Homework Assignment
Cell Membrane Simulations

Bioengineering 6000
Homework Assignment # 1
Simulation of Cardiac Action Potentials

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February 27, 2013

Question 1: All or Nothing?

- What is all or nothing?
  - Threshold
  - Only two states, all, or nothing, independent of variations other than threshold being reached.
- Does the model replicate this behavior?
- What consequences does the answer have on subsequent simulations?
  - Where to set threshold in later questions?

Probing the Stimulation Space

Stimulus Duration [ms]

Stimulus Amplitude [µA/cm²]

	1	2	4	6	8
5	No	No	No	No	Yes
10	No	No	No	No	Yes
15	No	No	No	No	Yes
20	No	No	No	No	Yes
25	No	No	Yes	Yes	Yes

Probing the Stimulation Space

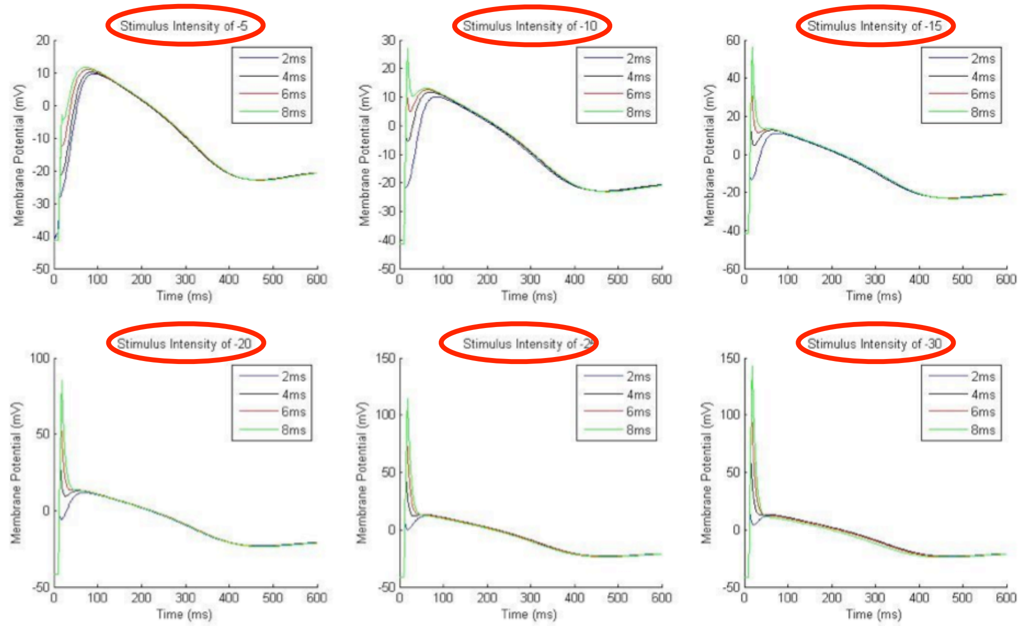
Stimulus Duration [ms]

Stimulus Amplitude [µA/cm²]

	1	2	4	6	8
5	No	No	No	No	Yes
10	No	No	No	No	Yes
15	No	No	No	No	Yes
20	No	No	No	No	Yes
25	No	No	Yes	Yes	Yes

Question 1: All or Nothing?

Probing the 2D simulation space

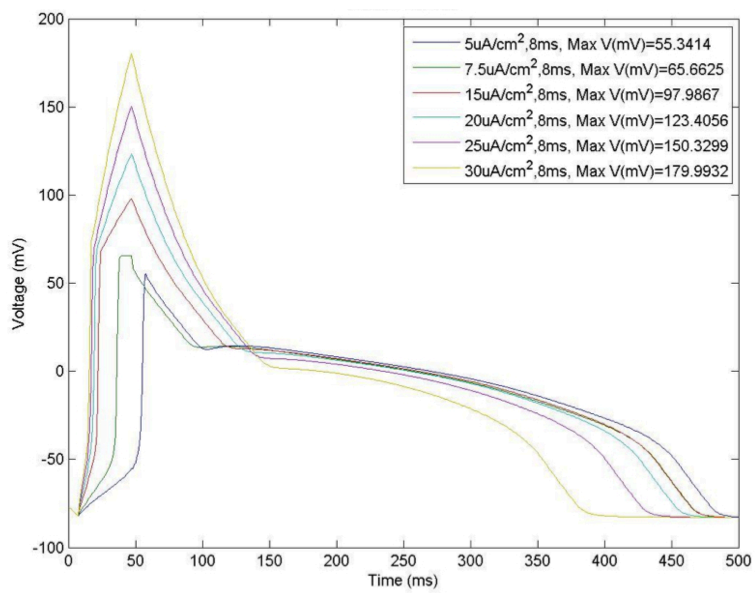


All or Nothing Example

Stimulus fixed at 8 ms
Varied in amplitude

The Problem?

