Hodgkin-Huxley Model Simulation Assignment

Run the model

a) What current intensities are injected into the cell?
b) How does the behaviour of your neuron react to the different intensities of injected current?

Part 1 Challenge: Change the Injected Current and Understand its effects on the action potential fired by the nerve cell

1. What is the minimum current needed to initiate one action potential? **Change the value of InjectedCurrent2**
2. Adjust the input current duration to stimulate the cell for the full duration of the simulation. **In the def I_inj function, change the return line from:**

```
return self.InjectedCurrent1*(t>100) -
self.InjectedCurrent1*(t>200) + self.InjectedCurrent2*(t>300) –
self.InjectedCurrent2*(t>400)
```

To:

```
return self.InjectedCurrent1*(t>0) - self.InjectedCurrent1*(t>450)
```

Change the value of variable **InjectedCurrent1** to adjust the amount of current that is injected into the cell.

What is the minimum current you need to inject 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 (i.e. InjectedCurrent1 * 10). Does this increase the nerve firing rate?

4. Now do a 100-fold increase (i.e. InjectedCurrent1 * 100). What happens and why is this occurring?

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

6. Single action potentials can also be elicited by transient current pulses, even when the duration of the current pulse is shorter than the action potential. 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 (You don’t need to write code for this, you can just run the existing code several times to find the data points and then make a plot). Is there a simple relationship between pulse width and threshold current?

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

2) **Case study: On January 12, 2007 KDND radio show held an on-air contest called "Hold your Wee for a Wii". Contestants had to drink as much water as they could without urinating. Every 15 minutes, contestants were handed an 8 oz (240 mL) water bottle to drink. One participant soon died of water intoxication. We will use the current model to understand what happened physiologically.**

   a) Drinking water faster than the rate at which your kidneys can remove it leads to water intoxication. What is the average amount of water that healthy kidneys excrete per hour? By how much did the game exceed this amount?

   b) With excess water in the body, Na+ is diluted in the blood and this leads to a decrease in the [Na+] in the extracellular fluid. 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?

   c) Reduce the sodium reversal potential in the model to20 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?

   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?

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

   f) Certain gene mutations can affect voltage-gated sodium channel conductivity which can lead to Epilepsy, Cardiac arrhythmias., and neuromuscular diseases. Scientists have started to looking into drugs that can increase Na-channel conductivity (called Nav inhibitors; https://www.intechopen.com/books/ion-channels-in-health-and-sickness/voltage-gated-sodium-channels-in-drug-discovery). If you have a low Na+ concentration but increase the conductivity of the Na-channels (g_Na), how does this affect the behavior of your nerve cell?

Part 3 Challenge: Adjusting the properties of Sodium (K)

1) Reduce the conductance density of K (g_K). What is the impact on the AP? Return the variable to its original value before part 2
2) **Case study: You are a doctor in the ICU and a patient experiencing heart arrhythmias comes in. When you look at the patient's heart activity using an ECG, you see that it is different than normal:**

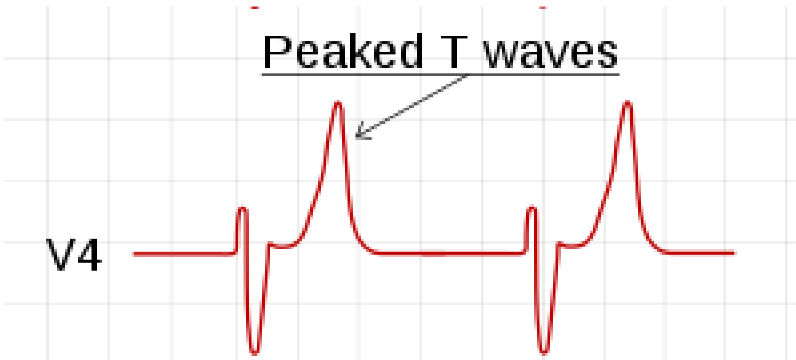

Figure 1 Abnormal ECG

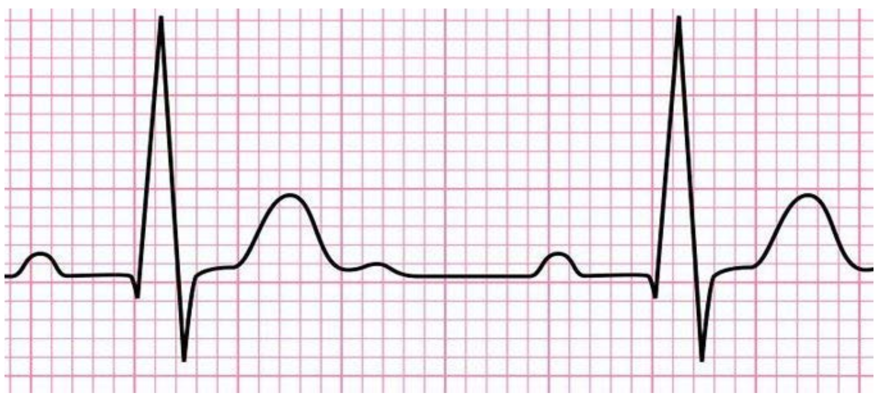

Figure 2 normal ECG

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:

- **Sodium level: 140 mmol/L**
- **Potassium Level: 6.5 mmol/L**

What do you suspect is happening to your patient?

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

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

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