Deconstructing Actual Neurons

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Reference: The many ionic currents used in the HVC neuron model are described in detail in the Hille book

The HVC and HVC Neurons

The HVC is a region of the brain in song birds that is largely responsible for the production of bird song. I, along with students and collaborating labs at FSU, have constructed models of the electrical activity of the three types of neurons in the HVC: neurons that project to the RA nucleus (HVC_{RA} neurons), those that project to the Area X nucleus (HVC_X neurons), and those that project to neurons only with the HVC, called interneurons (HVC_{int} neurons). In this chapter we see how to use the models to learn things about the cells that are hard or impossible to extract from experiments alone.

The model cells contain nine different types of ion channels, with expression levels differing among the cell types. This is very typical of neural cell bodies or somas (in contrast to the axon that was studied by Hodgkin and Huxley). Our task is to determine how the ionic currents through the different channels affect spiking properties of the cells. The voltage equation for each of the three neuron types is

$$C\frac{dV}{dt} = -(I_L + I_K + I_{Na} + I_{Nap} + I_{CaL} + I_{CaT} + I_A + I_{SK} + I_M + I_h - I_{app}) \tag{1}$$

where I_L is a leak current, I_K is a delayed rectifying K^+ current, I_{Na} is a standard Na^+ current, and I_{CaL} is an L-type Ca^{2+} current that was also the type of depolarizing current used in the Morris-Lecar model. There are also several types of currents we have not encountered before.

- I_{Nap} is a persistent Na^+ current that inactives more slowly than the standard Hodgkin-Huxley Na^+ current. It has the form $I_{Nap} = g_{Nap} m_{p\infty}(V) h_p (V - V_{Na})$ where activation is assumed to occur instantaneously (the factor $m_{p\infty}(V)$), and inactivation (the factor h_p) has a large time constant.

- I_{CaT} is a T-type Ca^{2+} current. This current is through channels that activate at a lower voltage than the L-type Ca^{2+} channels. These channels also inactivate and the inactivation is fairly rapid.

- I_A is an A-type K^+ current that activates at low voltages and also inactivates at low voltages. The activation is rapid, so we assume that it is instantaneous: $I_A = g_A a_\infty(v) e (V - V_K)$ where a is activation and e is inactivation.

- I_{SK} is a K^+ current with channels activated by the binding of intracellular Ca^{2+} ions to the channel, rather than voltage. So their activation is fundamentally different from any channels we have thus far encountered. The "SK" stands for "small conductance", so these are small

conductance Ca^{2+}-activated K^+ channels. The equation for the current is: $I_{SK} = g_{SK} k_\infty(Ca_c)(V - V_K)$, where $k_\infty(Ca_c) = \frac{Ca_c^2}{Ca_c^2 + ks^2}$. The Ca_c is the cytosolic Ca^{2+} concentration, which we will discuss in detail in future lectures. But note that there is a differential equation for Ca_c in this model, since the intracellular Ca^{2+} concentration changes over time as Ca^{2+} enters and leaves the cell.

- I_M is an M-type K^+ current, named from the fact that it can be activated by "muscarinic acetylcholine receptors". These channels slowly activate when the cell is depolarized and don't inactivate. The equation is: $I_M = g_M z(V - V_K)$ where z is the activation variable with a large time constant.

- I_h is an hyperpolarization-activated inward current. Unlike every other current it is activated when the membrane is hyperpolarized, and is deactivated when the membrane is depolarized. It is a mixed current, letting Ca^{2+} and Na^+ in and K^+ out, but the reversal potential is above the rest potential. Therefore, this is a depolarizing or inward current. It is also composed of two distinct proteins; one protein activates rapidly and the other much more slowly. The current is: $I_h = g_h[k_r r_f + (1 - k_r) r_s](V - V_h)$, where k_r is the fraction of the channels that are of the fast type (so $1 - k_r$ is the fraction that are

of the slow type), r_f is the fast-type activation variable, and r_s is the slow-type activation variable. The reversal potential in the model is $V_h = -43$ mV, which is above the cell's resting potential.

We will begin with voltage clamp simulations to see how some of the currents (we won't look at all of them) respond to clamping at different voltages. We will then move to current clamp to see the influence that each of these currents has on the spiking pattern of the cell.