Cardiac Action Potential - the Luo-Rudy Model

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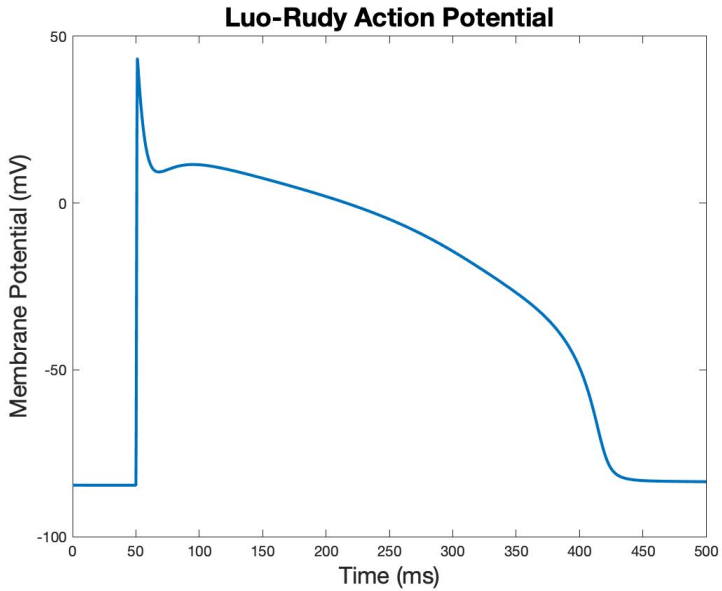
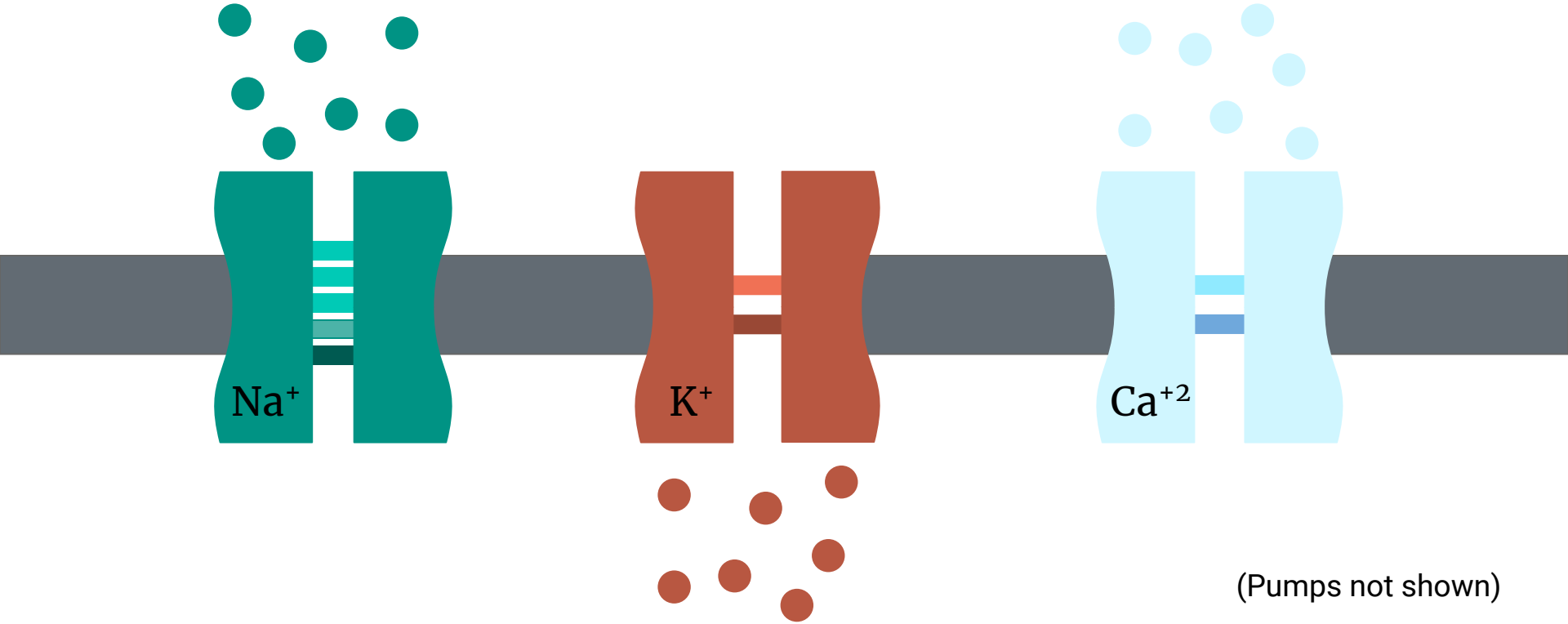
Biological background