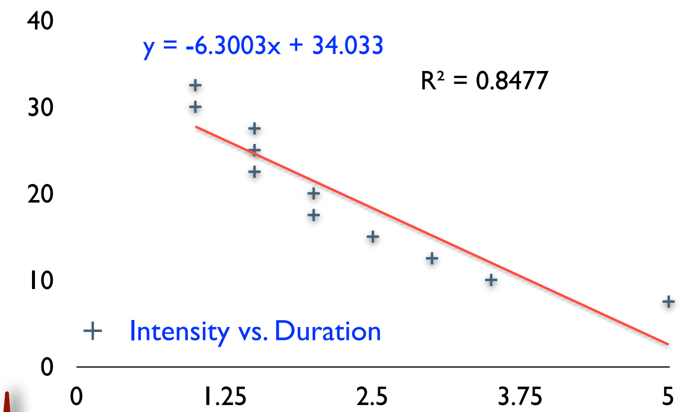
Stimulus carries over to the response of the membrane; it is too long.



Question #1: Cell Stimulation

$$R^2 = 0.85$$

$$y = -6.3x + 34.0$$

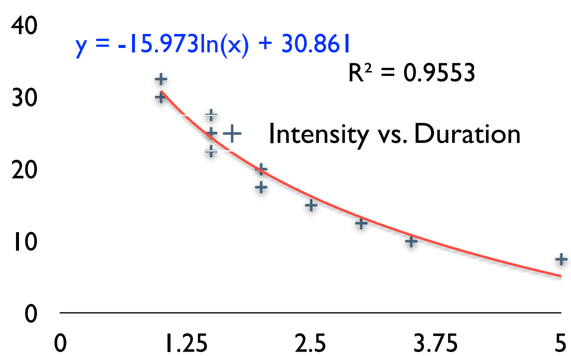


I_{th} (μA/cm^2)	ΔT_{th} (ms)	$1/\Delta T_{th}$
32.5	1	1.0
30	1	1.0
27.5	1.5	0.7
25	1.5	0.7
22.5	1.5	0.7
20	2	0.5
17.5	2	0.5
15	2.5	0.4
12.5	3	0.3
10	3.5	0.3
7.5	5	0.2

Question #1: Cell Stimulation

$$R^2 = 0.96$$

$$y = -16\ ln(x) + 30.86$$



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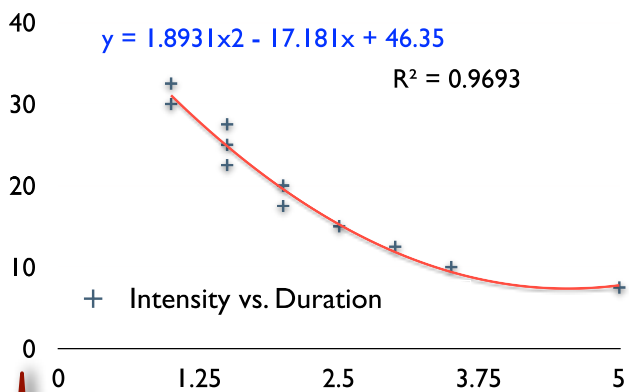
12.5	3	0.3
10	3.5	0.3
7.5	5	0.2

Question #1: Cell Stimulation

$$R^2 = 0.97$$

$$y = 1.89x^2 - 17.2x + 46.4$$



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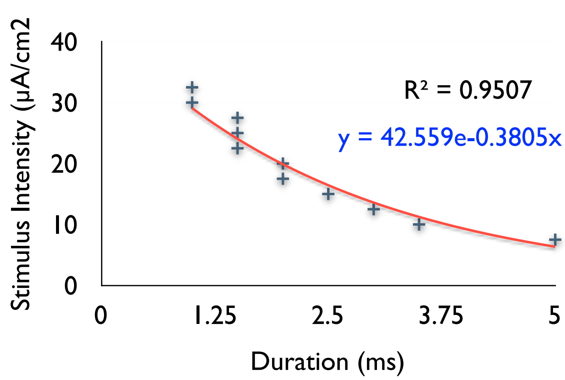
Question #1: Cell Stimulation

