BIO450/IBS534 Spring 2025 In class Experiments and Homework 7 Assignment

Load the Google Colab notebook for today’s session found here:

[Session 15-16 Colab Notebook](https://colab.research.google.com/drive/1FCJrqqzUfZrkWeNLqIeBBSjXM6uVt8vL?usp=sharing)

Save this notebook as a copy to your own drive – only this way will you maintain changes that you make.

In between simulations be sure to set parameters that were changed back for a specific preceding manipulation back to default. For example, if you are exploring the diameter of the dendrite in one simulation, put it back to default diameter of 2 micrometer before starting the next experiment. Lingering stray inputs and parameter settings were the most common error in previous homework submissions.

Also be sure to execute each simulation with ‘Run cell and below’ starting with the code block entitled ‘create the neuron’. Do not start execution with the parameter setting code block. To do so carries over some internal variables from the preceding simulation which thus influences your outcome.

Homework #4

**Experiment 2. Passive Synaptic Responses**

We are now looking at excitatory and inhibitory **synaptic inputs in** **passive neurons.** **‘Passive’ means that HH Na and K channels are NOT present.**

For all simulations, save the results plot as .png file and include those as figure in your homework. Give each plot a figure number and describe the results in your answer. Also note specific questions below for each simulation.

First, turn the current injection off by setting the stim.amp = 0. Keep the sec.Ra at 1E2.

Simulation 1

Turn on the soma synapse with a reversal potential of 0, and a gmax of 0.006 microS/cm^2.

Measure the EPSP amplitude in mV from baseline and the delay from the onset time of the input (at 25 ms) for each recording location, and make a table of these results. Explain the relative size and delay of the EPSP in different parts of the neuron.

*Answer:*

*Soma: as we set up the injection into a point at soma in the neuron, we would expect the EPSP to be largest at with minimal delay. This is because the size of soma is relatively large (diameter=10, length=10) to have low axial resistance and membrane resistance, which allow injected current to depolarize the soma directly without much delay. Furthermore, since the soma synapse’s reversal potential is set to be 0, the driving force for current (Vrev – Vrest) is strongest at the synapse itself, resulting in large EPSP magnitude.*

*Axon: The magnitude of EPSP is second largest and second smallest delay. This is because since the axon is directly connected to soma, there’s shorter distance for current to travel. As the axon typically have higher channel density that decrease membrane capacitance, and various structures like Nodes of Ranvier can decrease membrane capacitance (and decrease tau) and help it to be depolarized more quickly and efficiently, which would lead to relatively large EPSP magnitude and relatively small delay.*

*Dendrite: The magnitude of EPSP is smaller than soma and axon, and have larger delay than them because the nature of its shape – long and narrow – increase the dendrite’s axial resistance. Generally, proximal part of dendrite has largest EPSP magnitude and smallest delay followed by middle part of dendrite, then distal part has smallest EPSP magnitude and largest delay. Comparing across the two dendrite, dendrite 2 (longer) have smaller EPSP magnitude and larger delay compared to dendrite 1 (shorter).*

1. *Different part within same dendrite: The difference between different parts on the same dendrite is mainly because of the distance that the current have to travel to depolarize the part. The proximal part is closest to soma, where the current is injected, therefore the current reach to the proximal part first, followed by middle and distal part, causing the delayed transmission. Similarly, the axial resistance increase with increased length, causing the decay of EPSP magnitude (followed by the cable theory equation).*
2. *Different dendrite: The longer length of Dendrite 2 increases the axial resistance, causing more voltage drop as the EPSP propagates, which leads to a greater attenuation of the signal and thus a smaller EPSP magnitude. Additionally, the increased length results in a larger surface area would decrease membrane resistance and increase current leakage, further diminishing the EPSP magnitude. The greater axial resistance (longer dendrite) in Dendrite 2 also slows the propagation of the EPSP, leading to a larger delay.*

*Table 1 EPSP amplitude from baseline (mV) and delay from onset on input (ms) at various part of neuron when open the soma synapse.*

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*Figure 1 Simulated neuron response to stimulus injection upon opening the soma synapse.*

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Simulation 2

Turn off the soma synapse and put the same synaptic input (i.e. 0.006 microS/cm^2) on the tip of the distal dendrite of dendrite 2 this is ‘syn4’ in the code). Again make a table of EPSP amplitude and delay in each part of the neuron. Compare and contrast the results to simulation 1 and explain the differences.