What is an action potential?

- Electrical pulses to signal and trigger contraction
- Triggered by stimulus (pacemaker cells)
- Voltage drop across membrane via controlling ions
- Cell level vs fiber level



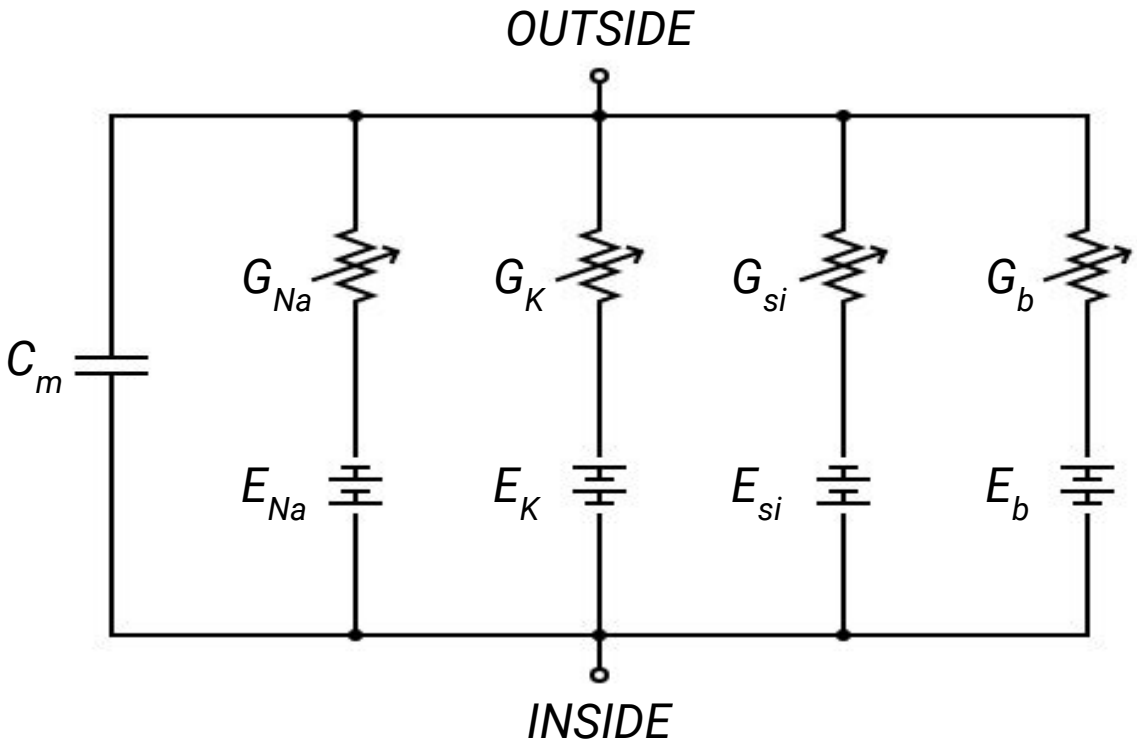
Ions at the cell membrane



(Pumps not shown)

