BME445 NEURAL BIOELECTRICITY
Lab 4: PROPAGATION OF NEURONAL ELECTRICAL ACTIVITY
November 1st , 2023 - PRA0102

Liza Babaoglu - 1006026532
Deniz Uzun - 1006035005
Nicholas Heeralal - 1005867475

Purpose

In this lab, we aim to investigate the effects of membrane properties and cable dimensions on signal transmission along dendritic and axonal cable models. We will investigate the effect of discretization and dendritic cable diameter, the spatial and temporal summation of synaptic inputs to understand the passive spread; the effect of axonal cable diameter on propagation velocity, and excitability and refractoriness of axonal cables to understand the active spread mechanisms underlying neural communication and information processing.

Results/Discussion

PART I: Passive Spread

- **Space and Time Constants**

1. ***Measuring space constant in a time clamp mode. Compute the measured λ and compare with its theoretical value. How does increasing the number of compartments change the measured λ.***

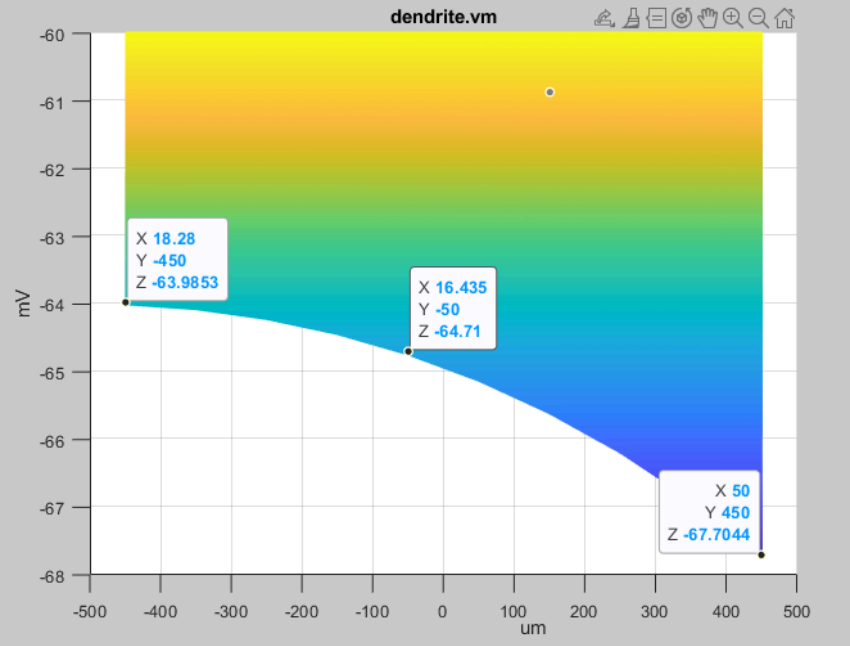

Figure 1: Measuring space constant in time clamp mode

Measured λ using values from *Figure 1*:

Vo = -67.7044 mV

Vf = -63.9853 mV

Vm = -64.71 mV

X = 550 µm

$$\frac{v_m - v_f}{v_o - v_f} = e^{-\frac{x}{\lambda}} \Rightarrow \lambda = -x / ln(\frac{v_m - v_f}{v_o - v_f}) = 416.452 \text{ m} \simeq 4.16 \text{ mm}$$

The theoretical value of λ:

$$\lambda = \left(\frac{R_m d}{4 R_a}\right)^{0.5} = \left(\frac{3.333 k\Omega * cm^2 * 0.0002 cm}{4 * 30\ \Omega - cm}\right)^{0.5} = 0.074 \text{ cm} = 7.45 \text{ mm}$$

The theoretical value is higher than the measured value of the space constant. As we increase the number of compartments, the accuracy and precision of our measurement increases, therefore the measured λ increases and becomes closer to the theoretical value.

2. ***Measuring time constant in a space clamp mode. Compare the measured τm with its theoretical value.***

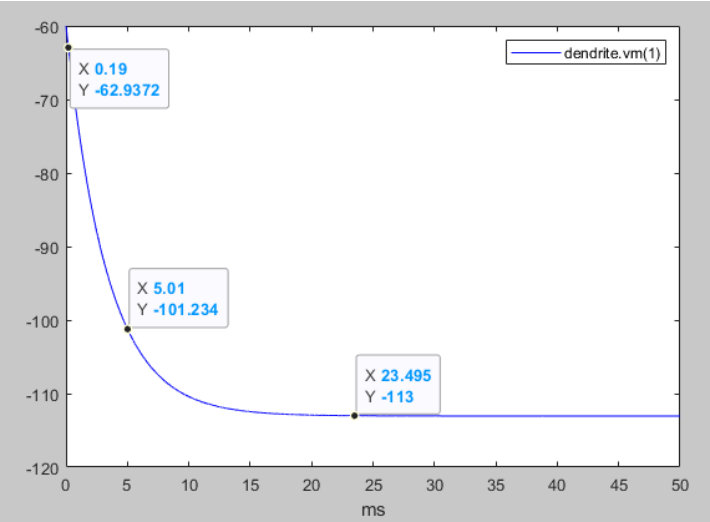

Figure 2: Measuring time constant in space clamp mode

Measured τ_m using values from *Figure 2*:

Vo = -62.9372 mV
Vf = –113 mV
Vm = -101.234 mV
t = 4.82 ms

$$\frac{v_m - v_o}{v_f - v_o} = 1 - e^{-\frac{t}{\tau}} \Rightarrow \tau_m = t/ln(1 - \frac{v_m - v_o}{v_f - v_o}) = 3.32871 \text{ ms} \simeq 3.33 \text{ ms}$$

The theoretical value of τ_m:

$\tau_m = R_m * C_m = 3.333\ k\Omega cm^2 * 1\ \mu F/cm^2 = 3.333\ ms$

Measured τ_m is the same as the theoretical value of τ_m.

