Mathematical Biology 5120-S14: Problem Set 2

Due March 27, 2014 at the beginning of class.

In this homework, you are to write a MATLAB program to solve the Hodgkin-Huxley equations and to use it to explore their dynamics under a variety of conditions. I have attached a sample MATLAB code for solving a different set of ODEs which should provide a template for much of what I ask you to do.

The Hodgkin-Huxley equations, related quantities, and parameter values are also attached.

A) Write a MATLAB function, say gateshh, that takes a value V of (transmembrane) voltage as input, and returns values for $m_\infty(V)$, $\tau_m(V)$, $n_\infty(V)$, $\tau_n(V)$, $h_\infty(V)$, and $\tau_h(V)$, for this voltage.

1. Plot the functions $m_\infty(V)$, $n_\infty(V)$, and $h_\infty(V)$ vs V for $-90 \leq V \leq 50$. Plot the three curves on the same axes but in different colors.

2. Plot the functions $\tau_m(V)$, $\tau_n(V)$, and $\tau_h(V)$ vs V for $-90 \leq V \leq 50$. Plot the three curves on the same axes but in different colors.

B) Write a MATLAB function, say odehh, that takes t, V, m, n, h, as input and evaluates the right-hand-sides of the ODEs Eqs.(1)-(4) below. This function needs to be able to evaluate $m_\infty(V)$, $\tau_m(V)$, $n_\infty(V)$, $\tau_n(V)$, $h_\infty(V)$, and $\tau_h(V)$, for the input voltage V. It could do this, for example, by using the function you wrote for part A). The function also needs to be able to evaluate the applied current I_{app}, for which it needs to know t_{delay}, $t_{duration}$, I_0, and t.

C) Write a MATLAB function, say drivehh, in which you specify an initial voltage $V(0)$, the parameters t_{delay}, $t_{duration}$, and I_0 needed for the applied current, a final time t_{end} and a time interval dt between the times for which solution values are reported by ode23s. The times at which the solution should be saved are tspan = [0:dt:tend], using MATLAB notation. Your MATLAB function should then solve the HH equations for this time interval, and it should plot the solutions and other variables as follows: Plot $V(t)$ vs t in one figure; plot $I_{app}(t)$ vs t is another figure; plot all of $m(t)$, $n(t)$, and $h(t)$ vs t in a third figure; plot $g_{Na}(t)$ and $g_K(t)$ vs t in a fourth figure. (You should look up how to use the 'subplot' command in MATLAB.) To test your program, compare its results to those shown in Figure 1 below.

D) With $I_{app} = 0$, determine (to within 1 mV) the threshold voltage needed to generate an action potential, that is, determine the minimum value of $V(0)$ that leads to an action potential? You should use $m(0)$, $n(0)$, $h(0)$ set to $m_\infty(V_{eq})$, $n_\infty(V_{eq})$, and $h_\infty(V_{eq})$, respectively, as explained below. What is different and what is the same about $V(t)$ for a simulation with $V(0)$ 1 mV above the threshold compared to that for a simulation with $V(0)$ 5 mV above the threshold?

E) Here, you will experiment with different magnitudes and durations of applied current I_{app}. i) What happens if a current with $I_0 = 5$ is applied for 5 msec? What happens if that current is applied for 50 msec? ii) What happens if a current with $I_0 = 10$ is applied for 50 msec? iii) What happens if a current with $I_0 = 15$ is applied for 50 msec? iv) What happens if a current with $I_0 = 20$ is applied for 50 msec? Run each of these simulations for 100 msec. Use the slow-manifold plots in Figure 2 below to help you explain the differences between these cases.

The Hodgkin-Huxley equations are:

$$\frac{dV}{dt} = \frac{1}{C}\Big(- g_{Na}(V - V_{Na}) - g_K(V - V_K) - \bar{g}_L(V - V_L) + I_{app}\Big) \tag{1}$$

$$\frac{dm}{dt} = \frac{1}{\tau_m(V)}\Big(m_\infty(V) - m\Big) \tag{2}$$

$$\frac{dn}{dt} = \frac{1}{\tau_n(V)}\Big(n_\infty(V) - n\Big) \tag{3}$$

$$\frac{dh}{dt} = \frac{1}{\tau_h(V)}\Big(h_\infty(V) - h\Big) \tag{4}$$

where $g_{Na} = \bar{g}_{Na} m^3 h$ and $g_K = \bar{g}_K n^4$.