The model for a single cell

The model as a circuit

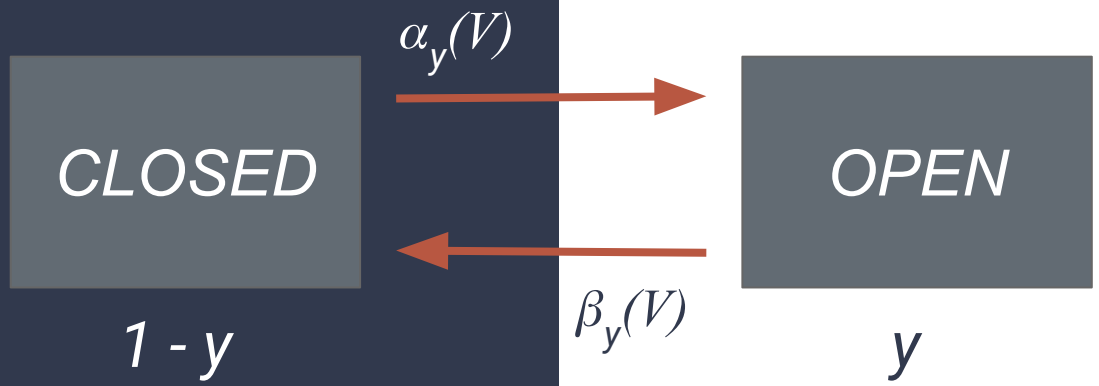


$$I_{C_m} = C_m \frac{dV}{dt}$$

$$I_{Na} = G_{Na} \cdot m^3 \cdot h \cdot j \cdot (V - E_{si})$$

$$I_{stim} = C_m \frac{dV}{dt} + I_{ion}$$

Gating variables



$$\frac{dy}{dt} = \alpha_y(V)(1-y) - \beta_y(V)y$$

The Luo-Rudy Model

$$I_{stim} = C_m \frac{dV}{dt} + I_{ion}$$

$$I_{ion} = I_{Na} + (I_K + I_{K1} + I_{Kp}) + I_{si} + I_b$$

$$I_{Na} = G_{Na} \cdot m^3 \cdot h \cdot j \cdot (V - E_{Na})$$

$$I_{si} = G_{si} \cdot d \cdot f \cdot (V - E_{si})$$

$$I_K = G_K \cdot X \cdot X_i \cdot (V - E_K)$$

$$I_{K1} = G_{K1} \cdot K1_\infty \cdot (V - E_{K1})$$

$$I_{Kp} = G_{Kp} \cdot Kp \cdot (V - E_{Kp})$$

$$I_b = G_b \cdot (V - E_b)$$

