AMS 332/BIO 332/NEU 536
– Project for Module 4 –

Part A: Hodgkin-Huxley model (30/60 points)

*** Remember to include: 1. your code (as an appendix) and 2. a statement of collaboration. ***

Box 1: The Hodgkin-Huxley model

- **Main equations:**

$$C\frac{dV}{dt} = -G_L(V-V_L) - G_{Na}m^3h(V-E_{Na}) - G_Kn^4(V-E_K) + I_e, \tag{1}$$

where V is the membrane potential, I_e is an external current and the gating variables m, n and h obey the first-order ODEs

$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m, \tag{2}$$

$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h, \tag{3}$$

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n, \tag{4}$$

with transition rates $\alpha(V)$ and $\beta(V)$ given by

$$\alpha_m(V) = \frac{0.1(V+40)}{1-e^{-0.1(V+40)}}\ ; \quad \beta_m(V) = 4e^{-0.0556(V+65)}, \tag{5}$$

$$\alpha_h(V) = 0.07e^{-0.05(V+65)}\ ; \quad \beta_h(V) = \frac{1}{1+e^{-0.1(V+35)}}, \tag{6}$$

$$\alpha_n(V) = \frac{0.01(V+55)}{1-e^{-0.1(V+55)}}\ ; \quad \beta_n(V) = 0.125e^{-0.0125(V+65)}. \tag{7}$$

- **Model parameters**:
  $G_{Na} = 400$ nS, $G_K = 200$ nS, $G_L = 2$ nS, $E_{Na} = 99$ mV, $E_K = -85$ mV, $V_L = -65$ mV, $C = 2$ pF and I_e as specified in the exercises.
- **Initial conditions**:
  $V(0) = V_L$, $m(0) = m_\infty(V(0))$, $h(0) = h_\infty(V(0))$, and $n(0) = n_\infty(V(0))$, where

$$m_\infty(V) = \frac{\alpha_m(V)}{\alpha_m(V)+\beta_m(V)}, \tag{8}$$

and analogous for $h_\infty(V)$ and $n_\infty(V)$.

1. (Main simulation) **Simulate $t_{max} = 200$ ms evolution of one HH neuron as defined in** Box 1. Use the forward Euler algorithm with **time step $dt = 0.01$ ms**. Stimulate the neuron from time $t_0 = 40$ ms with a constant current of amplitude $I_0 = 200$ pA and lasting until t_{max} (i.e., $I_e = 0$ for $t < 40$ ms and $I_e = I_0$ for $t > 40$ ms). Plot in the same figure but in different subplots:
   i) the membrane potential vs. time,
   ii) the total membrane current, $I_m = G_L(V-V_L) + G_{Na}m^3h(V-E_{Na}) + G_Kn^4(V-E_K)$, vs. time,
   iii) the sodium conductance ($=G_{Na}m^3h$) vs. time,
   iv) the potassium conductance ($=G_Kn^4$) vs. time, and
   v) the current I_e vs. time.

Include the plot in your report.

Matlab tip ⇒ Use `figure(1)` and then start each plot with `subplot(5,1,x)`, where x ranges from 1 to 5. □

2. (Spike detection) **Endow your code with a mechanism to detect each 'spike'** (=action potential). To do so, you must decide on a critical value V_{spk} at which you might say that a spike has been emitted (values between −30 and 0 mV should be good choices). **Make sure to count each spike only once.**

   Now, enlarge the previous plot from Exercise 1 to illustrate the dynamics of one single action potential, marking the time at which V_{spk} was reached. **Include the plot in your report.**

   Matlab tip ⇒ Use `xlim([`t_1 t_2`])` in each subplot to zoom in all subplots equally; choose as t_1 and t_2 the time just before and just after the action potential, respectively. □

3. (Action potential threshold) Determine the threshold current to elicit a single action potential. Start from a very small value of the input current (e.g., $I_0 = 2$ pA) and increase it **until you find the value of the current I_1 at which the neuron starts firing one action potential only, and then stops firing**. Report the value I_1 in your report.

4. (Rheobase current) By increasing the current beyond the value I_1, eventually 2, 3 or more action potentials will be generated, but then the neuron stops firing again. By increasing the current even more, eventually repetitive firing ignites (i.e., the neuron doesn't stop firing). **Find I_{rh}, defined as the smallest value of the current above which repetitive firing ignites.** Report the value I_{rh} in your report.

5. ($f - I$ curve) The previous exercise seems to imply that the HH model will switch from having zero firing rate to having a finite firing rate at a critical value I_{rh}. Run Exercise 1 again, this time for at least 40 values of the current with increasing amplitude, starting from values a bit lower than $I = I_{rh}$. **For each run, estimate the firing rate in that run, and then plot the current-frequency response function** once all firing rates have been estimated (see Box 2 below for the relevant definitions).

