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 23.5 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 conductance (gNa) then and the potassium current (I-K) and conductance (gK).

Change the intensity of the stimulus current (Parameters | Protocol | Injected current) and re-run the simulation at currents of 23.6, 23.7, 23.8, 23.9, and 24. Note the rise and fall of the Na^+ and K^+ conductances, as well as the timecourse of the Na^+ and K^+ currents at each step.

Do the Na^+ and K^+ currents match up well with the changes in Na^+ and K^+ conductance? Why or why not? At what current did the cell reach threshold?

Now, increase the maximum voltage-gated K^+ conductance to 2 (Parameters | Conductances | gK) and repeat the steps above. **At what current did the cell reach threshold? How did changing gK affect the threshold?**

Finally, overlay a simulation at 24nA stimulus intensity with gK at 1 and a simulation at 24 nA stimulus intensity with gK at 2 (doubling the voltage-gated K^+ conductance). **What key differences in the 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 much 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 at the peak of the action potential? Why does INa have such a weird timecourse? Explain the slight afterhyperpolarization. What does this have to do with K^+ channel kinetics and EK?

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 D2L to the dropbox for Homework 3.

1. What determines 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?