Signal Processing in Neurons

The goal of this lab is to explore the classic Hodgkin-Huxley model of neuronal activation and its properties. To achieve this, we will implement and simulate the Hodgkin-Huxley model as well as determine properties like the minimum stimulation required for activation or refractory periods. For your report, include all MATLAB code, figures generated, and answers to included questions.

Problem 1: Simulating the Hodgkin-Huxley Model (Demo)

The Hodgkin-Huxley model can be written as:

$$C_M \frac{dV}{dt} = I - \sum_i g_i (V - E_i)$$

where C_M is the membrane capacitance, $\frac{dV}{dt}$ is the change in voltage across the membrane, I is the total applied current flowing across the membrane, g_i is the conductance of ion channel i, V is membrane potential, and E_i is the Nernst potential for ion channel i. Consider a neuron with ion channels for sodium, potassium, and a leak channel. We know that the applied currents must equal the sum of currents across the membrane. Thus, we have

$$C_M \frac{dV}{dt} = I - \bar{g}_K n^4 (V - E_K) - \bar{g}_{Na} m^3 h (V - E_{Na}) - \bar{g}_L (V - E_L)$$

where $n, m,$ and h are gating variables representing on and off states of the sodium and potassium channels. The dynamics of n, m and h are given in the generic form as

$$\frac{dn}{dt} = \alpha_n(V)(1-n) - \beta_n(V)n$$
$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m$$
$$\frac{dh}{dt} = \alpha_h(V)(1-h) - \beta_h(V)h$$

where the on and off rates for each gate are

$$\alpha_n(V) = 0.01\left(\frac{10 - V}{e^{\frac{10-V}{10}} - 1}\right)$$
$$\beta_n(V) = 0.125 e^{-V/80}$$
$$\alpha_m(V) = 0.1\left(\frac{25 - V}{e^{\frac{25-V}{10}} - 1}\right)$$
$$\beta_m(V) = 4 e^{-V/18}$$
$$\alpha_h(V) = 0.07 e^{-V/20}$$
$$\beta_h(V) = \frac{1}{e^{\frac{30-V}{10}} + 1}$$

A) Write functions for on and off rates for each gating variable and plot $\alpha(V)$ and $\beta(V)$ for $V = [-20, 120]\ mV$.

B) Write a function that can be passed into an ODE solver for the Hodgkin-Huxley equations. Your function should use an applied input current I. Write a second function to generate the applied current given the function

$$I(t) = \begin{cases} 2 & 2 \leq t \leq 2.5 \\ 25 & 10 \leq t \leq 10.5 \\ 0 & otherwise \end{cases}$$

Simulate the Hodgkin-Huxley model given parameters $\bar{g}_K = 36 \frac{mS}{cm^2}, \bar{g}_{Na} = 120 \frac{mS}{cm^2}, \bar{g}_L = 0.3 \frac{mS}{cm^2}, E_K = -12mV, E_{Na} = 120mV, E_L = 10.6mV, C = \frac{1muF}{cm^2}$, and for $t = [0{:}\,0.02{:}\,20]\ ms$. Use initial conditions.

$$V_0 = 0\ mV$$
$$n_0 = \frac{\alpha_n(V_0)}{\alpha_n(V_0) + \beta_n(V_0)}$$
$$m_0 = \frac{\alpha_m(V_0)}{\alpha_m(V_0) + \beta_m(V_0)}$$
$$h_0 = \frac{\alpha_h(V_0)}{\alpha_h(V_0) + \beta_h(V_0)}$$

Plot membrane voltage, gating variables, conductance, channel currents, and the applied step current vs time.

Problem 2: Determining minimum stimulus to generate excitatory response

A) Using the same parameters and initial conditions as part B), determine the minimum input current of, I, over the duration of 0.5 $msec$, I_{min}, needed to stimulate an excitatory response in a neuron that is initially at rest. Start with $I = [2{:}\,25]\ \mu A/cm^2$ to determine the minimum applied current needed to generate an action potential. Plot the membrane voltage vs time for $I_{min} - 1$, I_{min}, and $I_{min} + 1$. Explain why action potentials are generated only for certain minimum applied current and beyone.

Problem 3: Determining refractory period in the Hodgkin-Huxley model

In problem 1, we saw that depolarization occurs given a sufficiently large stimulus. However, in the Hodgkin-Huxley model, sodium, potassium, and leak currents relax over a long-time scale relative to that of an action potential or spike. Once the membrane and ion channel gates have returned close to their original state, a subsequent stimulus could lead to an action potential.

A) Using the Hodgkin-Huxley model and functions for generating step currents from problem 1, Determine the minimum interval required to induce a second action potential in a neuron in the interval $t = [0\ 60]\ ms$ after applying an initial current. Use parameters $\bar{g}_K = 36 \frac{mS}{cm^2}, \bar{g}_{Na} = 120 \frac{mS}{cm^2}, \bar{g}_L = 0.3 \frac{mS}{cm^2}, E_K = -12mV, E_{Na} = 115mV, E_L = 10.6mV, C = \frac{1muF}{cm^2}, t = [0{:}\,0.02{:}\,40]\ ms$ and the same initial conditions as problem 1: $V_0 = 0\ mV, gate_i = \alpha_i(V_0)/\alpha_i(V_0) + \beta_i(V_0)$. Use results from problem 1 to determine appropriate step currents to generate action potentials.

1. Modify functions for generating applied currents to produce two step currents with a given duration between them.
2. Simulate the Hodgkin-Huxley model over several iterations varying the duration between two step currents.

3. Find duration between step currents that is long enough to allow for more than a single action potential to occur. Report the determined refractory period.

B) Plot membrane voltage, gating variables, conductance, channel currents, and the applied step current vs time for a current with two pulses that occur in a window shorter than the determined refractory period.

C) Repeat part B) for a current with two pulses that occur in a window longer than the determined refractory period.

D) Are your results consistent with the time scale of membrane voltage and ion channel gating kinetics in response to a stimulus?

Problem 4: Controlling the Beating of Neurons

The concepts of excitability and a refractory period begin to explain how neurons can exhibit oscillatory dynamics given a constant input.

A) Using similar parameters as 1-2, $\bar{g}_K = 36\frac{mS}{cm^2}, \bar{g}_{Na} = 120\frac{mS}{cm^2}, \bar{g}_L = 0.3\frac{mS}{cm^2}, E_K = -12mV, E_{Na} = 115mV, E_L = 10.6mV, C = 1\frac{muF}{cm^2}$, simulate the Hodgkin-Huxley model for $t = [0\ 80]\ ms$ using an applied current of 25 $\mu A/cm^2$ from $t = [10\ 30]$ and $t = [50\ 70]$ or 0 $\mu A/cm^2$ otherwise.. Plot membrane voltage vs time and the applied current vs. time. How do these results compare to that of a single pulse of 0.5 ms? What do you notice about subsequent action potentials after initiating firing.

B) Repeat part B), now with a constant current of 15 $\mu A/cm^2$. Plot membrane voltage, gating variables, conductance, channel currents, and the applied step current vs time. What do you observe about the result with constant current? Is the output constant or converge to a fixed point? If not, explain these results.

C) Repeat part B) with a constant current of 45 $\mu A/cm^2$. How do these results compare to those from part B? Explain any differences in response with different applied constant currents.