APPM 4370/5370, Computational Neuroscience: Homework 1

Due Fri. Jan 24, 2020
at 11am (in class)

Math exercises.

1. **Spike threshold.** The leaky integrate and fire neuron model evolves according to the differential equation

$$\tau_m \frac{du}{dt} = -[u(t) - u_{\text{rest}}] + RI(t).$$

(a) Treating $I(t)$ as an unknown function and assuming $u(0) = u_{\text{rest}}$, solve the above equation for $u(t)$ using an integrating factor or Laplace transforms.

(b) Assuming $I(t) = \bar{I}$ (constant) and $u(0) = u_{\text{rest}}$, determine the minimal $\bar{I} = \bar{I}_{\text{crit}}$ for the voltage to eventually reach threshold $u(t) = u_{\text{th}}$ and the neuron to 'spike.'

(c) Given $\bar{I} > \bar{I}_{\text{crit}}$, determine how the time T for the voltage to reach threshold $u(T) = u_{\text{th}}$ depends on model parameters (i.e., isolate T). Show T decreases as $\bar{I}$ is increased (if $\bar{I} > \bar{I}_{\text{crit}}$).

(d) *Periodic forcing.* Given $I(t) = A\sin(t)$, compute the evolution of $u(t)$ prior to the first spike. You may leverage your general solution from (a) or solve for $u(t)$ another way. In the limit $\tau_m \to 0$, how large must A be to generate a spike?

2. **Chains of linear equations modeling synaptic coupling.**

(a) *Chemical coupling.* A spike at $t = 0$ releases $x(t)$ neurotransmitter into the synaptic cleft according to

$$\tau_x \frac{dx}{dt} = -x + \delta(t), \quad x(0) = 0.$$

Neurotransmitter binds to the postsynaptic membrane and opens channels leading to a current $I(t)$ as

$$\tau_s \frac{dI}{dt} = -I + I_0 x(t), \quad I(0) = 0,$$

and the current charges the postsynaptic membrane as

$$\tau_m \frac{du}{dt} = -u + RI(t), \quad u(0) = 0.$$

Solve for the voltage response $u(t)$ as an integral, e.g., using Laplace transforms or integrating factors. You may assume none of the time constants are equal (e.g., $\tau_x \neq \tau_s$). Does the amplitude of the response increase or decrease with R? What about I_0? What happens in the limit as $\tau_s \to 0$ and $\tau_m \to 0$? Explain.

(b) *Gap junctions.* Electrically active cells (e.g., neurons or cardiac cells) can be coupled by gap junctions, so neighboring cells' voltages diffusively seek balance. Consider a pair of cells with a gap junction between (with conductance g ohms^{-1}), a constant input to the first neuron ($I(t) = \bar{I}_1$), and all other parameters set to unity ($\tau_m = 1$ time units, $R = 1$ ohms), so

$$\frac{du_1}{dt} = -u_1 + \bar{I}_1 + g\underbrace{(u_2 - u_1)}_{\text{gap junction}}, \quad \frac{du_2}{dt} = -u_2 + g\underbrace{(u_1 - u_2)}_{\text{gap junction}}, \quad u_1(0) = u_2(0) = 0.$$

Assuming neither neuron spikes (u_{th} is large), solve for $u_1(t)$ as it depends on $\bar{I}_1$ and g. What is the long time limit of the first neuron's voltage: $\lim_{t\to\infty} u_1(t)$? How does it change as g is increased? Discuss.

(c) Use your solution for $u_1(t)$ from (b) to write an implicit equation for the time T of the first spike $u_1(T) = u_{\text{th}}$. Assuming $\bar{I}_1 = 2$mA and $u_{\text{th}} = 1$mV, compare T when $g = 0$ as opposed to when $g \to \infty$ and explain the difference.

3. **Hodgkin Huxley model.** *Adapted from Ch.2 exercises in Gerstner et al (2014).*

(a) Using the Nernst equation (voltage diff: $\Delta u = \frac{kT}{q} \log \frac{n_2}{n_1}$), calculate the reversal potential of Ca^{2+} at room temp. (21°C) given intracellular concentration of 10^{-4}mM and extracellular concentration of 1.5mM.

