David Young

10/5/2013

Action Potential for various stimulus voltages 100 l_inj=0 Inj=1 l_inj=2 80 l_inj=2.5 Inj=2.6 60 I_,nj=2.61 Voltage (mV) 20 -20 L time (mS)

QP: CLAB 3 H-H Model

Looking at how variations in the injected current (acting as a stimulus) affect the resultant graph of membrane voltage over time, you can clearly outline the threshold voltage for an action potential (AP). See Figure 1. The graph shows how the membrane voltage rises, but no AP occurs for injected currents below 2.61. But at 2.61 a distinct AP occurs.

Looking at injected current variations above 2.61 (min to cause AP), one can see how the refractory period is affected by increasing stimulus. See Figure 2. As the stimulus increases, the relative refractory period decreases, but only until it reaches a certain point where the absolute refractory period dictates the axon cannot fire again so soon.



Next I varied Tau m and Tau n to see the effects on threshold. To do this I replicated Figure 1, but varied the gains on Tau_m and Tau_n. By contrasting the two extremes in Figure 3 with each other and the two extremes in Figure 4 with each other, and seeing how Figure 1 lays in-between, one can understand the effects on threshold. At gains of 1 for all time constants, the injected current required to surpass threshold was 2.61. Figure 3 shows how an increase in Tau n will cause a decrease in the required I inj to surpass threshold, and a decrease in Tau n will increase the required I_inj to surpass threshold. This means a smaller n time constant raises threshold. This is because potassium conductance increases as Tau_n decreases, and Potassium conductance pushes the membrane voltage toward Ek which is below normal threshold. Conversely, the inverse behavior is demonstrated for Tau_m. See Figure 4. As Tau_m increases, threshold increases because sodium conductance increases, pushing the membrane voltage toward Ena well above threshold.



Looking at the APs when varying Tau_m and Tau_n shows the effects the time constants have on the rise and fall of the action potential. I accomplished this analysis by adding gain blocks to the time constants in my Simulink which fed into my total equation for membrane voltage. Looking at the time constant associated with activation particles ("n") for potassium channels, it is clear that a decreasing time constant yields a quicker response from potassium. This is because decreasing Tau means increasing the speed at which n approaches n_inf, meaning potassium conductance will increase much faster and the flow of potassium ions occurs quicker as a result. The peak should therefore not be as high, because sodium won't have as long to work on increasing voltage before potassium brings it back down, and the return from peak will be sooner. See **Figure 5**.



Decreasing the time constant Tau_m on the other hand is increasing the speed at which m approaches m_inf. This means sodium conductance increases much faster, and the peak should therefore be higher (as K hasn't had a chance to react fully) but the return will actually be sooner relative to a larger Tau_m because increasing V also increases G_k as it is voltage dependent. See **Figure 6**.



All in all, this system is remarkably good at modeling the involved currents that influence action potentials. The fact that 60+ years ago Hodgkin and Huxley derived all this by hand (without the aid of computers) astounds me. The math is simple in design (a summation of currents) but remains powerful as a model. Working backwards with curve fitting before the intuition of voltage gated ion channels was genius. Now that the model exists, values can be easily manipulated to show changes in peak, width, rise time, fall time, overshoot, refractory period and probably more.

Extra Credit:

Decreasing time constant Tau_n increases the speed at which n approaches n_inf, and therefore the speed at which potassium conductance increases. An increase in potassium conductance is associated with an outward movement/current of potassium ions. This is shown with an increasingly more negative current as tau_n decreases in **Figure 7**.



Decreasing time constant Tau_m increases the speed at which m approaches m_inf, and therefore the speed at which sodium conductance increases. An increase in sodium conductance is associated with an inward movement/current of potassium ions. This is shown with an increasingly more positive current in **Figure 8** as tau_m decreases.