Parameter	Measured	Theoretical
λ	4.16 mm	7.45 mm
τ_m	3.330 ms	3.333 ms

- **Effects of Dendritic Cable Discretization**

1. ***Inject a current pulse (-l nA, 0.5ms) into the soma and investigate the effect that cable discretization has on the simulation results. Adjust the number of dendritic compartments and run the simulation for at least 1, 5, 10, and 20 compartments. How many compartments are required before the effect of discretization becomes negligible? Hint: Compare what you observe at different compartments with your expectations of what should occur in a dendrite.***

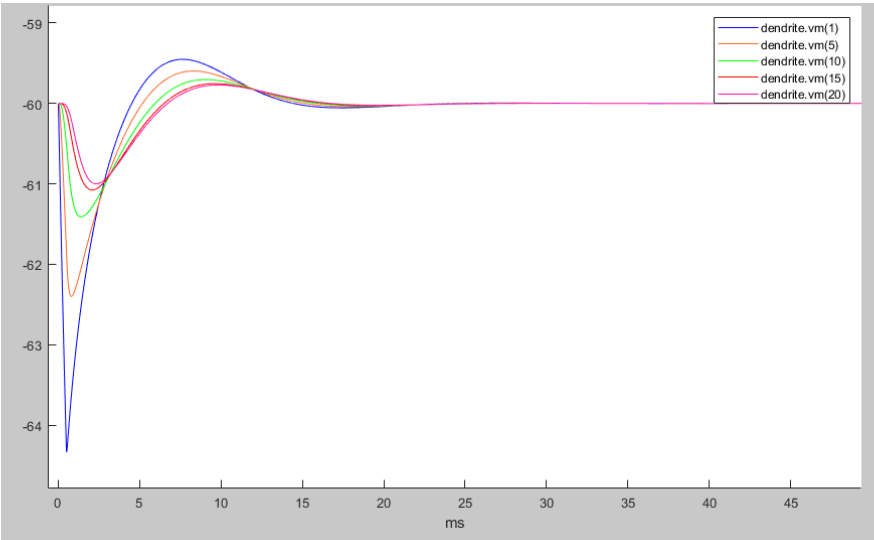

Figure 3: Graph illustrating the membrane potential response in a dendritic tree with different levels of compartmentalization (1, 5, 10, and 20 compartments) when a current pulse is injected into the soma

Observations:

- With only 1 compartment, the response seems quite distinct from the other curves. This suggests that a single compartment model might not capture the detailed dynamics occurring in the dendrite.
- As the number of compartments increases, the curves start to converge towards a more consistent response. This indicates that as we increase the number of compartments, we get a more accurate representation of the dendritic response.
- Beyond a certain number of compartments (in this case, somewhere between 10 and 20), adding more compartments doesn't seem to significantly alter the response. This suggests that after a certain point, the effect of discretization becomes negligible, and adding more compartments might not provide additional detail or accuracy.

What we know:

- Dendrites act as cables. When a current is injected at one end, we expect the signal to attenuate (decrease in amplitude) as it travels down the length of the dendrite. The degree of this attenuation is influenced by the dendrite's diameter, membrane resistance, and internal resistance. A longer electrotonic length means the signal can travel further without significant attenuation.
- With increased compartmentalization in simulations, we can capture more localized events and interactions in the dendrite. This is because real dendrites aren't just simple cables but have branches, varying diameters, and synapses. Therefore, increased compartmentalization should provide a more realistic representation.
- Increasing compartmentalization brings the simulated response closer to what we would expect in a real dendrite.
- Beyond a certain level of compartmentalization, the added detail might not significantly change the observed dendritic response, indicating that we've reached a point where the effect of discretization is negligible.

- **Effect of Dendritic Cable Diameter**

1. ***What is the velocity of propagation in the cable (for the default diameter = 2μm)?***

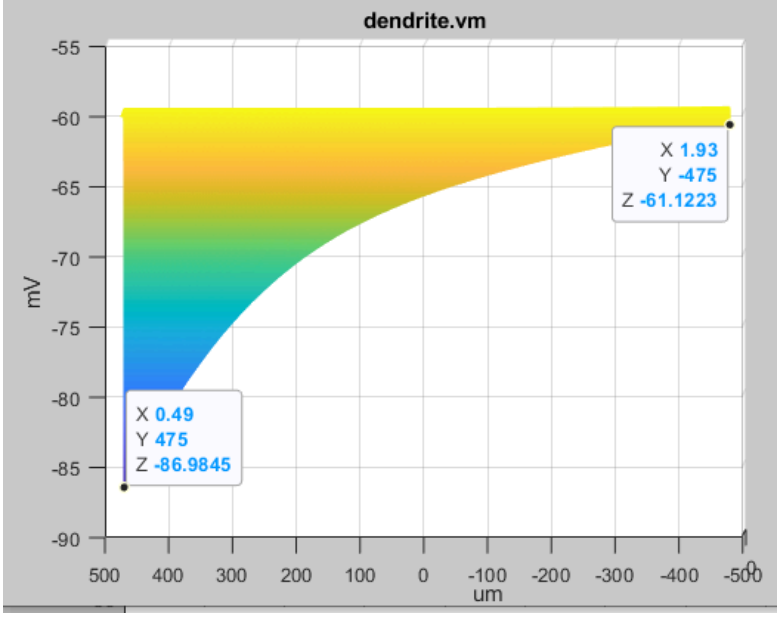

Figure 4: Default simple neuron model with 2μm dendritic cable diameter

From *Figure 4*:

$$x = -475\ \mu m$$
$$x_o = 475\ \mu m$$
$$t = 1.93\ ms$$
$$t_o = 0.49\ ms$$

The velocity of propagation in the cable with 2μm diameter:

$$\theta = \frac{(x - x_o)}{(t - t_o)} = -0.6597\ m/s$$

2. ***Measure the velocity of propagation for the following diameters (0.0001 cm, 0,0003 cm and 0.0004 cm). How do your measured velocities compare to the theoretical values?***

At d = 0.0001 cm = 1 µm

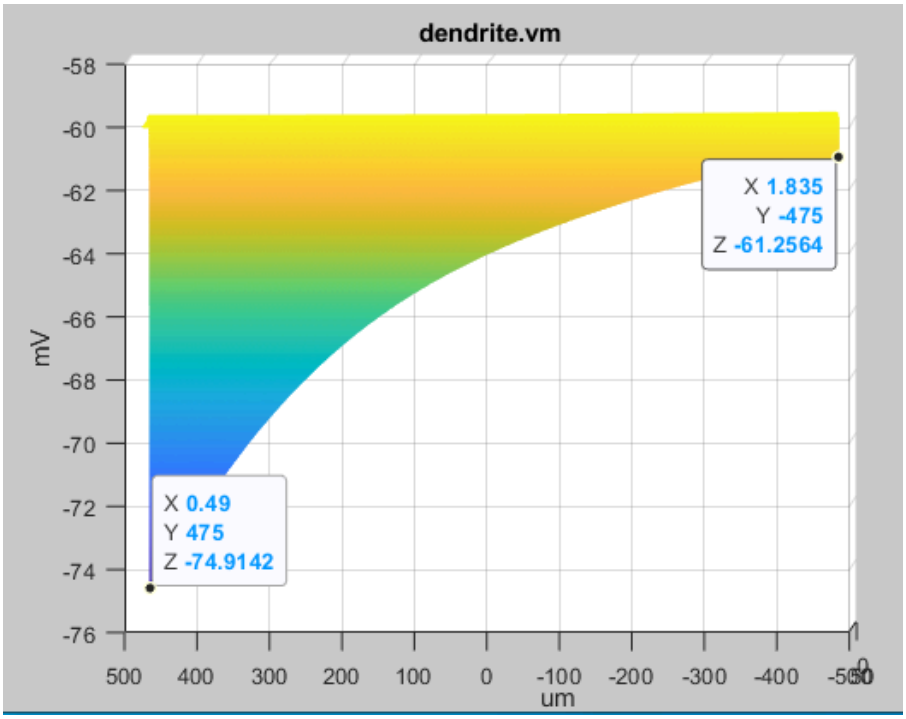

Figure 5: Simple neuron model with 1µm dendritic cable diameter

From *Figure 5*:

x = -475 µm

x_o = 475 µm

t = 1.835 ms

t_o = 0.49 ms

Velocity of propagation in the cable with 1µm diameter:

$$\theta = \frac{(x - x_o)}{(t - t_o)} = -0.706\ m/s$$

The theoretical value of θ:

