Synapse Construction Kit©
Student Handout

Part II: Modeling the Action Potential

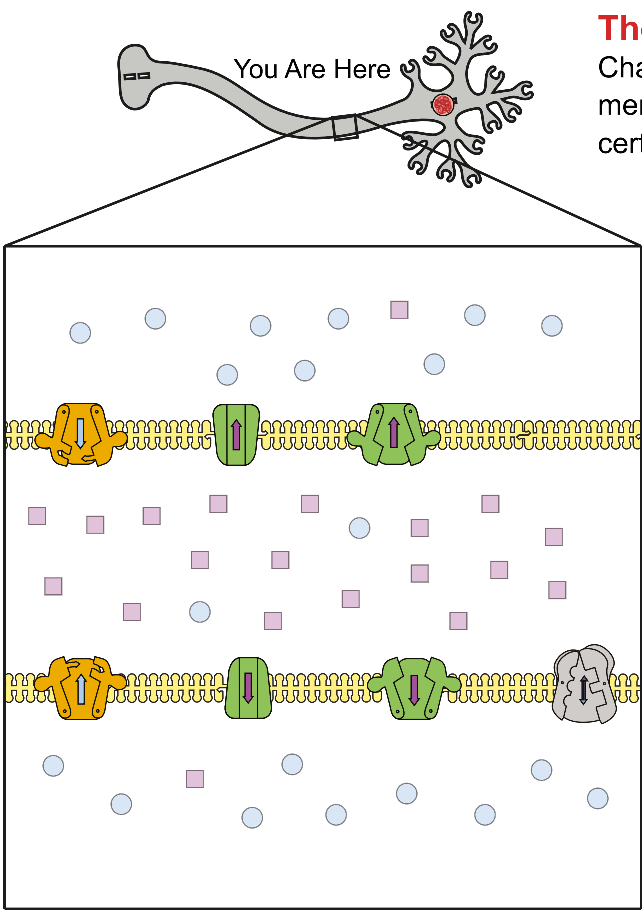
Voltage-gated sodium have three configurations:

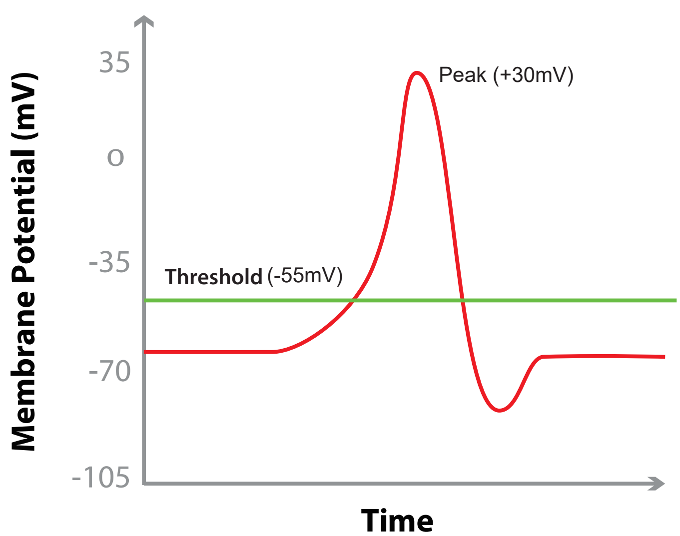
Voltage-gated potassium have two configurations:

Set up an axonal membrane as shown in the diagram below and to the left. Remember to set up your model so that there are more extracellular Na^+ ions than intracellular Na^+ ions and more intracellular K^+ ions than extracellular K^+ ions. You will also need to periodically refer to the graph shown below and to the right as you work your way through the modeling process:

The Action Potential

Changes in membrane potential in a local area of a neuron's membrane result from changes in membrane permeability to certain ions.





