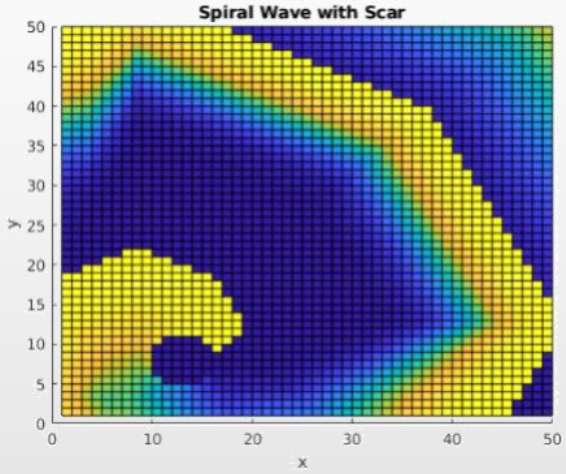


Results

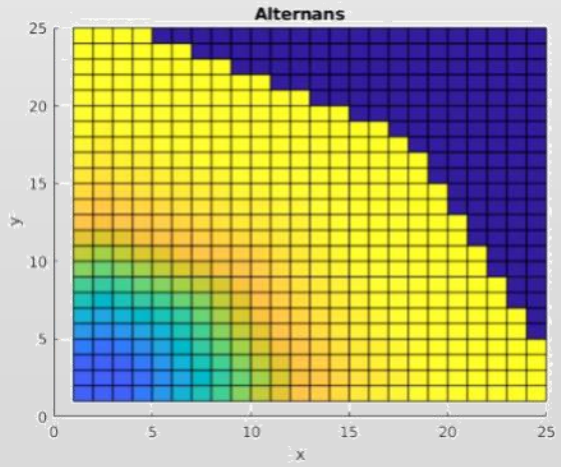
- Spiral Wave with Scar

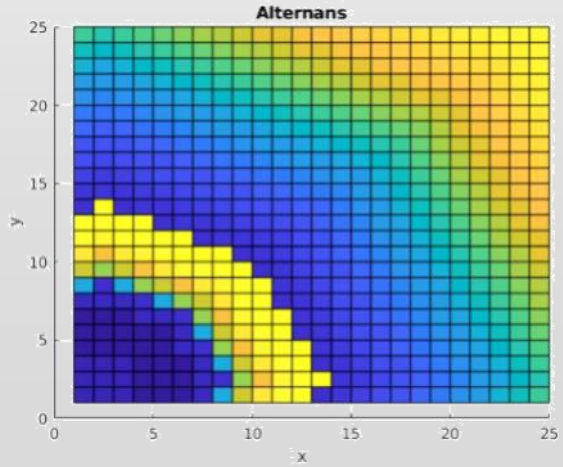