θ ≈ 6 * d = 6 * 0.1 = − 0.6 m/s

At d = 0.0003 cm = 3 µm

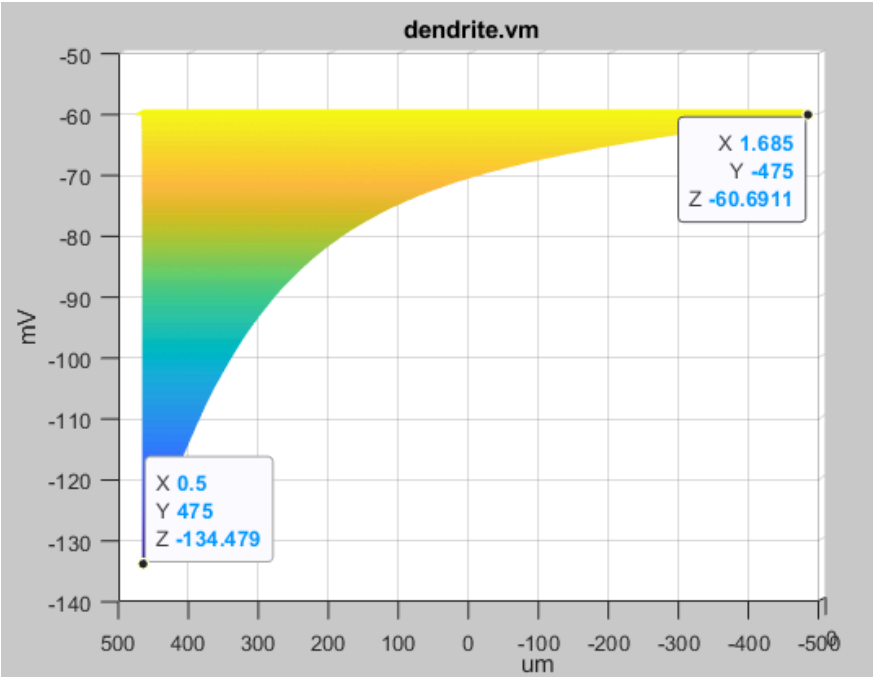

Figure 6: Simple neuron model with 3µm dendritic cable diameter

From *Figure 6*:

$$x = -475 \text{ µm}$$
$$x_o = 475 \text{ µm}$$
$$t = 1.685 \text{ ms}$$
$$t_o = 0.5 \text{ ms}$$

Velocity of propagation in the cable with 3µm diameter:

$$\theta = \frac{(x - x_o)}{(t - t_o)} = -0.802\ m/s$$

The theoretical value of θ:

$\theta \approx 6 * d = 6 * 0.3 = -1.8$ m/s

At d = 0.0004 cm = 4 µm

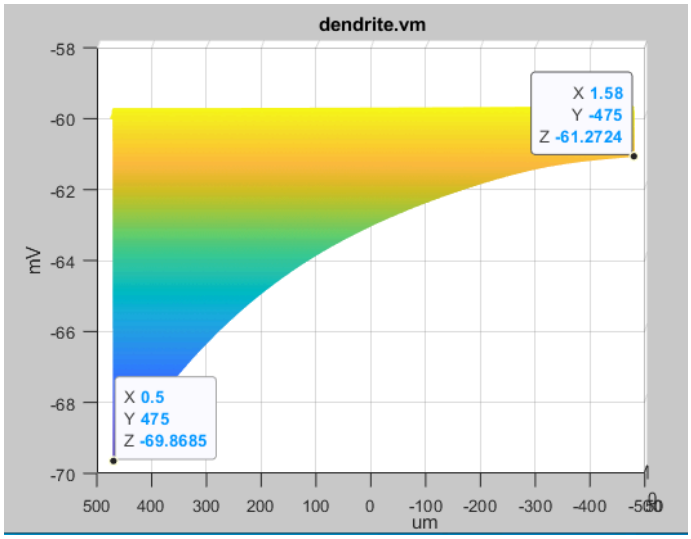

Figure 7: Simple neuron model with 4µm dendritic cable diameter

From *Figure 7*:

$$x = -475 \text{ µm}$$
$$x_o = 475 \text{ µm}$$
$$t = 1.58 \text{ ms}$$
$$t_o = 0.5 \text{ ms}$$

The velocity of propagation in the cable with 4µm diameter:

$$\theta = \frac{(x - x_o)}{(t - t_o)} = -0.879\ m/s$$

The theoretical value of θ:

$\theta \approx 6 * d = 6 * 0.4 = 2.4$ m/s

Although our measured values do not match the theoretical values exactly, we observe that the velocity of propagation increases as the diameter of the cable is increased. The negative sign denotes the direction of the propagation of the wave.

Diameter d	**Velocity of Propagation (Measured)**	**Velocity of Propagation (Theoretical)**
0.0001 cm	$-0.706\ m/s$	$-0.6\ m/s$
0.0003 cm	$-0.802\ m/s$	$-1.8\ m/s$
0.0004 cm	$-0.879\ m/s$	$-2.4\ m/s$

- **Spatial and Temporal Integration of Synaptic Inputs**

1. ***Describe the voltage response at compartment 20 and at the soma. Is there evidence of synaptic integration? What are the voltage responses?***

