Lab 4: Modeling neural recordings and stimulation

Introduction

In Labs 2 and 3, we used specialized software to model neural activity and current spread. To study neural interfaces, such as neural recordings and stimulation, these two types of models must be combined. By exporting currents from NEURON and K matrices from COMSOL, we can both incorporate neural currents and electrostatic models into a single model. At the end of this lab, you should be familiar with both analytical and computational approaches to solving this problem.

Software

This lab can be completed using MATLAB or Python, and also NEURON. Matlab has better signal processing tools, so please use Matlab by default (see the pink noise portion below) but Python is doable. These files will be provided in .mat and .csv format. You will also need the voltages you exported from Comsol in Part 2 of Lab 3.

Part 1) Analytical model of neural recording

An important question to ask about neural recordings is, "In what conditions should we be able to record an action potential?" How does distance from the neuron affect the recording? What about neuron size? Here, we'll create a simple model of neural recording outside of a single neuron.

Recall Cindy's favorite equation:

$$V_{ext} = \frac{I_0}{4\pi\sigma r}$$

By applying this equation to currents exported from NEURON, we can predict the voltage trace recorded by an electrode near the simulated neuron.

For this lab, we will be using the files currents_big and currents_small. These files are in the same format as the NEURON outputs from Lab 2.

1. Load currents_big. This file contains currents (in amps) from a NEURON simulation of an action potential from a layer V pyramidal neuron (which is often around 20 um in diameter). Each current is associated with a specific XYZ coordinate in space (in micrometers) indicating the part of the neuron that produced the current.
2. The axon hillock is located at the origin, with the soma and dendrite extending along the x-axis. Pick a point 50 um from the axon hillock, extending perpendicularly from the neuron's axis. (That is, don't pick a point inside the cell.)
3. Implement code for Cindy's favorite equation (above). Assume $\sigma = 0.3333\ S/m$. CHECK YOUR UNITS.

   Note: It will be helpful to write this step as a function of the form:

voltageTrace = calcVext(currentTrace, currentXYZ, electrodeXYZ)

You will need to reuse this calculation for several parts of this lab.

4. Now do this for every point along the neuron and use superposition of voltage to calculate the net voltage trace your chosen point would record from the whole neuron.
5. Repeat this process for points 100, 200, and 300 um from the axon hillock. Again, make sure your points extend radially away from the axis of the neuron.
6. At what distance would an action potential be no longer detectable above a $10\ \mu V_{pk-pk}$ noise floor?
7. Repeat 2-6 for currents in currents_small. The currents in this file might be closer to what we would expect from a small layer II neuron in cortex.

Part 2) Simulate electrode recording of multiple neurons

Real-world neural recordings usually don't occur in noise-free environments with just one neuron in the vicinity. Here, we will extend the model from Part 1 to a multi-neuron environment with tissue injury along with thermal and biological noise.

1. Using the coordinates and currents from currents_big, randomly distribute 10 neurons within a 100 um cube centered on a recording site. Just the axon hillocks need to be within the cube; don't worry if part of the dendrite or axon extends beyond. Serendipitously, pyramidal neurons in the cortex naturally tend to point in the same direction, so there's no need to randomize orientation.
2. Using the waveform from currents_big, generate a 2-50 Hz fixed pattern for each neuron that is one second long. I.e. pick an integer between 2 and 50 and put that many equally spaced spikes in a 1 second time bin. Assume $dt = 0.025\ ms$ in the current files.

   Note: This must be programmed in a way such that 1) action potentials from a single neuron do not overlap; and 2) action potentials from multiple neurons do not happen at *exactly* the same time. A handy way to do this is to randomize the time between spikes for each neuron.

3. In the same way as you did in Part 1, calculate the net potential recorded at the electrode, this time accounting for all ten neurons with their variable firing patterns.
4. Add $10\ \mu V_{pk-pk}$ pink noise to the recorded potential, using the following lines of code and scaling it appropriately:

   ```
   %Matlab Implementation
   cn = dsp.ColoredNoise('Color','pink','SamplesPerFrame',tTot/dt);
   recordedNoise = cn();
   ```

   Note: If you wish to do this in Python, there does appear to be a 'colorednoise' library (pip install colored noise, import colorednoise as cn). This produces a nice looking noise signal, but you're on your own with syntax.

