

## Hodgkin-Huxley Part 2

**8-15.** Given our discussion to this point we can summarize the ionic current through the membrane with the equation

$$I_{ion} = \bar{g}_{Na} m^3 h (V - V_{Na}) + \bar{g}_K n^4 (V - V_K) + g_L (V - V_L)$$

A compartmental approach will solve

$$c_{mj} \frac{dV_j}{dt} + (I_{ion} + I_{syn} + I_{stim}) = \left( \frac{V_j - V_{j-1}}{r_{j-1,j}} - \frac{V_{j+1} - V_j}{r_{j,j+1}} \right)$$

together with

$$\begin{aligned} dm/dt &= \alpha_m(V) (1 - m) - \beta_m(V) m \\ dh/dt &= \alpha_h(V) (1 - h) - \beta_h(V) h \\ dn/dt &= \alpha_n(V) (1 - n) - \beta_n(V) n \end{aligned}$$

and this could be solve analytically with  $n(t+\Delta t) = n_\infty - (n_\infty - n(t)) \exp(-\Delta t/\tau_n)$  for example. However, we often leave this in equation form, particularly if we want to use NEURON's variable time step method which is quite fast.

NEURON strives to obtain 2<sup>nd</sup> order accuracy and to do so it uses staggered time steps.

Voltage is solved at time t

m, n, and h are computed at t + Δt/2 using voltage at time t

Voltage is computed at time t + Δt using the m, n and h at time t + Δt/2

m, n, and h are computed at t + 3Δt/2 using the voltage at time t + Δt

etc.

**8-16.** To compute the m, n, and h we need to know the α and β values. The fitted functions used by HH are given on this overhead. We see here functions for α<sub>n</sub>(V) and β<sub>n</sub>(V) for potassium and α<sub>m</sub>(V), β<sub>m</sub>(V), α<sub>h</sub>(V), and β<sub>h</sub>(V) for sodium.

We also have the n<sub>∞</sub>, m<sub>∞</sub>, and h<sub>∞</sub> calculated from the α and β values at the current time step and also the τ<sub>n</sub>, τ<sub>m</sub>, and τ<sub>h</sub>.

The conductance is computed from the maximum conductance multiplied by n<sup>4</sup> for potassium and m<sup>3</sup>h for sodium.

**8-17.** Some notes. The rate constants, like all rate constants are temperature dependent. Transitions speed up as we increase temperature. The equations given above will calculate values for α and β at 6.3C. If we want to use a different temperature we need to use different values.

Temperature is introduced into rate constants via what is called a q<sub>10</sub> factor. This expresses how much the rate constants change for a temperature change of 10C. Mathematically we say  $\alpha_m(T) = \alpha_m(6.3C) Q^{(T-6.3)/10}$ .

For squid axon, for a 10 degree increase in temperature,  $\alpha_m$  increased 3-fold, so we say the rate constants have a  $q_{10}$  of 3.

HH experiments were done at 6.3C (the normal extracellular environment for squid), but some experiments were also done at 22C. In this case we would have to increase rate constants by  $3^{(22-6.3)/10}$ . You might try changing temperature in some of the computer exercises we have done. NEURON has a temperature menu from one of the drop down headings.

What happens to the action potential when temperature is increased? (It goes much faster)

Secondly, if you look at some of the equations for  $\alpha$ , you might note a possible problem. For example, in the equation for  $\alpha_n$  what happens when  $V=10$ , or in the equation for  $\alpha_m$  what happens when  $V=25$ ?

We have  $\alpha_n = \frac{0.01(10-V)}{\exp((10-V)/10)}$ . When  $V=10$  both the numerator and denominator are zero.

The solution blows up! What do we do? What is the proper value to use when  $V=10$ ? In calculus you probably dealt with this. You take the limit as  $V \rightarrow 10$ . In cases where you have 0/0 in the limit you use L'Hopital's rule. Remember this? You take the derivative of the numerator and denominator and then apply the limit. After taking the derivative here we have  $-0.01/[\exp((10-V)/10) * 0.1]$ . Now we can substitute  $V=10$  with no problem.

In situations like this, the NEURON .mod file for hh uses a vtrap function. We shall look at this later.

**8-18.** Third, be careful with alpha and beta functions to determine if they are given relative to a resting potential of 0 mV or a resting potential of -65 mV (or some other value). For example the  $\beta_m$  defined in the NEURON .mod file is  $\beta_m(V) = 4\exp(-(V+65)/18)$  whereas the original HH has  $\beta_m(V) = 4\exp(-V/18)$ . Note the +65 in the NEURON expression to compensate for a resting potential of -65. Be careful when taking values from the literature. Even some of mine are messed up because of this, but I blame this on the post-doc!

Fourth, for computational efficiency NEURON can pre-compute values and store them in a table, for example the minf, hinf, ninf or mexp, hexp, nexp or taun, taum, tauh values. Then a table lookup is done instead of an actual computation.

**8-19.** Here is a .mod file for the squid axon. This is not the default one. Note where temperature is defined. Also note the maximum conductances and the reversal potentials, including the leak conductance.

**8-20.** In this example the m, n, and h are computed analytically in the states() procedure. I believe that to use the variable step method you have to code differential equations here.

Note the definition of a TABLE and the grid. Note also how temperature is used in the rates procedure. Finally, note the vtrap function which takes care of the 0/0 situation.

**8-21.** This .mod file is the default one. Note that it has the suffix hh. So when you change a conductance at the command line you need to say `gnabar_hh=new value` with the `_hh` attached. In the previous example the suffix was `hh2`, so you would have to use `gnabar_hh2=new_value`.

In the ASSIGNED block, variables given values outside the program are specified first. Many of these are standard hard-coded parameters in NEURON such as `ena`, `ek`. You will have to change these in the main script, not here.

**8-22.** Here the `m`, `n`, and `h` are solved with their differential equations, but in a slightly different form that we saw earlier