Assignment 2
Theoretical Neuroscience

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Due 24 October, 2008

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

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

   where $R_\lambda \equiv r_m/2\pi a\lambda$.

   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.

   Hint #2: You will need a couple of facts about δ-functions. First, if

$$u(x,t) = \begin{cases} f(x,t) & t \geq 0 \\ 0 & t < 0\,, \end{cases}$$

   then

$$\frac{\partial u(x,t)}{\partial t} = \begin{cases} f(x,0)\delta(t) + \frac{\partial f(x,t)}{\partial t} & t \geq 0 \\ 0 & t < 0\,. \end{cases}$$

   Second, one of the (many) representations of the δ-function is

$$\delta(x) = \lim_{\sigma \to 0} \frac{\exp[-x^2/2\sigma^2]}{(2\pi\sigma^2)^{1/2}}\,.$$

(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. 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. **Steady-state solution for cables with different radii**

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 into the cable whose radius is a_1, at a distance x from their point of connection (assume a point current source: $I_{\text{injected}} \sim \delta(x)$).

(a) Solve for the voltage in both cables in terms of distance from the point of injection.

(b) Plot the voltage at the point of injection as a function of $(a_2/a_1)^{3/2}$, first with a_1 fixed, then with a_2 fixed.

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

Assume that a synapse has n release sites. When an action potential arrives at the synapse, each site releases an amount q of neurotransmitter. The release probability, denoted p, is the same for all sites, and release at one site is independent of release at another. The amount of release is also probabilistic; we'll denote its probability distribution $P(q)$. 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?

A couple of hints. First,

$$P(q_{tot}) = \sum_k P(q_{tot}|k)p(k)$$

where k is the number of sites that release neurotransmitter, q_{tot} is the total neurotransmitter released, and $P(q_{tot}|k)$ is the probability distribution of q_{tot} given that k sites released neurotransmitter. (Recall from class that $p(k)$ is multinomial.)

Second,

$$P(q_{tot}|k) = \int dq_1 dq_2 ... dq_k \, \delta\left(q - \sum_{l=1}^{k} q_l\right) \prod_{i=1}^{k} P(q_i).$$

Third, the moment generating function for the binomial is

$$\langle k^l \rangle = \left(p\frac{d}{dp}\right)^l \sum_{k=0}^{n} \frac{n!}{k!(n-k)!} p^k \rho^{n-k}$$

where the derivatives are evaluated at $\rho = 1 - p$. You should verify this for yourself!!!

4. **ML estimate of 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 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

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

   You are given a data set (which can be found on the review session's website). The way to load this into matlab is by "load hwk2data" - arrays called x and t will appear in your workspace. with 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). This data was generated with $\tau = 100$ ms and $P_0 = 0.6$. Find the maximum likelihood values of f_F and f_D. You will have to do this numerically (unless you're a lot smarter than we are, which is always possible). How certain are you of your answer?