An elementary numerical solution of the Hodgkin-Huxley equations in MATLAB

Kaushik Majumdar, Systems Science and Informatics Unit, Indian Statistical Institute, 8th Mile, Mysore Road, Bangalore – 560059, India; E-mail: kmajumdar@isibang.ac.in

The purpose of this note is to help any one who is intending to numerically solve the Hodgkin-Huxley (HH) equations and simulate an action potential in MATLAB for the first time. The effort has been guided by a single resource "Understanding neuronal dynamics by geometrical dissection of minimal models," A. Borisyuk and J. Rinzel, In: Chow C, Gutkin B, Hansel D, Meunier C, Dalibard J, eds. Models and Methodsin Neurophysics, Proc Les Houches Summer School 2003, (Session LXXX), Elsevier, 2005:19-72 (particularly Appendix A). Plenty of scope of improvements remain both in the mathematical approach to the solution and in the MATLAB implementation. Suggestions to improve are most welcome.

The equations

HH equations for action potential generation by a 1 cm^2 patch of membrane in a giant squid axon are as following:

$$C_m \frac{dV}{dt} = -I_{ion}(V,m,h,n) + I_{app}$$

$$= -g_{Na} m^3 h (V - V_{Na}) - g_K n^4 (V - V_K) - g_L (V - V_L) + I_{app} \quad (1)$$

$$\frac{dm}{dt} = \frac{\phi[m_\infty(V) - m]}{\tau_m(V)} \quad (2)$$

$$\frac{dh}{dt} = \frac{\phi[h_\infty(V) - h]}{\tau_h(V)} \quad (3)$$

$$\frac{dn}{dt} = \frac{\phi[n_\infty(V) - n]}{\tau_n(V)} \quad (4)$$

$$\phi = 3^{(T-6.3)/10}. \quad (5)$$

C_m is membrane capacitance in $\mu F / cm^2$, V is displacement of membrane potential from its resting value (depolarization, taken as negative) in millivolt (mv), m, h, n are dimensionless (hypothetical) gating variables respectively for sodium activation, sodium inactivation and potassium activation, I_{app} is the applied stimulation current in μA, g_{Na}, g_K, g_L are respectively maximum sodium, potassium, leak conductance in milli-mho (m.mho)/cm^2 or mS/cm^2, $V_{Na} = E_{Na} - E_r$, $V_K = E_K - E_r$ and $V_L = E_L - E_r$, where E_r is the value of resting potential in mv, E_{Na}, E_K, E_L are potentials in mv at which currents due to sodium, potassium and leakage (due to chloride and other

negatively charged ions) respectively become zero, $m_\infty(V), h_\infty(V), n_\infty(V)$ are steady state values of sodium activation, sodium inactivation and potassium activation respectively (dimensionless), $\tau_m(V), \tau_h(V), \tau_n(V)$ are time constants of sodium activation, sodium inactivation, potassium activation respectively in milliseconds (ms), T is temperature in centigrade. For a very detailed description of the quantities involved and physical significance of the equations one should see "A quantitative description of membrane current and its application to conduction and excitation in nerve," A. L. Hodgkin and A. F. Huxley, Journal of Physiology, vol. 117, p. 500 – 544, 1952.

$$\tau_x = \frac{1}{\alpha_x + \beta_x} \tag{6}$$

$$x_\infty = \frac{\alpha_x}{\alpha_x + \beta_x}, \tag{7}$$

where x stands for m or h or n.

$$\alpha_n = \frac{10 - V}{100(e^{(10-V)/10} - 1)} \tag{8}$$

$$\beta_n = 0.125e^{-V/80} \tag{9}$$

$$\alpha_m = \frac{25 - V}{10(e^{(25-V)/10} - 1)} \tag{10}$$

$$\beta_m = 4e^{-V/18} \tag{11}$$

$$\alpha_h = 0.07e^{-V/20} \tag{12}$$

$$\beta_h = \frac{1}{e^{(30-V)/10} + 1}. \tag{13}$$

Combining (6), (8) and (9) we get $\tau_n(V)$, which has been calculated by the routine tau_n.m. Combining (7), (8) and (9) we get $n_\infty(V)$, which has been calculated by the routine m_inf.m. Similarly for $\tau_m(V)$, $\tau_h(V)$, $m_\infty(V)$ and $h_\infty(V)$ calculated by the routines tau_m.m, tau_h.m, m_inf.m and h_inf.m respectively. For equations (8) to (13) modern convention for sign of the potentials has been followed and therefore the equations have been taken from Biophysics of Computation: Information Processing in Single Neurons, K. Koch, Oxford University Press, New-York, 1999 (Chapter 6).