$$R^2 = 0.95$$

$$y = 42.6e^{-0.38}x$$



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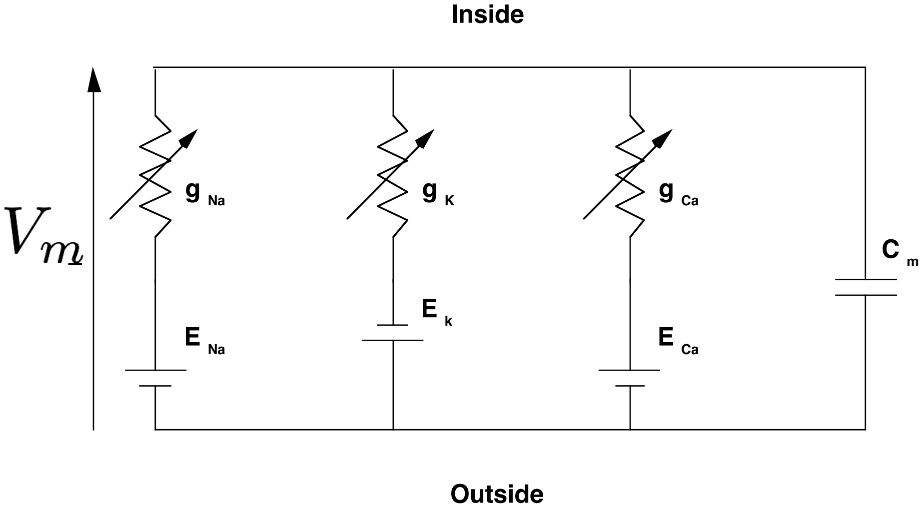
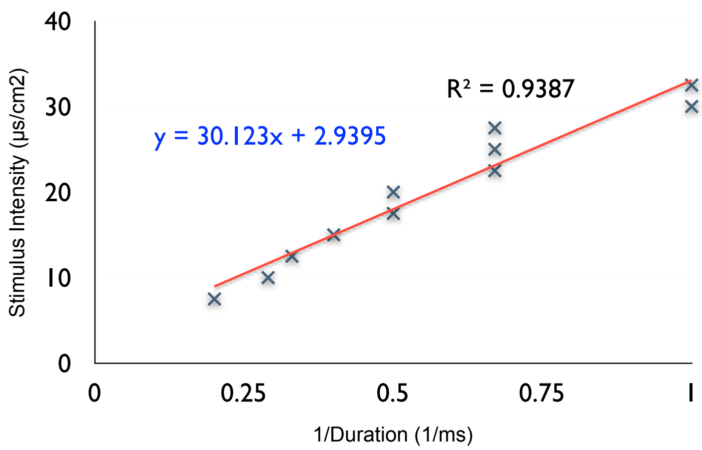
Membrane Voltage



Think Charge!

$$I_C = -C_m \frac{dV}{dt} \qquad V_m = \frac{Q}{C_m}$$

Question #1: Cell Stimulation



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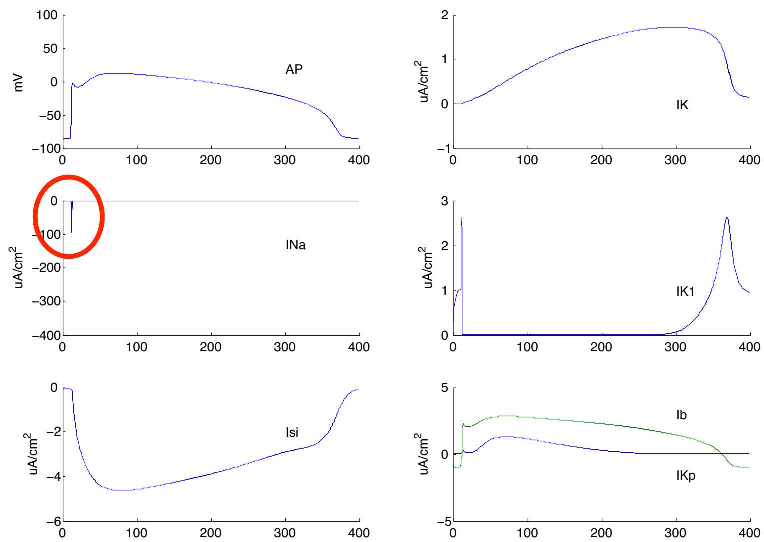
$$y = mx + b \qquad I_{th} = K(1/T_{th}) + I_0$$

