PROPAGATION OF NEURONAL ELECTRICAL ACTIVITY

INTRODUCTION

The propagation of bioelectricity within a neuron occurs both passively and actively. Propagation and integration of synaptic inputs along the dendritic tree is primarily passive, while action potentials are transmitted actively along axons. The passive resistive and capacitive properties of neuronal membranes have important effects on information processing within the nervous system. The focus of this lab is to study the ·effect of membrane properties and cable dimensions on signal transmission along dendritic and axonal cable models. There are two main parts to this lab. These are as follows:

I) Passive Spread
   A. The effect of cable discretization.
   B. The effect of dendritic cable diameter.
   C. Spatial and temporal summation of synaptic inputs.

II) Active Spread
   A. The effect of axonal cable diameter on propagation velocity.
   B. Excitability and refractoriness of axonal cables.

Specific sections for the lab report are marked with the  symbol.

BACKGROUND

The Model Neuron

The model cell used in this lab has three distinct components: a) the soma, a single spherical compartment with active membrane properties, b) the axon, a small diameter cable with active membrane properties similar to those of the soma, and c) the dendritic cable, a large diameter cable representing the cells dendritic tree with passive RC membrane properties. Figure lA is a sketch of a typical neuron with axon, soma and dendrites. The simplified cable model to be used in this lab is shown in Figure lB.

Rall's Cable Model

The Rall cable model reduces a complex, branching dendritic tree structure to a single equivalent cylinder. Each branch of the dendritic tree behaves like a cylinder with resistance values along its length (axial resistance), resistance across its thickness (membrane resistance), and capacitance values across its thickness (membrane capacitance).

In the cable model, in addition to length *"l"* and radius *"a",* the equivalent dendritic cylinder has the additional parameters – axial resistance, membrane resistance, and membrane capacitance. Specific resistances and capacitance represent the parameters of one unit area of membrane. However, frequently

in the cable model resistances and capacitance per unit length are more useful, since axons and dendrites can have long stretches of cable of the same diameter. The table below demonstrates the different resistances and capacitances, as well as their units. Note the upper and lower case of both the R/C as well as the subscript. Also, take a minute to make sure you understand the units of resistance/capacitance.

$$\lambda = \left(\frac{R_M . d}{4R_a}\right)^{0.5}$$

	Axial Resistance	**Membrane Resistance**	**Membrane Capacitance**
Specific	R_i^* (Ω*cm)	R_m (kΩ*cm^2)	C_m (μF/cm^2)
Unit length	$r_i = R_i/\pi a^2$ (Ω/cm)	$r_m = R_m/2\pi a$ (kΩ*cm)	$c_m = C_m * 2\pi a$ (μF/cm)
Total	$R_A^* = r_i l$ (Ω)	$R_M = r_m/l$ (kΩ)	$C_M = c_m l$ (μF)

*Generally, R_A refers to the total/lumped axial resistance, while R_i is the specific axial resistance.

In the GUI used for this lab, however, R_a is used to denote specific axial resistance.

