Problem Set 3

Due Wednesday, Oct 24, 2018

Random Points Generation

Randomly generate N points inside a ball with radius R. These points may be viewed as the cell body of a neuron. Compute the mean distance between any two points in the volume by taking into account volume exclusion: two points cannot be closer than d_{soma}, the diameter of the cell body. Plot the distribution of nearest neighbor distance. Compute the mean nearest neighbor distance and plot it as a function N.

Derivation of the Goldman-Hodgkin-Katz formula for reversal potential

The reversal potential we discussed in the class only take into account one type of ion. However, some channels are not quite selective, and we need to combine the current flow from multiple ions, and the result is the Goldman-Hodgkin-Katz formula for reversal potential. I will write down the equation here, and it is your homework to provide the derivation of this formula.

$$E_m = \frac{k_B T}{e} \ln \left(\frac{\sum_{i=1}^{N} P_{M_i^+}[M_i^+]_{out} + \sum_{i=1}^{N} P_{A_j^-}[A_j^-]_{in}}{\sum_{i=1}^{N} P_{M_i^+}[M_i^+]_{in} + \sum_{i=1}^{N} P_{A_j^-}[A_j^-]_{out}} \right). \tag{1}$$

Here P denotes the permeability of a given ion.

Integrate-and-fire neuron

The Integrate-and-fire model of neuron's firing consists of of the following equation for the membrane potential (in dimensionless units):

$$\begin{aligned} \tau \frac{dV}{dt} &= -V + I_e \\ V(t_{spike}^-) &= 1 \\ V(t_{spike}^+) &= 0 \end{aligned} \tag{2}$$

However, the model ignores two important biological observations. First, the action potential has a finite temporal width. Second, after firing an action potential, a neuron is less likely to fire an action potential in a short refractory period, contributed by the large persistent voltage-gated potassium current. To incorporate these ingredients into the model, Here we consider two different modifications.

1. We assume that after a spike the neurons potential is strongly refractory, namely it is unable to respond to an external input for a period of time, τ_r where τ_r is of the order of a few milliseconds. Mathematically, this assumption can be written as,

$$V(t) = 0, t_{spike} < t < t_{spike} + \tau_r. \tag{3}$$

(a) Please compute the $f - I_e$ curve (firing frequency vs applied current) of this neuron. Analyze its behavior for large I_e, and compare it to the behavior at large I of the normal I-F neuron (i.e., without refractoriness). *Hint*: Use Taylor expansion in $1/I_e$. Additionally, explore the effect of τ_r, by plotting the two curves (with and without refractoriness using the following parameters: $\tau = 20$ ms $\tau_r = 2$ ms.

2. We introduce a negative adaptation current I_a, induced by the spiking of a neuron itself. The effect is to decrease the firing rate of subsequent spikes. A simple model of the adaptation current is given by

$$\tau_a \frac{dI_a}{dt} = -I_a - J_a \tau_a \sum_i \delta(t - t_i^{spike}), \tag{4}$$

where τ_a is the time constant the adaptation current, J_a is its strength. Note that every time the neuron spikes I_a decreases discontinuously by an amount J_a. Now in Equation 1, the total applied current is $I = I_e + I_a$.

(b) *Please derive an implicit relationship for the firing rate of the neuron versus the applied constant current I_e, and solve it numerically for the following parameters: $\tau = 10$ ms, $\tau_a = 200$ ms, and $J_a = 0.1$, or $J_a = 1$. Discuss what are the main effects of the adaptation on the $f - I_e$ curve?

Hint: In the steady state, we shall assume that the neuron fires periodically with an interspike interval T (which is the inverse of the firing rate). (1) Under these conditions, i.e., $V(t) = V(t + T)$, show that the solution to Equation **??** is given by $I_a(t) = -J_a \sum_0^\infty e^{-\frac{nT+t}{\tau_a}}$ for $t \in [nT, (n+1)T]$. (2) Substitute in Equation 1 and derive the condition for threshold crossing. For $\frac{dx}{dt} + ax = x_0(t)$, prove that the general solution is $x(t) = x(0)e^{-at} + \int_0^t dt' e^{-a(t-t')} x_0(t')$.

(c) *Computer Simulation: You are provided with a sample MATLAB code for an integrate and fire neuron without the adaptation current which you may download from our website. Modify the code to include the adaptation current, and run the simulation to produce a curve of the firing rate as a function of the input with and without the adaptation current. Produce a plot of the membrane voltage in time for two different applied current values. Compare this f-I with the analytical solution. Also, compute the first inter-spike interval (ISI) for the different current values, and compare 1/ISI with the steady state firing rate. (Plot both on the same graph).

Note: Problems with * are optional. However, solving them will give you additional credits.