Assignment 3
Theoretical Neuroscience

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1. **Passive cables (one more time)**

   Consider two semi-infinite cables connected at their finite ends. Let the radii of the two cables be a_1 and a_2. Inject a steady current a distance x from their point of connection (assume a point current source: $I_{\rm injected} \sim \delta(x)$). Solve for the voltage in both cables in terms of distance from the point of injection. Is the transmitted voltage larger from the big to the small cable or the other way around?

2. **Synaptic adaptation**

   As in class, consider a model of short-term synaptic facilitation of the form

$$\tau \frac{dP_{\rm rel}}{dt} = P_0 - P_{\rm rel} \qquad \text{between spikes}$$

$$P_{\rm rel} \to P_{\rm rel} + F_f(1 - P_{\rm rel}) \qquad \text{when a spike occurs.}$$

   Question 2a. Consider two presynaptic spikes that occur a time Δt apart. Derive a relation for $P_{\rm rel}$ immediately before the second spike in terms of $P_{\rm rel}$ immediately before the first.

   Question 2b. Assume the presynaptic spikes arrive regularly – meaning all interspike intervals are the same. If the interspike interval is $1/r$, what is the value of $P_{\rm rel}$ after a large number of spikes?

   Question 2c. The mechanisms for depression and facilitation are different: one comes from a depletion of vesicles; the other from a buildup of calcium. Construct a single model that takes both into account. There's no right answer here – be creative.

   Question 2d. You are now going to build a more sophisticated model of synaptic release, based on the following:

   - There are two pools of vesicles: a readily-releasable pool and and a non-releasable pool. The former can be released when an action potential invades the synaptic terminal, the latter cannot. Let n_1 refer to the number of vesicles in the readily-releasable pool and n_2 to the number in the non-releasable pool.
   - Due to endocytosis, the number of vesicles in the non-releasable pool increase at rate $(N_2 - n_2)/\tau_2$.
   - The rate at which vesicles move from the non-releasable into the readily-releasable pool is $(\rho n_2 - n_1)/\tau_2$ where ρ is a positive constant (which is generally less than 1).
   - When an action potential invades the synaptic terminal, the probability that any vesicle in the readily-releasable pool is released is $P_{\rm rel}$. We'll assume, as usual, that $P_{\rm rel}$ is the same for all readily-releasable vesicles. We'll also assume (contrary to standard practice) that $P_{\rm rel}$ does not change over time.

Assume that both n_1 and n_2 are large enough that: a) they can be treated as real numbers rather than integers, and b) the number of readily-releasable vesicles that are released is exactly $n_1 P_{\rm rel}$ every time a spike occurs.

Now for the actual questions: First, write down a set of differential equations governing n_1 and n_2 between spikes, and describe what happens when a spike occurs.

Second, consider two spikes separated by time Δt. Write down an expression for n_1 and n_2 immediately before the second spike in terms of n_1 and n_2 immediately before the first.

3. **Long-term potentiation**

As discussed in class, NMDA receptors act as coincidence detectors: if the post-synaptic cell is depolarized when a spike arrives at the pre-synaptic terminal, NMDA receptors will be activated, which in turn opens calcium channels. The influx of calcium causes all sorts of things to happen, including a change in synaptic strength.

We will consider a very simple model for the amount of calcium present when the pre-synaptic neuron fires. Let $t_{\rm pre}$ and $t_{\rm post}$ be the times of the pre- and post-synaptic spikes, respectively. We will assume that these are the only spikes that occur. Of interest is the calcium concentration at the time of the pre-synaptic spike, and that clearly depends on the time difference between $t_{\rm pre}$ and $t_{\rm post}$: if the post-synaptic neuron fires first we expect calcium influx, otherwise we don't. Let $C(\Delta t)$ be the calcium concentration at the time of the pre-synaptic spike, and assume time dependence of the form

$$C(\Delta t) = 2e(\Delta t/\tau)\exp[\Delta t/\tau]\Theta(-\Delta t)$$

where τ is the decay time for calcium and $\Theta(z)$ is the Heaviside step function; it is 1 if $z > 0$ and 0 otherwise.

