In the name of God

Sharif University of Technology
School of Electrical Engineering
Principles of Biomedical Engineering
Dr. Ali Ghazizadeh
Fall Semester 1400

Homework 3 - Action Potential, H-H model

Note:

- Include all your answers in a zip file named HW3_Name_Student ID.zip.
- Your zip file should contain your written answers, MATLAB scripts, and a short pdf report for questions 5 and 6.
- Do not copy other students' answers.
- If you have any questions regarding this assignment, message *@asadian_ah* in Telegram or email *ahosseina98@gmail.com*.

Problem 1.

Choose the correct answer.

1. What effect does an intravenous injection of KCl have on behavior of neurons?
   (a) Extracellular K^+ decreases and therefore the membrane potential gets closer to Na^+ equilibrium potential.
   (b) The membrane potential becomes more negative and it becomes more difficult to generate action potentials.
   (c) Extracellular K^+ increases and therefore the membrane potential gets closer to Na^+ equilibrium potential.
   (d) None of the above.

2. Photoreceptors in the retina have special channels that are open to Na^+ in the dark. When light hits photoreceptors, these special channels close. What can you conclude from this?

   (a) Photoreceptors depolarize to light.
   (b) Photoreceptors hyperpolarize to light.
   (c) Photoreceptor voltage does not change in the presence of light.
   (d) None of the above.

3. According to the figure 1, the slow depolarization apparent in phase 4 is primarily due to:

   (a) The Slow L-type Ca^{2+} Channel.
   (b) A slow, inward Na^+ current (funny current).
   (c) A slow, outward Na^+ current (funny current).
   (d) None of the above.

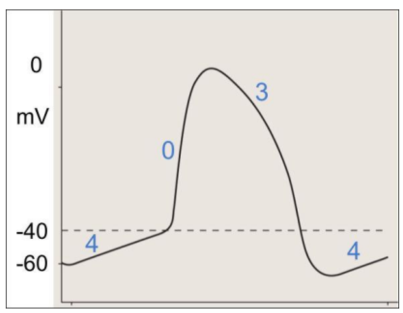

Figure 1: An action potential.

4. Drug X, when applied to a nerve axon, results in both a gradual decrease in the amplitude of individual action potentials and a depolarization of the resting potential, both of which develop over a period of several hours. The drug is most likely:

   (a) Blocking the voltage-dependent Na^+ permeability.
   (b) Blocking the voltage-dependent K^+ permeability.
   (c) Blocking the (Na^+ - K^+) pump.
   (d) Blocking the process of Na^+ inactivation.
   (e) Increasing the rate at which voltage-dependent changes in K^+ permeability occurs.

5. Reducing the concentration of extra-cellular Na^+, reduces the amplitude of action potential.

   (a) True

   (b) False

6. The rising phase of the action potential is controlled by the parameter:

   (a) m (The probability that a Na^+ activation gate is open.)

   (b) h (The probability that a Na^+ inactivation gate is open.)

   (c) n (The probability that a K^+ gate is open.)

   (d) All of the above.

Problem 2.

In an action potential, how many Na^+ ions must move into the axon to cause a depolarization of 100 mV?
Suppose the length of a cylindrical axon is 100 μm, and it has a radius of 4 μm. Assume the thickness of the membrane is 10 nm and the dielectric constant is 7.
(Equations and constants are provided. Please be sure that you show units.)

$\mathrm{Q} = \mathrm{C}\ .\ \Delta E, \quad \text{(coulombs)} = \text{(coulombs/volt) (volt)}$

$\mathrm{C} = \dfrac{\kappa.\epsilon_0.A}{d}$

$\epsilon_0 = 8.85\ .\ 10^{-12}$ (F/m)

Elementary charge $= 1.60\ .\ 10^{-19}$ coulombs

Problem 3. ***The effects of toxins on different channels.***

Researchers at Duke University discovered in the 1960s that a toxin (Tetrodotoxin (TTX)) isolated from the ovaries of the puffer fish could selectively block the sodium channel. TTX blocks all sodium-dependent action potentials and therefore is usually fatal if ingested.

(a) Another important compound that can affect certain ion channels is Tetraethylammonium (TEA). What does it do? (If you don't know, search the web)

(b) According to the figure 2 from a voltage-clamp experiment, we can see a time-dependent inward ionic current followed by a time-dependent outward ionic current. A hypothesis proposes that there are two sets of voltage-gated channels: Voltage-gated sodium and voltage-gated potassium channels. First, design an experiment to isolate Na^+ and K^+ currents and then draw Na^+ and K^+ currents separately.