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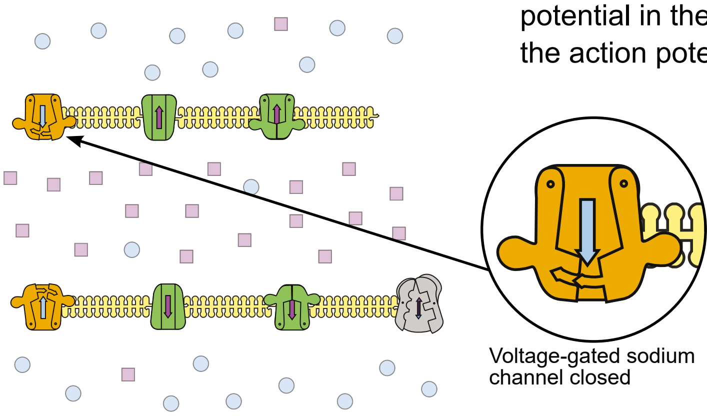
1. Resting Potential

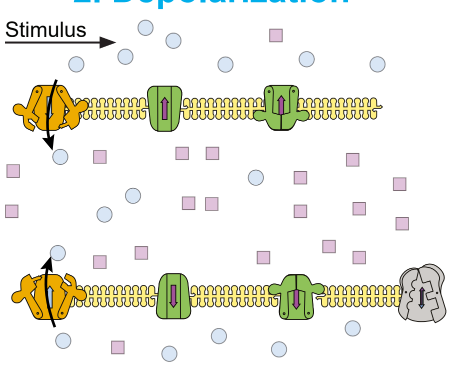


Next, you will simulate the mechanism that produces an action potential in the axon of the neuron. Follow the steps below to model the action potential.

Step 1 - Resting state:

The voltage-gated sodium and potassium channels are closed. Set your voltmeter at -70 mV.

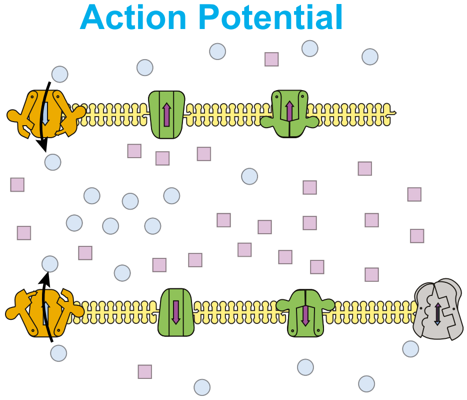
2. Depolarization



Step 2 - Depolarization:

A stimulus opens some voltage-gated sodium channels and Na^+ follows its concentration gradient into the neuron. The influx of Na^+ causes a depolarization across the cell membrane. An action potential will be triggered only if the depolarization reaches threshold (often between -5 and -15 mV higher than resting potential). Set the voltmeter at threshold. For the purposes of this activity, we will consider the threshold potential to be -55 mV.

3. Rising Phase of the Action Potential



Step 3 - Rising phase of the action potential:

During an action potential, depolarization opens most of the voltage-gated sodium channels. Move a few more Na^+ into the neuron through the open voltage-gated sodium channels. Depolarization continues until the inside of the membrane is positive with respect to the outside (usually +30 mV). Set the voltmeter at the peak value of the action potential. When the patch of neuron membrane is generating an action potential and its voltage-gated sodium channels are open, the neuron cannot respond to another stimulus no matter how strong.

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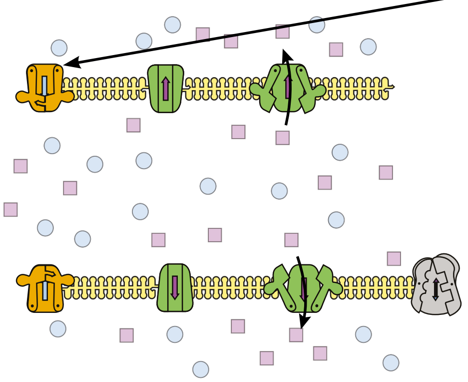
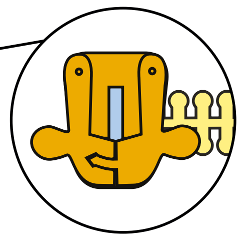
4. Falling Phase of the Action Potential