$$K = I_{th} T_{th} = Q_{th}$$

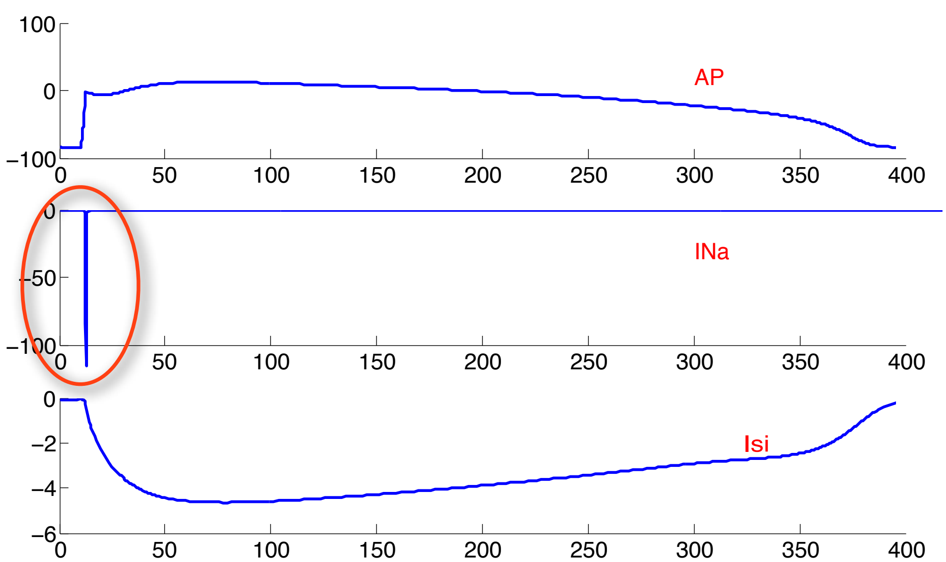
$$Q_{th} \approx 30\ \mathrm{nC/cm^2}$$

Question 2: Effect of $[Na^+]_e$

- Interpretation of low $[Na^+]_e$
  - Think of driving force; even is concentration gradient eliminated potential gradient exists!
  - Hypothesis about ICa
  - Both hypotheses are easy to test with simulation



When in Doubt, Check the Simulation



Be Careful with Axes

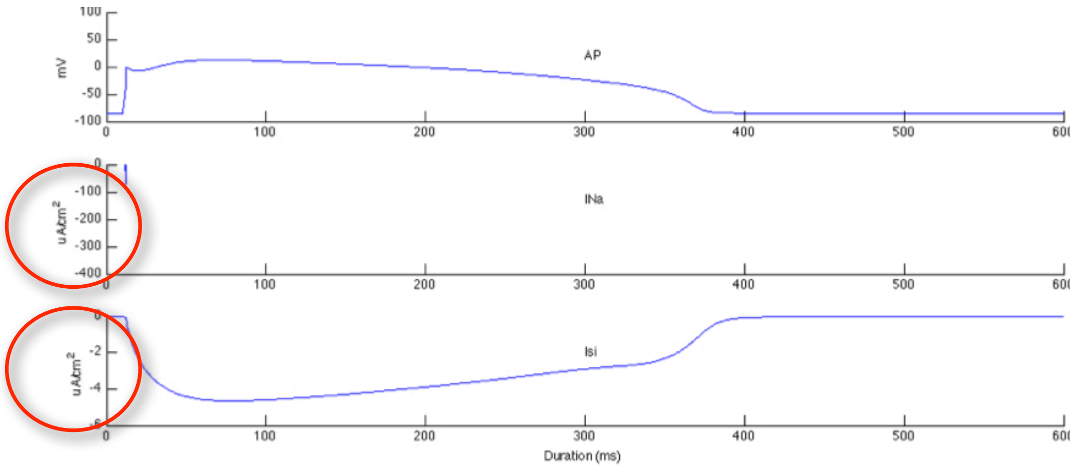


Figure 13: Action Potential when Sodium Gradient = 0. This figure also displays the sodium current and the calcium current.