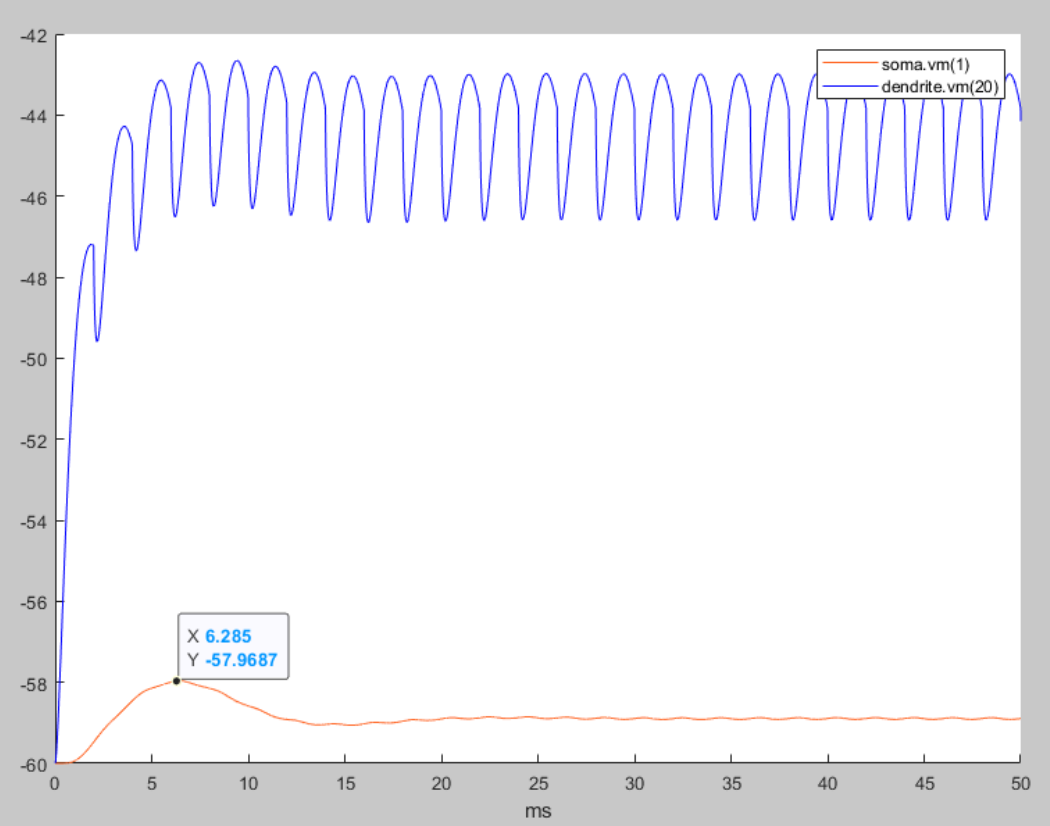

Figure 8: Graph illustrating the voltage response at compartment 20 and at the soma using a train of simulated synaptic current inputs, both excitatory and inhibitory postsynaptic potentials, applied to the dendritic cable, rather than using short pulse current injections into the dendrites

- Voltage Response at Compartment 20 (Dendrite)
    - It displays a series of oscillations, indicating repeated excitatory postsynaptic potentials (EPSPs).
    - The oscillations start with a sharp upward spike, indicating the arrival and impact of each EPSP.
    - There's a regular periodicity between the EPSPs, suggesting a uniform train of synaptic inputs.
    - Overall, the voltage oscillates sharply with each EPSP, indicating strong excitatory inputs. The voltage peaks then decay before the next input arrives.

- Voltage Response at the Soma
    - The response is relatively stable and less pronounced compared to compartment 20.
    - There's a mild wavelike pattern, which shows that the soma is registering the EPSPs, but the amplitude of these oscillations at the soma is dampened compared to the dendrite.
    - Overall, the voltage shows a milder oscillation pattern in response to the EPSPs. This suggests that while the soma is registering the excitatory inputs, the impact is less pronounced due to the electrotonic spread and other integrating factors of the neuron.

Yes, there is evidence of synaptic integration. Synaptic integration refers to the process by which multiple synaptic potentials (EPSPs or IPSPs) combine within a single postsynaptic neuron. The characteristics of synaptic integration can be seen in two ways:

- Temporal Summation: Temporal summation occurs when a single synapse fires multiple times in rapid succession. The repeated and regular EPSPs at compartment 20 show evidence of temporal summation. A one EPSP hasn't fully decayed before the next one arrives, their effects accumulate over time, and we see repeated peaks without returning to the baseline.

- Spatial Summation: Spatial summation occurs when different synapses fire at approximately the same time. The voltage response at the soma (despite being attenuated) shows that signals from different parts of the dendrite (like compartment 20) are being combined and integrated at the soma. The fact that the soma shows a response (even if dampened) to the EPSPs indicates spatial summation.

The steady state voltage amplitude spread for compartment 20 can be calculated as:
Amplitude Spread = Peak - Trough
Amplitude Spread= (-43 mV) - (-47 mV) = 4 mV

Similarly for soma,
Amplitude Spread = (-57.96 mV) - (-59 mV) = 1.04 mV

The periodicity (time between two successive peaks) for compartment 20 appears to be approximately 5 ms, whereas for the soma it appears to be around 2 ms

Site	Maximum Voltage (mV)	Steady State Voltage Amplitude Spread (mV and ms)
Compartment 20	-43	4 mV 5 ms
Soma	-57.96	1.04 mV 2 ms

2. ***Now alter the specific membrane resistance while retaining the same EPSP train. Study the effect of dendritic membrane resistance on temporal and spatial summation of synaptic inputs by calculating the following:***

Dendritic Membrane Resistance	Maximum Soma Voltage (mV)
Quarter default R_m	-59.51
Half default R_m	-58.87
Default R_m (3.333 k-ohm cm^2)	-57.96
Double default R_m	-57.03
Quadruple default R_m	-56.24

Dendritic Membrane Resistance and its Effect:
Membrane resistance (R_m) is a measure of how resistive the cell membrane is to the flow of ions across it. A higher resistance means that it's harder for ions to cross, and vice versa.

Effect on Temporal and Spatial Summation:

- Temporal Summation: With lower dendritic membrane resistance (e.g., quarter default R_m), the EPSPs generated by the train of synaptic inputs will decay faster. This might affect the overall summation of the PSPs if they are spaced closely in time.

- Spatial Summation: With lower resistance, the spread of voltage due to one synapse might affect neighboring synapses more strongly, leading to increased spatial summation. Conversely, higher resistance can limit the spread of voltage and reduce spatial summation.

3. ***For the same EPSP train, setting the R_m to default, find the minimum leakage conductance (gL) for soma which will result in an action potential at the soma for this EPSP frequency?***

The minimum leakage conductance (gL) for soma which will result in an action potential at the soma for this EPSP frequency was found to be 0.74 (mS/cm^2).

