Theoretical Neuroscience (BITS F317)

Assignment 1

You have to submit following problems. From part-1, problem nos. 4, 5, 8. From part-2, problem no.1. Deadline is 14-February 3 PM.
Part-2 problem-1 should be entirely uploaded on Moodle along with your MATLAB codes. One .doc/pdf file should contain all figures & your responses . The other file (include a .m file) should contain the code
Part-1 should be submitted in hard-copy.

1 Part-1

1. The axon of a certain mammalian neuron has a diameter of $0.5\mu m$ (typical in the mammalian brain) is $2.3mm$ long.

   Suppose that (a) the specific capacitence (capacitence per unit surface area) is $0.75\mu F/cm^2$ (Infact, this is the estimate for a pyramidal neuron of the Hippocampus region in brain), and (b) the specific membrane resistance* of the neuron (close to its rest membrane potential) is $100M\Omega cm^2$. For the $2.3cm$ long axon, calculate its

   (a) total capacitence

   (b) total membrane resistance

   *Read through first few pages of chapter 5 of textbook for the definition of specific membrane resistance (it is not the same as resistivity).

2. Squid's giant axon - Find the equilibrium potential for Na^+, Cl^- , K^+ given that the intracellular & extra cellular concentrations are as follows

	Ionic concentration ICF	Ionic concentration ECF
Na^+	$50mM$	$440mM$
K^+	$400mM$	$20mM$
Cl^-	$50mM$	$560mM$

Table 1: Ionic concentration - Squid giant axon

   Compare these against mammalian neuron discussed in the class (you can see the slides for ionic concentrations on Moodle).

3. Membrane of a neuron can be represented as RC circuit with a battery in series with R. This was discussed in the class.

   A small segment of neuron of length $= 1cm$ and diameter $= 2\mu m$ is initially maintained at its rest membrane potential $V = V_{rest} = -70mV$. A step current of magnitude$I_0 = 0.3nA$ is injected into the neuron at $t = 0$ and it lasts for $10msec$.

   (a) Calculate the membrane time constant.

   (b) Find the variation of membrane voltage with time $V(t)$. Sketch the variation.

   Take $C = 100pF$, $R = 100M\Omega$. The axon is space clamped ensuring no spatial variation of voltage.

4. In a voltage clamped HH neuron, steady state currents of various ions at membrane voltage V are -
   (a) $I_{Na,\infty} = \bar{g}_{Na}m^3_\infty(V)h_\infty(V)(V - E_{Na})$, (b) $I_{K,\infty} = \bar{g}_K n^4_\infty(V)h_\infty(V - E_K)$, (c) $I_{L,\infty} = \bar{g}_L(V - E_{Na})$, where

   $\bar{g}_{Na} = 120mS/cm^2$, $\bar{g}_K = 36mS/cm^2$, $\bar{g}_L = 0.3mS/cm^2$. Calculate the equlibrium potential for yourselves (problem-2).

(a) Plot $I_{Na,\infty} vs.\ V$ & $I_{K,\infty}\ vs.\ V$, and $I_{L,\infty}\ vs.\ V$. Comment on the results.

(b) Plot net ionic current across the mebrane for different membrane voltages $I_{ion} vs.\ V$.

(c) From the above plots, find the value of the resting membrane potential of a HH neuron

5. After firing an action potential the neuron the membrane potential first falls below its resting value and then approaches its rest value (figure below). Explain qualitatively why the membrane potential falls below its rest value.

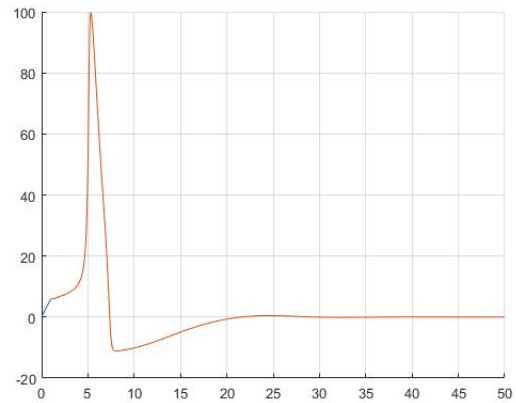

Figure 1: Action potential after a $1msec$ pulse of height $7\mu A/cm^2$ is injected into the HH axon

6. Suppose, h gates are absent in the Na+ channels of some neuron. Rest is all the same as in the HH neuron. Will this neuron fire an action potential if stimulated by a sufficiently strong pulse of current ?