The action potential did not disappear completely even when the sodium concentration gradient was near zero. In these instances, the calcium current provided most of the inward current, allowing the cell to still depolarize. The initial depolarization was likely due to a small sodium influx, but the majority of the depolarization was due to calcium. This was supported in

Scale is Essential

Scale is Essential

Creating Clear Graphs/Figures

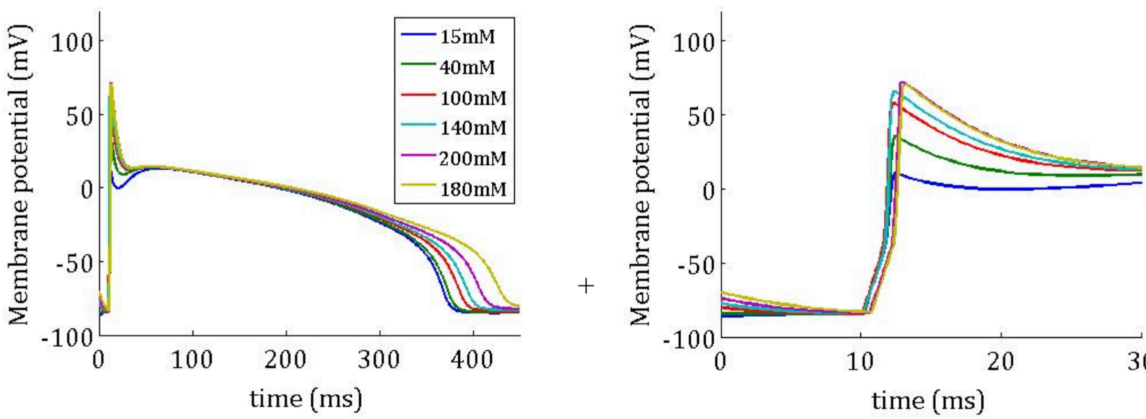
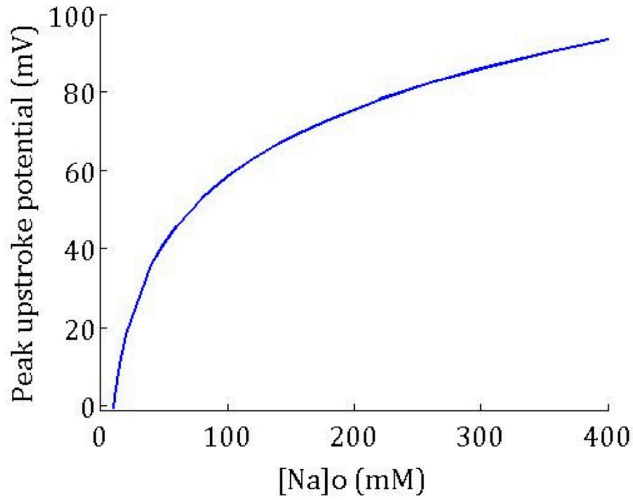


Figure 4 Graph of membrane potential against time; Extracellular sodium concentration was varied from 15 mM to 300 mM for a stimulus of amplitude -30 μA/cm² and duration 2 ms: (LEFT) Action potential over the entire duration (RIGHT) Closer view of the action potential upstroke

Generating Secondary Results



More Secondary Results

3.1 Effect of increased extracellular potassium concentration

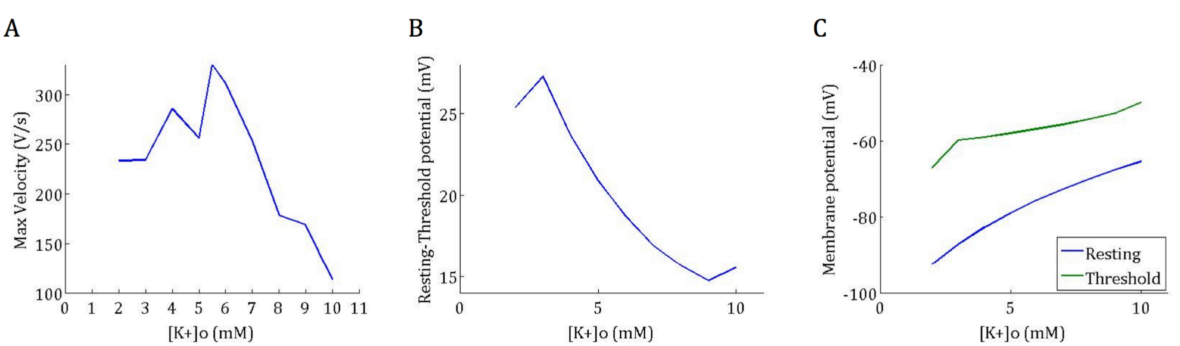
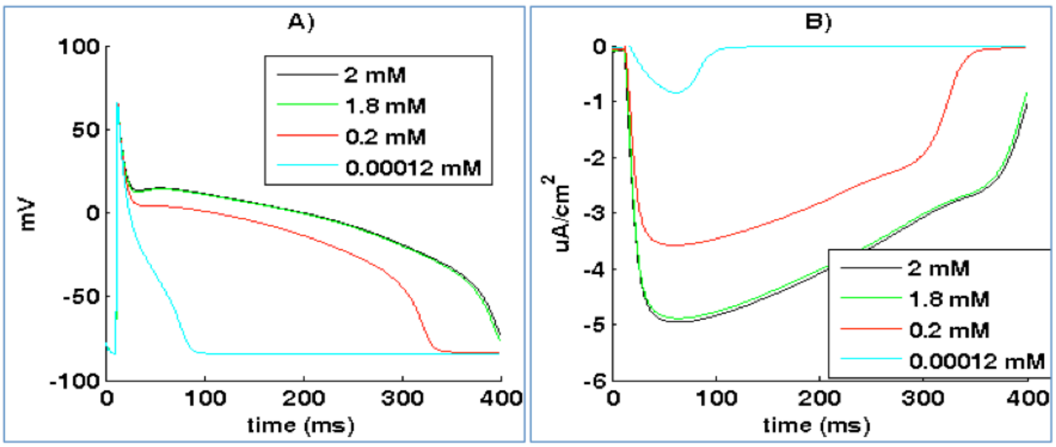