$$\frac{dy}{dt} = \alpha_y(V)(1 - y) - \beta_y(V)y$$

where y is gating variables m, h, j, d, f, X

$$E_{si} = 7.7 - 13.0287 \ln([Ca]_i)$$

$$\frac{d[Ca]_i}{dt} = -10^{-4} \cdot I_{si} + 0.07(10^{-4} - [Ca]_i)$$

Note: E_K, E_{K1}, and E_{Kp} all depend on $[K]_o$

Numerical results and analysis

Forward difference

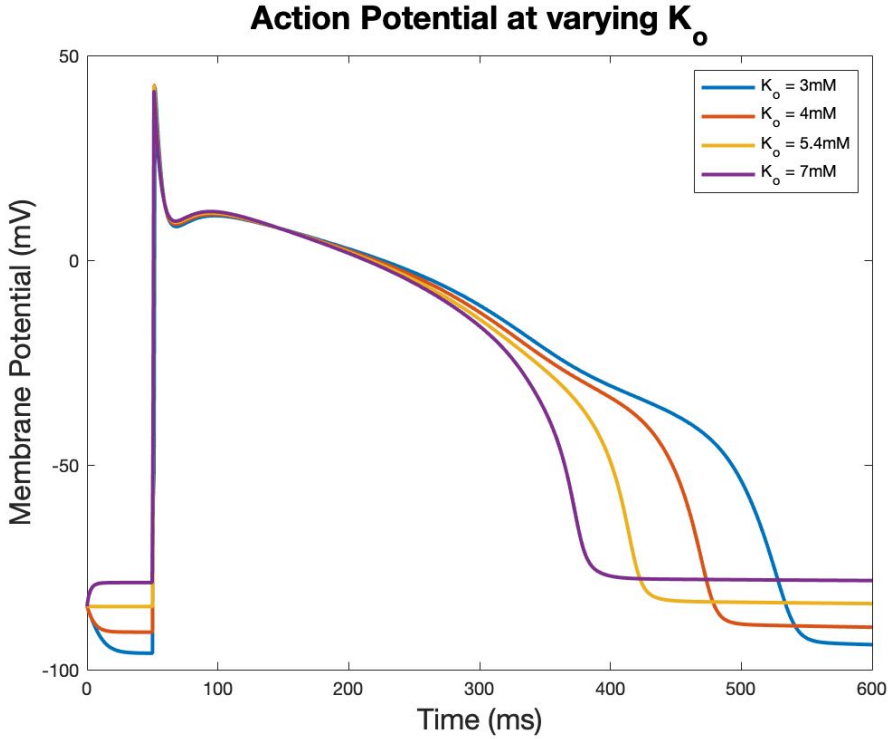
$$V_{i+1} = V_i + \Delta t \left(\frac{1}{C_m} \right) (I_{stim} - I_{ion})$$

$$y_{i+1} = y_i + \Delta t \left(\alpha_y(V)(1 - y_i) - \beta_y(V) y_i \right)$$

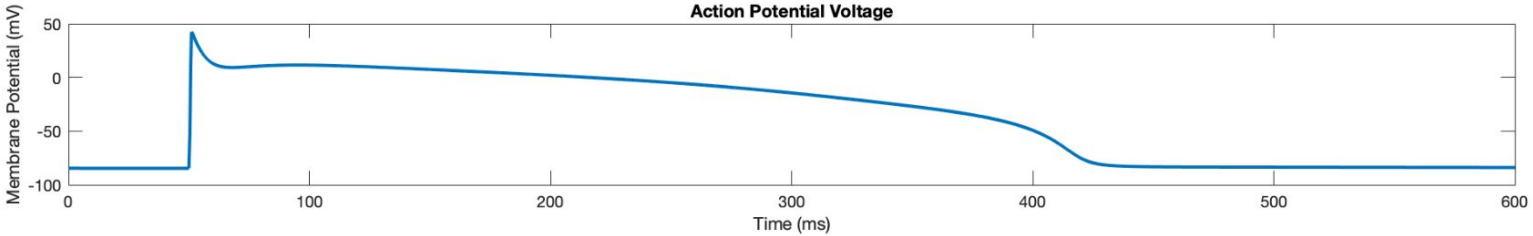
where y is gating variables m, h, j, d, f, X

$$Cai_{i+1} = Cai_i + \Delta t(-10^{-4} \cdot I_{si} + 0.7(10^{-4} - Cai))$$

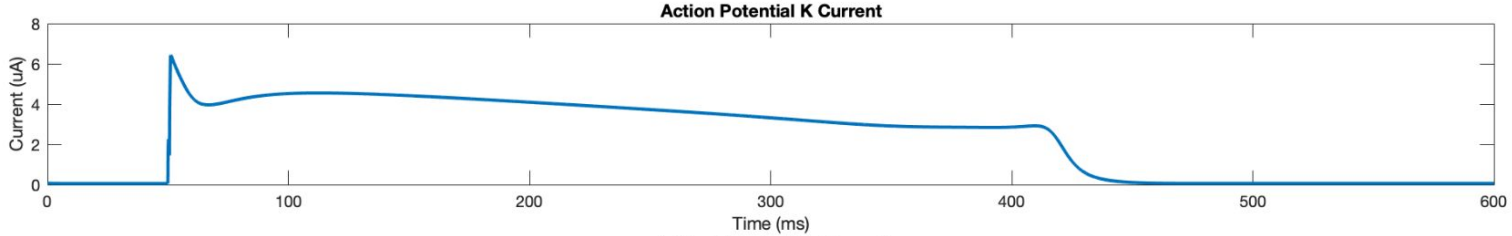
Results – Voltage (at varying $[K]_o$ levels)