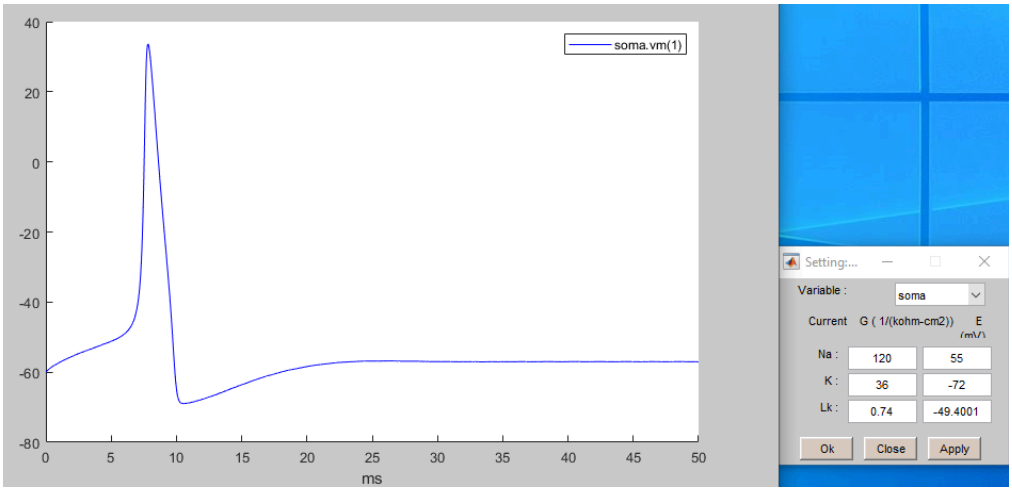

Figure 9: Graph showing resulting action potential from minimum leakage conductance at the soma for given EPSP frequency

4. ***Load Synaptic_Integration_2.m model, which includes an IPSP. What is the effect of the new model on the response at the soma?***

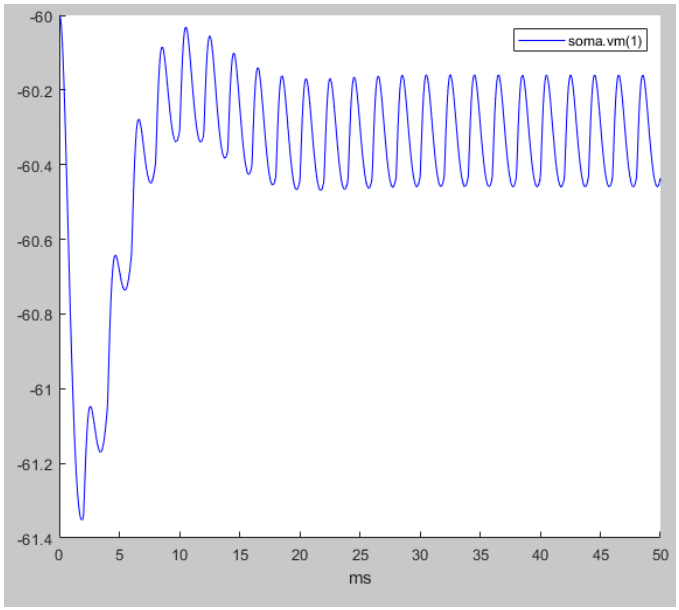

Figure 10: Graph showing the effect of the new model on the response at the soma with regard to the Synaptic_Integration_2.m model, which includes an IPSP

Observations:

- The graph starts with a rapid depolarization (increase in voltage).
- After the initial depolarization, the voltage seems to settle into regular oscillations or repetitive depolarizations and hyperpolarizations.
- The voltage appears to oscillate between roughly -60.1 mV and -60.6 mV.

The model incorporates the effect of inhibitory synapses on the neuron's membrane potential. IPSPs typically make the inside of the neuron more negative (hyperpolarization) and move the membrane potential further away from the threshold needed to generate an action potential

PART II: Active Spread

- **Effect of Axonal Cable Diameter on Propagation Velocity**

1. What is the velocity of propagation along the axon?

To find the velocity of propagation (θ) along the axon, we observe the relationship between distance and time, and calculate this slope.

$$\theta = \frac{\Delta distance}{\Delta time} = \frac{2450 - (-2450)}{19.76 - 1.21} = 264 \frac{\mu m}{ms}$$

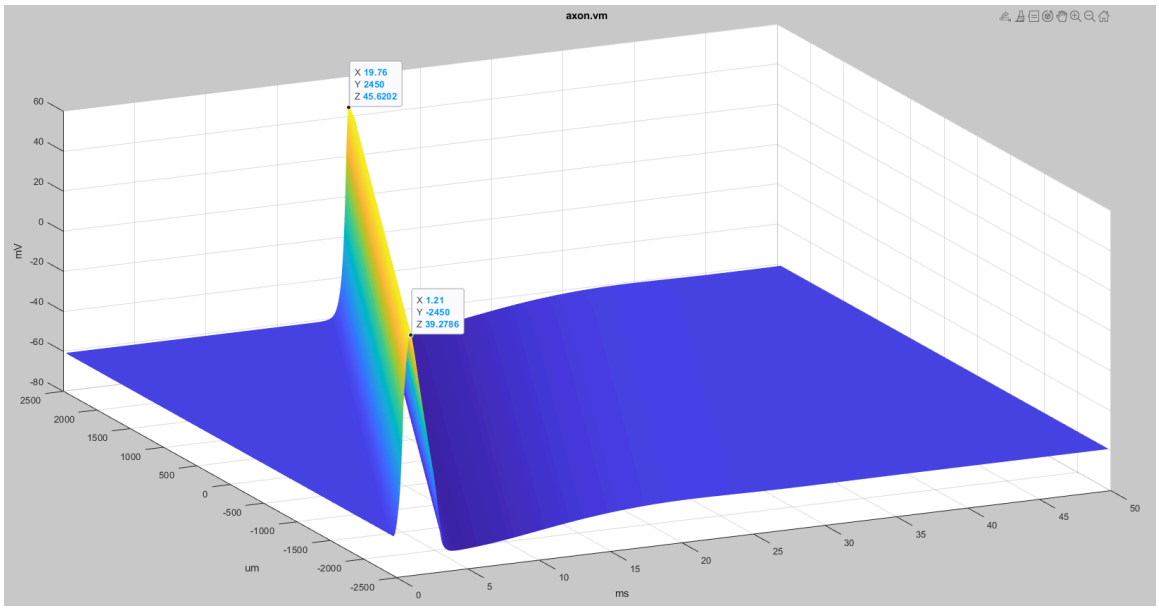

Figure 11: 3D-viewer of the action potential propagation along the axon

2. What is the space constant of the axonal cable?

As seen in *Figure 11,* there is no decay or reduction in the amplitude of the action potential due to propagation with an active spread. There is active lossless spread in unmyelinated axons. Since space constant is a passive property of membranes, we conclude that there is no space constant for the unmyelinated active axonal cable.