Figure 7 (A) Max change in voltage during upstroke against [K+]o (B) Change in resting membrane potential and threshold potential with varying [K+]o (C) Difference between membrane potential and threshold potential with varying [K+]o

Question 3

- Question #3
  - Try to motivate with some physiology or pathophysiology
  - Examine all parameters to try and identify mechanisms
  - Use the simulations to explore mechanisms--they reveal the answers many times in a way the experiments cannot!!

E.g., Vary Ca^{+2} concentration



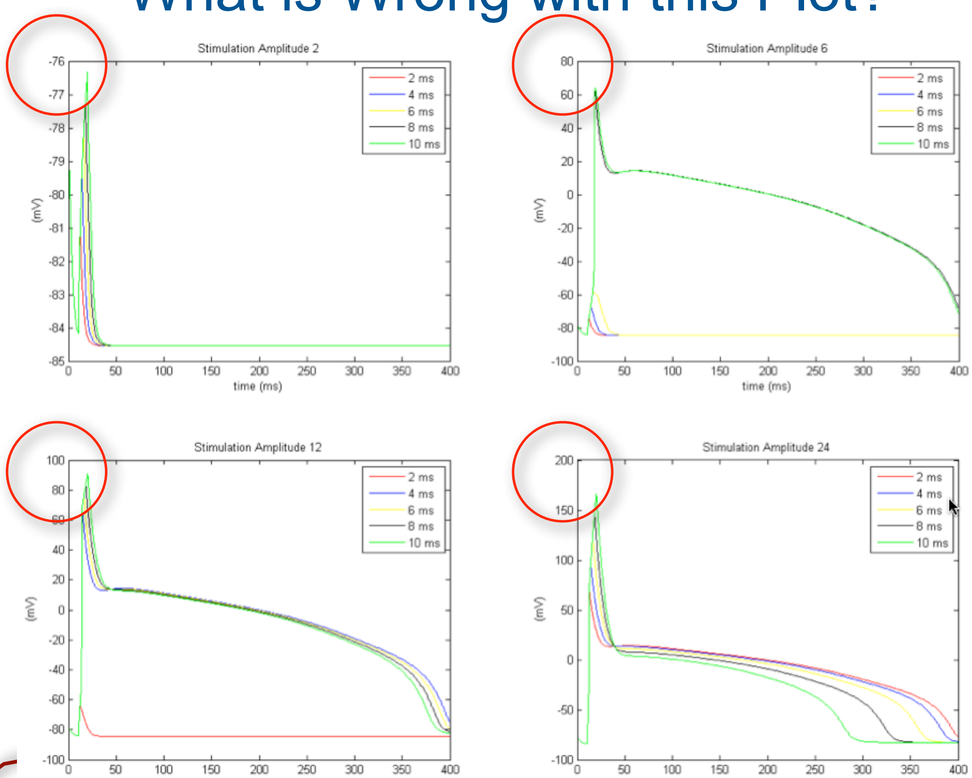
Cell Simulation: General I

- Organize simulations
  - Develop a strategy to answer the question
  - Vary as few parameters at a time as possible
  - Use reasonable (physiological) ranges of values
  - Examine the relevant parameters (often good to start by looking at all and identify relevant ones)
- Develop second order results where appropriate
  - e.g., plot of stimulus duration vs. stimulus
  - e.g., APD vs concentration
- Use results of analysis to motivate more simulations
  - Use to uncover mechanisms

