

Problem Set 6 (due Thurs Apr. 10)

Passive models of neurons

April 3, 2003

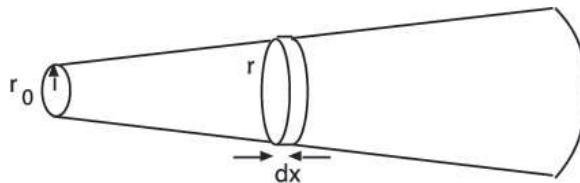
1. The membrane capacitance of a typical cell is $1 \mu\text{F}/\text{cm}^2$ (i.e., 10^{-6} uncompensated coulombs of charge on each side of 1 cm^2 of membrane are needed to produce 1 V across the membrane). Suppose that the concentrations of ions inside and outside the cell are about 0.1 M, and that the cell is spherical with radius $10 \mu\text{m}$.
 - (a) How many ions of surface charge are required to produce a transmembrane potential of 100 mV? These are called “uncompensated ions”, because they violate space-charge neutrality.
 - (b) What is the total number of ions inside the cell?
 - (c) What is the ratio of the number of uncompensated ions to the total number of ions?

The last number should be small, justifying my statement in lecture that space-charge neutrality is a very good approximation in neurons. Also, it means that we can treat ionic concentrations as constant in time, even though the membrane potential and amount of surface charge may vary rapidly in time.

2. A membrane is permeable to K^+ and Cl^- , but not to a large organic ion R^+ . Inside the membrane, the initial concentrations of RCl and KCl are both 150 mM. Outside the membrane, the initial concentration of KCl is 300 mM, while that of RCl is zero.
 - (a) What are the final concentrations of R^+ , K^+ , and Cl^- on each side of the membrane at equilibrium?
 - (b) What is V_m at equilibrium?
 - (c) Will there be any osmotic pressure? If so, in which direction?

Hint: At Donnan equilibrium, the Nernst potentials of potassium and chloride must be the same.

3. The drawing below depicts the business end of a glass capillary microelectrode. The hole at the tip has radius r_0 , and the radius r increases linearly away from the hole.



- (a) What is the resistance dR of the slab shown in the figure, in terms of the thickness dx , radius r , and resistivity ρ of the electrolyte? From this result, it should be clear why the tip dominates the total resistance of the electrode.
- (b) Let $r = kx$, so that k represents the steepness of the taper of the pipette. Calculate the total resistance R by integrating dR from $x = r_0$ to $x = \infty$. You can make the approximation that the cone above extends to infinity, rather than turning into a cylinder, which would be more realistic. This makes little difference to the result, since the resistance is dominated by the tip. Your answer should be inversely proportional to the hole radius r_0 and to the steepness of the taper k .

(c) Typical values for a patch electrode are $\rho = 100 \Omega \text{ cm}$, $r_0 = 0.5 \mu\text{m}$ and $k = 0.2$. Substitute these values into your expression for R , to find the electrode resistance. Your result should be on the order of $M\Omega$.

4. The **integrate-and-fire neuron** is a simple model of spiking behavior that sacrifices biophysical realism for mathematical simplicity. Below threshold, the membrane potential V obeys the differential equation

$$C_m \frac{dV}{dt} = -g_L(V - V_L) - g_{syn}(V - V_{syn}) + I_{app} \quad (1)$$

If V reaches a threshold V_θ , then the neuron is said to spike, and V is instantaneously reset to a value of V_0 , where $V_0 < V_\theta$. The term I_{app} models the current injected through an experimenter's microelectrode. The equation above is like Eq. (5.7) in the Dayan and Abbott book, though with slightly different notation. Also, I've added an extra term that models synaptic input as the product of a synaptic conductance g_{syn} , and a driving force that depends on the reversal potential V_{syn} . Let's consider the case of an excitatory synapse, so that V_{syn} is above V_θ .

(a) Response as a function of applied current I_{app} , with no synaptic input ($g_{syn} = 0$).

- i. Determine the threshold current I_θ (or rheobase) below which the neuron is inactive, and above which the neuron fires repetitively. The sign of I_θ should depend on whether V_θ is above or below V_L .
- ii. If I_{app} is held constant in time above threshold, the neuron should fire action potentials repetitively. Find the relationship between frequency of firing ν and I_{app} above threshold.
- iii. Show that ν behaves roughly linearly for large I_{app} , and determine the slope.
- iv. Make a sketch of ν as a function of I_{app} , annotating the important features.

(b) Response as a function of synaptic input g_{syn} , with no applied current ($I_{app} = 0$). Suppose that the synaptic conductance g_{syn} is constant in time. This could be approximately true in vivo when a neuron receives a constant barrage of inputs from many other sources, so that the summed input is approximately constant.

- i. Determine the threshold synaptic conductance $g_{syn,\theta}$ below which the neuron is inactive, and above which the neuron fires repetitively.
- ii. Find the relationship between frequency of firing ν and g_{syn} above threshold.
- iii. Show that the ν behaves roughly linearly for large g_{syn} , and determine the slope.
- iv. Make a sketch of ν as a function of g_{syn} , annotating the important features.

5. Simulate an integrate-and-fire neuron in MATLAB with $g_{syn} = 0$, $I_{app} = 1 \text{ nA}$, $C_m = 500 \text{ pF}$, $g_L = 25 \text{ nS}$, $V_L = -70 \text{ mV}$, $V_\theta = -54 \text{ mV}$, and $V_0 = -60 \text{ mV}$. To perform your numerical integration, use a step size of $dt = 0.2 \text{ ms}$, and follow the instructions around Eqs. (5.46) to (5.48) in Dayan and Abbott. As soon as V exceeds V_θ , reset it to V_0 in the next time step. Graph a train of 10 spikes, starting from the initial condition $V = V_L$. Just for looks, you can draw a vertical line whenever a spike happens, to make your graph look more realistic (as in Figure 5.5 of Dayan and Abbott). Compare your interspike interval with the formula for ν that you derived above.