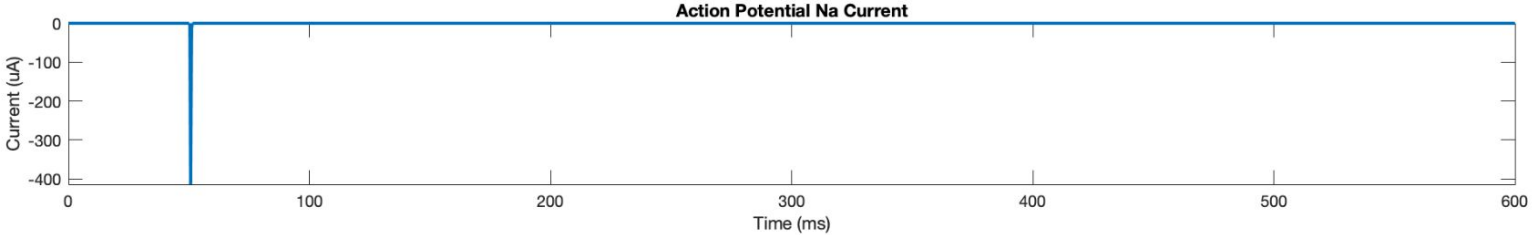
V


Action Potential Voltage
Membrane Potential (mV)
50
0
-50
-100
0
100
200
300
400
500
600
Time (ms)

