APPM 4370/5370, Computational Neuroscience: Homework 2

Due Wed. Feb 5, 2020
at 11am (in class)

THIS HOMEWORK IS ON FOUR PAGES. PAGES 1+2: THE FIRST THREE MATH EXERCISES.
PAGE 3: THE NO COLLABORATION PROBLEM. PAGE 4: PYTHON EXERCISES.

Math exercises. Relevant Gerstner et al sections: 3.1; 4.1-4.5

1. **Biophysical & heuristic synapse models.**

(a) Assume the amount of neurotransmitter in a synapse after a presynaptic spike at $t = 0$ is modeled by

$$N(t) = \begin{cases} \frac{1}{\tau_x} \mathrm{e}^{-t/\tau_x}, & t > 0, \\ 0, & t < 0. \end{cases}$$

Show $N(t) \to \delta(t)$ as $\tau_x \to 0^+$. That is, $\int_{-a}^{a} N(t)dt = 1$ for any $a > 0$ and $N(t) \to 0$ for any $t \neq 0$.

(b) Use your result from (a) to show $g_{\text{syn}}(t) = g_{\max} R(t) = g_{\max} \alpha \mathrm{e}^{-t/\tau}$, $t > 0$, when

$$\frac{dR}{dt} = \alpha N(t)(1 - R) - \beta R, \qquad R(0) = 0,$$

and $\tau_x \to 0$ and determine the time constant τ in terms of the other parameters.

(c) Some synapses facilitate and depress, as in the *Tsodyks-Markram model* where the baseline postsynaptic conductance $g(t) = x(t)y(t)\bar{g}$ is shaped by facilitating $x(t)$ and depressing $y(t)$ changes given by

$$\frac{dx}{dt} = -\frac{x - x_F}{\tau_F} + f_F(1 - x) \sum_{j=1}^{\infty} \delta(t - t_j), \tag{1a}$$

$$\frac{dy}{dt} = -\frac{y - 1}{\tau_D} - f_D y \sum_{j=1}^{\infty} \delta(t - t_j), \tag{1b}$$

where x_F is baseline facilitation, τ_F and τ_D are the facilitation and depression time constants, and f_F and f_D are facilitation and depression strengths. Assume the presynaptic neuron spikes periodically (at 10Hz), so $t_1 = 100$ms, $t_2 = 200$ms, and so on. What is the long term baseline post-spike conductance $g(t)$? To determine this, shift time and assume $x(0) = x(100) = x_0$ and $y(0) = y(100) = y_0$ (times right after spikes), and derive and solve equations for x_0 and y_0 using Eq. (1), noting $g_0 = x_0 y_0 \bar{g}$.

(d) Using your solution from (c), determine g_0 in the limit of fast facilitation and slow depression: $\tau_F \to 0$ and $\tau_D \to \infty$. Then, determine g_0 in the limit of slow facilitation and fast depression: $\tau_F \to \infty$ and $\tau_D \to 0$. Discuss your results biologically.

(e) Lastly, determine g_0 in the limit of strong facilitation $f_F = 1$ and weak depression $f_D = 0$. Then, determine g_0 in the limit of weak facilitation $f_F = 0$ and strong depression $f_D = 1$. Again, discuss your results biologically.

2. **Type I dynamics.** Near a *saddle node* bifurcation, the potential of the Morris-Lecar model behaves according to the following differential equation:

$$\frac{du}{dt} = a(I - I_{\text{SN}}) + b(u - u_{\text{SN}})^2, \tag{2}$$

where $a, b > 0$ are determined from model dynamics. This is the *quadratic integrate and fire model*.

(a) Consider the case in which $I < I_{\text{SN}}$. Find the fixed points (where $\frac{du}{dt} = 0$) and their stability. Call the

stable fixed point $u_{\rm rest}$ and the unstable one $u_{\rm th}$.

(b) For $I < I_{\rm SN}$, define $J = a(I_{\rm SN} - I) > 0$ and employ the change of variables $v = \sqrt{b}(u - u_{\rm SN})$ in Eq. (2). Show that if $u(0) = u_0 > u_{\rm th}$, then a spike occurs in finite time ($u \to \infty$ for $t = T < \infty$). Use separation of variables and integrate v from $\sqrt{b}(u_0 - u_{\rm SN})$ to ∞ and t from 0 to T. Find T.

(c) Show if $I > I_{\rm SN}$, then $u(t) \to \infty$ in finite time if $u(0) = -\infty$. Determine the time $t = T$ that $u(T) = \infty$. Hint: Set $J = a(I - I_{\rm SN}) > 0$ and $v = \sqrt{b}(u - u_{\rm SN})$ in Eq. (2) and use separation of variables. How does T change as J increases. Explain your finding.

(d) Assume the following change-of-variables:

$$u(t) = u_{\rm SN} + a \tan \frac{\theta(t)}{2}.$$

Plug this expression into Eq. (2) and use the chain rule to convert $\frac{du}{dt}$ to $\frac{d\theta}{dt}$, and thus show that $\theta(t)$ satisfies

$$\frac{d\theta}{dt} = c(1 - \cos(\theta)) + [I - I_{\rm SN}]\,(1 + \cos\theta),$$

where $c = ab$. This is called the *theta model* (or Ermentrout-Kopell model). Sketch the model's phase line (which is actually a circle from $0 \le \theta < 2\pi$) in each of the following cases: $I < I_{\rm SN}$, $I = I_{\rm SN}$, and $I > I_{\rm SN}$.