Note: Real thermal noise is not uniformly distributed over all frequencies, like white noise, which is why we use pink noise here. For more detail on thermal noise in neural recordings, read Lempka et al, 2011.

5. Oftentimes, electrode insertion results in a “dead zone” immediately around the electrode. Repeat this process, but exclude neurons that are within 25 um of the electrode.
6. Plot the resulting voltage traces with and without the “dead zone” in 2 subplots of the same figure. There should be many fewer large spikes when there is a dead zone.

Part 3) Model neural recording with a variable conductivity environment

In Parts 1 and 2, we used an analytical approach to calculate voltage recordings of neural firing. Complex conductivity environments, however, can make the calculation prohibitively complex. Here, we will approach the same problem with a computational approach and compare differences in output.

In Lab 3, Part 2, you generated a matrix of voltages in space that result from a 1 A current at the origin of a variable conductivity environment. We will use it as a K matrix to transform currents at a distance to voltages at the electrode. Recall the relationship described by the K matrix:

$$V_{ext}(x, y, z) = I_0(x, y, z) \times K(x, y, z)$$

1. Extract your K matrix from the COMSOL output into MATLAB or Python. CHECK YOUR UNITS.
2. Using currents and coordinates from currents_big, place a cell with the hillock 50 um from the origin, in the Y or Z direction.
3. Since the coordinates of the currents and the K matrix do not line up exactly, you will have to interpolate the coordinates of one to match the others. MATLAB’s griddata() function can be helpful for this.
4. Use your K matrix to model the extracellular waveform recorded 50 um from the axon hillock.
5. Compare to your results from Part 1. Does it make sense with respect to what was found in Moffitt and McIntyre, 2005 about the importance of the different conductivity regions?

Part 4) Model neural stimulation

In Part 1-3, we focused on simulations of neural recording. We now turn our attention to simulations of neural *stimulation*. To carry out this simulation, we will use the simple 20-um axon you created in Lab 2, Part 2.

1. Using your NEURON model, determine the threshold current necessary to trigger an action potential midway along the axon.
2. Assume that an electrode tip is 1 mm away from the middle of the axon. Using MATLAB, calculate the external voltage seen by every compartment along the axon, if the electrode were to inject +1 mA of current. Make your axon 5 mm in total length. Plot the results.

3. Using the equation described by Warman, Grill, and Durand (1992), calculate the equivalent intracellular current that comes from the injected extracellular current. Assume $g_a = 3 \times 10^{-5}\ S$.
4. Determine the minimum current necessary to activate an axon 1 mm away.

Guidelines for Lab Report (on Labs 3 and 4 together)

Introduction: The introduction should be one paragraph long summarizing the motivation for electrostatic models, what data they draw upon from past experiments, and a brief summary of everything you will show in this lab report.

Methods: From Lab 4, there should be methods paragraphs (and diagrams where necessary) on:

1. Assumptions of the models used (e.g. is this simplified vs reality?)
2. How the models were set up and arranged
3. The different things that were varied in the recording model (adding cells, cell size, noise, K matrix, etc)

Include the code as an Appendix to your report. Cite sources for any values used in your models.

Results: You should include the following in your Results:

1. Plots from big currents and small currents from Part 1, at distances of 50, 100, 200, 300 um (two plots total).
2. Plot neural traces from Part 2 (with/without "dead zone").
3. Plot your modelled voltage waveform from Part 3.
4. Include the minimum current you calculated in Part 4
5. Describe the effects of increasing model complexity and any implications for electrophysiological recordings and deep brain stimulation.

Include any other figures produced that could help explain and illustrate your findings.

Discussion: Should be ~2 paragraphs long describing whether your results match the literature discussed in lecture, and what you could use these models for in the future.

This report will be combined with Lab 3, to create one cohesive report. 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.

Please upload your report to Canvas.