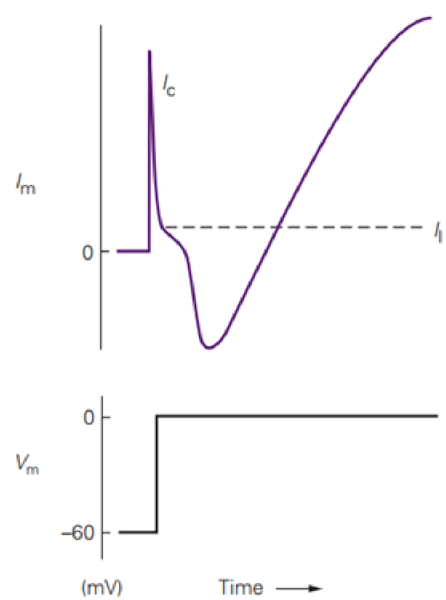

Figure 2: A voltage-clamp experiment demonstrates the sequential activation of voltage-gated sodium and potassium channels.

Problem 4.

In a physiological experiment, the following data is collected. The membrane thickness is 10 nm and We know that the rest potential is -88.5 mV. (kT/q $\simeq 26.7 mv$)

$[\mathrm{Na}^+]_i = 12 \quad mMol/lit$	$[\mathrm{K}^+]_i = 155 \quad mMol/lit$	$[\mathrm{Cl}^-]_i = 4 \quad mMol/lit$
$[\mathrm{Na}^+]_o = 145 \quad mMol/lit$	$[\mathrm{K}^+]_o = 5 \quad mMol/lit$	$[\mathrm{Cl}^-]_o = 110 \quad mMol/lit$

(a) Calculate V_{Na} and V_K.

(b) Calculate α and β for each parameter of Hodgkin-Huxley model. i.e. n, m, h. Using α and β parameters, find an equation for m(t), n(t) and h(t). What are their steady-state values?

$$\alpha_n(V) = \frac{0.1 - 0.01V}{e^{1-0.1V} - 1}, \qquad \alpha_m(V) = \frac{2.5 - 0.1V}{e^{2.5-0.1V} - 1}, \qquad \alpha_h(V) = 0.07\, e^{-\frac{V}{20}}$$

$$\beta_n(V) = 0.125\, e^{-\frac{V}{80}}, \qquad \beta_m(V) = 4\, e^{-\frac{V}{18}}, \qquad \beta_h(V) = \frac{1}{e^{3-0.1V} + 1}$$

(c) Calculate g_{Na} and g_K at rest. ($\bar{g}_K = 24.31$ mmho$/cm^2$, $\bar{g}_{Na} = 42.9$ mmho$/cm^2$)

(d) Assume g_L=0.3 mmho$/cm^2$. Calculate V_L so that it is compatible with the values you calculated in previous parts.

(e) Calculate I_{ext} (μ A$/cm^2$) so that V_{rest} becomes -80 mV.

Problem 5.

Plot the following graphs in MATLAB based on equations in the lecture slides.

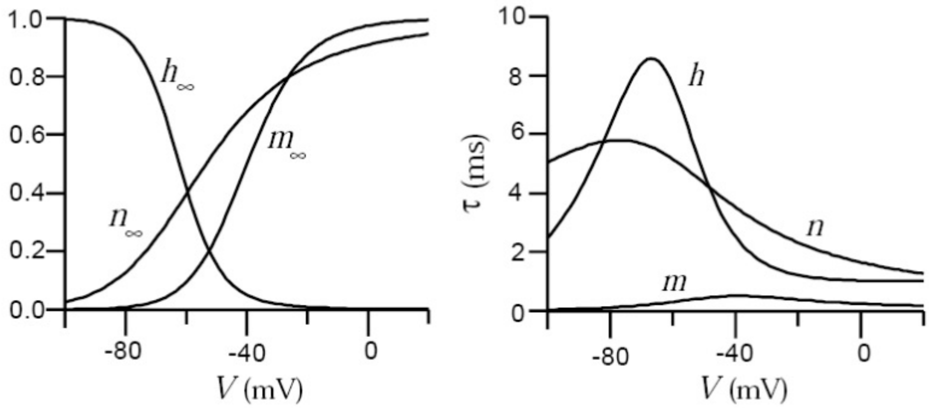

Figure 3: The voltage-dependent functions of the Hodgkin-Huxley model.

