

# Foundations of Neuroscience



# FOUNDATIONS OF NEUROSCIENCE

Open Edition

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East Lansing



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# INTRODUCTION

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*Foundations of Neuroscience* is aimed at undergraduate students new to the field of neuroscience. The first edition specifically targets students enrolled in Neurobiology at Michigan State University and primarily contains topics covered in that course. For example, only three sensory systems are discussed in this version of the text. Future editions will continue to expand the number of topics and concepts presented (see below for a list of planned topics).

Following the principles of Universal Design for Learning, multiple means of representation will be provided for students to engage with the content. Clear, accessible text will be divided into short, easily digestible chapters that focus on one concept. Numerous images and animations will be paired with the text, and a captioned video version of the text is shared for each chapter. The text is written with the undergraduate student that is new to neuroscience in mind. Neuroscience terminology will be introduced in an easy-to-understand manner, and supporting content will be clear and concise to minimize cognitive load not associated with understanding new material.

Each chapter will end with an interactive quiz for student self-evaluation of the content. All quiz answers (i.e. both correct and incorrect) will provide feedback, so students can self-check their understanding at the end of each concept and receive immediate feedback about their learning.

Find errors or have suggestions? Email FoundationsNeuroscienceOER at gmail dot com.

## Future topics include:

Emotions (winter 2021)

Learning and Memory (winter 2021)

Diseases and disorders for the different systems (2022)

Pain (2022)

Auditory (2022)

Vestibular (2022)

Olfaction (2022)

Autonomic nervous system (2022)

Color Vision

Cerebellum

Sleep

Circadian rhythms

PART I

# NEURON STRUCTURE & FUNCTION



## 1.

# THE NEURON

---

Neurons are the basic units of the brain. Their main function is to send electrical signals over short and long distances in the body, and they are electrically and chemically excitable. The function of the neuron is dependent on the structure of the neuron. The typical neuron consists of the dendrites, cell body, axon (including the axon hillock), and presynaptic terminal.