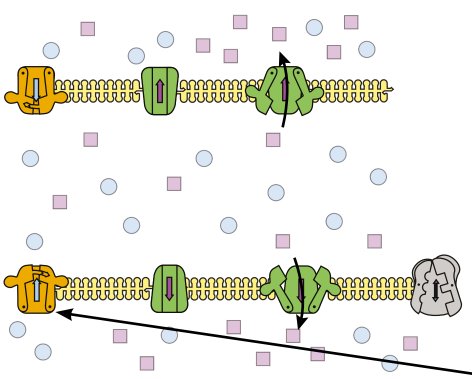




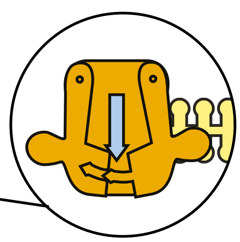
Voltage-gated sodium channel inactivated

Step 4 - Falling phase of the action potential:
Voltage-gated sodium channels become **inactivated**, at the peak of the action potential blocking Na^+ inflow. Voltage-gated potassium channels have been slowly opening permitting K^+ to follow its concentration gradient out of the cell. Once the peak of the action potential is reached, the membrane potential begins to move back toward the resting potential in a process known as **repolarization**, resulting in falling voltage across the membrane. Position the voltage-gated sodium channels to their inactivated position. Open the voltage-gated potassium channels and move the K^+ ions out of the neuron. Demonstrate a fall in voltage due to this ion movement on the voltmeter.

5. Hyperpolarization

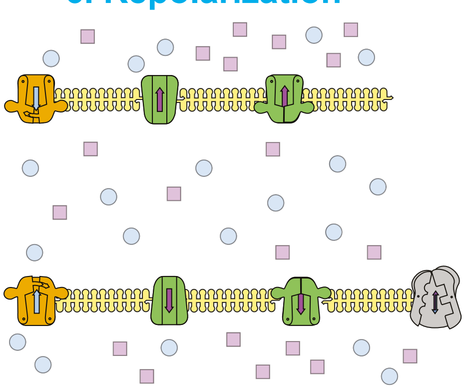


Step 5 - Hyperpolarization:
The voltage-gated potassium channels are still open, causing the voltage to undershoot the resting potential, set the voltmeter to dip below -70mV. The voltage-gated sodium channel reset back to their original closed position. Only a stronger-than-normal stimulus can reopen the voltage-gated sodium channels at this time.



Voltage-gated sodium channel closed

6. Repolarization



Step 6 - Restoring the Ion Concentrations:
Repolarization restores resting electrical conditions but does NOT restore resting ionic conditions. The ion redistribution is accomplished by the **sodium-potassium pump**.

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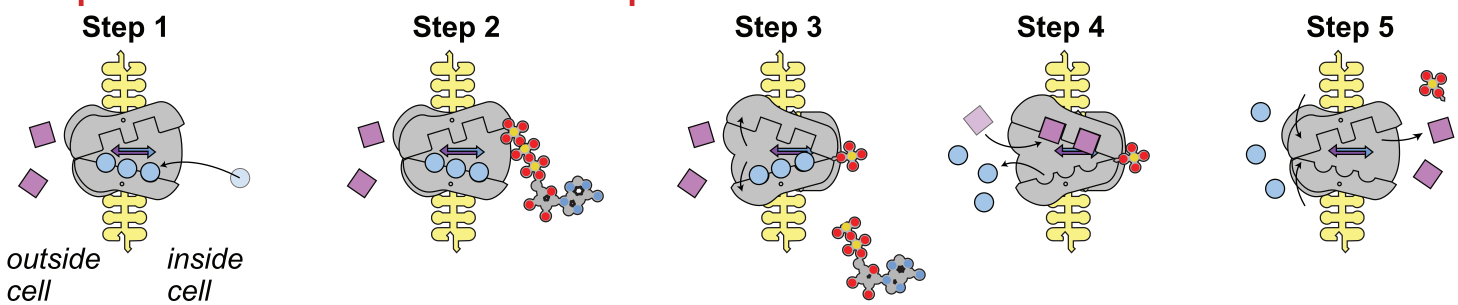
Step 7 - The Sodium-Potassium Pump:



7.1: Bind three three intracellular sodium ions to the appropriate spots in the protein.

7.2: Bring the ATP in close proximity to the pump. Sodium ion binding stimulates phosphorylation of the pump protein by ATP. In other words, a phosphate group is added to the sodium-potassium pump from the ATP molecule. Bind the phosphate group of the ATP to the sodium-potassium pump.

