Homework Assignment 3

*** Due Thursday 10/30/14 by noon on Sakai under HW3. Upload your submission as a Word document. ***

Please reaffirm the Duke Community Standard at the top of your assignment:
"I have adhered to the Duke Community Standard in completing this assignment." [Electronic Student Signature]

Please explain your methods, show all work, explain your results, include units, and label your axes. Upload your .hoc and .m files with clear filenames.

The objective of this assignment is to determine the effect of electrode geometry on the recorded compound nerve action potential (CNAP) and electroneurographic (ENG) signals. You are using a tripolar recording electrode with interelectrode spacing of *k* and the first and third (end) electrodes shorted together (averages potentials at these points) and acting as the reference. You will construct a virtual nerve bundle and use this to study the recorded signal. For simplification consider that your recording electrodes are simply point sources, that all fibers in your bundle are at the same "vertical" distance (r=1 mm) from the electrodes, and that the central node of all fibers is positioned directly beneath the center electrode.

Part 1 – The Source: Transmembrane Current during an Action Potential

Start with your code from Homework 2, Part 5. I suggest using dt=20us to reduce the computational demands, particularly for later parts. We will record the total transmembrane current at a node during propagation of an action potential.

a. How can you do this so that your recorded currents are not influenced by the stimulation current applied to initiate the action potential? Explain. Show plots to demonstrate that your recording does not have stimulation artifact.
b. Briefly explain how you recorded Im(t) in NEURON.
c. Plot the <u>total</u> transmembrane current for a node as a function of time for <u>$2 \leq D \leq 20\mu m$</u> in steps of 2μm with all curves on the same plot.
d. Plot the peak positive current as a function of diameter D for the range. On your plot, include a trendline and the trendline's equation.

Part 2 – Conduction Speed

We're going to use NEURON's NetCon ("network connection") objects to monitor spike times. The following code will monitor spike times at all nodes:

```
objref nc[num_nodes], spiketimes[num_nodes], nil
for i = 0, num_nodes - 1 {
        axon[i] nc[i] = new NetCon(&v(0.5), nil)
        nc.threshold = ap_thresh
        spiketimes[i] = new Vector()
        nc[i].record(spiketimes[i])
}
```

Note that NetCon's are usually used for synapses, but here, we're just using their functionality to record spike times. Some other useful lines of code:

```
spiketimes[<insert node number>].size()
spiketimes[<insert node number>].x[<insert spike number>]
```

Determine the conduction speed for each of fiber diameter: D=2 to 20um with Δ=2um. I suggest placing your electrode closer to one end, and recording far enough away from your stimulating electrode; otherwise the passive response will compromise the accuracy of your spike times for the purpose of conduction speed calculation.

a. Briefly explain how you determined the conduction speed (e.g. method in NEURON, method in Matlab after saving the spike times to a text file, etc.; explain what equation you used…).
b. Provide a table with your results.
c. Plot your results.
d. Fit a trendline to your data. Provide the trendline's equation and show it on your plot.

Part 3 – Compound Nerve Action Potential (CNAP)

In this problem, you will construct a virtual nerve bundle in Matlab and quantify how the spacing between your recording electrodes influences the evoked CNAPs. Create a bundle of at least 100 virtual axons, distributed among two different sub-populations of axon diameters (each with a distribution of diameters D, with a mean±s.d. that you select to represent two different types of nerve fibers present in peripheral nerve bundles). Note that superposition holds, so you can generate the recorded signals by summation of scaled (by distance) and time shifted (due to propagation) sources.

Part 3.A Provide a reference and histogram for your chosen axon diameters.

Part 3.B Initiate an action potential at one end of your nerve bundle and record the evoked signals with a tripolar recording electrode with *k*=10mm interelectrode spacings. Assume an extracellular resistivity of 500ohm-cm and a perpendicular electrode-fiber distance of 1mm.

a. What is the relationship between the current time course (Im(t)) and the fiber diameter?
b. Consider $Im(t=t_o)$ for a given node N of your axon. What is the equation for the potential at a recording electrode some distance r from N due to $Im(t=t_o)$ at node N? Define all your variables.
c. Given the potentials V1, V2, and V3 at each contact in a tripolar electrode (left, middle, and right, respectively), what is the equation for the net recorded voltage in response to $Im(t=t_o)$ from a given node N? Define all your variables.
d. Plot the recorded ECAP for two different distances between the axons' proximal end (where the action potentials initiate) and the middle recording electrode. Include one distance that is quite close to the proximal end. Briefly comment on the effect of changing this distance and the underlying cause for this effect.
e. Using your ECAPs from different stimulation-recording distances, determine the conduction velocity for the contribution to the CNAP from each fiber subpopulation. Explain your method and show your calculations. Are your results in keeping with your expected values? Explain.
f. Plot the recorded ECAP for three different interelectrode spacings (k). How do the recorded signals change?

Part 3.C Recording of CNAPs is used frequently to diagnose peripheral nerve dysfunction, but clearly cuff electrodes cannot be implanted for diagnostic purposes. Do some research to determine how CNAPs are recorded for clinical diagnostic purposes and summarize briefly (<100 words). Provide your reference(s).

Part 4 – Electroneurogram (ENG)

Use the virtual nerve bundle you developed in Part 3 to simulate spontaneous electroneurographic (ENG) signals and ENG signals evoked by natural (asynchronous) stimulation. Give each axon a spontaneous basal firing rate drawn from a uniform distribution of firing frequencies between 10 Hz and 20 Hz.

a. Show a histogram of your firing rates.
b. Explain your coding algorithm.
c. Plot your ENG for each fiber distribution separately. What is the primary difference between your two plots? Why is this the case?