Due August 13, 2014 at 11PM

Note: In all the problems, be mindful of the units of various quantities and the sign conventions for currents and voltages.

Your submission must include:

- 1. A .pdf or .doc file clearly documenting your code, figures, and results.
- 2. Your MATLAB code. The code must be saved in plain text files that can be immediately run in MATLAB; include a file called main.m that runs the functions you implemented and generates the figures described in your assignment write-up. You will lose credit if your code is absent or cannot be run.

Store your write-up and code in a single directory named hw1_yourID (for example hw1_12D423222) and submit it in moodle.

Do not wait till the last minute to start the Assignment as you will require at least at least 8 hours to complete all the questions.

Late submission policy:

Before the solution key is uploaded in moodle: If your original score is S and you submitted the HW X hours after the deadline, your score will be $S \exp(-X/24)$.

After the solution key is uploaded in moodle: 0 credit.

Spiking Neuron Models

In this assignment, we will learn how to model the activity of spiking neurons starting with the simplest model. We will also implement the Hodgkin-Huxley neuron model and use it to determine an estimate of the energy cost associated with a spike.

Problem 1: Leaky Integrate and Fire Model

The dynamics of the membrane potential V(t), in the LIF neuron model is given by the equation

$$C\frac{dV(t)}{dt} = -g_L(V(t) - E_L) + I_{app}(t)$$
(1)

C is the membrane capacitance, g_L is the leak conductance and E_L is the leak reversal potential. I_{app} is the externally applied current and is assumed to be positive for current flowing into the cell.

When $V \ge V_T$, a spike is issued and V is reset to E_L (We will write this as $V(t) \longrightarrow E_L$). (Assume that C= 300 pF, $g_L = 30$ nS, $V_T = 20$ mV and $E_L = -70$ mV).

- (a) Assume that a constant current I_0 is applied to the neuron. Write an expression for the steady state value of the membrane potential. Hence, determine the minimum value of the steady state current, I_c necessary to initiate a spike. **2 points**
- (b) In order to simulate the behavior of a set of N neurons, it is useful to define a $N \times 1$ column vector to the store the membrane potentials of the N neurons. Write a program to solve the equivalent difference equation numerically using Runge-Kutta second order method for a set of N neurons driven by external current input. (You should not use a FOR loop to calculate the potential of the N neurons, rather, the potential of all the neurons should be calculated in one step.)

Assume that the input to the program is a $N \times M$ column vector, representing the input current for the N neurons for M time-intervals where $M = T/\Delta t$. The output of your program should be a $N \times M$ matrix storing the values of the membrane potential for the N neurons, for the M time-intervals.

(c) We would like to now use this framework to study the dynamics of LIF neurons. Assume that you have a population of 10 identical neurons, with each neuron receiving a constant current. Let the magnitude of the input current for the k^{th} neuron be given by the expression

$$I_{app,k} = (1 + k\alpha)I_c \tag{2}$$

where $\alpha = 0.1$. (In this example, the current does not vary with time, so, all the values across any row of the input current matrix is a constant). Plot the membrane potential for neurons 2, 4, 6 and 8 from t = 0 to 500 ms. (Assume $\Delta t = 0.1$ ms and at t = 0, the neuron is in steady-state with $I_{app}(t) = 0$).

(d) Plot the average time interval between spikes from (c) as a function of $I_{app,k}$. 4 points

Problem 2: Izhikevich Model

The dynamics of the membrane potential V(t), in the Izhikevich neuron model is given by the equations

$$C\frac{dV(t)}{dt} = k_z(V(t) - E_r)(V(t) - E_t) - U(t) + I_{app}(t)$$
(3)

$$\frac{dU(t)}{dt} = a\left[b(V(t) - E_r) - U(t)\right] \tag{4}$$

When $V(t) \geq v_{peak}$, $V(t) \longrightarrow c$ and $U(t) \longrightarrow U(t) + d$.

By varying the parameters $C, E_r, E_t, k_z, a, b, c$ and d, a variety of neuronal behaviors can be modeled.

	C(pF)	$k_z(\mu S/V)$	$E_r(\mathrm{mV})$	$E_t(\text{mV})$	a (KHz)	b(nS)	c(mV)	d(pA)	$v_{peak}(\mathrm{mV})$
$\overline{\mathrm{RS}}$	100	0.7	-60	-40	0.03	-2	-50	100	35
IΒ	150	1.2	-75	-45	0.01	+5	-56	130	50
$\overline{\mathrm{CH}}$	50	1.5	-60	-40	0.03	+1	-40	150	25

(a) What are the steady state values of V and U for $I_{app} = 0$?

2 points

(b) Write the equivalent difference equations for (3) and (4).

2 points

(c) Write a program to solve the equivalent difference equation for a set of N Izhikevich model neurons using Runge-Kutta fourth order method. The neuron type should be a parameter in your function call, for each of the N neurons. You may use $\Delta t = 0.1$ ms and plot the response of the three neurons above from t = 0 to 500 ms, for $I_{app} = 400, 500, 600$ pA.