3. **Bifurcations of the Fitzhugh-Nagumo model.** Bifurcations can indicate the onset of limit cycles (oscillations, representing spiking) or the appearance of fixed points. You will validate some of this theory with python simulations in Exercise 5.

(a) Consider the following form of the Fitzhugh-Nagumo model:

$$u' = u(u - \frac{1}{2})(1 - u) - w + I, \tag{3a}$$

$$w' = \epsilon(u - w). \tag{3b}$$

Show the nullclines $w' = 0$ and $u' = 0$ have form $w = u$ and $I = u - u(u - \frac{1}{2})(1 - u) = h(u)$, and explain why there can be at most three fixed points (where $u' = w' = 0$. Given an equilibrium point $(\bar{u}, \bar{w})$, determine the Jacobian $J(\bar{u}, \bar{w})$ associated with its linear stability.

(b) Set $I = 0$ and show that $\bar{u} = \bar{w} = 0$ is the only equilibrium, and that it is always stable (as long as $\epsilon > 0$). Can the model sustain repetitive spiking in this case?

(c) Now, set $I = 1/2$ and show that $\bar{u} = \bar{w} = 1/2$ is the only equilibrium. Starting with $\epsilon = 1$ and decreasing ϵ towards zero, determine the value of ϵ at which the fixed point becomes unstable (where at least one eigenvalue has positive real part). When the fixed point becomes an unstable spiral, this implies the existence of sustained oscillations (spiking).

4. ***NO COLLABORATION PROBLEM!*** **Recap of LIF model.** (Relevant Gerstner et al (2014) section: 1.3) An *autapse* is a synapse formed by a neuron connecting its own axon back to its own dendrites (i.e. a self (auto) synapse). In this problem, you will study self-sustained spiking in an 'autaptically'-coupled neuron.

   Current is applied to a neuron u self-coupled by an autapse until it spikes at $u_{\text{th}} = 1\text{mV}$. After this, its voltage is reset to rest $u_{\text{rest}} = 0\text{mVs}$, the current is shut off, and a burst of neurotransmitter is released which rapidly initiates a synaptic current. Assuming membrane time constant is $\tau_m = 1\text{ms}$, neurotransmitter decay time constant $\tau_x = 2\text{ms}$, fast synaptic current time constant ($\tau_s \to 0\text{ms}$), membrane resistance $R = 1\Omega$, neurotransmitter release concentration $\Delta x = 2$, and unit current conversion, the equations for neuron voltage u and neurotransmitter x after the first spike and prior to any other spikes are

$$\begin{aligned} \frac{du}{dt} &= -u + x, & u(0) &= 0, \\ \frac{dx}{dt} &= -\frac{1}{2}x, & x(0) &= 2. \end{aligned}$$

   (a) Does the autapse generate a second spike? That is, will the voltage $u(t)$ ever reach threshold $u_{\text{th}} = 1\text{mV}$? If so, at what time t_{spike}?

   (b) If the effect of the autapse is inhibitory ($x(0) < 0$), is a second spike possible? Explain.

python exercises.

See relevant python and jupyter notebooks in github repo for reference.

5. **Spiking/excitability in the Fitzhugh-Nagumo model.** Use the Fitzhugh-Nagumo code `fn_mod.py`.

   (a) For Eq. (3), choose $\epsilon = 1$ and set $I = 0$. Simulate `fn_mod.py`, starting at $u(0) = w(0) = 0$. What happens? Now set $u(0) = w(0) = 0.1$. Explain your findings. Do you find sustained oscillations (spiking)?

   (b) Next, fix $\epsilon = 1$ and $I = 1/2$. Set $u(0) = w(0) = 0$ and simulate the model. Then set $\epsilon = 0.25$ and simulate again. Then set $\epsilon = 0.1$ and simulate again. Explain your findings in each case, in light of your results in Exercise 3. Is this consistent with your analysis from before? Do you find sustained spiking where you would expect to?

6. **Oscillations/bistability in the Morris-Lecar model.** Here you will code up and run some experiments on the Morris-Lecar model. You may use past python code to help get you started on coding up the model. You are welcome to use either forward Euler or a built-in ODE solver.

   (a) Write a python code implementing the Morris-Lecar model as described in Eqns. (4.6–4.10) in the Gerstner et al book using the parameters $\tau_w = 25$, $g_1 = 4.4$, $g_2 = 8$, $g_L = 2$, $V_1 = 120$, $V_2 = -84$, $V_L = -60$, $u_1 = -1.2$, $u_2 = 18$, $u_3 = 2$, $u_4 = 30$, $C = 20$, and $I = 120$ with $u(0) = w(0) = 0$. Plot the result both as functions of time (u vs. t and w vs. t) as well as in the phase plane (w vs. u). The model supports periodic spiking in this parameter range. Determine the period of these spikes – how long does it take between the beginning of spike 1 and the beginning of spike 2?

   (b) Now, set $I = 90$, and show that some initial conditions lead to periodic spiking, while others lead to the neuron remaining at a stationary steady state. Hint: To find the initial conditions that lead to the stationary steady state, search around inside of the limit cycle representing periodic spiking (you can more easily see this by plotting trajectories of the limit cycle in the phase plane: w vs. u).

   (c) Now set $u_3 = 12$, $u_4 = 17.4$, $\tau_w = 15$, and $g_1 = 4$ and find the rheobase (the minimum current I that generates periodic spiking).