Cell Simulation: General II

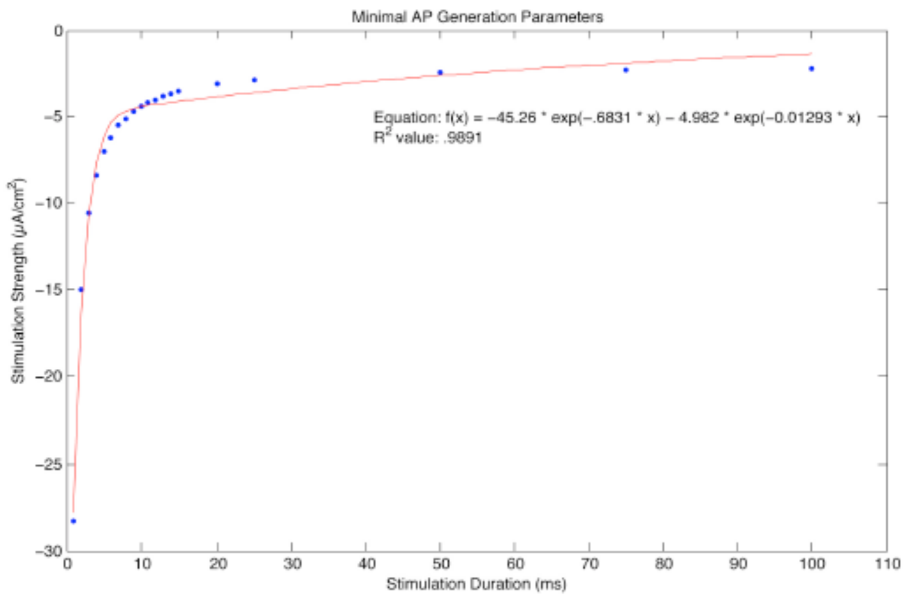
- Organization of report
  - Mimic the flow of the questions and answer all parts
- Plots and graphs
  - Include axes with labels
  - Include legends
  - Include concise captions
  - Export figures rather than screen capture
  - Embed all figures into the running text
- Text
  - Use past tense to report all methods and results
  - Adopt formal scientific prose style
  - Strive for concise, clear, accurate descriptions
- Use tables to show sets of results

What is Wrong with this Plot?



Homework: AP Simulation
Bioengineering 6000 CV Physiology

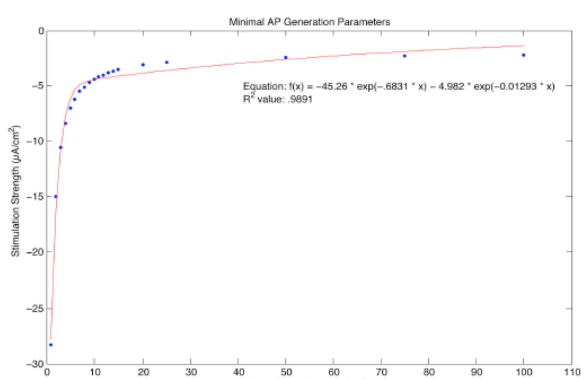
And this one...



Pixelated, especially text

And this one...

In this part of the assignment, I ~~am looking~~ at various combinations of current strength and amplitude that barely elicit a normal action potential. By tabulating numerous pairs of these parameters, it is possible to create a graph that shows the minimum requirements for an action potential. This graph is generated in Figure 2 and the combination of values are shown in Table 1.



Rule of thumb: Figure fonts should be approximately the same as surrounding text.

And one more...

