Lab 2: NEURON Simulations

Introduction

This lab introduces the use of NEURON simulation software to model neuron activity. We will start by creating some simple single-compartment models, examine the effects of modifying model parameters, replicate results from a widely used neuron model, and finish by building a simplified neuron model of our own. This lab will provide you with a primer on how to use NEURON software and its potential applications.

Software

This lab must be completed using NEURON using Python. Unless you have it already installed in another format prior to coming to class, please use colab.research.google.com and the installation and import code from Lecture 2-1.

Part 1) Build a single-compartment neuron model

If you have never previously used NEURON software, please start by going through the following tutorial, which will familiarize you with the basic syntax of creating a single active segment and stimulating it to spike. You only need to go through plotting the voltages and saving a CSV file in Step 8.

Tutorial link: https://neuronsimulator.github.io/nrn/tutorials/scripting-neuron-basics.html

Part 2) Model the effects of axon diameter on action potential speed

Now let's use the tools from Part 1 to model an action potential traveling along two axons of varying diameter—one 10 um across, and the other 20 um. Make them both 5 mm long with at least 1000 compartments.

1. Start by calculating the length constant for each of these axons. Use $R_m = 40{,}000\ \Omega * cm^2$ and $R_a = 200\ \Omega * cm$. Recall the length constant equation:

$$\lambda = \sqrt{\frac{r_m}{r_i}} = \sqrt{\frac{aR_m}{2R_i}}$$

   where a is the radius of the axon. These length constants should give you an idea of what to expect in the subsequent simulations.

2. Create a stimulus at one end of each of the axons the axons as demonstrated in Part 1. Make sure to apply stimulation at an axon compartment at the '0' portion.
3. To enable illustrating the speed of the action potential along each axon in a single plot for both axons, it may be easiest to have each stimulus start at a different time.

4. To measure the speed of the action potential along the axons, we will need to observe voltage from two different points along two different axons. Figure out how to plot voltages in various sections over time.
5. Calculate the speed of an action potential along the lengths of the two different axons. For your report, create a figure with an interpretable legend illustrating the speed of both axons. I.e. it should show four action potentials where one of the axons should be propagating faster than the other.

Part 3) Build your own simplified neuron model

Due to the complexity of the Mainen neuron, it can be difficult to scale it to different sizes while maintaining key characteristics, like action potential shape. Here we will build a simplified neuron model that is more easily scalable in size for different simulations.

1. Start by creating the cell soma, dendrite, and axon. Parameters below:

	length (um)	diameter (um)	nseg
soma	24	21	100
dendrite	50	12	222
non-myelinated axon	16	1	100
myelinated axon	300	1	100
axon hillock	16	*	9

*Have the axon hillock change size in 9 steps starting with the diameter of the soma and decreasing to the diameter of the non-myelinated axon. I.e. create a funnel shape

Note: The last part of this exercise asks you to model neurons at half and twice the size of the original, so you may wish to use variables for these dimensions.

2. Insert passive properties and extracellular properties (‘h.pas’, ‘h.extracellular’) into all of these compartments. Insert active hh channels into all of these compartments other than the myelinated axon. Reduce the cm of the myelinated axon to 0.04.
3. Add a current stimulus to make the cell fire. If you can’t see your action potential, try to get your current to the point where it just achieves an action potential rather than dominates the plots.
4. Plot the membrane current for the middle segment (0.5) of the dendrite, soma, non-myelinated axon and myelinated axon. The membrane current can be found in the variable ‘_ref_i_membrane’. Calculate how much bigger the non-myelinated axon current is than the soma current at the negative peak of each.
5. Now make this model slightly more realistic by increasing the density of the ion channels (found in ‘gnabar’, ‘gkbar’) by a factor of 10 in the non-myelinated section of the axon. Note the new negative peak current.

Note: To change a distributed property such as ion channel density, you can use:

```
for seg in soma:
seg.hh.property=X
```

6. From the 0.5 compartment from the axon hillock, soma, myelinated axon, non-myelinated axon, and dendrite, plot each of the currents in these compartments for your final report. Include **two** graphs to see with and without the 10x channel increase at the non-myelinated axon.
7. To see the effects of cell size on recorded action potentials, scale the all of the lengths and diameters from part 1 by a factor of 0.5x and 2.0x. Each of these sizes will have a different threshold current required to make them just barely fire, and you want to be near that threshold to make sure you're only looking at the current intrinsic to the neuron. If you're right at threshold, it will take the AP a ms or two to get going. Observe the peak negative currents recorded from these 3 models.
8. Noting that the '_ref_i_membrane' is in mA/cm^2, convert this into actual mA, and note the difference in absolute current between the 3 different sized cells. Discuss what this means for extracellular recording in your report.

Part 4) Explore ModelDB

Spend a few minutes exploring ModelDB. In the discussion section of your Lab Report where you discuss what these techniques could be used for, include a few sentences describing one of the models in this database. Think about for example, what you could use in a class project (whether or not you actually intend to have a NEURON component).

Guidelines for Lab Report (on Labs 1 and 2 together)

Introduction: The introduction should be one paragraph long summarizing what detailed single neuron simulations can be used for (motivation), what data they draw upon from past experiments, and a brief summary of everything you will show in this lab report.

Methods: From Lab 2, there should be three methods paragraphs (and diagrams if you like) on:

1. Assumptions of the models used (i.e. what kind of channels/neurons are these)
2. What the parameters are for axon models
3. The structure of your simplified neuron and the experiments carried out with it

Include the code as an Appendix to your report. It's fine to add a geometrical picture if that's easier than words. Always say where you looked up a value, for example from the Mainen paper.

Other Methods from Lab 1 will also go into the methods section. Make it one cohesive report.

Results: You should include the following in your Results:

1. Plot the effects of axon diameter on action potential propagation, with quantitative descriptions. Describe what should happen in the text based on your calculation of the length constants.
2. Plot and explain the output of the simplified neuron at different points along the cell for the normal and 10x density of channels in the non-myelinated axon. Also, describe the effects of scaling the neuron's size on the membrane currents.

Include all figures produced by NEURON that could help explain results.

Discussion: Should be ~2 paragraphs long. Describe what you learned about axon propagation. Also, describe the likely effect of neuron size on the ability to record signals. Also, describe what you could use these models for in the future. Include a few sentences about something interesting you found in ModelDB.

The report (not including Appendix) should be no longer than 4 pages. Use 12 pt. font and 1.15-1.5 line spacing. If your text is over the 4-page limit with figures, you can move your figures to an appendix section that goes beyond the 4-page limit. However, any text that goes beyond this limit will not be graded, except for figures, figure titles (no captions), and your code.

Please upload your report to Canvas as **a single file** (pdf or docx).