(b) An experimenter studies an unknown ion channel by applying a constant voltage u while measuring the injected current I needed to balance the membrane current through the ion channel. Sketch the current-voltage relationship (I as a function of u) assuming the current follows $I_{\text{ion}} = g_{\text{ion}} m h (u - E_{\text{rev}})$ with $g_{\text{ion}} = 1$ nS and $E_{\text{rev}} = 0\text{mV}$ where $m = 0.1$ and $h = 1.0$ independent of the voltage.

(c) An experimenter holds an unknown potassium ion channel with activation variable n and time constant τ_n at $u_0 = -50$ mV for a long time and then at time $t = 0$, switches to $u_1 = 0$ mV. Sketch the activation variable n, n^2, n^3 as a function of time for times much smaller than $\tau_n(u_1)$, where

$$n(t) = n_0(u_1) + [n_0(u_0) - n_0(u_1)] \exp\left[-\frac{t}{\tau_n(u_1)}\right].$$

(d) Show mathematically that for $0 < t < \tau_n$ the time course of the activation variable in (c) can be approximated $n(t) = n_0(0\text{mV}) + [n_0(-50\text{mV}) - n_0(0\text{mV})]\, t/\tau_n$. Hint: Use Taylor series and truncate.

(e) Considering your sketches in (c), how does the exponent p in the formula $I_{\text{ion}} = g_{\text{ion}} n^p (u - E_{\text{rev}})$ determine the 'delay' of activation?

python exercises.

These exercises are meant to ease you into using python and help you understand some of the math you did above. To help you along, you can adapt python code from the course website and should consult the accompanying jupyter notebooks.

4. **Firing rate of the LIF model.** Download the python code `lif_mod.py` and `lif_per.py` from the website and modify it to validate the spike threshold theory developed in exercise 1.

(a) Set $R = 1\Omega$, $\tau_m = 10\text{ms}$, $u_{\text{rest}} = 0\text{mV}$, $u_{\text{th}} = 1\text{mV}$, and use your formula from 1c to compute the time $T(\bar{I})$ for a spike given a constant input $\bar{I}$. Note the critical $\bar{I}_{\text{crit}}$. Plot this function $T(I)$ over the range $(I_{\text{crit}}, 10)$mA in python.

(b) Modify the code `lif_mod.py` to estimate $T(\bar{I})$ for $\bar{I} = 1.1\text{mA}$; $\bar{I} = 2\text{mA}$; $\bar{I} = 5\text{mA}$; and $\bar{I} = 10\text{mA}$. Then plot these as points overlaid on your theory curve from (a). Turn in a print out of this plot and your accompanying modified code. You are welcome to present this in a jupyter notebook.

(c) Set $R = 1\Omega$, $\tau_m = 0.1\text{ms}$, $u_{\text{rest}} = 0\text{mV}$, $u_{\text{th}} = 1\text{mV}$ in the periodically driven LIF model code `lif_per.py`. Using your theory from 1d (approximating $\tau_m = 0.1\text{ms}$ as $\tau_m \to 0$), determine how large A must be for a spike to be generated (call this value A_{crit}). Show in simulation what happens when you choose an $A < A_{\text{crit}}$ and then $A > A_{\text{crit}}$. Print this plot and modified code.

5. **Simulating the HH model.** Here you will adapt the code `hh_sim.py` to determine the *rheobase* of the model. The *rheobase* is the minimal current of infinite duration needed to generate repetitive spikes.

(a) Download `hh_spike.py` and keeping all the other parameters fixed, change the constant current `Id` to determine the minimal current required to generate repetitive spikes (rheobase). Report this minimal current and print plots of the neuron potential time series when the current is just over this value.

(b) Now change `gK` to 30 (mS/cm^2) and determine again the rheobase. Did it go up or down? Why?

(c) Change `gK` back to 36 (mS/cm^2) but change `gNa` to 100 (mS/cm^2) and again determine the rheobase. Is it higher or lower than in part (a)? Why?

(d) Change `gNa` back to 120 (mS/cm^2) but change `EK` to 0mV and again determine the rheobase. Is it higher or lower than in part (a)? Why?

(e) Change `EK` back to -12mV but change `ENa` to 100mV and again determine the rheobase. Is it higher or lower than in part (a)? Why?