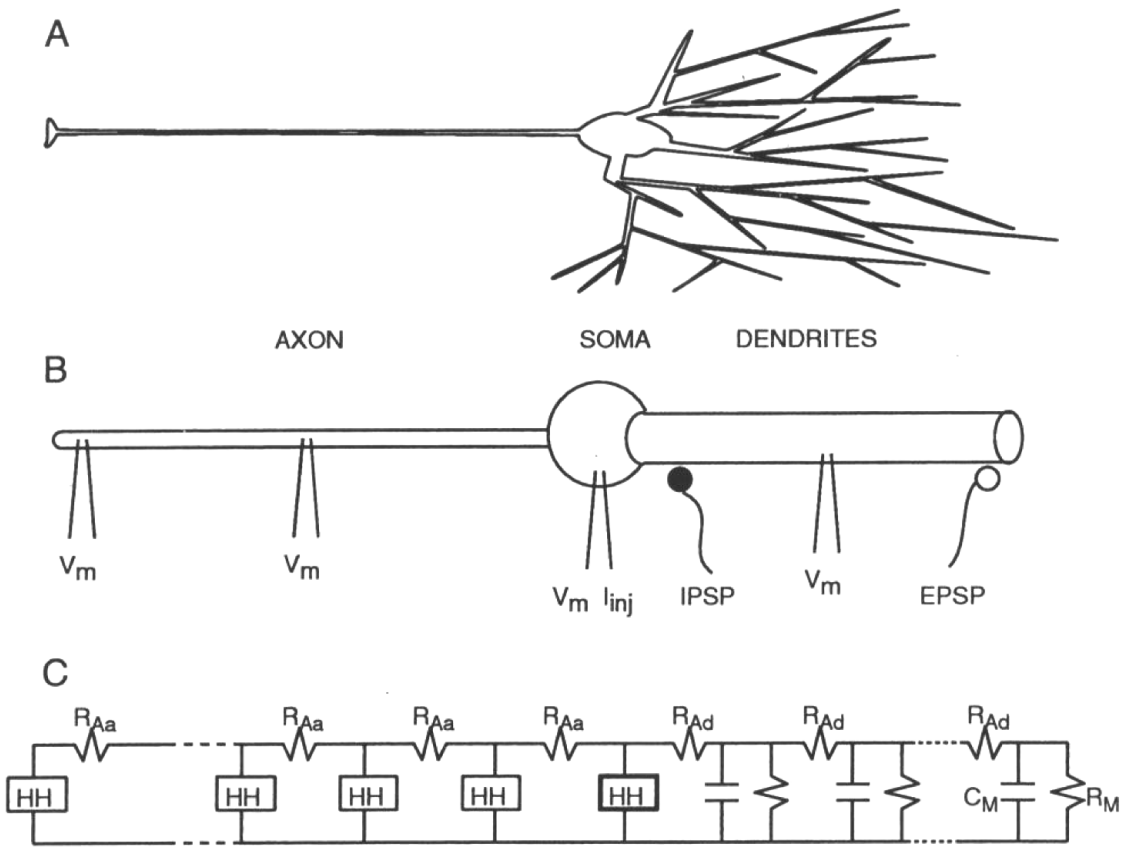


Figure 1: The model neuron. A) A typical morphology showing dendritic tree, soma, and axon. B) The simplified cylindrical model of the cell with dendrites replaced by an equivalent cylinder, the soma represented as an equipotential sphere, and the axon as a long, small diameter cylinder. Also shown are typical recording sites (V_m), the somatic current injection site (I_{inj}), and both inhibitory and excitatory synaptic inputs to the dendrites. C) The discretized ladder network used to model the cell. The dendritic cable is passive, with lumped parameters: membrane capacitance, C_M, membrane resistance, R_M, and axial resistance, R_{Ad}. The axonal cable is active, with each membrane patch represented by the Hodgkin-Huxley (HH) model and the lumped axial resistance of the axon (R_{Aa}).

The Compartmental Model

An alternate approach to modeling the behavior of the dendritic cable is to divide it up into compartments having lumped values of resistance and capacitance instead of distributed ones. This one dimensional representation of the cable is valid if one assumes that all current flow is axially symmetric and that only axial current flows in the intracellular and extracellular space. The one-dimensional discretized model of the cell is shown in Figure lC.

The values of R_A, R_M, and C_M (note capital letters with capital subscripts for lumped parameters) depend on the dimensions of the cable as seen in the table above; where l is the length of each compartment.

GETTING STARTED

Running the program

The lab will run in the GUI created for the MATLAB environment.

Linux:

To launch MATLAB from your terminal, run the command "*matlab -nodesktop -nosplash*". Once MATLAB loads in the terminal, change the directory by running "*cd /n/share/copy/ece445f/Prop_demo*", then run "neurocal":

```
[grigorov@p6 ~]$ matlab -nodesktop -nosplash

                            < M A T L A B (R) >
                  Copyright 1984-2017 The MathWorks, Inc.
                   R2017a (9.2.0.538062) 64-bit (glnxa64)
                             February 23, 2017


To get started, type one of these: helpwin, helpdesk, or demo.
For product information, visit www.mathworks.com.

>> cd /n/share/copy/ece445f/Prop_demo
>> neurocal
```

You should see the GUI like in Figure 2.