## Resources

- Key Takeaways
- Test Yourself
- Additional Review
- Video Version

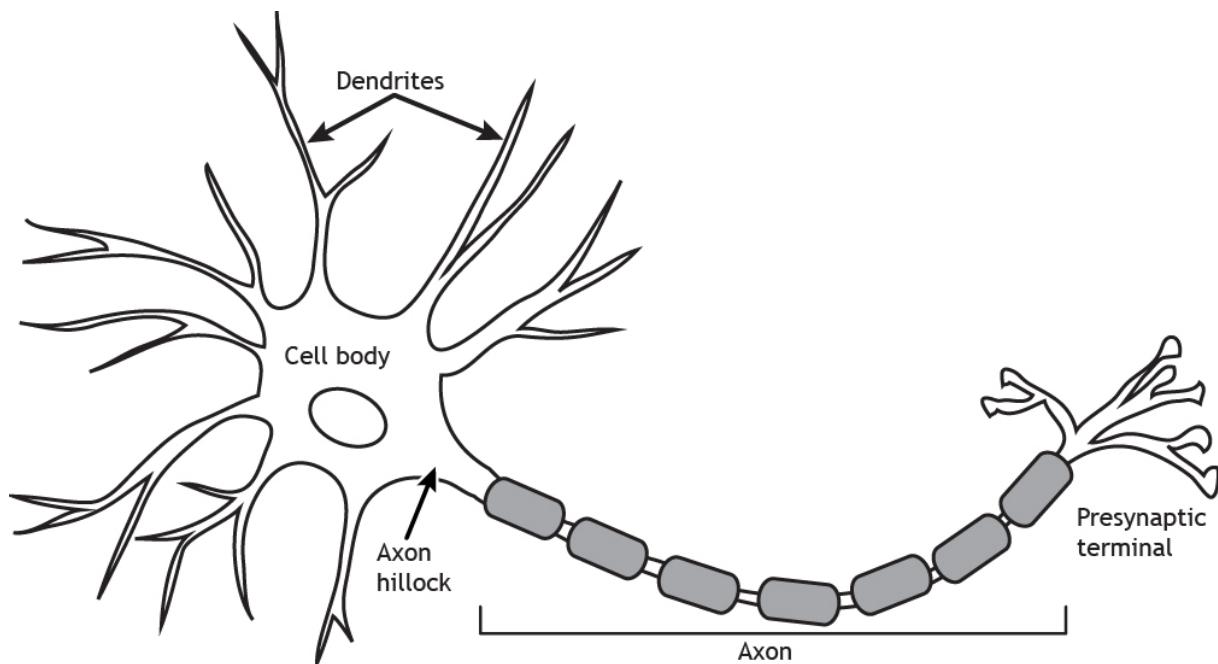


Figure 1.1. A typical neuron. Dendrites branch out from the cell body, where the nucleus is located. The axon hillock is located where the cell body transitions into the axon. The axon begins at the axon hillock and ends at the presynaptic terminal, which can branch into multiple terminals. ‘Neuron’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Dendrites

Dendrites, shown here in green, are processes that branch out in a tree-like fashion from the cell body. They are the main target for incoming signals received from other cells. The number of inputs a neuron receives depends on the complexity of the dendritic branching. Dendrites may also have small protrusions along the branches known as spines. Spines, illustrated in the inset box, are the sites of some synaptic contacts. Spines increase the surface area of the dendritic arbor, which may be an important factor in receiving communication.

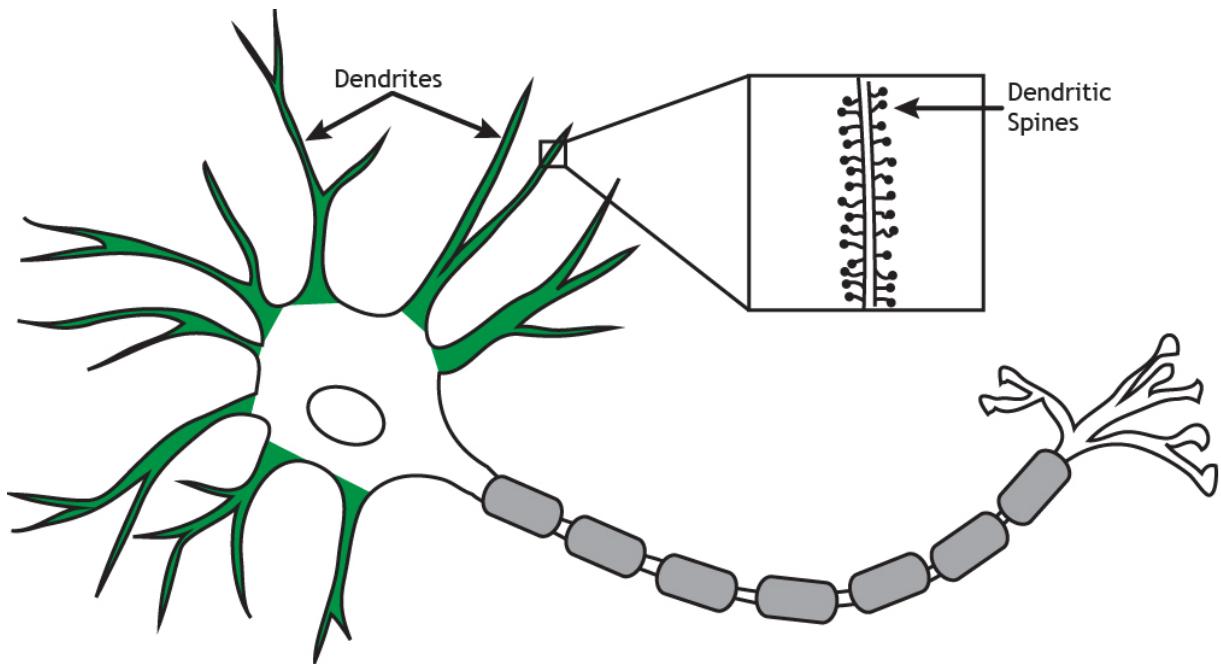


Figure 1.2. Dendrites branch out from the soma. Their function is to receive information from other neurons. Some dendrites have small protrusions called spines that are important for communicating with other neurons. 'Dendrites' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Cell Body

