Assignment 2
Theoretical Neuroscience

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

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

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

   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 #1: 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. **Noise in the amount of neurotransmitter per vesicle**

A synapse has 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, 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 amount of neurotransmitter released in terms of n, p, $\overline{q}$ and σ_q^2?

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

(c) Assume $P(q)$ is Gaussian. Plot the probability distribution of total neurotransmitter released. Assume $n = 10$ 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.

3. **ML estimate of a time-varying release model**

Assume the probability of release, P_r, obeys the equation

$$\tau \frac{dP_r(t)}{dt} = P_0 - P_r(t) + \tau [f_F(1 - P_r(t^-)) - x_i(1 - f_D)P_r(t^-)] \sum_i \delta(t - t_i) .$$

Here the t_i are the presynaptic spike times, $P_r(t^-)$ is the release probability evaluated immediately before a spike, and x_i is a random variable that can be 0 or 1; its value is determined by

$$x_i = \begin{cases} 1 & \text{with probability } P_r(t^-) \\ 0 & \text{with probability } 1 - P_r(t^-) . \end{cases}$$

The goal of this problem is to estimate the value of f_F and f_D given data. The data is the set of spike times, t_i, and whether or not transmitter was released, at that time, x_i.

(a) Assume you know $P_r(t_i)$ for all t_i. Write down an expression for the log probability of the data; that is, an expression for $\log p(\{t_i\}, \{x_i\})$ where $p(\{t_i\}, \{x_i\})$ is the probability of observing the whole data set, $\{t_i\}$ and $\{x_i\}$.

(b) Assuming you knew τ, P_0, f_F, and f_D, how would you find $P_r(t_i)$? (This is a one sentence answer.)

(c) A data set, which can be found on the course website, contains a set of spike times and x's. You can load the data set into matlab using "load hwk2data". Arrays called t and x will appear in your workspace; these are a list of spike times (the t_i) and whether or not there was a release (the x_i, where 1 means release and 0 no release). Find the maximum likelihood values of f_F and f_D. Use $\tau = 100$ ms and $P_0 = 0.6$, which are the true values. How certain are you of your answer?