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.

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 1A 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 1B.

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 addition to length "l" and radius "a", the equivalent dendritic cylinder has the specific parameters: axial resistance, $R_i[\Omega cm]$, membrane resistance, $R_m[\Omega cm^2]$, and membrane capacitance, $C_m[\mu F/cm^2]$. These passive electrical parameters may also be expressed as distributed (per unit

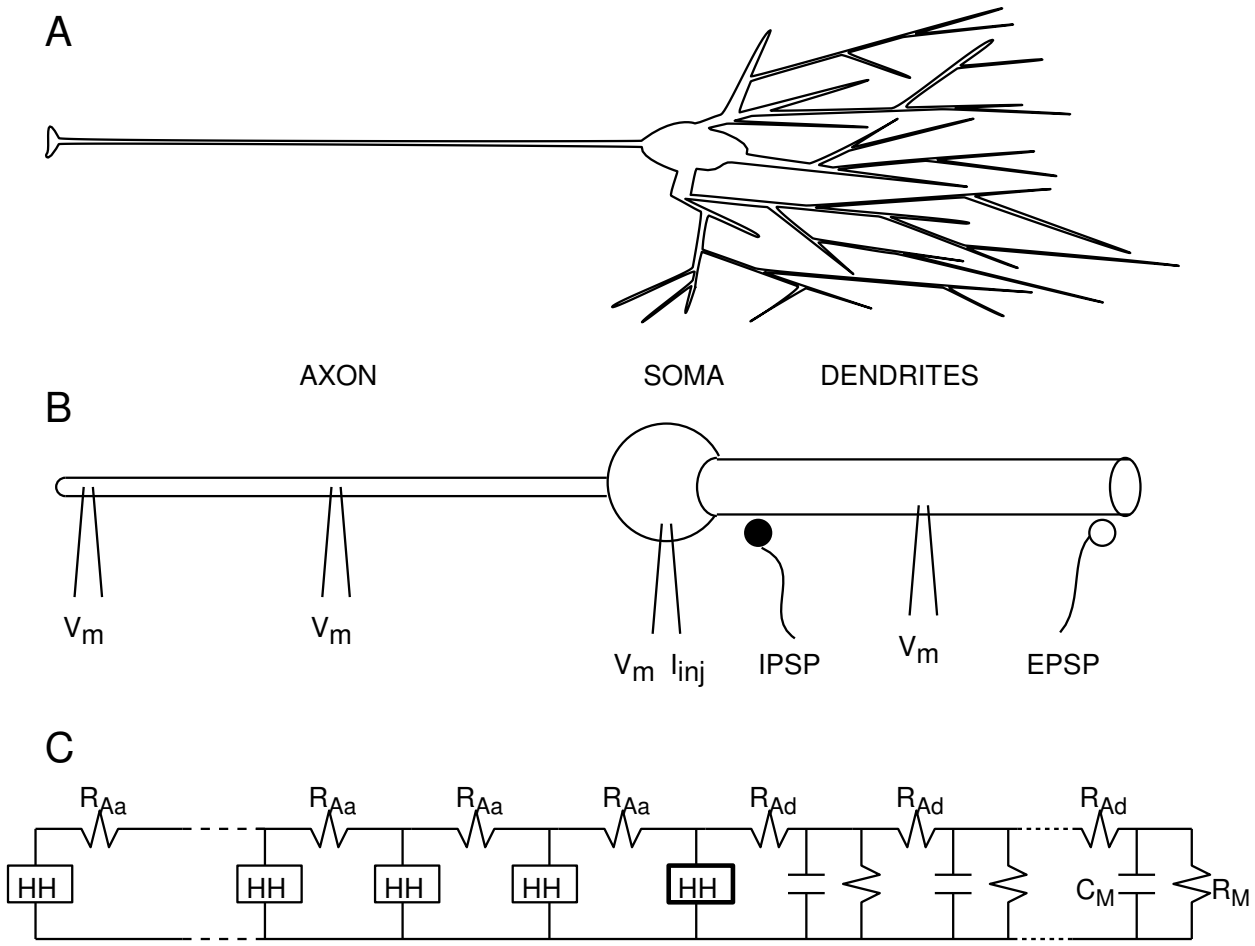

Figure 1: The model neuron. A) A typical morphology showing dendritic tree, soma, and axon. B) The simplified cylindrical model of the cell with dendrites replaced by an equivalent cylinder, the soma represented as an equipotential sphere, and the axon as a long, small diameter cylinder. Also shown are 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}).

length) values. Using upper case letters to denote specific parameters and lower case letters to denote per unit length values the three relationships are

$$\begin{aligned} r_i &= R_i/\pi a^2 \\ r_m &= R_m/2\pi a \\ c_m &= C_m 2\pi a \end{aligned}$$

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 1C.
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 and the compartments as follows:

$$\begin{aligned} R_A &= r_i l_c \\ R_M &= r_m/l_c \\ C_M &= c_m l_c \\ l_c &= l/N \end{aligned}$$

where l_c is the length of each compartment and N is the number of compartments.