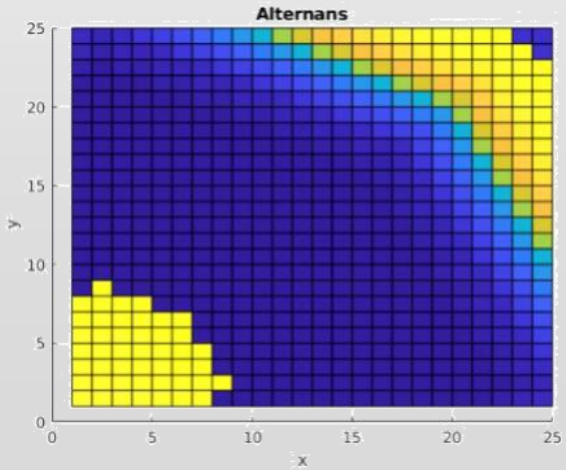




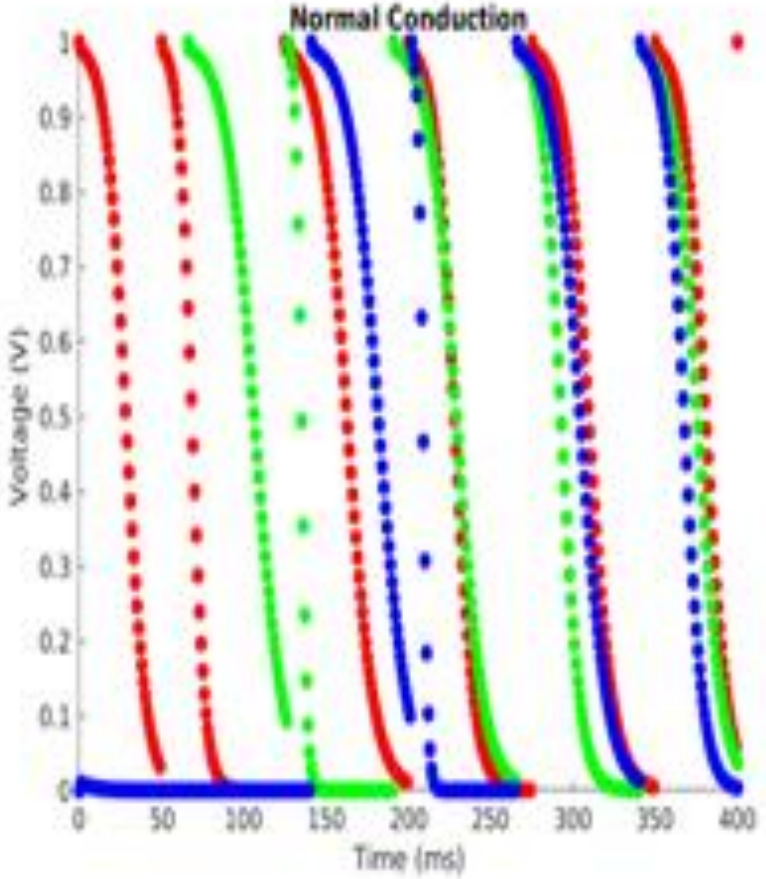
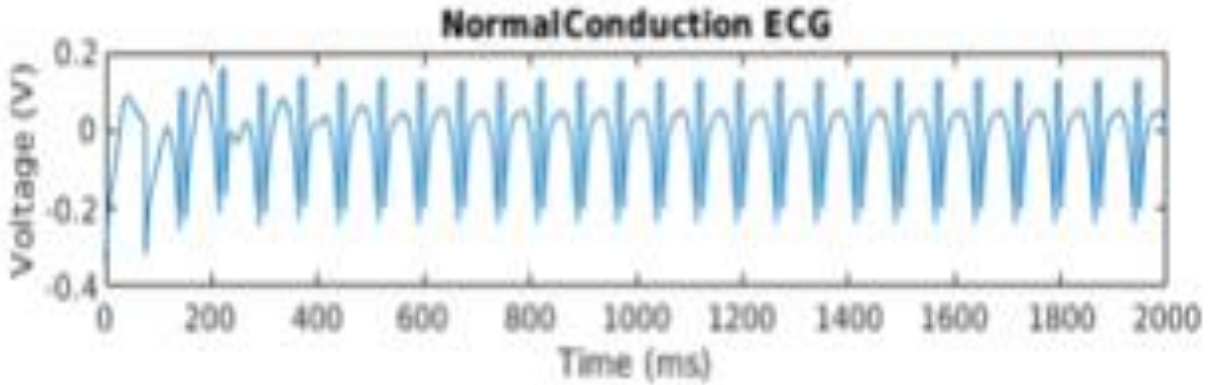
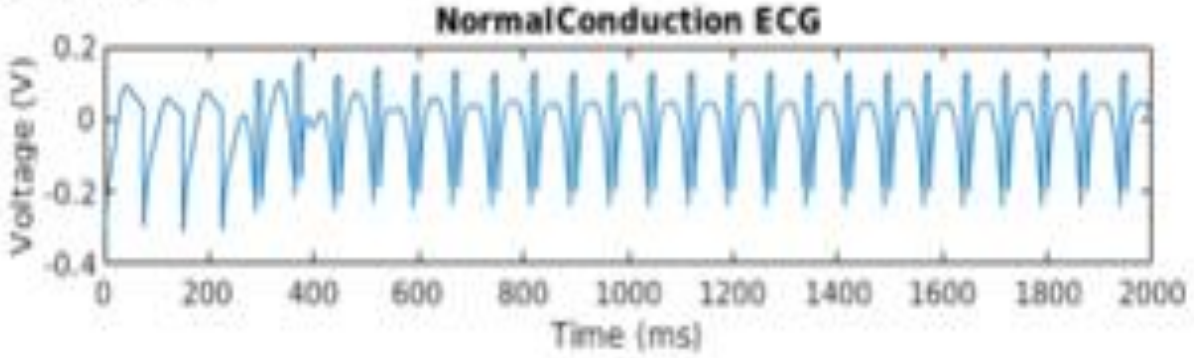
- Alternans







