BME205 PRA Block 2

RUN THE MODEL

a) What current intensities are injected into the cell?

The two current intensities are 10 micro-Amps/cm^2 and 35 micro-Amps/cm^2

b) How does the behaviour of your neuron react to the different intensities of injected current?

The voltage is directly proportional to current intensity. Therefore, for higher current intensity, there is higher voltage.

PART 1 CHALLENGE: CHANGE THE INJECTED CURRENT AND UNDERSTAND ITS EFFECTS ON THE ACTION POTENTIAL FIRED BY THE NEVER CELL

1. What is the minimum current needed to initiate an action potential?

Approximately 2.3 micro-Amps/cm^2 is required to initiate an action potential.

2. What is the minimum current you need to inject to get the cell to fire for the full duration?

Approximately 6.3 micro-Amps/cm^2 is required to get the cell to fire for the full duration.

3. Increase the value of the injected current that you found in part (b) 10-fold. Does this increase the nerve firing rate?

Yes. The fire rate increases.

4. Now do a 100-fold increase. What happens and why is this occurring?

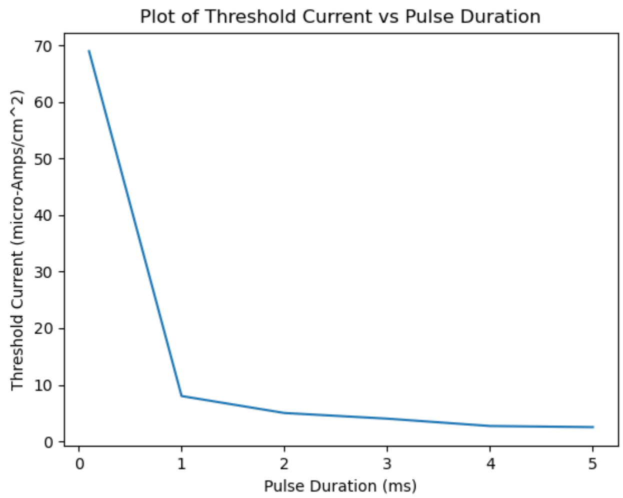
For a sufficiently high injected current, the action potential is initiated but only one cycle of polarization and depolarization occur. The equilibrium is also higher than a cell initiated with a lower injected current.

This phenomenon is because the stimulus is too strong for the physical ion channels. The current is too high for the ion channels to repolarize normally where it would normally hyperpolarize and consequently depolarize again to produce oscillating action potentials.

5. Is there any current you can inject to get a half height action potential?

No, it is not possible to get a half height action potential. Action potentials are governed by a threshold where depolarization beyond the threshold causes a full action potential. This threshold is lower than half the height of the action potential so depolarization to half height always surpasses the threshold and triggers an action potential.

6. What is the effect of pulse duration on threshold current for eliciting a single action potential? Generate a plot of threshold current vs. pulse duration for pulse widths between 0.1 ms and 5 ms. Is there a simple relationship between pulse width and threshold current?



Generally, threshold current is inversely proportional to pulse duration.

PART 2 CHALLENGE: ADJUSTING THE PROPERTIES OF SODIUM (NA)

1. Reduce the conductance density of Na (g_Na). What is the impact on the AP? Return the variable to its original value before part 2.

Reducing the conductance density decrease the action potential peak voltage. Also, whether the action potential is triggered continuously changes as lower conductance density stop action potentials from being triggered continuously.

2. Case Study
    a. What is the average amount of water that healthy kidneys excrete per hour?

62 mL/h

    b. What happens to the electrochemical gradient across the cell membrane when there is a significant decrease in Na+ ion concentration? What do you predict will happen to the cell APs?

The electrochemical gradient decreases as the extracellular concentration of Na+ ions decreases. Although the intracellular concentration may remain constant, the decreased concentration of extracellular ions reduces the potential difference.

Due to the reduced gradient, I expect the cell APs to reduce in voltage and for initial depolarization due to the injected current to be lower. With a reduced gradient and extracellular ion concentration, it will be more difficult to generate a sufficient potential difference by pumping ions to reach the threshold voltage.

    c. Reduce the sodium reversal potential in the model to 20 mV to simulate a decrease in the extracellular Na concentration that is similar to the intracellular concentration. Run the model. Does the outcome match with your prediction? What is the impact on the height/waveform of the action potential?

Yes, the outcome matches with my prediction. The threshold current increases and the voltage of action potentials decreases.

Regarding the impact on the height/waveform of the action potential. The peak voltages decrease. Also, the waveform does not oscillate for lower sodium reversal potentials as depolarization does not reach the threshold voltage unlike.

d. Now reduce the sodium reversal potential in the model to 10 mV to simulate a decrease in the extracellular Na concentration that is less than the intracellular concentration. Run the model. Does the outcome match with your prediction? What is the impact on the height/waveform of the action potential?

The same behaviour as in the previous case is observed. The threshold current continues to increase and the voltage of action potentials decreases. In this case, even more current is required to trigger an action potential as the concentration of ions decreases.

e. Seeing the effects of changing Na+ on neuron behaviour, how could this have caused death (i.e. what organs are controlled by neurons an how would they be affected)?

Most importantly, the brain is controlled by neurons and as the control center for several other organs, malfunction of the brain is fatal.

f. If you have low Na+ concentration but increase the conductivity of Na-channels (g_Na), how does this affect the behaviour of your nerve cell?

Increasing the conductivity of Na-channels would increase the throughput and transport of Na ions. This would negate the transport loss due to low Na+ concentration.

PART 3 CHALLENGE: ADJUSTING THE PROPERTIES OF SODIUM (K)

1. Reduce the conductance density of K (g_K). What is the impact on AP? Return the variable to its original value before part 2.

The magnitude of APs is reduced significantly. Also, there are now repeating cycles of APs.

2. Looking at your patient's medical history, you note that they have been diagnosed with chronic kidney disease. You do a blood panel on the patient and get the following levels for Na and K. What do you suspect is happening to your patient?

Compared to normal levels of Na and K, the Na level is at normal levels while K level is approximately double that of normal. Due to higher concentration of potassium in the blood, there is less potassium concentration inside the blood. Thus, the resting membrane potential is higher than normal. With a higher resting membrane potential, APs are more prone to triggering.

3. Let’s look at the effect of potassium level on action potentials. An increase in K+ ions would increase the extracellular voltage leading to the E-k measurement to decreases (become less negative). Adjust E_K to reflect this difference. How does it affect your AP?

Making E_K less negative makes it easier to trigger APs. With increased equilibrium potential, the resting membrane potential is increased while the threshold level is constant. Therefore, less excitation is required to trigger APs.

4. Change E_K back to its original value and now reduce the potassium conductivity (g_K). What happens to your AP? Is this different from the response to a lower Na+ conductance?

Reducing potassium conductivity causes repeating APs thus implying that it is easier to trigger APs due to hyperexcitation. This opposes lower Na+ conductance which follows theory as K+ and Na+ conductances affect the position of the resting membrane potential.

5. From the effects of K+ on nerve behaviour, do your patient's symptoms make sense? What would you diagnose them with?

Yes, my patient's symptoms make sense. I suspect that K+ active carriers and channels specifically the Na+/K+ pump may be malfunctioning. While Na+ concentration is normal, K+ concentration outside of the cell is too high.