Assignment 1 - Due March 9

1. For a neuron with a surface area of 0.025 mm^2, a specific membrane capacitance of $c_m = 10$ nF/mm^2, a specific membrane resistance of $r_m = 1$ MΩ·mm^2, and a resting membrane potential $E = -70$ mV:

   a) What is the total membrane capacitance C_m?

   b) What is the total membrane resistance R_m?

   c) What is the membrane time constant τ_m?

   d) How much external electrode current would be required to hold the neuron at a membrane potential of -65 mV?

   e) If this amount of current is turned on at time $t = 0$, with the cell initially at -70 mV, and held constant at this value, at what time t will the neuron reach a membrane potential of -67 mV?

2. Consider a passive neuron model receiving a single synaptic input caused by a presynaptic action potential at time $t = 0$. The synaptic current decays exponentially and delivers a total charge of q_s, so it is given by

   $$i_s(t) = \frac{q_s}{\tau_s} \exp\left(-\frac{t}{\tau_s}\right) .$$

   To make the mathematics easier, write the membrane potential as

   $$V = V_{rest} + v .$$

   Then, the equation for v with this synaptic current is

   $$\tau_m \frac{dv}{dt} = -v + \frac{R_m q_s}{\tau_s} \exp\left(-\frac{t}{\tau_s}\right) . \tag{1}$$

   a) Compute v(t), for $t > 0$, assuming that $v(0) = 0$. To do this, it is useful to know that v takes the form

   $$v(t) = A \exp\left(-\frac{t}{\tau_s}\right) + B \exp\left(-\frac{t}{\tau_m}\right) ,$$

   where A and B are constants to be determined as functions of the other parameters. A is determined by inserting this form into equation 1 and requiring that the left and right sides match, and B is determined by imposing the condition $v(0) = 0$.

   b) At what time does $v(t)$ reach its maximum value. This is determined by setting $dv/dt = 0$.

   c) What is the value of $v(t)$ at its maximum? This is called the PSP (postsynaptic potential) amplitude.

3. Build an integrate-and-fire model neuron,

$$\tau_{\mathrm{m}} \frac{dV}{dt} = V_{\mathrm{rest}} - V + R_{\mathrm{m}} I_{\mathrm{e}} \,.$$

With $V_{\mathrm{rest}} = V_{\mathrm{reset}} = -65$ mV, $V_{\mathrm{th}} = -50$ mV, $\tau_{\mathrm{m}} = 10$ ms, and $R_{\mathrm{m}} = 10$ MΩ. Reset the potential to $V = V_{\mathrm{reset}}$ whenever it goes to or above V_{th}, and then the neuron fires an action potential.

Apply different levels of current I_{e}, count spikes over a suitable period of time to compute firing rates, and plot these rate as a function of $R_{\mathrm{m}} I_{\mathrm{e}}$. Compare your results to the analytic formula

$$r = \left(\tau_{\mathrm{m}} \ln \left(\frac{R_{\mathrm{m}} I_{\mathrm{e}} + V_{\mathrm{rest}} - V_{\mathrm{reset}}}{R_{\mathrm{m}} I_{\mathrm{e}} + V_{\mathrm{rest}} - V_{\mathrm{th}}} \right) \right)^{-1} \,.$$

4. Build a Hodgkin-Huxley model neuron by numerically integrating the equations for V, m, h, and n:

$$c_{\mathrm{m}} \frac{dV}{dt} = -i_{\mathrm{m}} + \frac{I_{\mathrm{e}}}{A} \,,$$

where

$$i_{\mathrm{m}} = \overline{g}_{\mathrm{L}}(V - E_{\mathrm{L}}) + \overline{g}_{\mathrm{K}} n^4 (V - E_{\mathrm{K}}) + \overline{g}_{\mathrm{Na}} m^3 h (V - E_{\mathrm{Na}}) \,.$$

and

$$\tau_n(V) \frac{dn}{dt} = n_\infty(V) - n \,,$$

$$\tau_n(V) = \frac{1}{\alpha_n(V) + \beta_n(V)}$$

and

$$n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)} \,,$$

and similar equations for m and h, with

$$\alpha_n = \frac{.01(V + 55)}{1 - \exp(-.1(V + 55))} \quad \beta_n = 0.125 \exp(-0.0125(V + 65)) \,,$$

$$\alpha_m = \frac{.1(V + 40)}{1 - \exp(-.1(V + 40))} \qquad \beta_m = 4 \exp(-.0556(V + 65))$$

$$\alpha_h = .07 \exp(-.05(V + 65)) \qquad \beta_h = 1/(1 + \exp(-.1(V + 35))) \,,$$

In these equations, time is in ms and voltage is in mV. Take $c_{\mathrm{m}} = 10$ nF/mm^2 and, as initial values, take: $V = -65$ mV, $m = 0.0529$, $h = 0.5961$, and $n = 0.3177$. The maximal conductances and reversal potentials used in the model are $\overline{g}_{\mathrm{L}} = 0.003$ mS/mm^2, $\overline{g}_{\mathrm{K}} = 0.36$ mS/mm^2, $\overline{g}_{\mathrm{Na}} = 1.2$ mS/mm^2, $E_{\mathrm{L}} = -54.387$ mV, $E_{\mathrm{K}} = -77$ mV and $E_{\mathrm{Na}} = 50$ mV. The best method to use to integrate all of these equations over time is the exponential integration scheme discussed in class, but any routine that works is OK. Make your integration step size small enough to get accurate results.

a) Use an external current with $I_e/A = 200$ nA/mm^2 and plot V, m, h, and n as functions of time for a suitable interval.

b) Plot the firing rate of the model as a function of I_e/A over the range from 0 to 500 nA/mm^2.

c) Apply a pulse of negative current with $I_e/A = -50$ nA/mm^2 for 5 ms followed by $I_e/A = 0$ and show what happens. Why does this occur?

