**Homework 6: Cables and Synapses (Jaeger)**

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Note: For submitting plots you can just do screen captures of the plots and paste them into your Word document. To highlight the important features of a graph for explaining your findings, you may want to use the ‘keep lines’ feature to superpose results from 2 or more simulations. (You get the keep lines option by clicking the white square box in the top left of each plot). Similarly you can use the Zoom features using this graph interface to highlight a specific region of the graph for explanations. It may be useful to mark a specific feature of the plot with a letter or an arrowhead in Word to refer to it in your written explanations.

For measuring the signal at any point in time or space it is ok to just use crosshair measurements from the graph menu of the plotting window.

Make use of both the voltage vs. time and the voltage vs. space graphs. Make sure to stop the simulation at an opportune time for capturing relevant voltage vs. space results.

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**Part 1: Cable Experiments.**

**Use the Passive Tutorial in Neuron (passive.nrm)**

**Explain all your results!! Show your relevant simulation data. 40 points total!**

Using ‘Axon Parameters’ interface from the Panel Manager, set up the simulation with a cable of length 20 mm (20,000 µm) and diameter 10 µm and default ‘Axon Parameters’ and with current injection at the leftmost end of the cable (default in ‘Stimulus Control). To make things consistent, throughout use the default value of +5 nA for the current amplitude and start the current pulse at a delay of 1 ms. This can be set in Stimulus Control after you activate the ‘IClamp’ menu. Run your simulations for a total of 30 ms.

1. Inject the current pulse for 25 ms (duration setting). Experimentally determine λ and *L* (the electrotonic length) for the cable (*L* = actual length/λ). You will want to see the ‘Voltage vs. Space’ plot for one of these measurements. Show your plots and the method you get your answer.

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The length constant, lambda, is the distance it takes for the membrane voltage to decay to 37% of its initial value, which in this case is the maximum voltage (Vmax). Thus, once the membrane was charged, we captured the spatial distribution of voltage, observing that the initial value was 34.644 mV. The distance to which the voltage decays to 0.37 \* 34.644 = 12.8, which also known as 37% of the initial value, is approximately 1.5 mm as demonstrated by the crosshairs. We were not able to pinpoint the exact value at 12.8 mV due to the skipping of the crosshairs, so we picked the closest value. Our length constant lambda is thus 1.5 mm. Then, L = actual length/λ, so 20/1.5 = 13.3.

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1. Now decrease the diameter of the cable to 5 µm and repeat your experiment and measurements. What has changed? Explain the changes based on the cable theory slides shown by Dr. Calabrese.
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The first value is 98.1909 mV, so we would want to see the distance to 0.37 \* 98.1909 = 36.3. The distance at which the voltage has decayed to 37% of its initial value is around 1 mm. This is our length constant: 1 mm. Our L then is 20/1, or 20.

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We see that compared to a larger diameter cable, the smaller diameter cable charges/discharges with smaller distances, and thus the length constant is shorter. This is because the length constant depends on the membrane resistance and the axial resistance, or sqrt(rm/ra). Thus, when decreasing the diameter of the cable, we see that our circumference gets smaller, and thus the axial resistance increases. A larger axial resistance means that there is more resistance to ion flow through the neuron, which in turn means that an area will become charged/discharged more before moving down the cable. This results in a smaller length constant—it takes less distance to charge/discharge the cable.

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**Part 2: Synaptic Integration**

**Use the 3dendpassive.nrn Tutorial in Neuron**

**Explain all your results!!! Show all relevant simulation data with figures. 60 points total!**

30 pts. Start 3dendpassive.nrn. Run the simulations at half-speed (speed slider in the middle). Using the ‘Train, Single Location’ controls, determine what the temporal spacing between 3 inputs elicits an AP the fastest (measured by the black node[5] plot crossing 0) for a conductance of 2.8 microS. For any given simulation, keep the time difference between first, second and third activation of the synapse equal (use an increment of 0.1 ms, i.e. start with 1,1,1 then 1 1.1, 1.2, then 1, 1.2, 1.4 ms etc). Always start the first activation at t= 1 ms. Also determine the longest interval between inputs that still elicits an AP. Why is firing all inputs at once not the optimal solution?