7. Continuation of above problem. Suppose that the time constants of m & n-gates are not the ones given above. Instead, assume that the time constant curves for the two gates are swapped. If we now stimulate this neuron, will or won't this neuron fire an action potential ?

8. For the Hodgkin-Huxley neuron the rest membrane potential is approx -65 mV. In its resting state, the gating variables m, h, n will also be constant in time. Find the resting values of m, h, n in terms of the rate constants $\alpha's$ and $\beta's$

   Hint: Resting values can be calculated from the requirement that m, h, n are independent of time which would imply that $\frac{dm}{dt} = \frac{dh}{dt} = \frac{dn}{dt} = 0$.

2 Part-2 (Simulation of Hodgkin-Huxley neuron)

1. Here you will carry out computer simulations of the Hodgkin-Huxley model of the axon subjected to a steady external current I_{ext} starting at time $t = 0$. Prior to this, the membrane potential is at its resting value.

   (a) Write a MATLAB code to solve the Hodgkin-Huxley equations using the ODE solve ode45. Remember, that at $t = 0$:

   - Values of the membrane potential should be taken to be its resting value $\approx -65mV$ AND
   - Gating variables m, h, n must also be assigned their resting values. You have been asked to find the expressions for their resting values in terms of the expressions of rate constants $\alpha's$, $\beta's$. Expressions of $\alpha's$ and $\beta's$ as a function of voltage have been put up on Moodle.

   (b) Explore the dynamics of the HH neuron with$I_{ext} = 2, 6, 8, 10, 12, 16, 18\mu A/cm^2$.

   i. Plot $V\ vs.\ t$ for each I_{ext}. Does the neuron spike for all injected currents?

   ii. Plot the gating variables $m, h, n\ vs.\ time$. Comment on the dynamics (open/closed) of the gating variables, at different stages of the voltage changes & correlate these with the action potential.

   iii. Comment on the time duration of the spike & time duration over which the neuron returns to its resting value.

iv. Are the spikes periodic ?

v. Comment on the frequency of spikes f (in Hz) on varying I_{ext}.

vi. Does the peak value of membrane voltage in a spike vary with I_{ext} ? Comment whether the result surprises you and why/why not?

For squid giant axon (modeled by Hodgkin-Huxley), $C = 1\mu F/cm^2$, $\bar{g}_{Na} = 120mS/cm^2$, $\bar{g}_K = 36mS/cm^2$, $\bar{g}_L = 0.3mS/cm^2$. These are obtained experimentally. Calculate the Equilibrium potential E_{Na}, E_K , E_L (a problem in part-1) and use these in the simulations.

Very Important Note: In the HH equations , voltages and time are in units of mV & $msec$ respectively AND values of C, $\bar{g}'s$ are in units of $\mu F/cm^2$, and mS/cm^2 respectively.

2. Here lets consider the response of the HH neuron to short $1msec$ pulses of different magnitudes (eg. $1, 2, ...\mu A/cm^2$).

   Action potentials are often regarded as $All - or - none$ events. It means the following. If voltage is below a threshold valueV_{th} at the time when the current pulse switches off, the voltage ceases to increase and drops to rest value. However, if the voltage goes above some threshold value V_{th}, it rises all the way up to its peak before returning to rest. When $V > V_{th}$, There is no half-way up. Hence, either the rising voltage goes all the way to its peak (forming an action potential) or it returns to rest without rising further.

   In the simulations, here you will explore the $All - or - none$ event of an action potential

   (a) Modify your MATLAB code to include an external current pulse of a chosen magnitude and of $1msec$ duration.

   (b) Select & experiment with different current magnitudes in your simulations. Find a voltage threshold.