Windows:

1- Open MATLAB

2- Open '*S:/BME445/Source/Lab4'* by selecting "File" icon

3- Type neurocal in command window

<u>Important notes</u>

- In the GUI, click OK to save the parameter changes, and Apply to run the simulation.
- The resting membrane voltage for this lab is set at -60 mV.
- Both 3D and 2D graphing capabilities are available for this lab under the "Graph" menu. Note that 3D graphing works only when more than one compartment is present.
- Some help in running the GUI is available by clicking the Help menu.

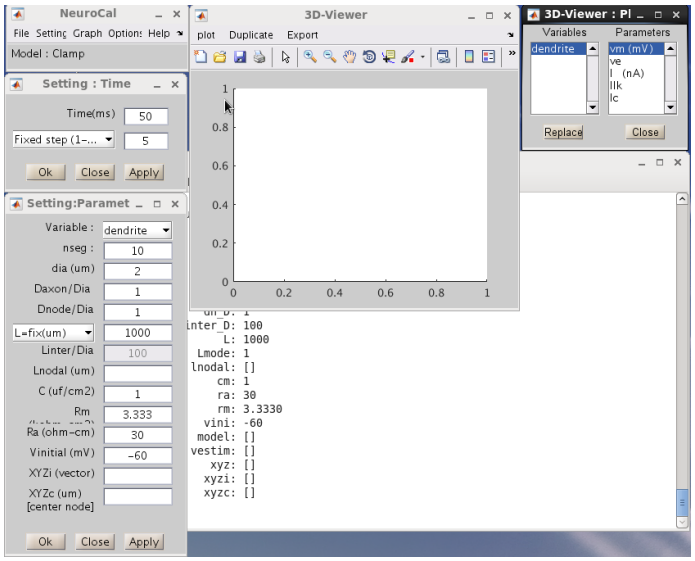


Figure 2. Starting GUI for the Propagation Lab

EXPERIMENTS

PASSIVE SPREAD

Space and Time Constants

The space constant λ and the membrane time constant τ_m characterize the dendritic cable equation. If *Clamp.m* model is not automatically loaded, load it from the *Model* directory using "File->Open model".

1. Measuring space constant in a time clamp mode. With at least 10 compartments inject a hyperpolarizing current pulse of -0.1 nA into the end of the **dendritic** cable (position 1). Set the duration of the pulse to be long enough that the cable attains a steady state voltage distribution. Compute the measured λ and compare with its theoretical value. How does increasing the number of compartments change the measured λ.

   Hint: If you are not sure how to find measured λ, consider what the space constant represents, and how it can be analogous to a time constant.

2. Measuring time constant in a space clamp mode. In space clamp mode, the same current is injected into all **dendritic** compartments. In order to simulate it, set the number of compartments to 10 and inject -0.1 nA into all of them in the "Settings -> Intracellular Simulation". Using a short pulse input and observing the response at the end of the cable, compare the measured τ_m with its theoretical value.

Parameter	Measured	Theoretical
λ		
τ_m		

NOTE: For both λ and τ_m, be sure to provide calculations and justification for measured and theoretical results

Effect of Dendritic Cable Discretization

Load *Simple_Neuron.m* model consisting of a single somatic compartment and a single dendritic compartment with length lmm.

1. Inject a current pulse (-lnA, 0.5ms) into the **soma** and investigate the effect that cable discretization has on the simulation results. Adjust the number of **dendritic** compartments and run the simulation for at least 1, 5, 10, and 20 compartments. How many compartments are required before the effect of discretization becomes negligible?

Hint: Compare what you observe at different compartments with your expectations of what should occur in a dendrite.

Effect of Dendritic Cable Diameter

Using *Simple_Neuron.m* model with at least 20 **dendritic** compartments and -1 nA injection at the end of the **dendrite** answer the following:

1. What is the velocity of propagation in the cable (for the default diameter = 2μm)?
2. Measure the velocity of propagation for the following diameters. How do your measured velocities compare to the theoretical values?

