APPM 4370/5370, Computational Neuroscience: Homework 2

Due Wed. Sept 22, 2021
at 11:30am (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. **An LIF Neuron with an 'autapse'.** 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 the emergence of 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 τ_m (ms), neurotransmitter decay time constant τ_x (ms), fast synaptic current time constant ($\tau_s \to 0\text{ms}$), membrane resistance $R = 1\Omega$, excitatory neurotransmitter release concentration x_0, and unit current conversion, the equations for neuron voltage u and neurotransmitter x after the first spike and prior to any other spikes are

$$\tau_m \frac{du}{dt} = -u + x, \qquad u(0) = 0,$$
$$\tau_x \frac{dx}{dt} = -x, \qquad x(0) = x_0.$$

   (a) If $\tau_x > \tau_m$ and $x_0 = 2$, show it is possible for the neuron to spike a second time if τ_x is large enough as long as the spike threshold $u_{\text{th}} < 2\text{mV}$. To do this, solve for x and then for u. Determine the maximum value of u as a function of time t (assuming first u stays subthreshold). This formula should depend on τ_m and τ_x. Argue the resulting formula can be made arbitrarily close to 2 by increasing τ_x.

   (b) Now, assume $\tau_x = \tau_m \equiv \tau$, so the membrane and synapse have the same timescale. Again, determine the maximum value u_{max} of $u(t)$ as a function of time t when $x_0 = 2$. Is there any value of τ that will lead to u reaching above a threshold value of $u_{\text{th}} = 1\text{mV}$? Hint: Determining the maximum of u_{max} as a function of τ, optimize this, and compare this to 1mV. Does it go above?

   (c) Lastly, determine the critical value of x_0 for the τ-optimized u_{max} value to exactly reach 1.

2. **Synapses and short term synaptic plasticity.** (a) Consider a model of supralinear neurotransmitter $N(t)$ decay and saturating receptor uptake of neurotransmitter $R(t)$ given by the following

$$\frac{dN}{dt} = -N^2, \qquad N(0) = 1,$$
$$\frac{dR}{dt} = N(1-R) - \beta R, \qquad R(0) = 0.$$

   Solve for $N(t)$ and then $R(t)$. Discuss what happens for very large or very small inactivation rates β of the receptors in terms of the trajectory of $R(t)$.

   Hint: The receptor equation has solution of form $R(t) = A\mathrm{e}^{-\beta t}/(1+t) + B/(1+t)$. You can derive this from scratch, or just plug it in and specify the constants.

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

$$\frac{dx}{dt} = -\frac{x - x_F}{\tau_F} + f_F(1-x)\sum_{j=1}^{\infty}\delta(t-t_j), \qquad x(0) = x_F \tag{1a}$$

$$\frac{dy}{dt} = -\frac{y-1}{\tau_D} - f_D y\sum_{j=1}^{\infty}\delta(t-t_j), \qquad y(0) = 1. \tag{1b}$$

where x_F is baseline facilitation, τ_F and τ_D are facilitation and depression time constants, and f_F and f_D are facilitation and depression strengths. Assume the presynaptic neuron spikes periodically at 10Hz (every 100ms) so $t_1 = 100$ms, $t_2 = 200$ms, and so on. Assume facilitation and depression are full strength and have the same 100ms timescale so $f_F = f_D = 1$ and $\tau_F = \tau_D = \tau = 100$ms and that $x_F = 0.5$. What is the long term pre-spike conductance $g(t)$?

To determine this, examine the solution $x(300^-) = x(j \cdot 200^-) = x_\infty$ and $y(300^-) = y(200^-) = y_\infty$, values of the facilitation and depression variables right before each spike. Multiply these together with $\bar{g}$ to get the total conductance. The solution to each equation in Eq. (1) will be analogous to the periodically forced integrate and fire model solution from HW1. There will just be decay in between inputs and then an abrupt increase/drop in the variables with each spike.

(c) Now for a general baseline facilitation strength x_F, general timescale τ, and pre-synaptic spike interval (so $t_1 = T$ms, $t_2 = 2T$ms, etc), determine long term pre-spike conductance. Then determine the interval T that maximizes this. How does it vary with τ and x_F? Also, find the value of this maximum. Interpret and explain your results.

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:

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

$$w' = \epsilon(u - w). \tag{2b}$$

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: Nonlinear integrate and fire models.** We have primarily considered the linear integrate-and-fire model, but there are many variations that incorporate more complicated nonlinear integration dynamics, to try to better mimic the typical spike shape. This non-collaboration problem will investigate a couple of these.

   (a) The simplest version of the quadratic integrate and fire model has the form

   $$\frac{dx}{dt} = I + x^2 = f(x)$$

   where x is the 'voltage' and I is the input. Note, this is the normal form of a saddle-node bifurcation. Show there are two fixed points x^* (where $\frac{dx}{dt} = 0$) of the model when $I < 0$: one stable where $f'(x^*) < 0$ and another where $f'(x^*) > 0$. What happens to these fixed points as $I \to 0$? And then as $I > 0$? What do you think this represents in terms of spiking?

   (b) Determine the time $T/2$ until $x \to +\infty$ given $I > 0$ and $x(0) = 0$. This is half the time between spikes given a constant positive input. How does T change with I? Hint: You will need to solve the ODE using separation of variables and the change of variables $x = \sqrt{I}\tan u$.

   (c) Now, let's examine the AIF – absolute integrate-and-fire model – which has form

   $$\frac{dx}{dt} = 1 + |x|, \qquad x(0) = -1,$$

   where a spike occurs when $x = 1$. Obtain an explicit solution to the above initial value problem, and determine how long it will take for a spike to occur.

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. (2), 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).