Mathematical solution

Next comes the calculation of the actual activation (inactivation) variables or in other words the gating variables, which are denoted by n, m, h for potassium activation, sodium activation, sodium inactivation respectively. (2), (3), (4) can be written in a generic form as

$$\frac{dx}{dt} = \phi \frac{x_\infty(V) - x(V)}{\tau_x(V)}, \tag{14}$$

where $x = n$ or m or h. Solving (14) gives us

$$x = x_\infty - (x_\infty - x_0)e^{-(\phi t/\tau_x)}. \tag{15}$$

For $x = m$, τ_m is very small. Hence by (15) it is going to be

$$m = m_\infty. \tag{16}$$

The routine gating_variable.m has been used to compute (15) for $x = n$ and $x = h$. Now we are ready to tackle equation (1). First consider Fig. 1.

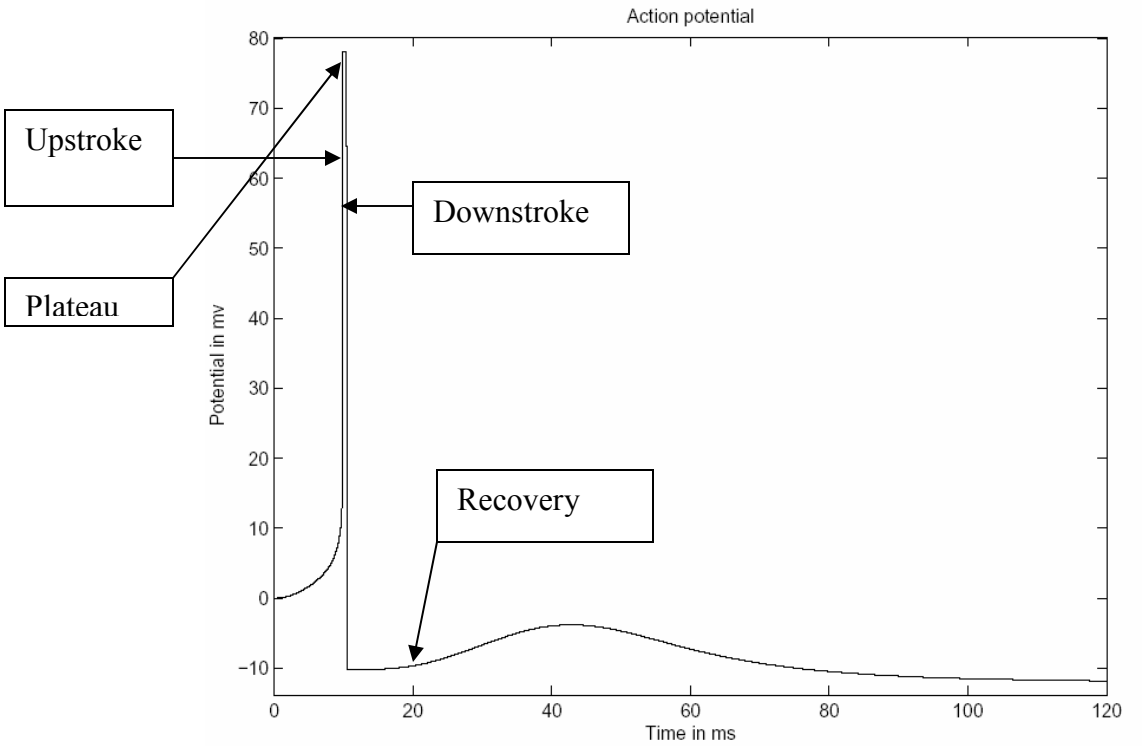

Fig. 1. Hodgkin-Huxley action potential generated by hhbr.m. First the variables time (t) and voltage (v) have been loaded in the MATLAB work space by commands t = 0:0.01:120; and v = -20:0.01:100; Then the command [D] = hhbr(v, t, 18.3, 1, 0.65, 0, 120, 36, 0.3, 80, -12, -60, 15, 50, 10); generated the figure. (Plateau and Downstroke arrows are not pointing accurately).

There are four phases of generation of an action potential as shown in Fig. 1, as a numerical solution of equation (1).

Phase 1: Upstroke – is characterized by very rapid activation of Na^+ channels (the very rapid, almost vertical with respect to time, rising phase in Fig. 1). Compared to the sharp change in m, changes in h and n are so slow that in this phase they can be assumed as constant. So that $\frac{dh}{dt} = 0$ and $\frac{dn}{dt} = 0$. For this phase we take $h = h_0$ and $n = n_0$. For the action potential in Fig. 1 $h_0 = 0$ and $n_0 = 0.65$ (in Koch's book n_0 has been taken to be 0.32 (p. 147)). Equations (1), (2), (3), (4) reduce to

$$C_m \frac{dV}{dt} = -g_{Na} m^3 h(V - V_{Na}) - g_K n^4 (V - V_K) - g_L (V - V_L) + I_{app}$$

$$m(V) = m_\infty(V)$$

$h = h_0 = 0$ and $n = n_0 = 0.65$, which can be written as

$$dt = \frac{dV}{-AV + B + I'_{app}}, \qquad (17)$$

where $A = \frac{g_{Na} m_\infty^3 h_0 + g_K {n_0}^4 + g_L}{C_m}$, $B = \frac{g_{Na} m_\infty^3 h_0 V_{Na} + g_K {n_0}^4 V_K + g_L V_L}{C_m}$ and $I'_{app} = \frac{I_{app}}{C_m}$.