16 points

Note: Try to re-run 2(c) with larger values of Δt . You will notice that the overall dynamics can change drasticially, especially for neuron CH. This is because of the inaccuracy in determining the exact time when V(t) exceeds v_{peak} . For a good description of this issue and how to get around it, see: Hybrid spiking models, Phil. Trans. R. Soc. A November 13, 2010 368 (1930) 5061-5070.

We will ignore these issues here, and for the sake of displaying, you may chose to artificially set the value of membrane potential just before reset to v_{peak} in your code.

Problem 3: Adaptive Exponential Integrate-and-Fire Model

The dynamics of the membrane potential V(t), in the AEF neuron model is given by the equations

$$C\frac{dV(t)}{dt} = -g_L(V(t) - E_L) + g_L \Delta_T \exp\left(\frac{V(t) - V_T}{\Delta_T}\right) - U(t) + I_{app}(t)$$
 (5)

$$\tau_w \frac{dU(t)}{dt} = a \left[V(t) - E_L \right] - U(t) \tag{6}$$

When $V(t) \ge 0$, $V(t) \longrightarrow V_r$ and $U(t) \longrightarrow U(t) + b$.

As before, by varying the parameters a variety of neuronal behaviors can be modeled.

	C(pF)	$g_L(ns)$	$E_L(\text{mV})$	$V_T(\mathrm{mV})$	$\Delta_T(\mathrm{mV})$	a(nS)	$\tau_w(\mathrm{ms})$	b(pA)	$V_r(mV)$
$\overline{\mathrm{RS}}$	200	10	-70	-50	2	2	30	0	-58
IΒ	130	18	-58	-50	2	4	150	120	-50
СН	200	10	-58	-50	2	2	120	100	-46

(a) Write the equivalent difference equations for (5) and (6).

2 points

- (b) What are the steady state values of V and U for $I_{app}=0$? (Determine the answer numerically, such that the value of V is accurate within $\pm 1\mu V$).
- (c) Write a program to solve the equivalent difference equation for a set of N AEF model neurons using Euler method. The neuron type should be a parameter in your function call, for each of the N neurons. You may use $\Delta t = 0.1$ ms and plot the response of the three neurons above from t = 0 to 500 ms, for $I_{app} = 250,350,450$ pA.

 12 points

Problem 4: Spike energy based on Hodgkin-Huxley neuron model

The dynamics of the membrane potential V(t), in the Hodgkin-Huxley neuron model is given by the equations

$$C\frac{dV(t)}{dt} = -i_{Na}(t) - i_{K}(t) - i_{l}(t) + I_{ext}(t)$$
(7)

where

$$i_{Na}(t) = g_{Na}m^3h(V(t) - E_{Na})$$
 (8)

$$i_K(t) = g_K n^4 (V(t) - E_K) \tag{9}$$

$$i_l(t) = g_l(V(t) - E_l) (10)$$

The variables n, m and h lie in the interval [0, 1] and obey the equation

$$\frac{dx}{dt} = \alpha_x(t)(1-x) - \beta_x(t)x\tag{11}$$

where

$$\alpha_n(t) = \frac{0.01(V(t) + 55)}{1 - \exp(-(V(t) + 55)/10)} \qquad \beta_n(t) = 0.125 \exp(-(V(t) + 65)/80) \tag{12}$$

$$\alpha_m(t) = \frac{0.1(V(t) + 40)}{1 - \exp(-(V(t) + 40)/10)} \qquad \beta_m(t) = 4\exp(-0.0556(V(t) + 65)) \tag{13}$$

$$\alpha_h(t) = 0.07 \exp(-0.05(V(t) + 65))$$
 $\beta_h(t) = \frac{1}{1 + \exp(-0.1(V(t) + 35))}$ (14)

V(t) is assumed to be measured in mV in the above expressions.

Assume that C=1 μ F/cm², $E_{Na} = 50$ mV, $E_{K} = -77$ mV and $E_{l} = -55$ mV and $g_{Na} = 120$ mS/cm², $g_{K} = 36$ mS/cm² and $g_{l} = 0.3$ mS/cm².

- (a) Solve the equivalent difference equations for (7) and (11) to determine the ion currents and the membrane potential for a step current waveform described as follows: $I_{ext}(t) = I_0[H(t-2T) H(t-3T)]$ where H(x) is the Heaviside step function defined as H(x) = 1 if $x \ge 0$ and H(x) = 0 otherwise. You should set your initial conditions such that there are no spikes when there is no external input current to the neuron. Assume $I_0 = 15\mu\text{A/cm}^2$, $\Delta t = 0.01$ ms, T = 30ms.
- (b) The instantaneous power dissipated (per unit area) in the various ion channels can be approximated by the expression

$$P_x(t) = i_x(t)(V(t) - E_x)$$
(15)

Similarly, the power spent in charging/discharging the membrane capacitance (per unit area) can be approximated as

$$CV(t)\frac{dV(t)}{dt} = [-i_{Na}(t) - i_{K}(t) - i_{l}(t) + I_{ext}(t)]V(t)$$
(16)

Plot the relative magnitudes of the instantaneous power dissipated in the three ion channels and in the membrane capacitor as a function of time for one cycle of the action potential. **4 points**

(c) Numerically integrate the power in (b) to determine the total energy dissipated in one cycle of the action potential for a patch of the cell membrane with area of 1 μm^2 4 points.