Background Information

Neurons are a type of excitable cell. The three main components of an excitable cell are

1) the charged ions that are located on the inside and outside of the cell
2) the cell membrane which separates charges and prevents charged molecules from entering and leaving the cell
3) and, voltage-gated ion channels which are proteins in the cell membrane that provide a pathway for charges to move from one side of the cell to the other.

The ionic current is based on the movement of three major ions: sodium current (I_{Na}), potassium current (I_K), and the leakage current (I_L). When charges pass in and out of the cell, the change in the transmembrane potential (membrane voltage)(V_m) across the cell is called an action potential. The ion channels have gates that open and close at different times during the action potential and this helps to govern the diffusion of ions across the membrane. The convention for the transmembrane potential is that vm = Vm – Vrest, where Vrest is the membrane voltage at equilibrium. Vrest = -80 mV, so at rest we consider vm = 0.

Each ion also has a membrane voltage for which it is at equilibrium. This is called the Nernst potential for the ion (eNa, ek, el).

$$e_{Na}=115 \text{ mV}$$

$$e_K=-12 \text{ mV}$$

$$e_L=10.613 \text{ mV}$$

The Hodgkin-Huxley model of the neuron action potential is based on the parallel conductance model of an excitable cell. The cell membrane is represented by a capacitor (C_m) and the ion channels are represented by resistors. In accordance with Ohm's Law, the movement of each of these currents is proportional to the conductance times the voltage. The conductances of the channels are based on the kinetics of the gates (gating variables). The sodium current has an activation gate (m) and an inactivation gate (h). The potassium current has an activation gate (n). Consequently the equations for sodium, potassium, and leakage currents can be in terms of the gating variables and the maximum conductances:

$$I_{Na} = \overline{g_{Na}} m^3 h (v_m - e_{Na})$$

$$I_K = \overline{g_K} n^4 (v_m - e_K)$$

$$I_L = \overline{g_L}(v_m - e_L)$$

where

$$\overline{g_K} = 36.0\ mS/cm^2,$$

$$\overline{g_{Na}} = 120.0 mS/cm^2$$

$$\bar{g_l} = 0.3\mathrm{mS/cm^2}\ .$$

A membrane patch is a space-clamped simulation where the transmembrane potential is allowed to vary in time but not in space. The entire membrane functions as a unit; therefore, the transmembrane potential V_m is the same at all points at a given time. This type of simulation is a good place to start when coding a kinetic model. If HH kinetics are used, there are four parameters that depend on time: V_m, m, n, and h. All four parameters have differential equations that describe their behavior.

The transmembrane potential is governed by the differential equation, I_{stim} is the current injected into the cell and C_m is the specific membrane capacitance of $1\mu F/cm^2$.

$$\frac{dv_m}{dt} = -\frac{1}{C_m}(I_{Na} + I_K + I_L + I_{Stim})$$

The gating variables are governed by the following differential equations, where alpha and beta are the voltage dependent rate constants for the gate.

$$\frac{dm}{dt} = \propto_m (1-m) - \beta_m$$

$$\frac{dh}{dt} = \propto_h (1-h) - \beta_h$$

$$\frac{dn}{dt} = \propto_n (1-n) - \beta_n$$

The rate constants, alpha and beta are calculated as follows:

$$\propto_m = 0.1\frac{25-v_m}{\exp\left(\frac{25-v_m}{10}\right)-1} \qquad \beta_m = 4.0\left(\frac{-v_m}{18.0}\right)$$

$$\propto_n = 0.1\frac{10-v_m}{\exp\left(\frac{10-v_m}{10}\right)-1} \qquad \beta_m = 0.125\left(\frac{-v_m}{80.0}\right)$$

$$\propto_h = 0.07exp\left(\frac{-v_m}{80.0}\right) \qquad \beta_h = 0.1\frac{1}{exp\left(\frac{30-v_m}{10}\right)+1}$$

Some numerical method must be used to find the solutions of these equations at each time step.

Solving the HH Model numerically

The approach we will use is to solve all the governing ODE using an explicit method. The simplest of these (and least accurate) is the Forward Euler method. Using the Forward Euler approximation, we can represent the differential equations as

$$v_m(t+1) = v_m(t) - \frac{\Delta t}{C_m}(I_{Na} + I_K + I_L + I_{Stim})$$

$$m(t+1) = m(t) + \Delta t(\alpha_m(1 - m(t)) - \beta_m m(t))$$

$$h(t+1) = h(t) + \Delta t(\alpha_h(1 - h(t)) - \beta_h h(t))$$

$$n(t+1) = n(t) + \Delta t(\alpha_n(1 - n(t)) - \beta_n n(t))$$

Given vm, m, n, and h at time t, it is easy to compute the values at t+ 1. **Remember that the smaller the time step (Δt), the more accurate the answer.**

The code for a membrane patch requires only a time loop and some method of calculating the model parameters at each time step. Given a set of initial conditions, the solutions can be built up iteratively within the time loop.