

Assignment 2

Theoretical Neuroscience

TAs:

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1. Infinite cable response to arbitrary time-varying input

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

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

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

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

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

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

- (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 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 \bar{q} and variance σ_q^2 .

- (a) What is the mean total amount of neurotransmitter released in terms of n , p , \bar{q} and σ_q^2 ?
- (b) What is the variance of the total amount of neurotransmitter released in terms of n , p , \bar{q} and σ_q^2 ?
- (c) Plot the probability distribution of total neurotransmitter released. Assume $P(q)$ is Gaussian with standard deviation 0.5, $\bar{q} = 1$, $n = 10$ 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**:39913996, 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 $t = t_0$.

- Assume that $1 + \rho > C_0 > C_1 > \max(1, \rho)$. List several reasons why we make this assumption.
- Derive an expression for $C(t)$.
- Derive an expression for the total change in weight (at a time long after the pair of spikes) versus t_0 .
- 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. Oja's rule

In an incredibly simple model of a neuron, the output, y , is related to the input, \mathbf{x} , via

$$y = \mathbf{w} \cdot \mathbf{x}.$$

The weight, \mathbf{w} , is updated after each presentation of \mathbf{x} according to

$$\Delta \mathbf{w} = \eta y (\mathbf{x} - y \mathbf{w})$$

- (a) Show that the average change in weight, $\langle \Delta \mathbf{w} \rangle$, is given by

$$\langle \Delta \mathbf{w} \rangle = \eta(\mathbf{w} \cdot \Sigma - \mathbf{w} \cdot \Sigma \cdot \mathbf{w} \mathbf{w})$$

where

$$\Sigma \equiv \langle \mathbf{x}\mathbf{x} \rangle$$

is the covariance matrix of the input (assuming it's zero mean; otherwise Σ has another name).

- (b) Show that in equilibrium (when $\langle \Delta \mathbf{w} \rangle = 0$), the weights have unit length: $\mathbf{w} \cdot \mathbf{w} = 1$.
- (c) Show that in equilibrium (when $\langle \Delta \mathbf{w} \rangle = 0$), the weight points in the direction of the eigenvector of Σ with the largest eigenvalue.
- (d) What happens if there are two eigenvectors with largest eigenvalue?