How to Solve and Program the Hodgkin - Huxley Equations

James Kenyon
Department of Physiology & Cell Biology
MS 352
University of Nevada School of Medicine
Reno, NV 89557

kenyon@physio.unr.edu
How to Solve and Program the Hodgkin - Huxley Equations

Revised in 2001 in anticipation of the 50th Anniversary of the publication of the J. Physiol. (Lond.) papers. The original document was prepared c.1990 to document a program that calculated Hodgkin-Huxley action potentials. That program was written in Turbo C to run on an XT computer at the time. Technology changes but the equations and the math stay the same. Some years ago I saw a poster at the Society for Neuroscience demonstrating these calculations in an Excel spreadsheet and for this revision I have prepared a spreadsheet of my own that is attached to this update.

A note on the voltage and current conventions

When Hodgkin, Huxley and Katz did what have become the classical experiments in membrane biophysics (Hodgkin & Huxley, 1952a; Hodgkin & Huxley, 1952b; Hodgkin et al., 1952; Hodgkin & Huxley, 1952c; Hodgkin & Huxley, 1952d) they did not have the technical advantages that we take for granted today. In particular, they were unable to measure absolute membrane potentials but had to be content with recording changes in the membrane potential from the resting potential. The convention that they adopted was that the resting potential was 0 mV and the action potential was a negative excursion from the resting potential. In addition, they adopted a current convention that is reversed from that which we use today. Namely, positive charge entering the axon was plotted as a positive current, i.e. normal sodium currents are positive while normal potassium currents are negative.

Note that while these conventions are completely arbitrary even Hodgkin and Huxley plotted action potentials going upwards along a negative voltage scale in their figures. In this discussion I have kept the original conventions for historical reasons and to avoid errors in converting all of the equations. To convert from the Hodgkin and Huxley convention we assume that the average resting potential of their axons was -60 mV and convert:

\[ V_{\text{modern}} = (-1 \cdot V_{\text{HH}}) - 60 = -1.0 \cdot (V_{\text{HH}} + 60) \]

I note that in the years following the original work the "normal" resting potential value crept more and more negative. An effect attributed to increased technical skill of later workers.

Introduction of the equations

If you want to model the action potential of the Hodgkin-Huxley axon you will need the equations and a computer on which to solve them. The original authors (Hodgkin & Huxley, 1952a) should be consulted. The equations are also reviewed in more recent publications (Hille, 1992; Moore & Ramon, 1974). The paper by Moore and Ramon specifically discusses how one might go about solving the equations on 1974 computers with "only 4000 words of core memory".

The main equation is:

\[ I = C_M \cdot \frac{dV}{dt} + g_k \cdot n^4 (V - V_k) + g_{Na} \cdot m^3 \cdot h \cdot (V - V_{Na}) + g_L \cdot (V - V_L) \]

Which gives the membrane current density (\(\mu A/cm^2\)) as the sum of the capacity current (\(C_M \cdot dV/dt\)) plus the ionic current through the resistive elements of the axon (i.e the channels).
The sodium and potassium currents are described by the maximum possible conductance (denoted by a $g$ under a bar in the original paper and hence referred to as $g_{\text{barK}}, g_{\text{barNa}}$ here) times time and voltage-dependent gating variables ($n, m, h$) times the driving force on the respective ions. In addition to these two main ionic conductances, there is a small "leakage" conductance that was invoked (essentially as a fudge) to cover the remaining current and force the resting potential of the model to fit the observations.

The time- and voltage- dependent elements of the model are the $n, m, h$ gating parameters which are given by the following relationships. The "time" dependencies are given by the differential equations:

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

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

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

with the voltage -dependencies of the underlying rate constants ($\alpha$ and $\beta$ values)

$$\alpha_n = 0.01 \cdot (V + 10) / \{\exp[1 + (0.1 \cdot V)] - 1\}$$

$$\beta_n = 0.125 \cdot \exp(V / 80.0)$$

$$\alpha_m = 0.1 \cdot (V + 25.0) / \{\exp[(0.1 \cdot V) + 2.5] - 1.0\}$$

$$\beta_m = 4.0 \cdot \exp(V / 18.0)$$

$$\alpha_h = 0.07 \cdot \exp(V / 20.0)$$

$$\beta_h = 1.0 / \{\exp[3.0 + (0.1 \cdot V)] + 1\}$$

The initial conditions needed to solve this system of equations may be obtained by assuming that the membrane potential is at some value (typically the resting potential of 0 mV) for a long time. In this case, $n, m, h$ assume their "steady state" values given by
The properties (i.e. constants) of the Hodgkin-Huxley axon are

\[ n_m = \frac{\alpha_n}{(\alpha_n + \beta_n)} \]

\[ m_m = \frac{\alpha_m}{(\alpha_m + \beta_m)} \]

\[ h_m = \frac{\alpha_h}{(\alpha_h + \beta_h)} \]

The goal of this exercise is to introduce students to how the Hodgkin Huxley equations work. Accordingly, I have restricted the discussion to the calculation of a "membrane" action potential. This is a non-conducted action potential that is generated when the length of an axon is space-clamped, i.e. all of the membrane is at the same potential. This situation is clearly nonphysiological in that normal action potentials are conducted, indeed one can argue that consideration of a membrane action potential eliminates a critical part of the model. However, the calculation of the membrane action potential is very much simpler than the calculation of a conducted action potential. Conceptually, we consider that we have access to a square centimeter of squid axon membrane and will calculate the current flow and potential drop across it. Note that the membrane action potential is not without some interest; the membrane action potential is what one records from space clamped preparations (i.e. cells that one can voltage-clamp).

We start with the main equation (equation 4):

\[ I = C_M \cdot \frac{dV}{dt} + g_K \cdot n^4 (V - V_K) + g_{Na} \cdot m^3 \cdot h \cdot (V - V_{Na}) + g_L \cdot (V - V_L) \]

During the action potential the ionic currents flowing across our square cm of membrane all go towards charging the membrane capacitance of that square cm and do not go anywhere else. In particular, the current does not go to discharge neighboring membrane nor does it go to an electrode to be collected for a current measurement. Mathematically this can be stated in two ways. (1) The current through the resistive elements equals -1.0 times the current through the capacitive element.
The net current, I, equals zero. I have found that #2 is not easy to accept and have developed a line of thought to help. Consider that in order to generate an action potential one uses a stimulator to inject current into the cell to shift the voltage to and above threshold. This current can be measured with your current meter in current-clamp mode, I = 0. When threshold is reached the stimulating current can be turned off and the action potential will be generated as the endogenous currents of the excitable cell discharge and recharge the membrane capacitance. These endogenous currents will not be measured in current-clamp mode, I = 0. However, one knows they are flowing because they are discharging and recharging the membrane capacitance (see #1 above). The mathematical consequence of I = 0 is

\[ -C_M \cdot \frac{dV}{dt} = -g_K \cdot n^4(V - V_K) + \frac{g_{Na}}{m^3} \cdot h \cdot (V - V_{Na}) + \frac{g_L}{(V - V_L)} \]  

or, since \( C_M = 1.0 \)

\[ -\frac{dV}{dt} = -g_K \cdot n^4(V - V_K) + \frac{g_{Na}}{m^3} \cdot h \cdot (V - V_{Na}) + \frac{g_L}{(V - V_L)} \]

We can evaluate our work so far and get an idea of how the solution is going to work by considering this form of the equation. It says that if the sum of the ionic currents is positive then \( dV/dt \) is negative. That is, positive currents make the membrane potential go more negative. Recalling the conventions (see above), we see that sodium currents are positive and they make the negative excursion of the action potential. Thus, all is well.