Normal Conduction

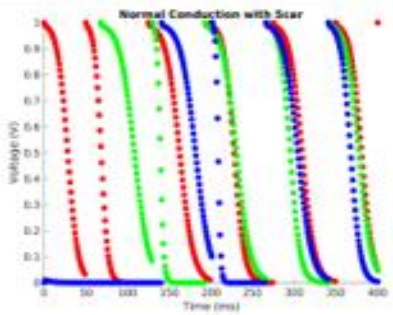
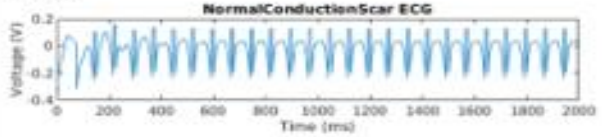
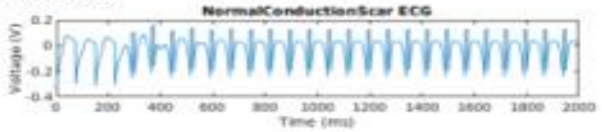
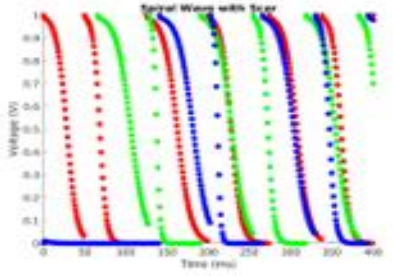
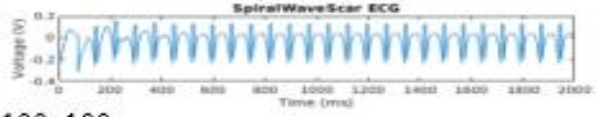
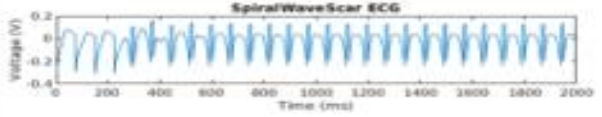
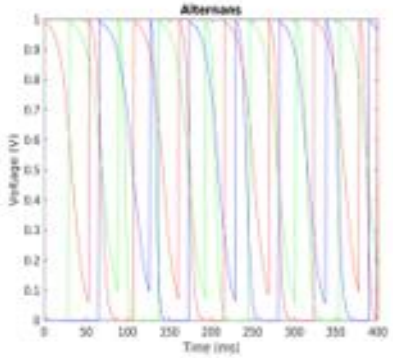
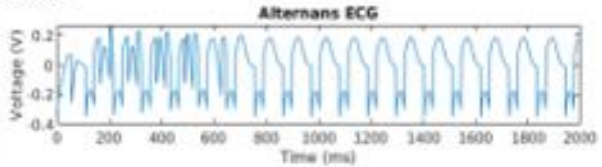
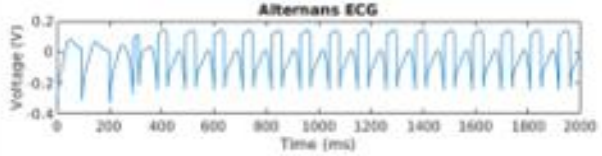
	Single Cell	Tissue
Normal Conduction		50x50  100x100 