Diameter d	Velocity of Propagation
0.0001 cm	
0.0003 cm	
0.0004 cm	

NOTE: As you might get somewhat different results depending on which compartments you choose for velocity calculation, be consistent in which ones you choose.

Spatial and Temporal Integration of Synaptic Inputs

In the following section, you will investigate the effect that changes in membrane resistance have on temporal and spatial summation of signals. Instead of using short pulse current injections into the dendrites, you will use a train of simulated synaptic current inputs, both excitatory and inhibitory post-synaptic potentials, applied to the **dendritic** cable.

Load *Synaptic_Integration.m* model that represents a train of EPSPs and run it.

1. Describe the voltage response at compartment 20 and at the soma. Is there evidence of synaptic integration? What are the voltage responses?

Site	Maximum Voltage (mV)	Steady State Voltage Amplitude Spread (mV and ms)
Compartment 20		
Soma		

2. Now alter the specific membrane resistance while retaining the same EPSP train. Study the

effect of dendritic membrane resistance on temporal and spatial summation of synaptic inputs by calculating the following:

Dendritic membrane resistance	Maximum Soma Voltage (mV)
Quarter default R_m	
Half default R_m	
Default R_m	
Double default R_m	
Quadruple default R_m	

3. For the same EPSP train, setting the R_m to default, find the minimum leakage conductance (gL) for soma which will result in an action potential at the soma for this EPSP frequency?
4. Load *Synaptic_Integration_2.m* model, which includes an IPSP. What is the effect of the new model on the response at the soma?

ACTIVE SPREAD

Effect of Axonal Cable Diameter on Propagation Velocity

Examine propagation along the axon. Load *Axon.m* model, set the axon diameter to 0.2 μm and inject a depolarizing current pulse into the **soma** of sufficient magnitude and duration to fire an action potential. Observe the propagation of the action potential along the axon.

1. What is the velocity of propagation along the axon?

2. What is the space constant of the axonal cable? Hint: Think carefully about this question
3. Vary the diameter of the axon and observe new velocities of propagation. Given the relationship $\theta = kd^n$ between velocity of propagation θ and axon diameter d, estimate values for k and n.

Myelinated Axon

Examine the effects of myelin sheath on the axon. Reset the parameters to default values (or reload the model) and set the following values (for explanation of values, see Appendix):

Daxon/Dia	0.6
Dnode/Dia	0.33
Lnodal	10

1. What happened to the velocity of propagation along the axon?
2. What happens if you reduce Lnodal to 1?
3. Are the results what you would expect? Why or why not?