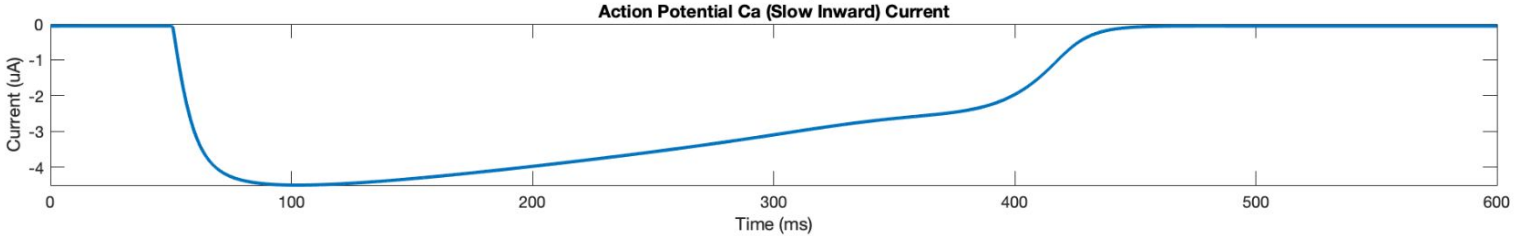
K

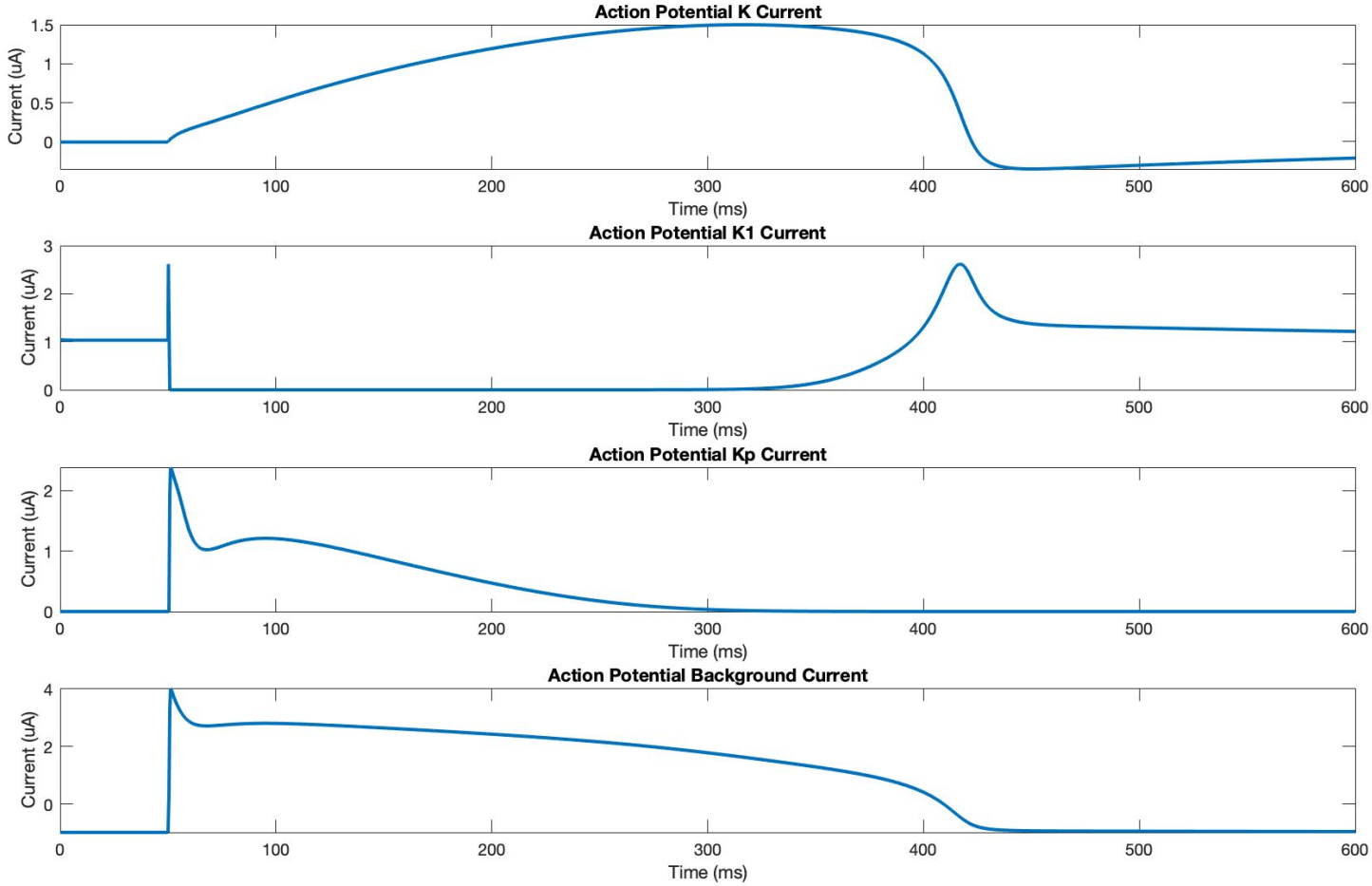

Action Potential K Current
Current (uA)
8
6
4
2
0
0
100
200
300
400
500
600
Time (ms)

Na


Action Potential Na Current
Current (uA)
0
-100
-200
-300
-400
0
100
200
300
400
500
600
Time (ms)

Ca


Action Potential Ca (Slow Inward) Current
Current (uA)
0
-1
-2
-3
-4
0
100
200
300
400
500
600
Time (ms)


Action Potential K Current
Current (uA)
1.5
1
0.5
0
0
100
200
300
400
500
600
Time (ms)
Action Potential K1 Current
Current (uA)
3
2
1
0
0
100
200
300
400
500
600
Time (ms)
Action Potential Kp Current
Current (uA)
2
1
0
0
100
200
300
400
500
600
Time (ms)
Action Potential Background Current
Current (uA)
4
2
0
0
100
200
300
400
500
600
Time (ms)

