# 15-386/686 Neural Computation
# Problem Set 1: Neuronal Model

**Credit: 10 points. Out: 1/25, 2023.**
**Due 11:59 p.m. 2/8, 2023.**

*Rules:*

You are encouraged to help each other, but you have to do your own work. *For the first two assignments, you are allowed to discuss with your classmates and share information over Piazza or Canvas.* **However, Part 3. Creative Exploration is a competition and has to be done by yourself, no collaboration allowed.**

Late policy: You have seven free-late-days allowance to submit homework late without penalty for the entire semester. You can use these seven late allowance in whatever way you wish. Beyond that, for each late day, you will incur a 5% deduction of your earned grade of that problem set. No homework will be accepted one week after the due day. Late by one hour or twenty-three hours behind due day will use one free day allowance. Each student should submit a soft copy to the Canvas Homework1 folder and to Gradescope. If you submit late, the submission day is the day you submit the soft-copy to Canvas.

Your report should be type-written and submitted as a pdf file (Latex or Word). You can choose your own format. For Math derivation, you could write it by hand and include them as a photo picture of it in your report. Submission to CANVAS assignment folder should be a zip file including your report, your codes. For the codes, you should submit a script for each part of the question e.g. part1a.m part1b.m. Note that you do not need to include every graph you have generated in the report. Include in the report graphs we explicitly ask for and those you consider pertinent for illustrating your observations. You should also submit your report, but not the codes, to Gradescope to facilitate grading.

**Matlab Tutorial Session**

Wed and Thursday 8:00 p.m. TA will provide Matlab tutorial over class zoom link. The sessions will be zoom-recorded and posted on CANVAS.
Matlab primers and previous' years tutorials are also available on CANVAS.

**Notes on Installing and using Matlab off campus.**

Go to https://www.cmu.edu/computing/software/all/matlab/ for instruction for installing Matlab. Standard version is fine. You do need to use CiscoVPN software provided by CMU to connect to CMU network to allow Matlab to access the licensing server if you are using the standard version at home. Standalone version is available only to students in CS and CIT. Once you install that, you don't need VPN to connect to campus network to use Matlab. **Say something about using the online version of Matlab**

**Part 1: Understanding membrane potential (6 points)**

When Hodgkin and Huxley visited Kenneth Cole's laboratory in Woods Hole, they were amazed at first by Cole's ingenuity in measuring the conductance change in the membrane using the voltage clamp technique. However, they also noticed that the peak of the action potential measured went all the way up to about +50 mV in the oscilloscope, while Bernstein's membrane break-down theory would have predicted 0 mV. To them, this implied that the membrane did not not simply broken down, but changed its permeability transiently and differently for the different ions.

Let's say the concentrations of the various chemicals inside the squid giant axon are $[Na^+] = 50$ mM, $[K^+] = 500$ mM, $[Cl^-] = 40$mM, and $[A^-] = 400$mM, while the outside concentrations of these ions are, $[Na^+] = 460$mM, $[K^+] = 20$mM, $[Cl^-] = 540$mM, and $[A^-] = 400$mM, other ions being equal inside and outside roughly.

(a) [0.5 pt] Write down the Nernst potential equation and compute the Nernst potential for each ion (K, Na, Cl) that will balance its respective chemical gradient.

(b) [1 pt] What could Hodgkin and Huxley conclude about which ion channel in the membrane has undergone changes in its permeability during spike generation based on the observation that the peak of the spike is at 50 mv? Explain why.

(c) [1.0 pt] Calculating the resting potential of the membrane should take into account not only the concentrations of the different ions but also their respective permeability. Goldman (1947) derived the following equation to calculate the membrane's resting potential at room temperature ($25^oC$)

$$V_m = \frac{RT}{F} ln(\frac{P_K[K^+]_{out} + P_{Na}[Na^+]_{out} + P_{cl}[Cl^-]_{in}}{P_K[K^+]_{in} + P_{Na}[Na^+]_{in} + P_{cl}[Cl^-]_{out}})$$

where $P_K, P_{Na}, P_{Cl}$ are the membrane permeability of the three different types of ion channels. Absolute permeability is hard to measure, but relative permeability can be used instead, and the relative permeability among the three ion channels are determined to be $1 : 0.03 : 0.1$ for $K$, $Na$ and $Cl$ respectively. Substitute all these numbers to compute the resting potential of the membrane at which the electrical potential balance the chemical gradients. This is the electrical potential of the neuron inside relative to outside when the neuron is at rest. At this resting state, What happen to the $K$, $Na$ and $Cl$ ions? Do they stop moving or continue to flow in or out of the cells?