5. Use the Hodgkin-Huxley model you built for problem #4 to construct a multiple compartment model of an axon. Built the axon out of 100 compartments, each of which has a radius of 2 μm and a length of 100 μm. Each compartment should contain the Hodgkin-Huxley conductances used in problem #4. Inject a current pulse sufficient to evoke a single action potential into the first compartment of the cable. All the other compartments should receive no external current. Use the Euler integration method or one of the build-in Matlab integration routines with a time step no bigger than around 0.01 ms.

   a) What is the propagation speed of the resulting action potential.

   b) Now change the cable radius to 20 μm. What is the propagation speed now? Show that the velocities you get in a and b are proportional to the square-root of the axon radius.

6. Build and simulate the Itzekevitch model, defined by the equations

$$\tau_{\mathrm{m}} \frac{dV}{dt} = V_{\mathrm{rest}} - V + \frac{(V - V_{\mathrm{rest}})^2}{\Delta_V} - U + R_{\mathrm{m}} I_{\mathrm{e}} \, ,$$

   and

$$\tau_U \frac{dU}{dt} = b(V - V_{\mathrm{rest}}) - U \, ,$$

   with the additional condition that when $V \geq V_{\mathrm{max}}$ it gets reset to $V = V_{\mathrm{reset}}$ and U gets incremented by $U \to U + d$. To start, use (in units of ms, mV, MΩ and nA) $\tau_{\mathrm{m}} = 1.67$, $\tau_U = 50$, $\Delta_V = 15$, $V_{\mathrm{rest}} = -70$, $V_{\mathrm{max}} = 0$, $V_{\mathrm{reset}} = -50$, $b = 0.33$, $d = 3$, $R_{\mathrm{m}} = 10$ and $I_{\mathrm{e}} = 0.63$.

   a) Make plots of V versus t and U versus t for a long enough time period to show what is happening.

   b) In the V-U phase plane (V as the horizontal axis and U as the vertical axis), plot the nullclines along which $dV/dt = 0$ and $dU/dt = 0$. Also plot a V-U trajectory from the data plotted in part a, but now with U plotted versus V over the time period, rather than plotting these variables against time.

c) Explain the trajectory you see in b in terms of the nullclines and other features of the model. For example, why does the trajectory cling to one of the nullclines over part of the trajectory.

d) By playing with the parameters, see if you can get the model to do something else interesting.

7. Simulate the pair of equations

$$\frac{dx}{dt} = -x(x-1)(x+1) + y \quad \frac{dy}{dt} = -k(2x+y)$$

with different values of k in the range $0 < k < 2$.

a) Find the largest value of k for which these equations produce oscillations.

b) Compute this value analytically by considering the fixed point $x = y = 0$ and finding the value of k where this state makes the transition from being stable to being unstable. When this state is stable, is the approach to the fixed point exponential or oscillatory? When the state is unstable, is the motion away from the fixed point exponential or oscillatory?

c) Show that your analytic results on the approach to and escape from the fixed point match your simulation results.

8. Construct an integrate-and-fire model responding to a "noisy" input representing the *in vivo* environment. This model is based on the equation

$$\tau_{\mathrm{m}} \frac{dV}{dt} = V_{\mathrm{rest}} - V(t) + \eta(t) + R_{\mathrm{m}} I_{\mathrm{e}}$$

with $\tau_{\mathrm{m}} = 10$ ms and $V_{\mathrm{rest}} = -56$ mV. The threshold and reset potentials for the model are $V_{\mathrm{th}} = -54$ mV and $V_{\mathrm{reset}} = -80$ mV. η is white-noise given by

$$\eta = \sigma_V \sqrt{\frac{2\tau_{\mathrm{m}}}{\Delta t}}\ \mathrm{randn}(1, \mathrm{length(t)})$$

where Δt is the time step size in your program, σ_V is a parameter (see below), randn is the matlab random number generator for a normal distribution, and t is the vector of times in your program.

a) Set $I_{\mathrm{e}} = 0$ and turn off the spike generation mechanism in your model. Plot the standard deviation of the membrane potential fluctuations that arise from different σ_V values in the range $0 \le \sigma_V \le 10$ mV.

b) Plot the average firing rate of the neuron (defined by counting spikes over a sufficiently long time interval and dividing by the duration of that interval) as a function of $R_{\mathrm{m}} I_{\mathrm{e}}$ for $\sigma_V = 2$, 6 and 10 mV. You may have to include negative I_{e} values to stop the neuron from firing. How does this differ from the firing-rate curve for the integrate-and-fire model without noise?