The model for a chain of cells

Cable equation

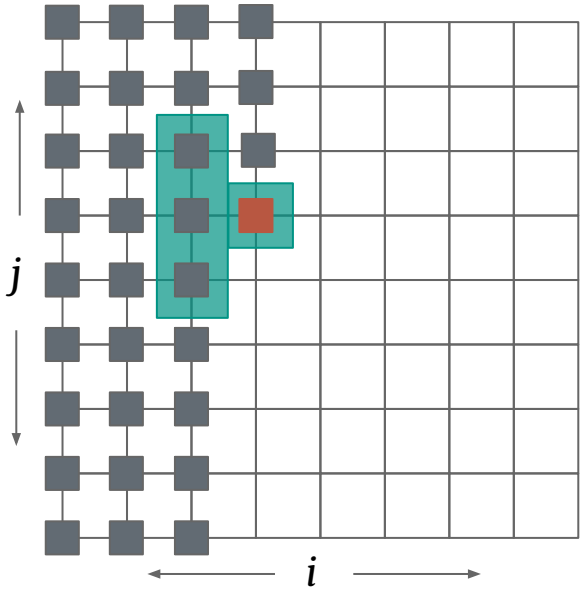
- Stimulus can be from neighboring cells
- Consider the cells in thin fiber, signal propagating via diffusion
- Each point in space has its own variables associated, only V is spatially dependent

$$I_{stim} = C_m \frac{dV}{dt} + I_{ion}$$

$$\frac{1}{R_a} \frac{\partial^2 V}{\partial x^2} + I_{stim} = C_m \frac{\partial V}{\partial t} + I_{ion}$$

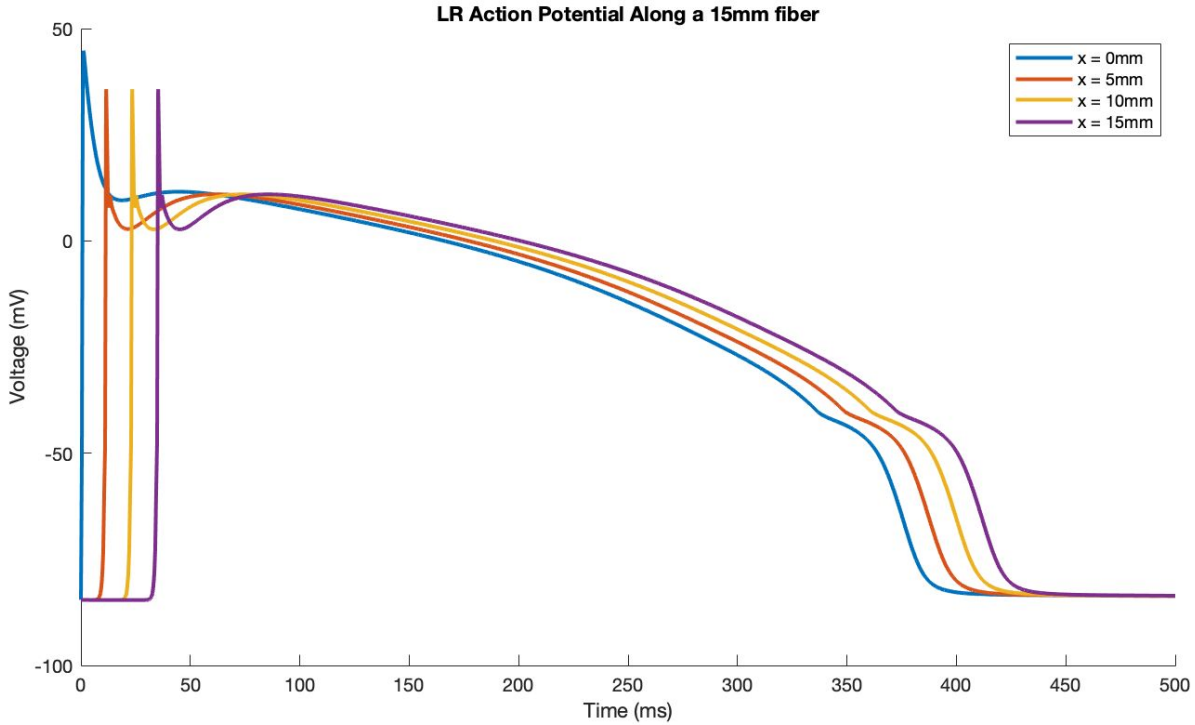
Central difference

$$V_{i+1}^{j} = V_i^j + \Delta t \left(\frac{1}{C_m}\right)\left(I_{stim} - I_{ion} + \frac{V_i^{j-1} - 2V_i^j + V_i^{j+1}}{R_a \Delta x^2}\right)$$