The normal values of the parameters are

C	$\bar{g}_{Na}$	$\bar{g}_K$	$\bar{g}_L$	V_{Na}	V_K	V_L
1.0 μF/cm^2	120 (μA/mV)/cm^2	36 (μA/mV)/cm^2	0.3 (μA/mV)/cm^2	45 mV	-82 mV	-59 mV

Note that with these parameter values and the gating functions given below, the equilibrium potential is $V_{eq} = -69.8977$. This should be the initial voltage for most of your simulations, and $m(0)$, $n(0)$, and $h(0)$ should be set to the values of $m_\infty(V_{eq})$, $n_\infty(V_{eq})$, and $h_\infty(V_{eq})$, respectively.

The gating functions are given by

$$m_\infty(V) = \frac{\alpha_m(V)}{\alpha_m(V) + \beta_m(V)} \qquad \tau_m(V) = \frac{1}{\alpha_m(V) + \beta_m(V)} \tag{5}$$

$$n_\infty(V) = \frac{\alpha_n(V)}{\alpha_n(V) + \beta_n(V)} \qquad \tau_n(V) = \frac{1}{\alpha_n(V) + \beta_n(V)} \tag{6}$$

$$h_\infty(V) = \frac{\alpha_h(V)}{\alpha_h(V) + \beta_h(V)} \qquad \tau_h(V) = \frac{1}{\alpha_h(V) + \beta_h(V)} \tag{7}$$

where

$$\alpha_m(V) = \begin{cases} \frac{0.1(V+45)}{1-\exp\left(-\frac{V+45}{10}\right)} & \text{if } V \neq -45 \\ 1 & \text{if } V = -45. \end{cases} \tag{8}$$

$$\beta_m(V) = 4\exp\Big(-\frac{V+70}{18}\Big) \tag{9}$$

$$\alpha_n(V) = \begin{cases} \frac{0.01(V+60)}{1-\exp\left(-\frac{V+60}{10}\right)} & \text{if } V \neq -60 \\ 0.1 & \text{if } V = -60. \end{cases} \tag{10}$$

$$\beta_n(V) = 0.125\exp\Big(-\frac{V+70}{80}\Big) \tag{11}$$

$$\alpha_h(V) = 0.07\exp\Big(-\frac{V+70}{20}\Big) \tag{12}$$

$$\beta_h(V) = \frac{1}{1+\exp\left(-\frac{V+40}{10}\right)} \tag{13}$$

Consider applied stimuli of the form:

$$I_{app}(t) = \begin{cases} 0 & \text{if } t < t_{\text{delay}} \text{ or } t > t_{\text{delay}} + t_{\text{duration}} \\ I_0 & \text{if } t_{\text{delay}} \leq t \leq t_{\text{delay}} + t_{\text{duration}}. \end{cases} \quad (14)$$

Here is an example solution of the Hodgkin-Huxley equations for the conditions indicated. Your code should produce results for those conditions that match the results shown here.

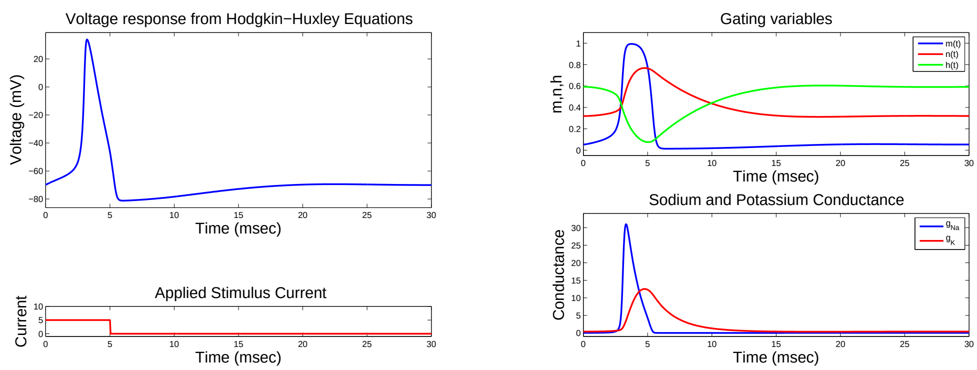

Figure 1: Solution to the Hodgkin-Huxley equations with an applied current of 5 for 5 msec.

