Assignment 2
Theoretical Neuroscience

TAs:
Roman Pogodin (roman.pogodin.17@ucl.ac.uk)
Franziska Broeker (franziska.broeker.15@ucl.ac.uk)
Ilyes Khemakhem (ilyes.khemakhem.17@ucl.ac.uk)

Due 15 February, 2019

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, $\lambda = (r_m a / 2 r_L)^{1/2}$ 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**: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 $t = t_0$.

   (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. **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

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

where

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

is the covariance matrix of the input (assuming it's zero mean; otherwise $\mathbf{\Sigma}$ 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 $\mathbf{\Sigma}$ with the largest eigenvalue.

(d) What happens if there are two eigenvectors with largest eigenvalue?