Now we come to the actual weight change. Assume that the change in synaptic strength, denoted, Δw, is of the BCM form:

$$\Delta w(C) = -C + C^2$$

Question 3a: Sketch Δw as a function of Δt. How does this compare to STDP?

Question 3b: By judiciously adding delays, can you make it look more STDP-like? By changing the time-course of $C(\Delta t)$, can you make it look even more STDP-like?

4. **Phase plane analysis**

In the Hodgkin-Huxley model we noticed that $n \sim 1 - h$ and that m was essentially always at equilibrium due to its tiny time constant. Letting $m(t, V) = m_\infty(V)$ and $h = c(1 - n)$ where c is some proportionality constant, rescaling the axes and then fitting polynomials to the nullclines we arrive at the equation

$$\begin{aligned} C\frac{dV}{dt} &= -(17.81 + 47.71V + 32.62V^2)(V - .55) - 26R(V + .92) + I \\ \frac{dR}{dt} &= \frac{1}{\tau}(-R + 1.35V + 1.03) \end{aligned}$$

where $\tau = 1.9$ms and $C = .8\mu\mathrm{F/cm}^2$. Simulate this system. Plot the phase portrait with the nullclines. Find the stable point using the MatLab `root` function and plot the eigenvalues of the Jacobian for a few values if I. Show that this system goes through a Hopf bifurcation and is type II.

Most neurones in the cortex are type I. Adding a quadratic to the recovery variable can convert type II behaviour into type I behaviour and in that sense is what I_A does. These are the simplified and rescaled equations for that case:

$$\begin{aligned} \frac{dV}{dt} &= -4(V^2 - V/10)(V-1) - R(V+1/5) + I \\ \frac{dR}{dt} &= 1/5(-R + 3V^2) \end{aligned}$$

Do the same as for the type II equations. Reduce the time constant of the R equation from 5 to 1.4. What happens? Why? Simulate the equations with initial conditions V = 0.4 and R = 0.3 and I=0. What happens? Why?

5. **Phase plane analysis II**

Consider a single neuron that synapses on itself (i.e., its axons connect to its own dendrites, forming what are called autapses). The time evolution of its firing rate might then be given by

$$\tau \frac{dx}{dt} = \phi(Jx - \theta) - x$$

where J and θ are constants and ϕ, which is referred to as the "gain function," is threshold-concave-nondecreasing, meaning

$$\begin{aligned} z < 0: &\qquad \phi(z) = 0 \\ z \geq 0: &\qquad \phi'(z) \geq 0 \text{ and } \phi''(z) \leq 0\,. \end{aligned}$$

For example, we might have $\phi(z) = \max[0, \tanh(z)]$.

This model has a natural interpretation: the neuron likes to decay to rest and not fire (thus the $-x$ in the equation), but if it gets enough input (from itself), it is activated via the term $\phi(Jx - \theta)$. If this activation is strong enough it can exhibit sustained firing.

Question 5a: Find the equilibria graphically. To do this, plot $\phi(Jx - \theta)$ versus x and look for intersections with the 45° line; that is, with the line $y = x$. Show that as θ varies there are three regimes, with 1, 2 and 3 equilibria. Make plots in each of the three regimes. For each plot indicate the stability of each fixed point(s).

Question 5b: Your experimental friends tell you that a neuron making autapses exhibits bursting – it fires for a while, then stops, then starts up again. In our model, this would mean x switches between two states: $x = 0$ and $x > 0$. To reproduce this behavior, you decide to include -frequency adaptation, which you model as

$$\tau_0 \frac{d\theta}{dt} = \theta_\infty(x) - \theta$$

Assume that θ varies slowly compared to x, meaning $\tau_0 \gg \tau$. For this neuron to burst, should $\theta_\infty(x)$ be an increasing or decreasing function of x? Why?

Question 5c: Suppose that you decided that the neuron exhibited synaptic adaptation rather than spike-frequency. This you model using

$$\tau_0 \frac{dJ}{dt} = J_\infty(x) - J\,.$$

Show that this mechanism alone can*not* lead to bursting.