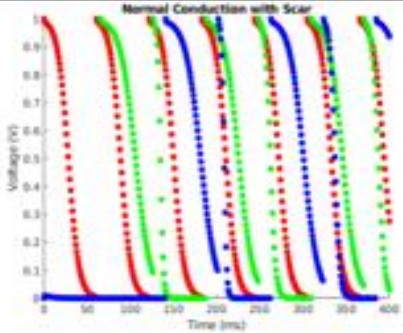
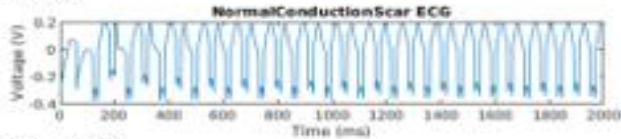
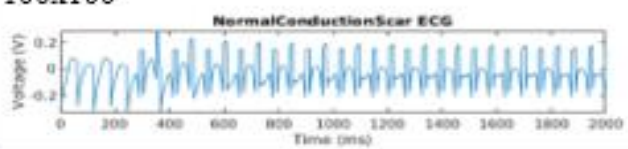
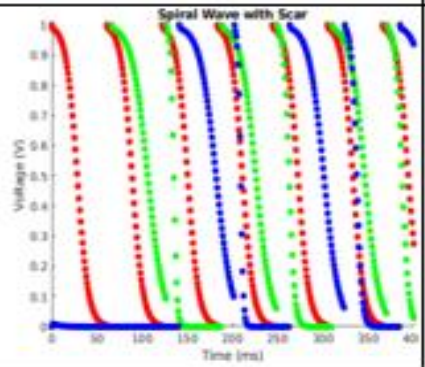
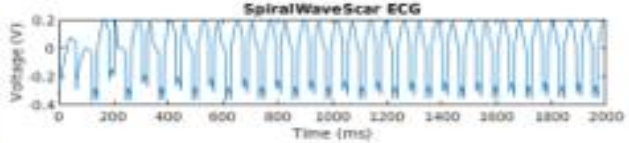
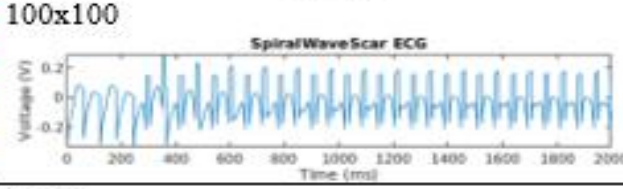
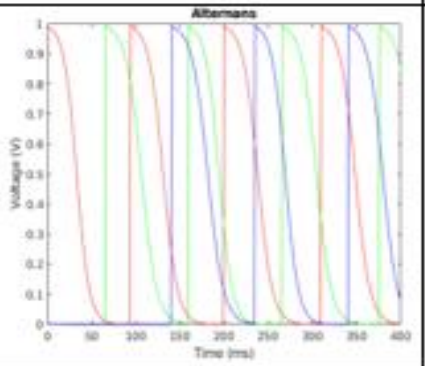
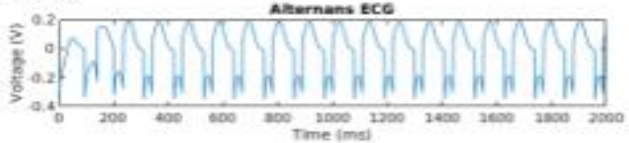
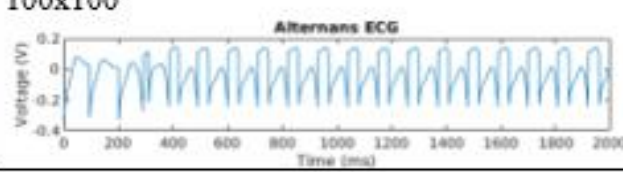
No Control vs Constant DI Control

- No Control
  - tstart = t
  - tend = tstart + BCL
- Constant DI
  - tstart = t
  - tend = tstart + APD(1,1) + DI_target

- DI_target = BCL – APD(1,1)
- APD(1,1) = 56.5466ms
- Normal Conduction with Scar & Spiral Wave with Scar
  - BCL = 75ms
  - DI_target ≈ 19
- Alternans
  - BCL = 54ms
  - DI_target ≈ -2

No Control vs Constant DI Control

	Single Cell	Tissue
Normal Conduction with Scar		50x50  100x100 
Spiral Wave with Scar		50x50  100x100 
Alternans		50x50  100x100 

	Single Cell	Tissue
Normal Conduction with Scar		50x50  100x100 
Spiral Wave with Scar		50x50  100x100 
Alternans		50x50  100x100 

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

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