GENESIS

Running the program

To run the program on a Sun Spark workstation, type the following commands:
host> **setenv LD_LIBRARY_PATH /local/X/lib**
host> **cd /local/packages/genesis2.0**
host> **cp .simrc ~**
host> **genesis**
genesis #0 >**cd Scripts/prop**
genesis #1 >**Prop**

Important notes

- after changing model parameters you *must* either hit return or click on the corresponding label.
- the RESET button must be clicked before each run.
- in order to start the simulation click on the STEP button.

EXPERIMENTS

I. Passive Spread

A. Effect of Dendritic Cable Discretization

The program starts up in the default configuration with a single somatic compartment and a single dendritic compartment with length 1mm.
Inject a current pulse (-1nA, 0.5ms) into the soma and investigate the effect that cable discretization has on the simulation results. With the *total cable length fixed* at 0.1cm, adjust the number of compartments and the length per compartment and run the simulation for 1, 10, 20, and 30 compartments. How many compartments are required before the effect of discretization becomes negligible?

B. The Effect Of Dendritic Cable Diameter

The space constant λ and the membrane time constant τ_m characterize the dendritic cable equation. With a 1mm (total length) cable consisting of at least 20 compartments (and using the default cable radius of 1μm) inject a hyperpolarizing current pulse into the end of the dendritic cable. Observe the signal at the injection site and one other point along the cable using time and space clamps respectively.

While injecting current only into the end of the cable, set the duration of the pulse to be long enough that the cable attains a steady state voltage distribution.

1. Under these steady state conditions compare the measured λ with its theoretical value.

In order to simulate a space clamp, type 'all' into the INJECT COMPARTMENT field to automatically inject the prescribed current pulse into all of the dendritic compartments. Reduce the input current to -0.1 nA for the space clamp.

2. Using a short pulse input in space clamp mode, and observing the response at the end of the cable, compare the measured τ_m with its theoretical value.

Return now to a -1nA short pulse injection into only the end compartment of the dendritic cylinder.

3. What is the velocity of propagation in the cable?

4. Chose three or four more diameter values and calculate the velocity of propagation for each diameter.

5. Given the relationship, $\theta \propto d^n$, where θ is the velocity of propagation and d is the diameter of the cable, estimate n.

C. 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 simulated synaptic current inputs applied to the dendritic cable.

First, disable the current injection (Change Current Injection Menu). Next reset all parameters to their default values and then add a 20 compartment, 0.1cm long dendritic cable.

Observe the effect of a train of Excitatory Post Synaptic Potentials (EPSP's) applied to the distal end (compartment 20) of the dendritic cylinder. In the Change Synaptic Current Menu, enable synaptic input 1 (leave the second disabled) and have it applied to compartment 20. Toggle the Single EPSP button to produce an EPSP train and, using a period of 2ms, run the simulation.

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

Now alter the specific membrane resistance. Observe the effect of quartering, halving, doubling, and quadrupling this parameter.

2. Describe the effect that membrane resistance has on temporal and spatial summation of synaptic inputs.

3. What is the minimum specific membrane resistance which will result in an action potential at the soma for this EPSP frequency?

Apply the IPSP resulting from synaptic input 2 onto compartment 2 (near the soma).

4. What is the effect of the IPSP on the response at the soma?

II. Active Spread

A. Effect of Axonal Cable Diameter on Propagation Velocity

Examine propagation along the axon. Disable all synaptic inputs to the dendritic cylinder and inject a depolarizing current pulse into the soma of sufficient magnitude and duration to fire an action potential. Display the axon plot and 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 signal traveling along the axon?

Increase the radius of the axon and observe the new velocity of propagation.

3. Determine the relationship between velocity of propagation and axon diameter.

B. Excitability and Refractoriness of Axonal Cables

With the cell parameters reset to their default parameters, disable current injection to the soma and activate axonal current injection. Inject a suprathreshold current into the midpoint of the axon.

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.

- Conclude by comparing active and passive signal propagation within neurons. What are the benefits of the two approaches and what are their respective roles in nervous system function?