Excitability and Refractoriness of Axonal Cables

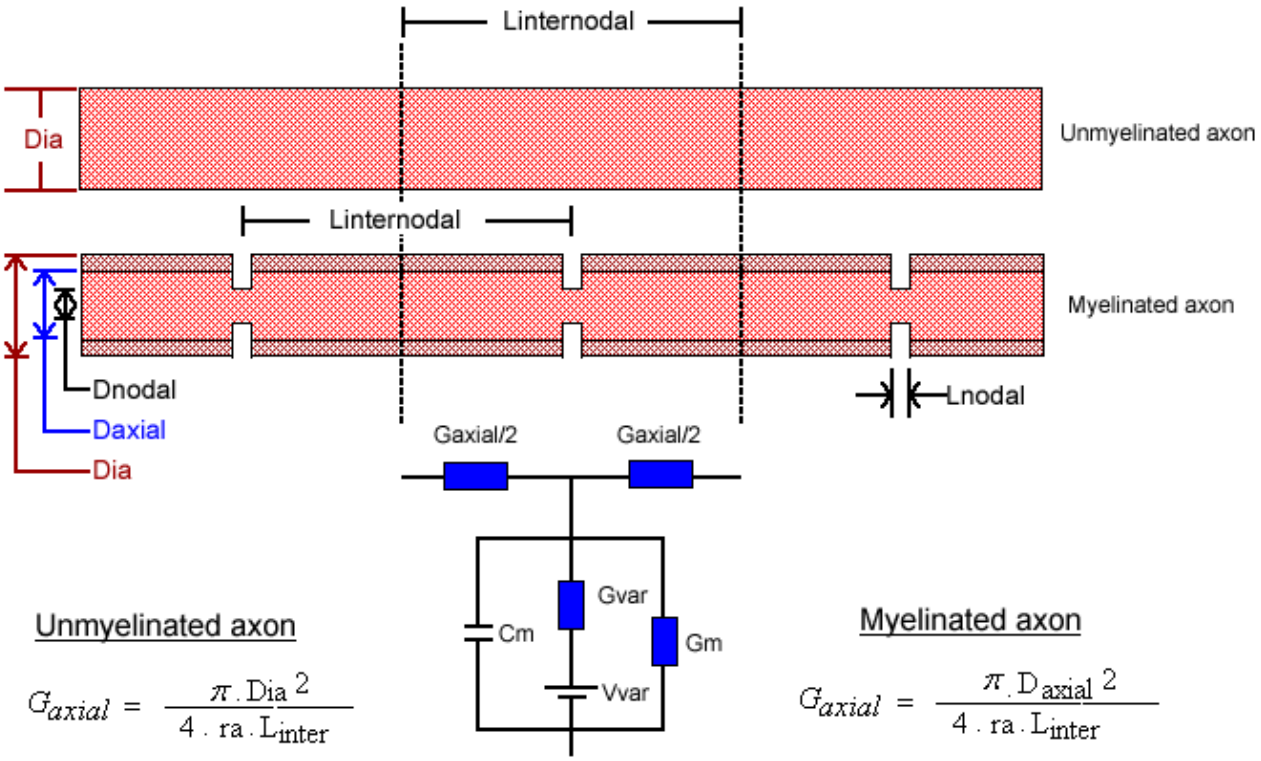
With the cell parameters reset to their default parameters, inject 1 nA current into the **midpoint** (0.5) of the axon. For easier observation, you can increase the total length of the axon, as well as the number of compartments.

1. How does the axon respond to this stimulation?
2. Account for the presence or absence of any reflection of the signal at the somatic end of the axonal cable.
3. Conclude by comparing active and passive bioelectrical signal propagation within neurons. What are the benefits of the two approaches and what are their respective roles in nervous system function?

Lab Write-up Format

title/date	Laboratory title and date the experiment was performed
name	Names of **everyone** in the laboratory group [one **(1)** lab report is to be submitted by each lab group]. Include full names and all student numbers.
purpose	One or two sentences identifying the objective or purpose of the investigation
results/discussion	All questions from the lab investigation and write-up section should be answered here. Any additional observations, analysis performed during the laboratory may be included. In addition, a simple one paragraph explanation of what you did and what you found out should be included at the end of the observations/discussion section. Write this paragraph as if you were explaining your results to someone who is not familiar with the laboratory topic (i.e. someone who hasn't taken this course before). **(maximum of 200 words for this paragraph).**
figures	Print out and include all figures and/or screen shots (All figures/screen shots requested in the lab investigation and write-up section must be included, along with any additional figures that may complement your observations/results).

APPENDIX:



Unmyelinated axon

$$G_{axial} = \frac{\pi \cdot Dia^{2}}{4 \cdot ra \cdot L_{inter}}$$

$$G_m = \frac{1}{r_m} \pi \cdot Dia \cdot L_{inter}$$

$$C_m = c_m \cdot \pi \cdot Dia \cdot L_{inter}$$

Myelinated axon

$$G_{axial} = \frac{\pi \cdot D_{axial}^{2}}{4 \cdot ra \cdot L_{inter}}$$

$$G_m = \frac{1}{r_m} \pi \cdot D_{nodal} \cdot L_{nodal}$$

$$C_m = c_m \cdot \pi \cdot D_{nodal} \cdot L_{nodal}$$

If Dnodal is not specified, Daxial will be used.
If Daxial is not specified , Dia will be used.
If Lnodal is not specified, Linter will be used.