(d) [1 pt] In the lecture, we showed that the membrane dynamics with injected current $I_o$ is modeled by the following RC circuit equation:

$$C\frac{dV_m}{dt} + \frac{V_m(t) - V_{rest}}{R} = I_o(t)$$

The solution for membrane potential $V_m$ of this circuit in response to a step current $I_o$ turned on at $t = 0$ is given by

$$V_m(t) = RI_o(1 - e^{-\frac{t}{\tau}}) + V_{rest}$$

where $\tau = RC$ and $R$ is the membrane resistance, and $C$ is the membrane capacitance.

Likewise, when the injected current is turned off at $t_{off}$, i.e. from $I_o$ to zero, the membrane potential is given by,

$$V_m(t) = RI_o(e^{-\frac{t-t_{off}}{\tau}}) + V_{rest}$$

Write the Matlab code (part1d.m) to plot this solution of $V_m$ on a graph, with y-axis showing $V_m$ in mV, and x-axis showing time in msec (lasting from -50 ms to 200 msec), as was shown in the lecture slide. Let us say the injected current $I_o$ level turns from 0 to 0.3 nA at $t = 0$, and stays at that level until $t = t_{off} = 100$ msec; $V_{rest} = -70$ mV, R = 100 M Ohm, C = 100 pF, $\tau = 10$ msec. See if you can reproduce the plot shown in the lecture slides. Adjust the parameter values if needed. The purpose of this question is to familiarize you with Matlab plotting functions. Submit the code with your the plot.

(e) [1.5 pt] While the solution to $V_m$ can be analytical solved to obtain closed form solution as in (d), we can also obtain the solution by numerical integration. In this case, we can use the Euler method to obtain $V_m(t)$. The Euler method iteratively determines the value of $V_m$ by determining its value at each successive time point by taking the previous time point value of $V_m$ and adding to it the value of the derivative evaluated at the previous time multiplied by our time step.

Earlier, we were given that the model of the system is represented by the RC equation:

$$C\frac{dV_m}{dt} + \frac{V_m(t) - V_{rest}}{R} = I_o(t)$$

After some basic algebraic manipulation, we can obtain the desired form of the update equation suitable for the Euler method:

$$\frac{dV_m}{dt} = \frac{(I_o(t) - \frac{V_m(t)-V_{rest}}{R})}{C}$$

Create a new Matlab script called `part1e.m` to implement the Euler method to simulate the evolution of $V_m$ based on the differential equation in Part 1d, with the same parameter specifications. Plot the numerical integration result on a graph and compare it with the plot of the analytical result from 1d.

Since some of you might not have done any numerical integration, we provide you with a `part1e_provided.m` file to do this. Your task is to fill in only one line – the Euler update equation above, as commented in the code, and make the code run for 200 ms (changing one number in the constant lists). Note that dVm = Vm(next time step t) - Vm (current time step). and dt is the time step. Try several time step sizes (dt = 0.001, dt = 0.1 for example) to see what difference step size would make in this numerical simulation?

For more instructions, you can study the Matlab tutorial in Appendix E of Trappenberg, posted in Canvas which contains a section on numerical integration. The neuron simulation routines in that chapter, as used in Part 2 below, also provide an example on the simple Euler method.

(f) [1.0 pt] **Individual Exploration: This part you should work by yourself** Your task is to explore how parameters resistor R and capacitor C of the model influence the behavior of the model to different kinds of input. The goal here is for you to gain better understanding of how resistors and capacitors work. You are encouraged to read up on these elements. Discuss your experimental observations and understanding of these circuit elements and provide some graphs to support your observation. Best 5 answers (most creative or thorough exploration) will be awarded up to 1 additional bonus point. Interesting run-up might get some partial bonus points.