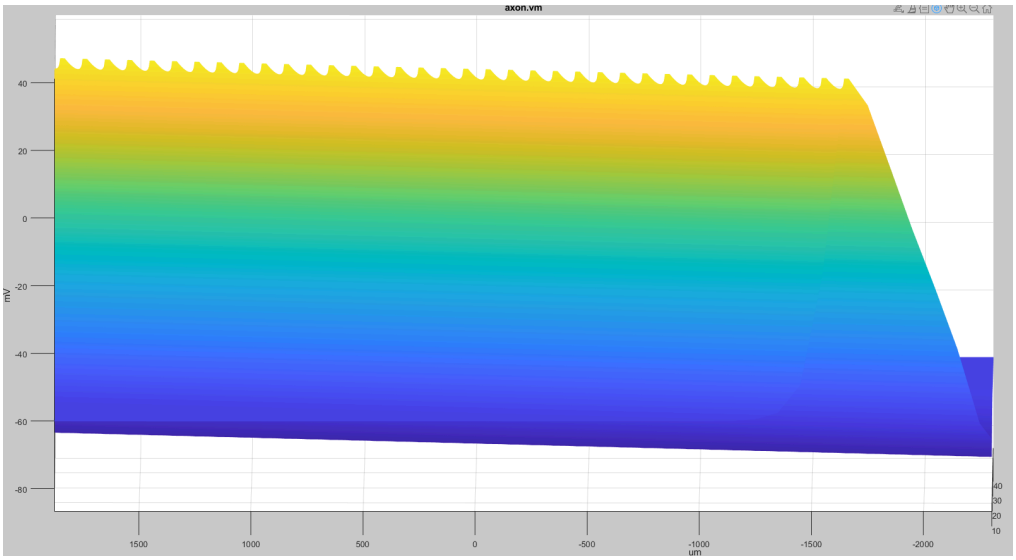

Figure 12: Planar view of the 3D-viewer of the action potential propagation along the axon

3. ***Vary the diameter of the axon and observe new velocities of propagation. Given the relationship θ = kd^n between velocity of propagation θ and axon diameter d, estimate values for k and n.***

Table 1 and *Figure 13* show our experimental data points and the relationship between these values, respectively. As seen in *Figure 13,* the equation for this relationship is estimated to be:

$$\theta = 604d^{0.53},$$

where $k \approx 604$ *and* $n \approx 0.53$.

The value of K depends on the radius, types of the membrane, temperature, and type of species. Our K value may have been overfitted by Excel's trendline. It is important to note that the relationship between θ and d was as expected since Hodgkin and Huxley have reported $\theta \propto \sqrt{d}$.

Table 1: Data for Diameter of Axon vs. Velocity of Propagation

d - Diameter of Axon (μm)	0.1	0.2	0.3	0.4	0.5	0.8	1.0
θ - Velocity of Propagation ($\mu m/ms$)	178	257	317	369	432	525	607

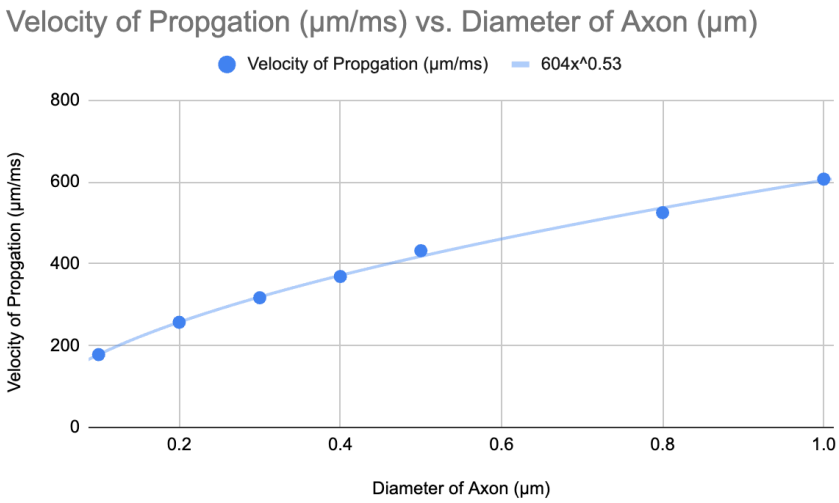

Figure 13: Diameter of Axon vs. Velocity of Propagation

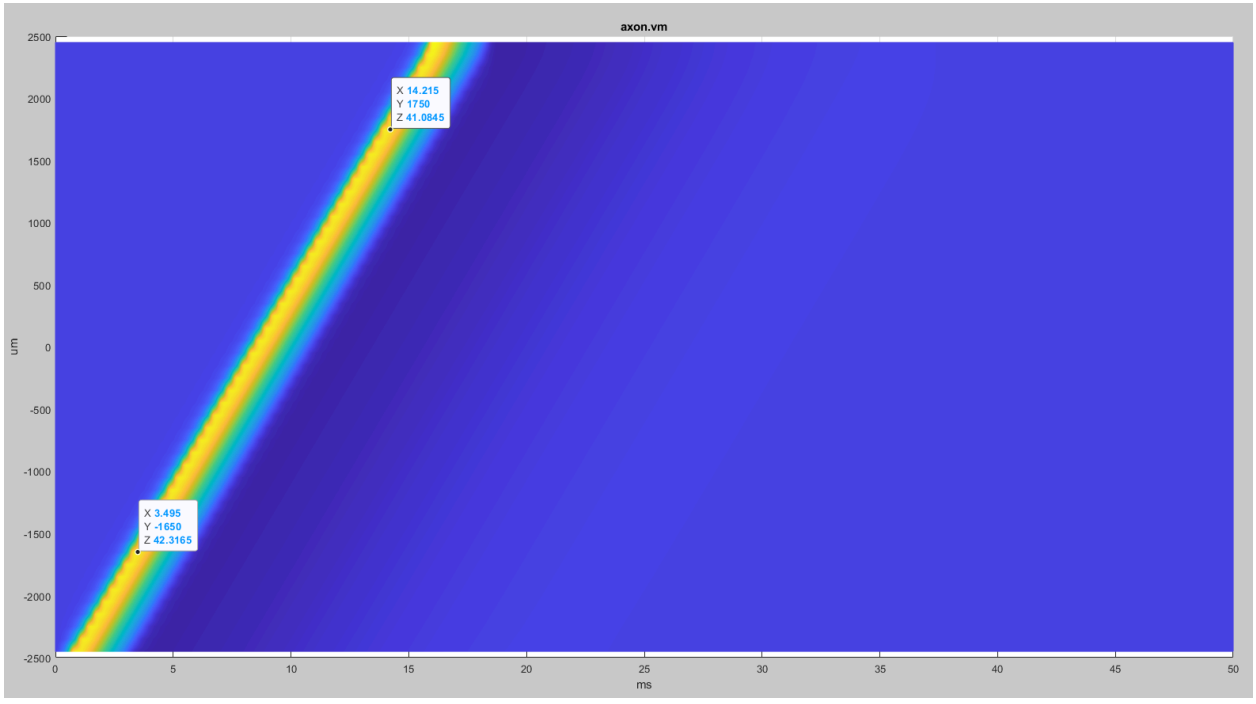

Figure 14: Example velocity calculation when diameter = 0.3µm for unmyelinated axon

- **Myelinated Axon**

1. ***What happened to the velocity of propagation along the axon?***

The velocity of propagation values for the myelinated axon increased. The comparison is shown below, where the default diameter of 1µm is used:

$$\theta_{unmyelinated}\,(d = 1\mu m) = \frac{2050 - (-1950)}{8.400 - 1.815} = 607.44\ \frac{\mu m}{ms}$$

$$\theta_{myelinated}\,(d = 1\mu m) = \frac{1850 - (-2150)}{3.025 - 1.075} = 2051.28\ \frac{\mu m}{ms}$$

$$\theta_{myelinated} > \theta_{unmyelinated}$$

In myelinated axons, the myelin sheath is not continuous; there are gaps shown as "Lnodal". Action potentials jump from node to node in a process called saltatory conduction, which is much faster than the continuous wave of depolarization that occurs in unmyelinated axons. In contrast, unmyelinated axons conduct action potentials along their entire length, which is a slower process. Hence, the relationship makes sense. Additionally, as reported by Hodgkin and Huxley $\theta \propto d$ in passive spread (myelinated axons), suggesting a higher velocity of propagation than the active spread.