Now put the synapse at the distal end of the dendrite, and put the conductance of a single input at 8 microS. Does the best timing for summation differ from a mid-dendritic location? Hand in plots of your simulations and explain your findings.

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For a mid-dendritic location, as shown in the plots above, at intervals of 1, 1, 1, and 1, 1.1, 1.2, no spike is elicited. At higher intervals, a spike is elicited between the following times: (explain about two times)

2.66-2.68 ms for intervals of 1, 1.2, 1.4.

2.65-2.66 ms for intervals of 1, 1.3, 1.6. This interval elicits an AP the fastest.

2.77-2.78 ms for intervals of 1, 1.4, 1.8.

2.96-2.97 ms for intervals of 1, 1.5, 2.0.

3.21-3.23 ms for intervals of 1, 1.6, 2.2.

3.52-3.53 ms for intervals of 1, 1.7, 2.4.

4.01-4.02 ms for intervals of 1, 1.8, 2.6. This is the longest interval that still elicits an AP.

At an interval of 1, 1.9, 2.8, the spike is no longer elicited.

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Firing all inputs at once is not the optimal solution because it does not take advantage of temporal summation. Temporal summation occurs when these potentials are able to summate with each other before fading, resulting in an AP. Thus, a larger potential is generated than if the individual inputs were fired individually at once.

For a synapse at the distal end of the dendrite:

Intervals below 1, 1.4, 1.8 elicited no spikes. This is in contrast to a mid-dendritic synapse, which was able to elicit a spike below 1, 1.4, 1.8.

A spike is elicited between the following times:

3.60-3.70 ms for intervals of 1, 1.4, 1.8.

3.37-3.38 ms for intervals of 1, 1.5, 2.0. This interval elicits an AP the fastest.

3.46-3.47 ms for intervals of 1, 1.6, 2.2.

3.91-3.92 ms for intervals of 1, 1.8, 2.6.

4.33-4.34 ms for intervals of 1, 1.9, 2.8. This is the longest interval that still elicits an AP.

At an interval of 1, 2, 3, the spike is no longer elicited.

The best timing for summation in a distal location differs from a mid-dendritic location. Both the best timing interval as well as the longest interval that still elicits an AP is shorter for a mid-dentritic location and longer for a distal location. For example, the best timing for our mid-dentritic location was 1, 1.3, 1.6, while the best timing for our distal location was 1, 1.5, 2.0. This may be because the potential must travel a longer distance to reach the soma, so temporal summation must act in a way where it does not fire in succession too quickly?

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30 pts. Restart 3dendpassive.nrn. Run the simulations at half-speed (speed slider in the middle). Use the ‚All Synaptic Variables’ control panel.

Set the top (Syn0) synapse at a delay of 1 ms, the middle one at a delay of 1.4 ms, and the bottom one at delay at 1.8 ms. Always set all 3 synapses to the same conductance strength. With a precision of 0.1 microS, determine the smallest conductance level that can still trigger an action potential. What is this conductance? Show a plot at threshold and explain how the 3 synapses contribute to the spike initiation.

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Description automatically generatedThe smallest conductance level that triggers an AP is 1.9 uS. At 1.8 uS, an AP is no longer triggered. The three synapses contribute to the spike initiation through summation, as each raises the membrane potential, summating until threshold, or when a spike occurs. Synapse 0 fires first, then synapse 1, and then synapse 2. We can see the membrane potential at different points in the axon, given by the black, red, and blue nodes in the voltage vs. time graph. After the summation, we can see that the membrane potential rises above threshold for a spike.

Now reverse the timing of the 3 synapses, i.e. activate Syn0 at 1.8 ms, and Syn3 at 1.0 ms. Repeat the determination of the smallest conductance triggering an action potential now. What is the value now and why is it different than before? Include simulation plots and explain how the trajectory of voltage explains your finding.

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Also, inflection in the spike means that it is the sodium channels opening

And look at cable theory equations

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