Introduction to Computational Neuroscience (Spring 2018)

Applications of Voltage Clamp

In this exercise we'll work with just one of the model HVC neurons, the HVC_{RA} model neuron. This time we'll see what can be done in the lab using a voltage clamp protocol, and then examine additional information that can be obtained from a model with the voltage clamp protocol. The first thing to remember about voltage clamp is that voltage is, well, clamped! So there won't be an ODE for V. Instead, it will be a parameter that can be set at any reasonable voltage value. All the gating variables will then respond. This response helps to set the dynamics of the ionic currents.

Exploration

Download the HVCRA_vc.ode file from my web site.

(1) Start up the HVC_{RA} code and run it. You should see a voltage pulse that starts at -70 mV, then goes to -30 mV for 300 ms, and then returns to -70 mV. The initial voltage is called the *holding potential*, and the more depolarized voltage is called the *test potential*. You should now open one or more additional windows and put the various ionic currents into them. I have defined these as auxiliary variables, so you can plot any of them.

(2) Plot the total current, I_{tot}. This is what would be measured in the lab. Why do you think it is initially positive, and then becomes much greater during the test pulse? Why is there a downward jump at the end of the test pulse? Why does the current then slowly decline? (You will better be able to answer these questions after doing the other parts of the exercise, but for now make your best guess.)

(3) To measure the time-dynamics of a specific ionic current, the typical experimental approach is to use the voltage protocol before and after application of a drug that blocks a specific type of ion channel underlying the current. One then subtracts the two measurements, before and after drug application. The difference is the current blocked by the drug. This is useful for measuring one current, assuming that there is a channel blocker specific to that type of ion channel (sometimes there is, sometimes there is not). It is difficult to measure more than one current per cell though, since the time required to add one drug at a time, and then wash it off before adding another can be so long that the seal to the cell degrades, changing the electrical properties of the cell. It's way easier to examine individual currents with the model. Plot the delayed rectifying K^+ current. Why does it do what it does during the test pulse?

(4) Next plot the Na^+ current. Explain why it does what it does during the pulse. Recall that you can also plot individual activation and inactivation variables (something you can't do in the lab), and this could help answer this and other questions.
(5) Next plot the persistent Na^+ current. Why does its response to the test pulse look so different from that of the other Na^+ current?
(6) Plot the T-type Ca^{2+} current and explain why it does what it does.
(7) As a final inward current to examine, explain why the h-current does what it does.
(8) Back to the outward currents, the M current is a bit similar to the delayed rectifier during the pulse, but there is a difference. Describe what's different and why. Also, what happens after the test pulse, and why?
(9) Plot the A-type K^+ current and explain what it does.
(10) Plot the leak current and explain why it does what it does.
(11) Finally, why does the SK current do what it does?
(12) Now instead of a depolarizing pulse to -30 mV, make the test pulse a hyperpolarization to -100 mV. Is there much response in the total current to the test pulse? Which currents are activated? Why do they do what they do?
(13) The parameter controlling the fraction of h current that is fast is kr. It is currently set at 0.95, meaning that 95% of the h current is gated by fast-activated channels. Change this now to 0.05, so that 95% are activated by the slowly-activated channels. How does this affect the response of the h current to a test hyperpolarization?