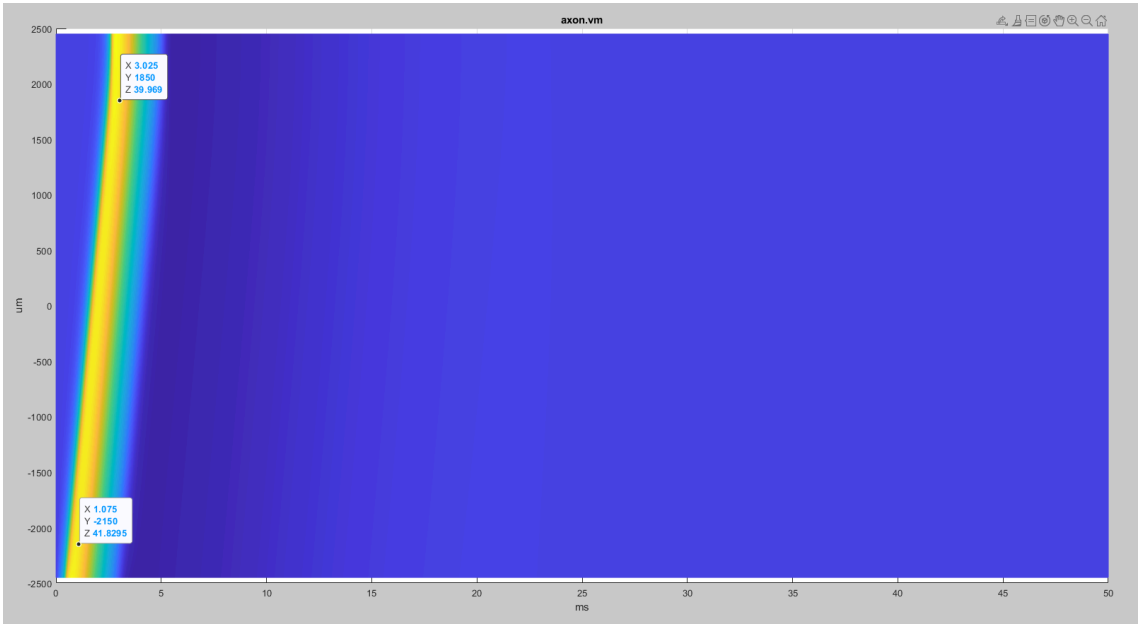

Figure 15: Velocity calculation when diameter = 1.0 µm for myelinated axon with L_{nodal} =10

2. ***What happens if you reduce L_{nodal} to 1?***

When we reduce the L_{nodal} value, that is, shorten these unmyelinated gaps along the myelinated axons, we get an even higher velocity of propagation, as shown below:

$$\theta_{myelinated}\,(d = 1\mu m,\ Lnodal = 1) = \frac{2050-(-2150)}{1.275-0.705} = 7368.42\ \frac{\mu m}{ms}$$

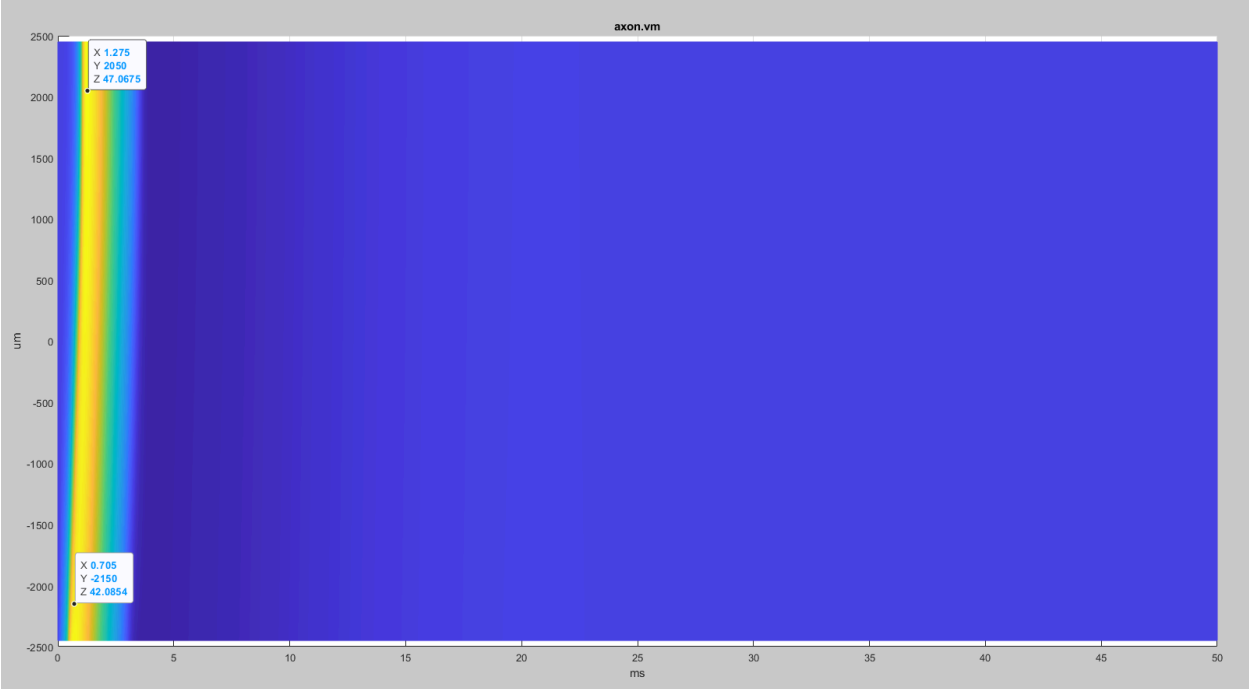

Figure 16: Velocity calculation when diameter = 1.0 µm for myelinated axon with L_{nodal} = 1

3. ***Are the results what you would expect? Why or why not?***

The results are as expected. Action potentials occur only at these "L_{nodal}" gaps, and the signal jumps from node to node through saltatory conduction. By reducing the length of the unmyelinated section, the speed of conduction is increased because the electrical signal can be transmitted more rapidly across the longer passive lengths.