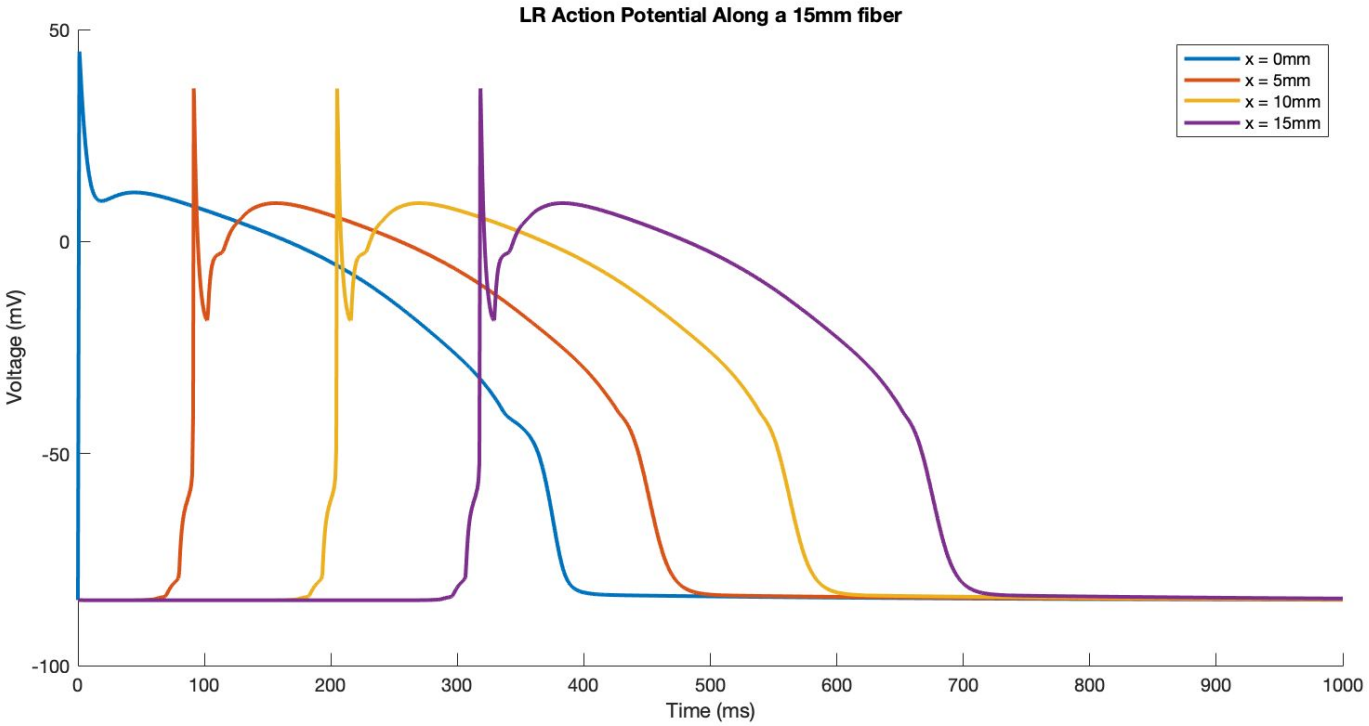


- Dimension and computational complexity
- Step sizes in t and x

Luo-Rudy PDE


LR Action Potential Along a 15mm fiber
x = 0mm
x = 5mm
x = 10mm
x = 15mm
Voltage (mV)
50
0
-50
-100
0
50
100
150
200
250
300
350
400
450
500
Time (ms)

Effects of higher resistance



Conclusion