Slow Manifold: For the reduced (V, n) 'slow' system obtained from the full Hodgkin-Huxley equations by setting $h(t) = 1 - n(t)$ and assuming that $m = m_\infty(V)$, the n-nullcline is $n = n_\infty(V)$ and the V-nullcline is $\bar{g}_{Na}\big(m_\infty(V)\big)^3(1-n)(V-V_{Na})+\bar{g}_K n^4(V-V_K)+\bar{g}_L(V-V_L)-I_{app} = 0$. Recall that the V-nullcline is also called the 'slow manifold'. For each value of V, I solved this equation for n using the MATLAB function fzero.

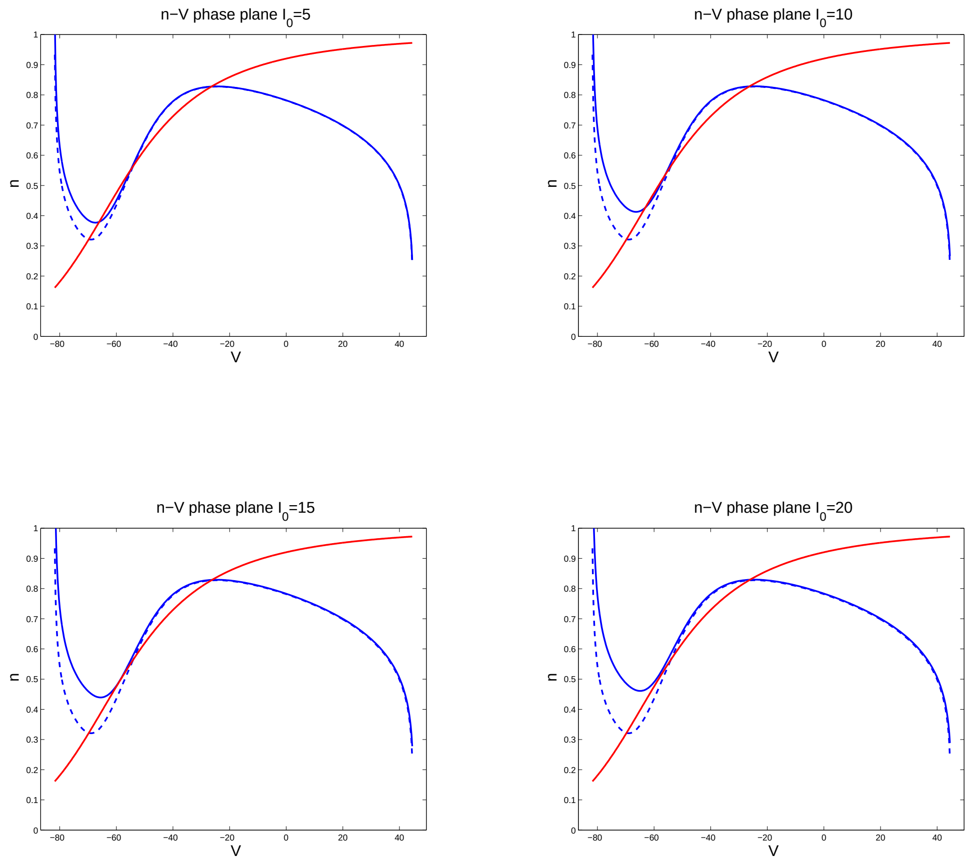

Figure 2: In each panel, the graph shows the n-nullcline $n = n_\infty(V)$ (red), the V-nullcline for the indicated value of the applied current I_0 (solid blue) and the V-nullcline for an applied current $I_0 = 0$ (dashed blue).