Problem 6.

In this exercise, we will use a MATLAB script (HH.m) that implements a simulation a single-neuron action potential based on Hodgkin-Huxley model using Euler's method under a current clamp experiment.
Current clamp means that we control the external current applied and measure the membrane potential in response to our manipulation. Note that this is different from voltage clamp in which we control the membrane potential and measure the ionic current.

In particular, this script is set to apply a depolarizing external current of 10 μA/cm^2 for 10 milliseconds.

(a) Complete the provided MATLAB code (file HH.m) and plot output voltage for a depolarizing external current of 10 μA/cm^2 for 10 milliseconds. Your output should be similar to figure 4.

(b) Find minimum amplitude of external current with duration of 10 milliseconds causes an action potential.

(c) Find minimum duration of external current with amplitude of 3 μA/cm^2 causes an action potential.

(d) Does the threshold for firing an action potential depend on the shape of the current pulse injected into the cell or does it only depend on the total charge injected? Explain your answer.

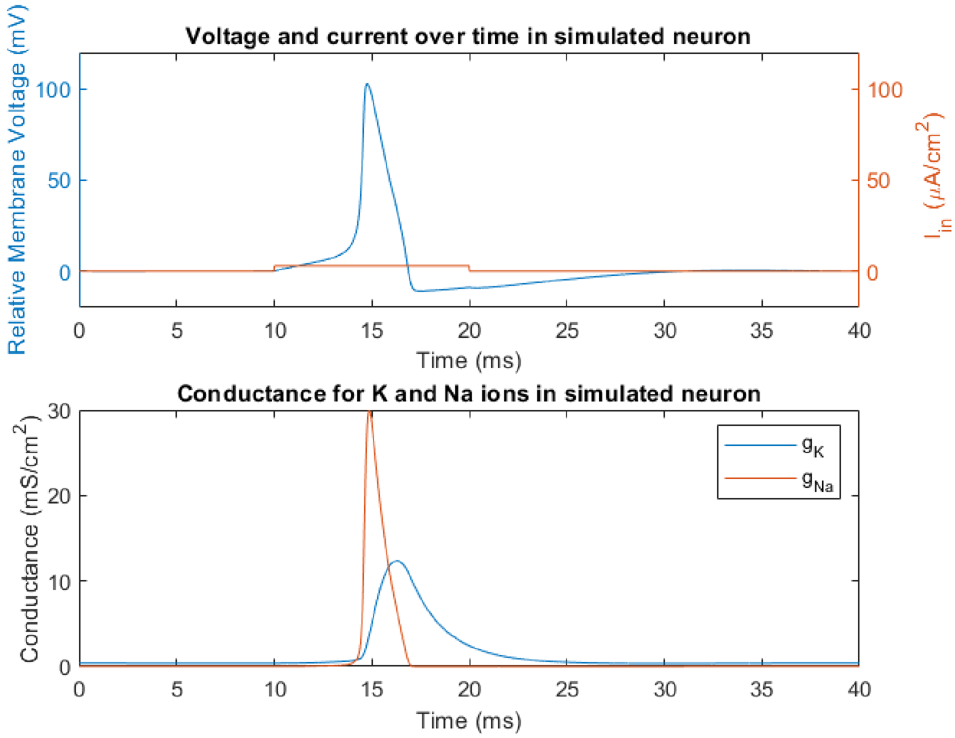

Figure 4: Membrane voltage (relative to resting potential) and voltage-dependent conductances for the Hodgkin-Huxley model.

(e) Make a copy of HH.m and call it HHpaired.m. Modify this file to apply two current pulses, each of amplitude 3 μA$/cm^2$ and a duration of 10 milliseconds. The pulses should have an inter-pulse interval of 10 milliseconds which means they are separated by 10 milliseconds measured from the end of the first pulse to the start of the second pulse. Look at the plots and comment on what you see.

(f) Modify the code so that the inter-pulse interval is now 2 milliseconds but keeping the amplitude at 3 μA$/cm^2$. Look at the output plots, what has changed from the previous case? Find minimum inter-pulse interval that causes an action potential.

(g) (**Extra question**) Plot HH variables (m, n, h) and the membrane currents (I_K, I_{Na}, I_{Leak}) using HH.m on the same figure vs time.