Assignment 2
Theoretical Neuroscience

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Just for practice!

1. **Infinite cable response to arbitrary time-varying input**

   As we all know, the passive cable equation can be written

$$\tau_m \frac{\partial u}{\partial t} - \lambda^2 \frac{\partial^2 u}{\partial x^2} + u = r_m i_e \tag{1}$$

   where $u(x,t) = V(x,t) - \mathcal{E}_L$ is the membrane potential relative to the leak reversal potential, τ_m is the membrane time constant, $\lambda = (r_m a/2r_L)^{1/2}$ is the length constant, r_m is the specific resistance of the membrane, r_L is the longitudinal resistivity, and a is the radius of the cable.

   (a) Let $i_e = r_m^{-1}\delta(x)\delta(t)$. (Yes, we know this has the wrong units but, as you'll see below, there's a reason for this.) Show that

$$u(x,t) = \frac{1}{\tau_m} \frac{\exp[-x^2/(4\lambda^2 t/\tau_m) - t/\tau_m]}{(4\pi\lambda^2 t/\tau_m)^{1/2}} \Theta(t)$$

   where $\Theta(t)$ is the Heaviside step function ($\Theta(t) = 1$ if $t > 0$ and 0 otherwise).

   Hint: Fourier transform both sides of Eq. (1) with respect to x (but not t), solve the resulting differential equation in time, then Fourier transform back.

   (b) Plot the time course of the voltage at position $x = 0, \lambda, 2\lambda$. Write down an expression for the maximum amplitude of the voltage (with respect to time) as a function of x. Use this expression to determine the "speed" at which signals travel in a passive cable. Here speed is defined as $x/t_{\max}(x)$ where $t_{\max}$ is the time at which the voltage reaches a maximum at position x. Why is speed in quotes?

   (c) Let $u_\delta(x,t)$ be the solution to Eq. (1) with $i_e = r_m^{-1}\delta(x)\delta(t)$. This is the Green function for the infinite, linear cable. The Green function is useful because it allows us to solve the equation

$$\tau \frac{\partial u}{\partial t} - \lambda^2 \frac{\partial^2 u}{\partial x^2} + u = r_m i_e(x,t)\,. \tag{2}$$

Show that the solution to Eq. (2) is

$$u(x,t) = \int_{-\infty}^{\infty} dt' \int_{-\infty}^{\infty} dx' u_\delta(x-x', t-t') r_m i_e(x', t') \,.$$

The Green function method for solving linear inhomogeneous ODEs is an extremely powerful one; you should remember it.

2. **Propagation in axons**

Between nodes of Ranvier, the membrane potential in axons obeys the equation

$$\frac{\partial V}{\partial t} = D\frac{\partial^2 V}{\partial x^2} + c_0 a_1 \delta(t)\delta(x)$$

where a_1 is inner radius of the axon. This equation implies that a bolus of charge is injected at position $x = 0$ (the location of a node of Ranvier) at time $t = 0$

(a) Why is the total injected charge proportional to the inner radius?

(b) Verify, by directly computing the derivatives, that this has the solution

$$V(x,t) = c_0 a_1 \frac{e^{-x^2/4Dt}}{(4\pi D t)^{1/2}} \Theta(t).$$

(c) We want to know how long it takes the voltage to reach a value large enough to cause a spike in the next node of Ranvier. Assume "large enough" is V_0, so the goal is to find the value of t_0 that satisfies

$$V(L, t_0) = V_0.$$

Show that

$$t_0 = \gamma(L/a_1, V_0)\frac{L^2}{4D} \tag{3}$$

where γ is an increasing function of V_0.

Note that if $a_1 \propto L$ (as it is in real axons), the time to reach V_0 is is independent of the inner diameter of the axon.

(d) Show that there is a critical value of V_0 above which the membrane potential never reaches V_0.

(e) Show that at the critical value, $\gamma(L/a_1, V_0) = 2$.

3. **Noise in the amount of neurotransmitter per vesicle**

It is common to model the neuromuscular junction as a synapse with n release sites. When an action potential arrives at the synapse, neurotransmitter is released (or not) from each site *independently.* The probability of release for all sites is p. If neurotransmitter is released from a particular site, the amount released, which we'll call q, is drawn from a distribution, denoted $P(q)$. This distribution has mean $\overline{q}$ and variance σ_q^2.

(a) What is the mean total amount of neurotransmitter released in terms of n, p, $\overline{q}$ and σ_q^2?

(b) What is the variance of the total amount of neurotransmitter released in terms of n, p, $\overline{q}$ and σ_q^2?

(c) Plot the probability distribution of total neurotransmitter released. Assume $P(q)$ is Gaussian with standard deviation 0.5, $\overline{q} = 1$, $n = 10$ and $p = 0.25$.

(d) Why is the Gaussian assumption unrealistic?

