Simulation Exercises – Action Potential Part 1

Begin by running the CCWin program. This simulates patch-clamp experiments in the "current-clamp mode", which is to say that the experimental configuration allows you to deliver current to the cell while recording the voltage of the membrane.

1. Simulations: Subthreshold conductances and current. Open the file SingleAP_1.CC5 and run this simulation. This simulation delivers a 200 microsecond current stimulus and the initial value is 24.0 nA. At the top of the screen is the membrane potential of the neuron. Just below that is the stimulus current (I-Inj), followed by the sodium current (I-Na) and the potassium current (I-K).

Change the intensity of the stimulus current (Parameters | Protocol | Injected current) in 0.1 nA increments until you find the current that will just barely elicit an action potential. Then change the stimulus current in 0.01 nA steps until you find the lowest current that will still elicit an action potential. This is the threshold current for this cell.

At what current did the cell reach threshold? Run a single sweep of data at this current.

Now, increase the maximum voltage-gated K^+ conductance to 3 (Parameters | Conductances | gK) overlay this sweep on the previous one. Note how the timecourse of the Na+ and K+ currents change. **How did changing gK affect the threshold?**

Finally, overlay a simulation at 25 nA stimulus intensity with gK at 1 and a simulation at 25 nA stimulus intensity with gK at 3 (tripling the voltage-gated K^+ conductance). **What key differences in the action potential (AP) are caused when gK increases?**

2. Simulations: Conductance and current during the action potential. Open the file **SingleAP_3.CC5** and run this simulation. This is the same action potential as the previous simulation, but the currents are on a larger scale so you can see their progression during the action potential, and the duration of the sweep is shorter to make the timing of events easier to see.

Do the conductances and currents match up well? In particular, compare the timecourse of the Na^+ conductance changes and the timecourse of INa. What happens to the Na+ current at the peak of the action potential? Why does INa have such a weird timecourse?

3. Simulations: How much can you do with just one type of sodium channel and one type of potassium channel?

Open the file SingleAP_6.CC5 - this simulation delivers a 50 ms current step to help you find out how good your neuron is at encoding stimulus strength in its firing frequency. Run the simulation, which starts with a current intensity of 1.0 nA. Repeat the simulation, increasing the stimulus intensity each time by 0.2 nA. Plot the number of action potentials (Y axis) by the stimulus intensity (X axis). This is known as an F-I plot (for Frequency x Current). A spike only counts as an action potential if it crosses -10 mV! This plot tells you how well your neuron encodes stimulus intensity in its firing rate.

Challenge: Try to make a cell that does a better job of encoding stimulus intensity in its spike frequency (covering a broader range of stimulus values, or creating a smoother "F-I curve". Try to make a cell that goes to a higher firing frequency. **The catch? All you can do is change the density of Na^+ channels (Parameters | Conductances | gNa) or the density of K^+ channels (Parameters | Conductances | gK). How did you solve this challenge?**

Homework 3 Questions:

Answer the following questions, using the data from your simulations to support your answers. Submit your document through Canvas for Homework 3.

1. What is your best explanation of what factors determine the action potential threshold?

2. What effects does increasing gK (increasing the density of K^+ channels) have on action potential timing and waveform?

3. Why is the timecourse of the ionic currents (like INa) sometimes so different from the timecourse of changes in conductance for those ions, and different from the changes in membrane voltatge?

4. Explain the hyperpolarization that sometimes occurs after the action potential.

5. Based on your results to the final challenge, what was the most important factor for creating a cell that had the widest range of firing frequencies?