**Part 2: Numerical Integration of Spiking Neuron Models (4 points)**

In the course assignment 1 folder, you should find a number of Matlab routines that simulate different models of spiking neurons. Here, we will consider the Hodgkin-Huxley's model (`hh.m`). Please refer to the description of these programs in Chapters 2 and 3, as well as Appendix E of Trappenberg's Fundamentals of Computational Neuroscience that we are providing in the Course Materials folder in Blackboard.

Study the code in `hh.m` and modify the code appropriately to perform the following experiment to obtain the so-called frequency-current (f-I) curve, which specifies the input-output relationship of the neuron.

(a) [1 pt] First, we will run a few simulations on the HH model with 200 ms stimulation of different external input current $I_{ext}$ = 2, 4, 7, and 14. The provided hh.m set the input current to 2 at 0 ms and set it to 0 at 200 ms. In your report, provide 200-ms duration plots of spiking activities of neurons with stimulation current $I_{ext}$ = 2, 4, 7, and 14. Note that the resting membrane voltage in this routine is not set to -70 mV, but to -10 mV, with the Nernst potentials adjusted accordingly. Don't worry about this. Your task is to substitute in different external stimulation current and observe what happen, and include the membrane potential plots under the stimulation of the four currents. What do you observe, noting anything you find interesting? Comment and explain your observations.

(b) [1 pt] We provide you with a 'window discriminator' in spikeFrequency.m which is a Matlab function that takes a time series of membrane potential, a defined threshold, and the duration of the time series as input, and returns the spiking rate (# of spikes/second or Hz) computed from the time series. Set your threshold based on the observation on the spike height so that the window discriminator will count the number of spikes in the input time series. You should generate a long duration of membrane potential such as 5000 ms as input so that you can have a more accurate estimate of the spike rate. Test the neuron with $I_{ext}$ value ranging from 0 to 15, at 0.5 increment (or finer if you wish), and plot the frequency-current (f-I) curve, with spiking rate on the y-axis and input current strength in the x-axis.

Include in your report this input-output or f-i curve. Describe at least two features of this f-I curve of the basic HH model. What could have contributed to these features? Are these features desirable or not desirable from a computational perspective? What are the implications on the computation that a neuron can perform? You are welcome to speculate, and you don't have to answer all the questions, but should think hard about it, or read about it and provide some meaningful ideas. Submit your graphs, observations and discussions in your report.

(c) [2 pt] While the current we inject to the neuron is deterministic, in an animal, the neuron's input can come from many different sources, such as top-down feedback, cognitive state of the animals, other neurons' interaction, stochasticity in synaptic transmission. We call those unknown input noises and can model them using a Gaussian noise. There are at least two possible approaches you can add Gaussian white noise to the HH model neuron: (1) adding $\sigma * randn$ to the input or (2) directly to variable $x$ in the integration step in the program. Here

$\sigma$ is a scalar specifying the standard deviation of the Gaussian white noise provided by $randn$. Is there a difference between these two approaches? Study the effect of noises on the spiking of the neurons and the f-I curve for a range of $\sigma$ ( the appropriate range might be different depending on how you add the noises, e.g. you might need to use smaller value if added to x than if you add to the input, or HH model might crash). In generating the f-I curve, for each particular fixed input current, you may want to repeat the simulations 20 times and then compute the average so that your f-I curve would be more smooth. Plot the new spike train for 200 msec as well as the new f-I curve with a number of $\sigma$ you choose. How does the noise change the f-I curve? What is the significance or implications of such change? Is this desirable or not desirable? How does the change vary with the noise level? Treat this as a scientific experiment to discover of the impact of noises on the "effective activation function" of the neuron. Back up your claims and conclusions with graphs and observations.

**Part 3: Competition: Additional Creative Exploration ( Maximum bonus points: 2 points)**

This part is optional and is a competition. Excellent entries (up to 10 entries) can be awarded up to 2 points bonus. Very good entries (up to the next 10 entries) can be awarded up to 1 point bonus. Your answer to this part cannot be more than 5 pages. In this part, you are to perform a self-directed study to explore membrane models or neuronal models related to this assignment in whichever way you wish. Usually an investigation begins with a question or a hypothesis. So state your question, and then do some research and perform creative experiment to see if you can find the answer or observe something interesting, or to gain a better understanding of the behaviors of the membrane potential or spiking neuron models. A good question and answer can become a part of a future version of this assignment of the course. Selected outstanding answers will be discussed in the class.