**The solution**

We desire the course of membrane potential, \( V \), over time but the equation gives us the rate of change of membrane potential at some instant, \( dV/dt \). A strategy that will work is the following. If you know the value of \( V \) at some instant, say \( V(t) \), and you know how \( V \) is changing at that instant of time, then you can predict the value of \( V \) at a future time, say \( t+\Delta t \). The equation is

\[ V(t + \Delta t) = V(t) + \frac{dV}{dt} \cdot \Delta t \]

where \( dV/dt \) is evaluated under any conditions imposed by \( V(t) \). (Note: Any mathematical purists who have managed the text this far may be outraged at the notation. This is not being written for mathematicians, who will not have needed this anyhow, but is written for innocents with the short term goal of managing a numerical solution to a system of differential equations.) This equation is fundamentally the Euler method for numerical integration and is an approximation of a true solution (see Moore and Ramon (1974)) or any text on numerical methods). It should be clear that the smaller the value of \( \Delta t \) the closer to the true solution we will be and the longer the solution will take to compute. Without going into detail, other integration methods are available that can reduce the number of calculations and provide a more accurate solution. Contemporary computers allow us to keep it simple and calculation intensive.

What is a good value for \( \Delta t \)? In my experience 0.01 ms is a good number. Larger values may be unstable (i.e. the solution can go off the track) and smaller values prolonged the computation time.
A simple strategy a working program can take is this:

1. Choose a membrane potential and solve for the steady state values of the gating variables n, m, and h. That is, we say that the membrane potential has been at some value for a very long time and all time dependent processes have relaxed. One can choose any value for V but a sensible and realistic value is V = 0 mV, the resting potential. In order to calculate n, m, and h one inserts V = 0 into equations (5) through (10) to calculate the values of the α and β rate constants. The rate constant values are then inserted into equations (11) to calculate the steady state values of n, m, and h. These gating parameters are inserted, into equation (13) along with the constants for gbarK, V_K, etc. to solve for dV/dt. Because we chose V equal to the resting potential we should have known that dV/dt = 0. The goal of step one is not to calculate dV/dt, rather it is to get the initial values for n, m, and h.

2. Now, choose a new membrane potential and "let the system go". A good value should be -20 (i.e. an instantaneous depolarization from -60 to -40 in modern terminology).

3. Calculate the new values for the rate constants using equations (5) through (10) and the new value for V.

4. Calculate the new values for dn/dt, dm/dt, and dh/dt using the new values for the rate constants and equations (4).

5. Calculate new values for n, m, and h using an Euler integration scheme, i.e.

   \[ n(t + \Delta t) = n(t) + \frac{dn}{dt} \cdot \Delta t \]

6. Calculate a new value for dV/dt using these new values of n, m, and h in equation (13).

7. Calculate a new value of V using this new value of dV/dt and the Euler integration (equation 14).

8. Take the new value of V, write or plot it someplace useful, and then take it up to step 3 above. Do this loop about 1000 times.

The display of the action potential is up to the user. One suggestion is to print out the values of V as they are calculated. They should get more and more negative before turning around to return towards the resting potential. This is a traditional observation which gives the modern student a small taste of the excitement that the original workers must have felt when doing these calculations by hand. For a more sophisticated output, a graph of voltage vs time is called for. Many computer languages support the graphics capabilities of laboratory computers and this can be implemented with relatively little effort. Alternatively, V and t can be written to a file and plotted with Sigmaplot, GraphPad, or Lotus.

While the calculation described above is a good way to start, it does not model the usual sort of experiment. That is, the action potential is evoked by an instantaneous shift of V while one typically uses a step of current. This can be achieved by adding an I_{stim} term to equation 13:

\[- \frac{dV}{dt} = \bar{g}_K \cdot n^4 (V - V_K) + \bar{g}_{Na} \cdot m^3 \cdot h \cdot (V - V_{Na}) + \bar{g}_L \cdot (V - V_L) + I_{stim} \]
where $I_{\text{stim}} = 0$ most of the time but can be set to a requested number of $\mu\text{A/cm}^2$ during the "stimulation". This modification is simple to implement after the version described above is working.

The following figures illustrate the voltage-dependence of the $\alpha$ and $\beta$ gating variables and the steady state values of $n$, $m$, and $h$. They are useful in isolating errors in your equations.

**Figure 1** Rate constants and steady-state voltage dependence of $n$.

**Figure 2** Rate constants and steady-state voltage-dependence of $m$. 
Figure 3 Rate constants and steady-state voltage-dependence of h.

Reference List