No titles for figures

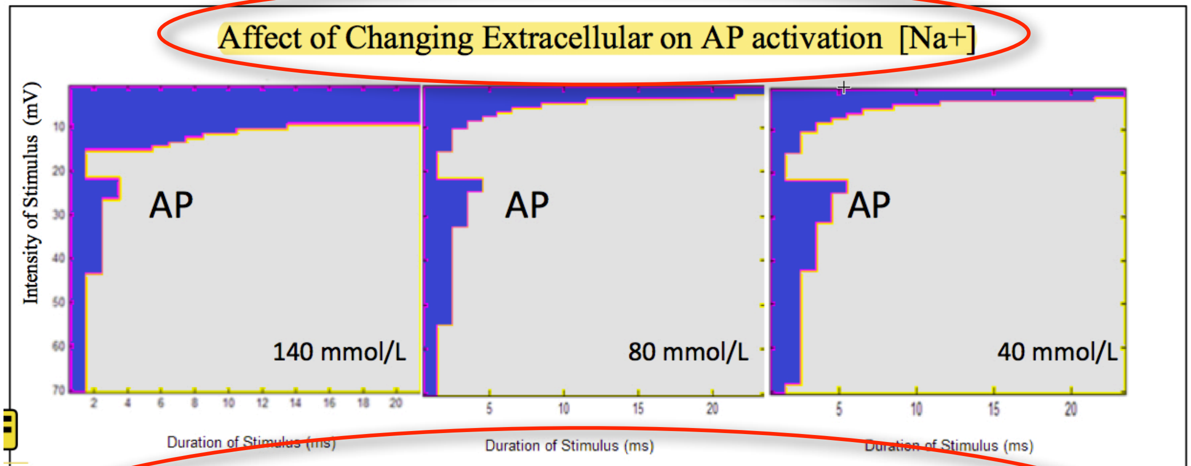
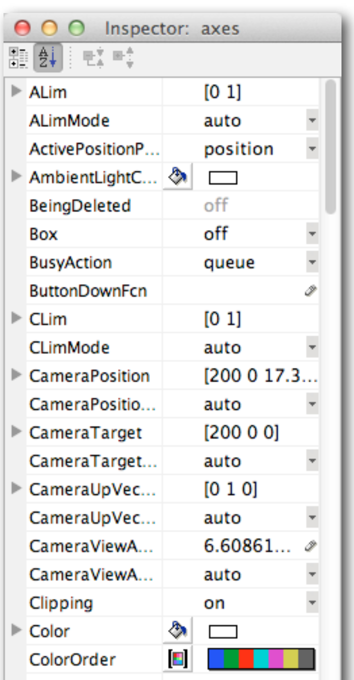
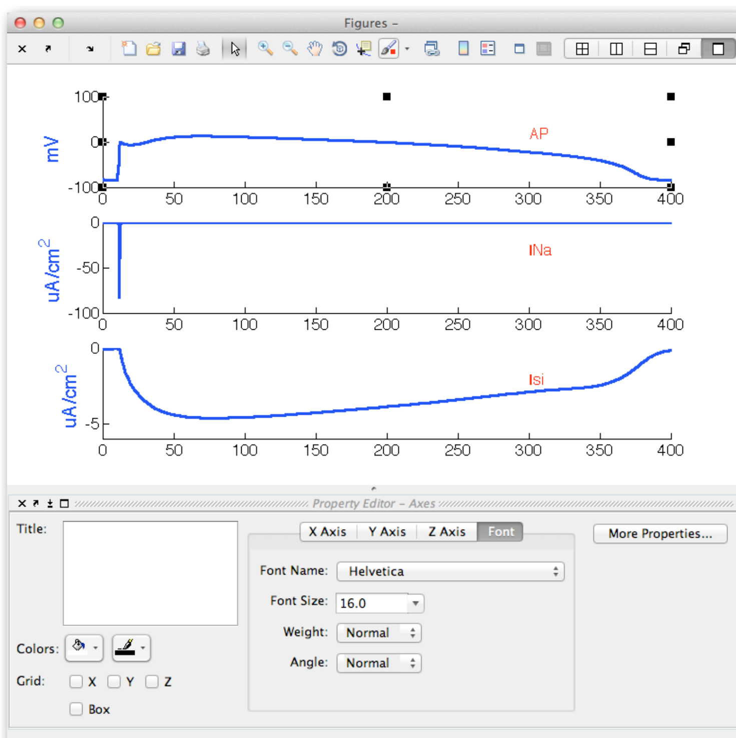


Figure 4: Reduction of Sodium Concentration. ****Note different hash marks on x-axis.** Reduction of extracellular sodium concentrations from 140 mmol/L → 80 mmol/L → 40 mmol/L showed decreased time of stimulus to AP at lower applied intensities due to increased relative opposing effect of Potassium on the gradient, as well as an increased effect of higher stimuli at smaller durations of time due to the gap in the gradient caused by decreased sodium. In the scope of this general broad overview, Calcium remained relatively unaffected.

Caption should not contain interpretation.

Mastering MATLAB Plots





Including Only What is Useful

Replace all this

Include only What you Refer To!

with this!