7.3: Phosphorylation causes a change in the shape of the protein. You can demonstrate this by “swinging” the sides of the protein so that it opens to the outside of the cell.

7.4: The shape change reduces the protein’s binding affinity for sodium ions and increases the binding affinity for potassium ions. Remove the sodium ions from the protein and deposit them outside the cell and bind two potassium ions to the appropriate spots in the protein.

7.5: Potassium ion binding triggers the release of the phosphate group from the protein.

7.6: Loss of the phosphate group results in the restoration of the protein’s original shape which then releases the potassium ions. Swing the sides of the protein back so that they open to the inside of the cell and deposit the potassium ions.

7.7 : Repeat this process until the ion concentrations are at resting potential.

...where molecules become real ™

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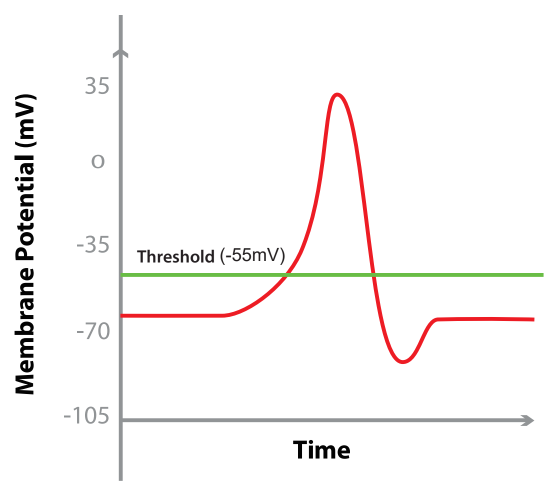
2a. What value is being used for the resting potential in your model neuron?

2b. What "factors" may cause a change in the voltage established across the membrane this neuron?

2c. Of what significance is a rise in membrane potential to -55mV in this neuron? Identify and describe the key protein channel and how it is affected by this change in voltage.

2d. What is meant by depolarization?

2e. Color the area on the graph below where depolarization has occurred.



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2f. Sketch the axon membrane that has been depolarized. Be sure to include all channels and ions in their proper locations and positions.

2g. What events occur at the peak of the action potential?

2h. Why is it important that another action potential cannot be generated during the rising phase of an action potential?

2i. Why does the voltage across the neuronal membrane fall?

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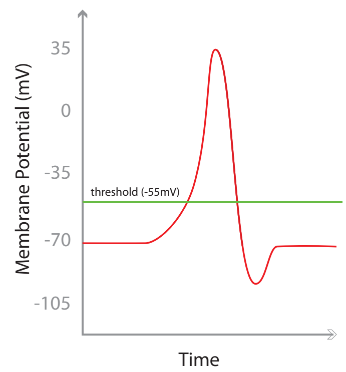
2j. Color the area on the graph to the right where repolarization has occurred.



2k. Sketch the axon membrane that has been repolarized. Be sure to include all channels and ions in their proper locations and positions.

2l. Why does the voltage "undershoot"?

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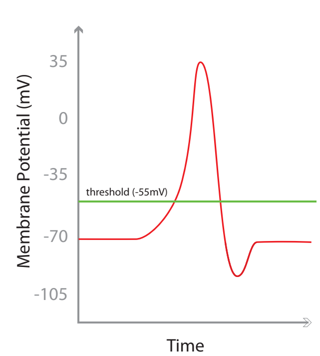
2m. Color the area on the graph to the right where hyperpolarization has occurred.



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2n. Fill in the following table to compare voltage fluctuations and ion concentration changes that occur during an action potential. When referring to concentrations use words like increasing, decreasing, high or low.

Action Potential Step	Voltage	Relative Intracellular Na^+ Concentration	Relative Extracellular Na^+ Concentration	Relative Intracellular K^+ Concentration	Relative Extracellular K^+ Concentration
Resting					
Threshold					
Peak Depolarization					
Repolarization					
Hyperpolarization					

2o. Why is the sodium-potassium pump necessary after an action potential has been generated?

2p. What happens to the ADP after the sodium-potassium pump has been phosphorylated?

2q. What would happen if a toxin (blue plug) were to bind to the voltage-gated **sodium** channels?

2r. What would happen if a toxin (blue plug) were to bind to the voltage-gated **potassium** channels?