(17) has been calculated in lines 42 through 47 in the routine hhbr.m. No differential equation solver has been used. The calculation has been done from the scratch.

Phase 2: Plateau – With rapid depolarization due to swift influx of Na^+ ions inside the cell the maximum value of potential is reached quickly. Immediately afterwards slow Na^+ influx inhibition and slow K^+ outflux activation together dominate the process. The change in action potential with respect to time becomes so slow that we can assume $\frac{dV}{dt} = 0$. Equation (1) becomes

$$0 = -g_{Na} m^3 h(V - V_{Na}) - g_K n^4 (V - V_K) - g_L (V - V_L) + I_{app}. \qquad (18)$$

Solving (18) we get

$$V = \frac{B1}{A1} + \frac{I}{C_m A1}, \tag{19}$$

where $A1 = \frac{g_{Na} m_\infty^3 h + g_K n^4 + g_L}{C_m}$ and $B1 = \frac{g_{Na} m_\infty^3 h V_{Na} + g_K n^4 V_K + g_L V_L}{C_m}$. (19) has been calculated in line 56 of hhbr.m, which makes up the flat part of the action potential in Fig. 1, called 'plateau'. Duration of plateau is roughly about 1 ms, the usual duration of an action potential. If resolution of time is 0.01, i.e., time has been generated by the MATLAB command t = 0:0.01:120; 100 time points will make 1 ms. So the length of the plateau is also 100 time points (in Fig. 1. the plateau is only 50 time points long). The duration of the plateau and the downstroke can be set in hhbr.m by choosing the values for the arguments 'width' and 'duration'.

The slow-fast dissection made in Phase 1 and Phase 2 is the trick to generate the action potential by the Hodgkin-Huxley equations. This will be carried over to the next two phases.

Phase 3: Downstroke – After each depolarization Na^+ channels become inactive for a few milliseconds. At the same time because of outflux of K^+ during phase 2 the cell undergoes a hyperpolarization. Although K^+ outflux is slow, once it reaches a certain level this hyperpolarization is very rapid. The following mechanism, as shown in Fig. 2, is responsible for rapid depolarization and rapid hyperpolarization of the membrane consisting of Na^+ and K^+ channels (Principles of Neural Science, 4th ed., E. R. Kandel, J. H. Schwartz, T. M. Jessell, McGraw Hill, 2000, p. 151).

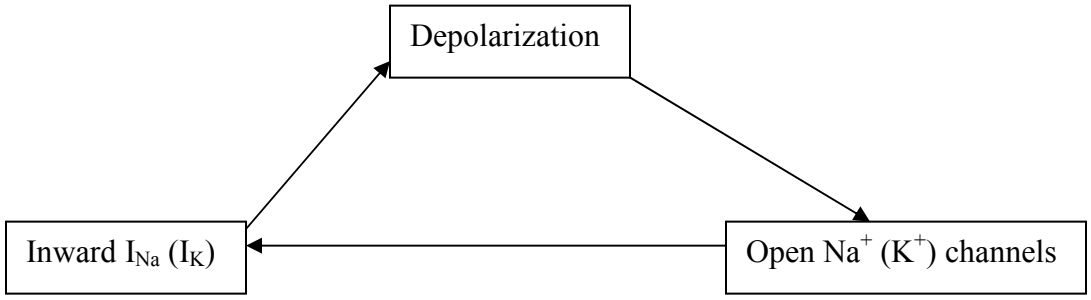

Fig. 2. If the membrane is depolarized sufficiently to open some of the Na^+ (K^+) channels, inward Na^+ (K^+) current (I_{Na} (I_K)) flows through these channels and causes further depolarization. The additional depolarization causes still more Na^+ (K^+) channels to open and consequently induces more inward Na^+ (K^+) current.

So we again resort to fast calculation according to equation (17). The downstroke of hyperpolarization follows.

Phase 4: Recovery or Refractory – The action potential is followed by a brief period of diminished excitability, or refractoriness, which can be divided into two phases. The

absolute refractory period comes immediately after the action potential. During this period it is impossible to excite the cell no matter how great a stimulating current is applied. This phase is followed directly by the *relative refractory period*, during which it is possible to trigger an action potential, but only by applying stimuli that are stronger than those normally required to reach threshold. These periods of refractoriness, which together last just a few milliseconds, are caused by the residual inactivation of Na^+ channels and increased opening of K^+ channels (Kandel et al., p. 157). In other words there is diminished h and enhanced n. So the entire refractory period is a candidate for modeling by slow dynamics.