   Important: Assign zero firing rate in the case of no spikes; and assign zero firing rate every time the neuron emits a few action potentials and then stops firing. In all other cases (*repetitive firing*) the firing rate will be a positive number. When plotting the firing rate vs. the amplitude of the input current, make sure to include the simulations which resulted in zero firing rates. □

   Include the plot of the f-I curve in your report and answer the following questions:

   i) Describe briefly the salient characteristics of this $f - I$ curve.

   ii) Via the $f - I$ curve, can you get an independent estimate of I_{rh}? Can you locate I_{rh} on the plot?

   iii) Imagine you wanted to use this model neuron to encode a graded input (i.e., spanning a continuous range of input currents) into the neuron's output firing rate. Does this $f - I$ curve suggest that this would be an efficient way to do so? Why or why not?

Box 2: Firing rate estimation

The Current-frequency response function (or '$f - I$ curve' for short) is the curve depicting the firing rate as a function of the amplitude of the input current I_e.

You can calculate the firing rate in either of two ways:

i) as the number of spikes per second between t_0 and t_{max} (make sure to use a **longer simulation time** t_{max}, e.g., 2000 ms, to obtain better estimates of the firing rates);

ii) as the *inverse* of the mean inter-spike interval (ISI), where the ISI is the interval of time between two successive action potentials.

Use method ii) as it is more accurate (if you try out both methods you will be able to notice the difference. Can you tell what is the reason behind this difference?). Note that either method requires the use of the spike detection mechanism developed in Exercise 2 (make sure to count each spike only once!).

Part B: Leaky Integrate-and-Fire neuron model (30/60 points)

*** Remember to include: 1. your code (as an appendix) and 2. a statement of collaboration. ***

Box 3: The Leaky Intergrate-and-Fire model

- **Main equation:**

$$C\frac{dV}{dt} = -G_L(V - V_L) + I_e, \tag{9}$$

  where V is the membrane potential and I_e is an external current.

- **Model parameters**:
  $C = 1$ nF, $G_L = 50$ nS, $V_L = -65$ mV and I_e as specified in the exercises.

- **Boundary conditions**:
  A spike is said to occur whenever V hits a threshold $V_{spk} = -45$ mV, after which V is reset to $V_r = -65$ mV for an absolute refractory period $\tau_{arp} = 2$ ms. Afterwards, the dynamics of Eq. 9 resumes.

- **Initial conditions**:
  $V(0) = V_L$.

Consider the leaky integrate-and-fire (LIF) neuron model as defined in Box 3.

1. (Main simulation) Repeat Exercise 1 of Part A for the LIF neuron: replace the equations for the HH model with the equations for the LIF neuron (remember to include the boundary conditions for the emission of a spike) and repeat the same exercise. This time, use the forward Euler algorithm with **time step** $dt = 0.1$ **ms** and choose a value for $I_e = 1.1$ nA. **Plot**, in the same figure but in two different subplots: **the membrane potential vs. time and the external current vs. time. Include the plot in your report.**

   Note The boundary conditions amount to a mechanism of spike initiation followed by clamping the membrane potential to the reset value for some time. In the LIF neuron, the time of spike initiation is also the time of spike detection (compare with Exercise 2 of Part A). If you found a way to detect each spike only once in Exercise 2 of Part A, the same code can be used to implement the refractory period here. But remember that in this case $V = V_r$ during the refractory period. □

2. ($f - I$ curve) Repeat Exercise 5 of Part A for the LIF neuron. Use at least 40 different values for the current. Make sure to use currents which elicit a range of firing rates from zero to at least 60 or 70 spikes/s. **Plot the $f - I$ curve and include the plot in your report.** Answer the following questions in your report:

   i) What type of $f - I$ curve do you observe in this case? Is this different from the $f - I$ curve of the HH model? In what way?

   ii) Is it possible, in the LIF model, to have only a few action potentials and then stop firing?

   iii) From the $f - I$ plot, locate the rheobase current (analogous to I_{rh} in Part A) and compare it with the theoretical rheobase current given by $I_{rh}^{LIF} = G_L(V_{spk} - V_L)$. Do they match?

3. (Running time) Answer the following questions:

   i) Do your simulations of the HH model work if you use $dt = 0.1$ ms? And if you use $dt = 0.05$ ms? **Include one plot in your report.**

   ii) Do your LIF neuron results change significantly when you use $dt = 0.2$ ms instead of $dt = 0.1$ ms?

   iii) Run both the LIF and the HH model with $dt = 0.01$ ms and $dt = 0.002$ ms, and measure how long each simulation takes (see Box 4). **Log these values in your report.** Is there an appreciable difference in running times between the HH and the LIF model neurons, at parity of dt? Which one runs faster? Is there a big difference?

Box 4: Estimate of running time

You can estimate how long your simulations take with the `tic` and `toc` instructions:

```
tic
(start simulation code)
...
(end simulation code)
toc
```

Matlab will output a message such as:

```
Elapsed time is 2.451381 seconds.
```

Note: make sure to use the same simulation time t_{max} with both models.