For part c, you'll need to know that the probability that neurotransmitter is released at exactly k sites, denoted $p(k)$, is

$$p(k) = p^k (1-p)^{n-k} \frac{n!}{k!(n-k)!} \,.$$

This is the famous binomial distribution.

4. **Spike-time dependent plasticity**

In an STDP model proposed by Graupner and Brunel (*PNAS* **109**:3991–3996, 2012), and simplified by me, the calcium concentration, C, in postsynaptic terminals obeys the differential equation

$$\frac{dC}{dt} = -\frac{C}{\tau} + \sum_i \delta(t - t_i^{pre} - D) + \rho \sum_j \delta(t - t_j^{post})$$

where t_i^{pre} are the times of the presynaptic spikes, t_j^{post} are the times of the postsynaptic spikes, and $\delta(\cdot)$ is the Dirac delta-function. The delay, D is positive, as is ρ. The strength of the synapse, denoted w, evolves according to

$$\tau_w \frac{dw}{dt} = \Theta(C - C_0) - \Theta(C - C_1)\Theta(C_0 - C)$$

where $\Theta(\cdot)$ is the Heaviside step function. Under this rule, the weight increases when $C > C_0$ and decreases when $C_0 > C > C_1$; it can also be written

$$\Delta w = \frac{(\text{total time for which } C > C_0) - (\text{total time for which } C_0 > C > C_1)}{\tau_w}$$

where Δw is the change in weight.

For simplicity, in what follows, assume that there is only one presynaptic spike at time $t = 0$, and one postsynaptic spike at time $t = t_0$.

(a) Assume that $1 + \rho > C_0 > C_1 > \max(1, \rho)$. List several reasons why we make this assumption.

(b) Derive an expression for $C(t)$.

(c) Derive an expression for the total change in weight (at a time long after the pair of spikes) versus t_0.

(d) Plot the expression for the total change in weight versus t_0, using $\rho = 1, C_0 = 1.2$ and $C_1 = 1.1$. How would you choose D to make this look as much as possible like classical STDP?

5. **Bag of synapses model**

Assume there are N two-state synapses. These are, of course, connected to neurons, but we'll ignore that. Instead, we're going to ask how long the synapses can hang on to a signal.

The idea is as follows. On each time step synapses are either potentiated or depressed, so that they can store information about the past. The rule for potentiation and depression is

$$P(\text{potentiated} \rightarrow \text{depressed}) = \lambda$$
$$P(\text{depressed} \rightarrow \text{potentiated}) = \lambda \,.$$

Of course, a synapses can only be potentiated if it's depressed and vice-versa. What we want to figure out is how long before information is effectively erased.

(a) Show that the probability that a synapse is potentiated at time t, denoted $\rho(t)$, evolves according to

$$\rho(t+1) = \lambda + (1-2\lambda)\rho(t)\,.$$

What is the equilibrium value of ρ?

(b) At time $t = 0$, n synapses (out of N) undergo a potentiation event: if they are already potentiated, nothing happens; if they are depressed, they are potentiated with probability λ. Show that the average number of potentiated synapses at $t = 0$, denoted $\overline{n}(0)$, is

$$\frac{\overline{n}(0)}{n} = \frac{1+\lambda}{2}\,.$$

(c) Show that

$$\frac{\overline{n}(t)}{n} = \frac{1}{2} + \frac{\lambda(1-2\lambda)^t}{2}\,.$$

(d) This expression indicates a remembering-forgetting tradeoff: larger λ means a larger initial signal ($\overline{n}(0)$ is larger), but faster forgetting (because memories decay exponentially at rate $1-2\lambda$). We want to optimize λ for long memory. For that we'll compute how long it takes before we can't tell, by looking at our n synapses, that a memory was embedded. Essentially, we're looking at n binary signals, and asking if the number of potentiated synapses is more than we would expect from chance. Here "chance" follows from the usual binomial expression: the mean number of potentiated synapses is $n/2$ and the variance is $n/4$. We can thus define the signal/noise ratio, S/N, as

$$S/N \equiv \frac{(\overline{n}(t) - n/2)^2}{n/4}\,. \tag{5}$$

Suppose we set a threshold for detection at $S/N = \Theta$. Show that the time it takes to reach threshold, t^*, is

$$t^* = \frac{\log(\Theta/n\lambda^2)}{2\log(1-2\lambda)}\,. \tag{6}$$

(e) Show that in the large n limit, the value of λ that maximizes the time it takes to reach threshold, denoted λ^*, is

$$\lambda^* \approx \sqrt{\frac{e^2\Theta}{n}}\,, \tag{7}$$

at which point

$$t^* \approx \sqrt{\frac{n}{4e^2\Theta}}\,. \tag{8}$$

The $\sqrt{n}$ scaling is not bad, but it turns out that you can do better, at the cost of considerable complexity (see Benna and Fusi's paper on the website, http://www.gatsby.ucl.ac.uk/~pel/tnlectures).