- **Excitability and Refractoriness of Axonal Cables**

1. ***How does the axon respond to this stimulation?***

When we stimulate excitation from the middle of the axonal membrane, we observe propagation in both directions, as seen in *Figures 17 and 18.* Inherently there is no structural difference between the two sides that would favor one direction of propagation over the other, and both sides are capable of propagation through local circuit currents, hence the bidirectionality.

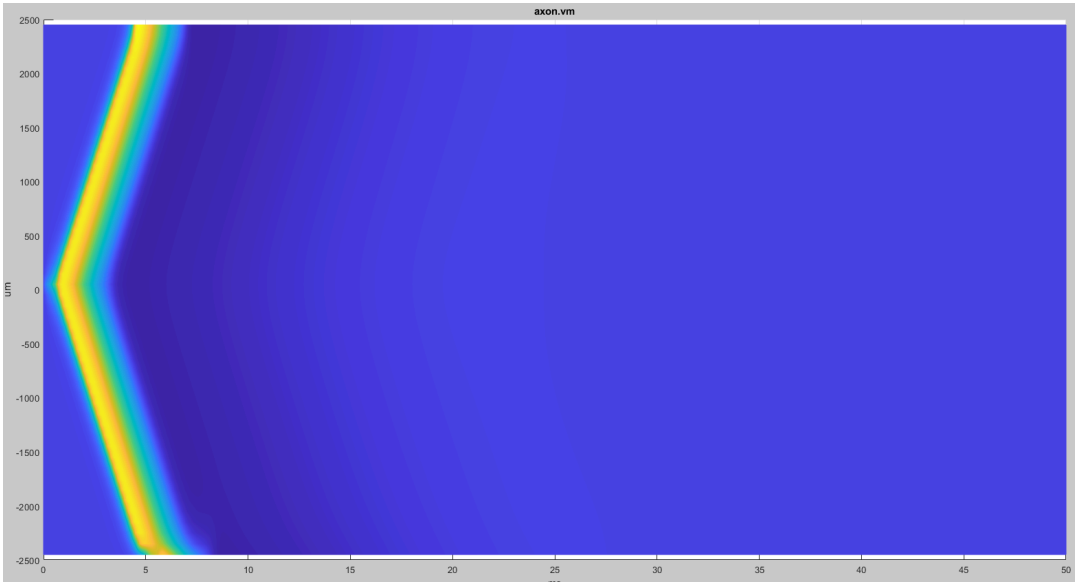

Figure 17: Top view of the propagation

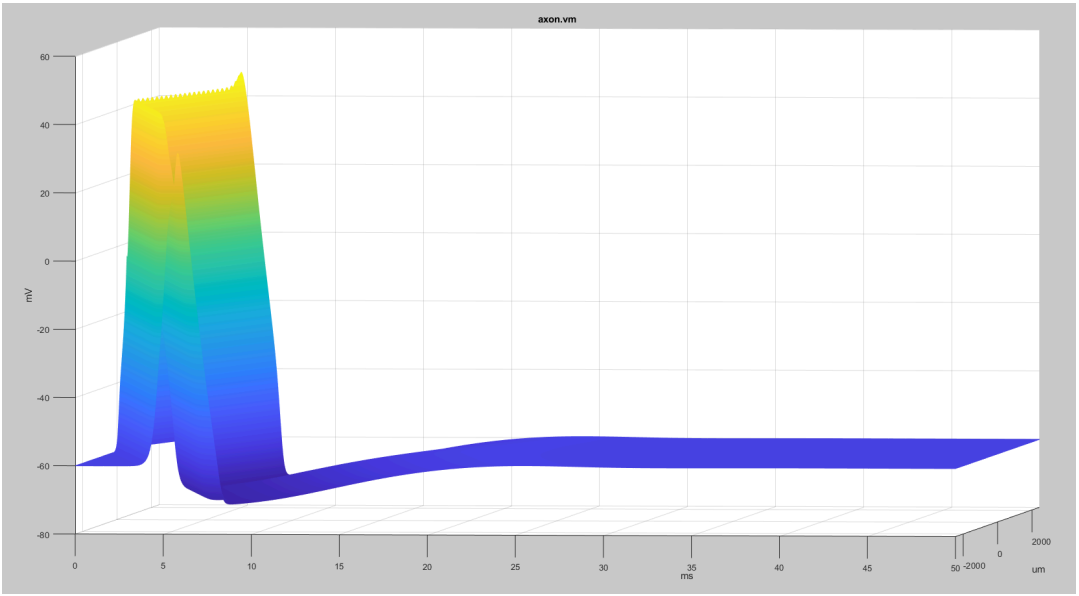

Figure 18: 3D-viewer of the propagation

2. ***Account for the presence or absence of any reflection of the signal at the somatic end of the axonal cable.***

Figure 17 depicts a continuous propagation of the signal without any evident bouncing back or reflection. Similarly, in *Figure 18,* after the initial simulation at the midpoint, there is continuous propagation without any visible reflection. This makes sense because once a section of the axon has fired, it becomes refractory, preventing the action potential from moving backward.

3. ***Conclude by comparing active and passive bioelectrical signal propagation within neurons. What are the benefits of the two approaches and what are their respective roles in nervous system function?***

Active propagation or action potentials ensure signals can travel long distances without diminishing in strength, and conduct frequency encoding. This is essential for long-distance communications in the nervous system, since the regeneration of the action potential at each segment of the axon ensures that the signal does not weaken, even over considerable distances. It also allows for frequency encoding, allowing neurons to convey different intensities or types of information.

Passive propagation is faster due to the absence of ion channel gating processes, and allows for the spatial and temporal summation of signals for synaptic integration. Passive propagation is predominant in rapid short-distance communication, providing quick transmission over short distances, such as within dendrites or initial segments of the axons. It is also essential for signal integration, as multiple inputs can be summed up at the dendrites or cell body, influencing whether a neuron will generate an action potential.

While active propagation ensures reliable and long-distance communication within the nervous system, passive propagation plays a role in quickly integrating and processing incoming signals.

Summary of Results/Discussion

In this lab, we focused on understanding the structures and roles of dendrites, myelinated axons, and unmyelinated axons in neural communication and processing. Our observations revealed that dendrites are passive and efficient in integrating signals both temporally and spatially. They do not actively generate signals but are crucial in processing incoming information. Myelinated axons, also passive, are characterized by their rapid signal transmission capabilities. This speed is essential for the quick transfer of information over long distances within the brain. In contrast, unmyelinated axons are active in signal generation. Most importantly, they employ frequency coding, where the frequency of signal transmission conveys information, rather than the amplitude. Though this process is slower compared to myelinated axons, it is crucial for certain neural communication pathways. We also investigated the effects of dendritic and axonal cable diameters on propagation velocity. Additionally, we investigated the effects of excitability and refractoriness in axonal cables. The combined functionalities of these components are fundamental to the effective processing and communication within the neural system.