*Answer:*

*In the two simulations, the key difference lies in the location where the current is injected: the first simulation injects current at the soma, while the second simulation injects current at the distal part of Dendrite 2. This difference significantly influences the observed EPSP magnitude and delay across the various parts of the neuron.*

*In the first simulation, where the current is injected at the soma, the EPSP magnitude is highest at the soma because that is where the current is injected directly. As the current propagates to the dendrites and axon, it encounters attenuation due to axial resistance and the increasing distance it travels. The EPSP magnitude decreases progressively in the dendrites and axon, with the largest magnitude observed in the soma, followed by the axon and then the dendrites. The delay is shortest at the soma, as there is no need for the signal to propagate, and it increases as the current moves farther from the soma to the dendrites and axon.*

*In contrast, in the second simulation, where the current is injected at the distal part of Dendrite 2, the EPSP magnitude is largest at the distal part of Dendrite 2. This occurs because the current is injected into the distal dendrite, where it begins its propagation. The signal travels through the length of the dendrite before reaching the soma, causing the EPSP magnitude to be larger in the more distal parts initially. However, as the current moves toward the soma, it experiences attenuation due to the axial resistance of the dendrite, resulting in a decrease in EPSP magnitude. The magnitude continues to decrease as the signal propagates through the soma and axon. The order of EPSP magnitude in this simulation is Dendrite 2 Distal > Dendrite 2 Middle > Dendrite 2 Proximal > Soma > Axon > Dendrite 1 Proximal > Dendrite 1 Middle > Dendrite 1 Distal.*

*The delay in the second simulation follows a reversed pattern. Since the current is injected at the distal part of Dendrite 2, the delay is longest at the distal dendrite. This is because the current needs to travel a longer distance to reach the soma and axon, which leads to greater signal attenuation and a longer delay. As the current moves toward the soma and axon, the delay decreases progressively, with the shortest delay at the soma and axon, as the current has less distance to travel from those regions. The overall pattern of EPSP delay in this simulation is reversed compared to the first simulation, where the delay increases as the current moves farther from the soma.*

*The differences in the results of these two simulations are primarily due to the location of current injection. In the first simulation, the current injection at the soma results in a large EPSP magnitude at the soma and shorter delays as the current propagates outward. In the second simulation, injecting current at the distal part of Dendrite 2 leads to a larger EPSP magnitude in the distal dendrite and longer delays as the signal propagates back toward the soma and axon. Additionally, in both simulations, the propagation of the signal is influenced by the axial resistance of the dendrites and axon, which causes the signal to decay as it travels through the neuron. In the second simulation, the longer dendrite increases axial resistance, which causes greater attenuation of the EPSP magnitude and a larger delay compared to the first simulation, where the signal is injected directly into the soma.*

*Table 2 EPSP amplitude from baseline (mV) and delay from onset on input (ms) at various part of neuron when open the synapse 4.*

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*Figure 2 Simulated neuron response to stimulus injection upon opening the synapse 4.*

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Simulation 3

Now make the diameter of dendrite 2 = 1 micrometer (instead of 2 micrometers). Rerun your simulation 2 with this change. Now you only need to measure the EPSP amplitudes and delays for the 3 positions in dendrite 2 and the soma, i.e. you can disregard dendrite 1 and the axon. Explain differences you see in comparison to simulation 2 using concepts from cable theory (length constant, decay etc).

*Answer:*

*Reducing the diameter of Dendrite 2 significantly increases its axial resistance. According to cable theory, axial resistance is inversely proportional to the square of the dendrite’s diameter. By reducing the diameter from 2 µm to 1 µm, the axial resistance is quadrupled. Increased axial resistance impedes the flow of current, causing more voltage to drop along the dendrite’s length. As a result, the EPSP signal decays more rapidly with distance.*

*This increased axial resistance also affects the length constant (lambda), which determines how far a voltage signal can propagate before it decays significantly. The length constant is given by: lambda = sqrt (r\_m / r\_a). Since reducing the diameter increases r\_a, the length constant decreases. This reduction in lambda causes the EPSP amplitude to diminish more sharply as the signal travels toward the soma.*

*The EPSP amplitude data reflects these effects. In Simulation 3, the EPSP amplitude is much larger at the distal end of Dendrite 2 (44.01 mV compared to 25 mV in Simulation 2) but decays far more rapidly as the signal moves toward the soma. By the time the EPSP reaches the soma, the amplitude is reduced to 1.2 mV in Simulation 3, lower than the 2.6 mV observed in Simulation 2. This sharper decline aligns with the decreased length constant due to the increased axial resistance.*

*The delay measurements also highlight the impact of increased axial resistance. With higher resistance, the current moves more slowly through the dendrite, increasing the EPSP delay. By the time the EPSP reaches the soma, the delay is noticeably longer (11.55 ms vs. 8.25 ms). This increased delay reflects the combined effects of slower current movement and greater voltage drop along the dendrite.*

*Table 3 EPSP amplitude from baseline (mV) and delay from onset on input (ms) at various part of neuron when diameter of dendrite 2 is half original (1 micrometer).*

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*Figure 3 Simulated neuron response to stimulus injection when diameter of dendrite 2 is half original (1 micrometer).*

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**Experiment 3 Synaptic responses in active neurons**

We are now looking at excitatory and inhibitory synaptic **inputs in active neurons.** **‘Active’ means that HH Na and K channels** are now added to the axon and the soma.

Simulation(s) 1

Return dendrite 2 to a 2 micrometer diameter. Further, enable the HH channels by setting the insertHH variable at the beginning of the ‘Create Neuron’ code block to ‘True’.

Rerun synaptic input conditions from simulation 1 from Experiment 2 with HH channels present. Explain the differences in outcomes compared to Experiment 2. (Turn on the soma synapse with a reversal potential of 0, and a gmax of 0.006 microS/cm^2.)

*Answer:*

*Table 2 EPSP amplitude from baseline (mV) and delay from onset on input (ms) at various part of neuron when diameter of dendrite 2 is half original (1 micrometer).*

*Figure 3 Simulated neuron response to stimulus injection when diameter of dendrite 2 is half original (1 micrometer).*

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What is happening to the resting membrane potential before the synaptic input starts in the presence of HH channels? Why is this happening (you have to dig back to your knowledge of HH kinetics and voltage dependence).

*Answer:*

*Reducing the diameter of Dendrite 2 significantly increases its axial resistance. According to cable theory, axial resistance is inversely proportional to the square of the dendrite’s diameter. By reducing the diameter from 2 µm to 1 µm, the axial resistance is quadrupled. Increased axial resistance impedes the flow of current, causing more voltage to drop along the dendrite’s length. As a result, the EPSP signal decays more rapidly with distance.*

Now change the gmax of the soma synapse to 0.007 microS/cm^2 and rerun synaptic input conditions from simulations 1 and 2 from Experiment 2 above.

*Answer:*

*Reducing the diameter of Dendrite 2 significantly increases its axial resistance. According to cable theory, axial resistance is inversely proportional to the square of the dendrite’s diameter. By reducing the diameter from 2 µm to 1 µm, the axial resistance is quadrupled. Increased axial resistance impedes the flow of current, causing more voltage to drop along the dendrite’s length. As a result, the EPSP signal decays more rapidly with distance.*

In which condition do you see an action potential? What is the critical factor for the AP to occur? Where is the action potential initiated in the neuron? Does it occur at the time that the EPSP peak is reached at the synapse or some other time? What factors determine the timing do you think?

*Answer:*

*Reducing the diameter of Dendrite 2 significantly increases its axial resistance. According to cable theory, axial resistance is inversely proportional to the square of the dendrite’s diameter. By reducing the diameter from 2 µm to 1 µm, the axial resistance is quadrupled. Increased axial resistance impedes the flow of current, causing more voltage to drop along the dendrite’s length. As a result, the EPSP signal decays more rapidly with distance.*

Simulation(s) 2

Now make synapse 4 a lot stronger by increasing the gmax to 0.02 microS/cm^2.

Before you run the simulation, would you expect an action potential to be triggered or not?

Slide the position of this synapse along the dendrite by changing ‘dend2\_syn4\_location’ to values between 0.8 and 0.2 in increments of 0.2. Note that ‘1’ corresponds to the distal tip of dendrite 2, ‘0’ is right next to the soma, and all other values are proportionally in between. Measure the EPSP size at the soma for each simulation, and assess how much HH Na and K current is elicited. What do you conclude about the contribution of distal synapses to the control of action potential initation? There are lot of distal synapses in the neurons of our brain. How could that be useful?

**Experiment 4 The interaction of excitation and Inhibition in active neurons.**

Design your own experiment that combines inhibitory with excitatory input. Describe the design of the experiment and your hypothesis. Than execute your simulations and describe your results. Be sure to include a mention of your specific parameter settings in each simulation.

Note: You turn any synapse on our simulated neuron into an inhibitory one by setting its reversal potential (eg. syn2.e) to -70 or -80 mV. Often inhibitory synapses also have a longer synaptic conductance time course than excitatory ones. You can prolong the conductance by setting the time constant to a bigger value like 3 or 5 (e.g. syn2.tau = 5). And you can put any dendritic synapse at any distance from the soma by setting the location to a value betwee 1 and 0 as described under experiment 3.