The cell body, shown here in green and also known as the soma, contains the nucleus and cellular organelles, including endoplasmic reticulum, Golgi apparatus, mitochondria, ribosomes, and secretory vesicles. The nucleus houses the DNA of the cell, which is the template for all proteins synthesized in the cell. The organelles, illustrated in the inset box, in the soma are responsible for cellular mechanisms like protein synthesis, packaging of molecules, and cellular respiration.

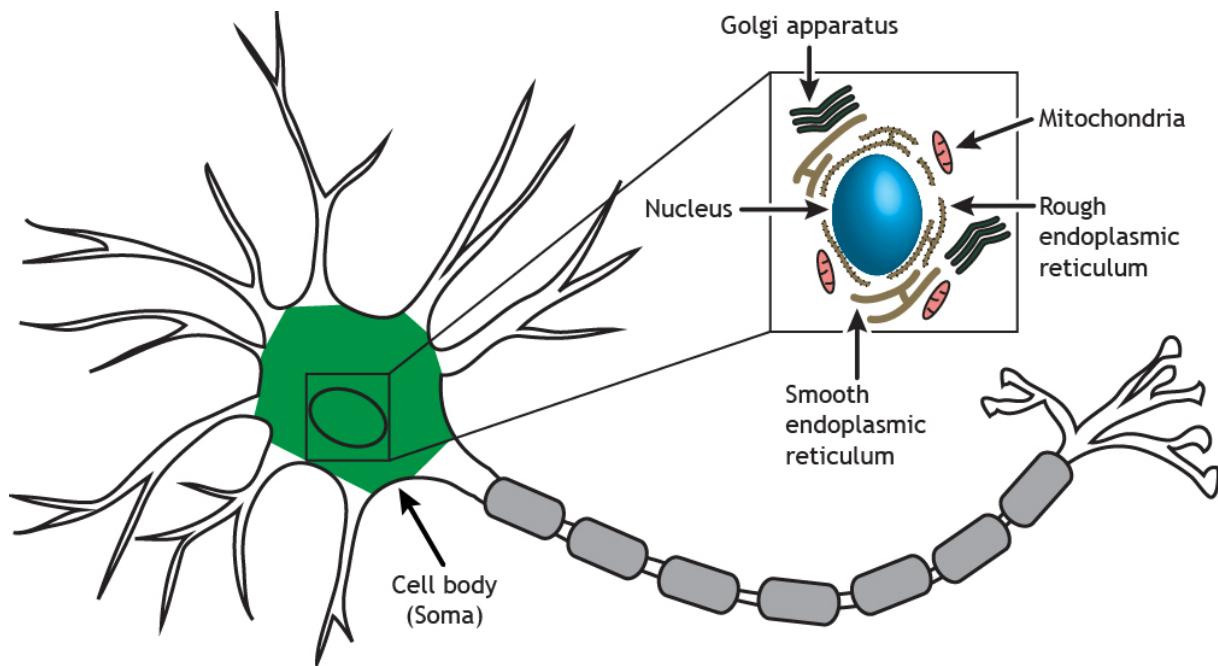


Figure 1.3. The cell body, or soma, of the neuron contains the nucleus and organelles that are commonly found in other cell types and are important for basic cellular functions. These organelles include mitochondria, endoplasmic reticulum, and Golgi apparatus. 'Soma' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Axon

The axon, highlighted in green, is usually a long, single process that begins at the axon hillock and extends out from the cell body. The axon hillock is located where the cell body transitions into the axon. Axons can branch in order to communicate with more than one target cell.

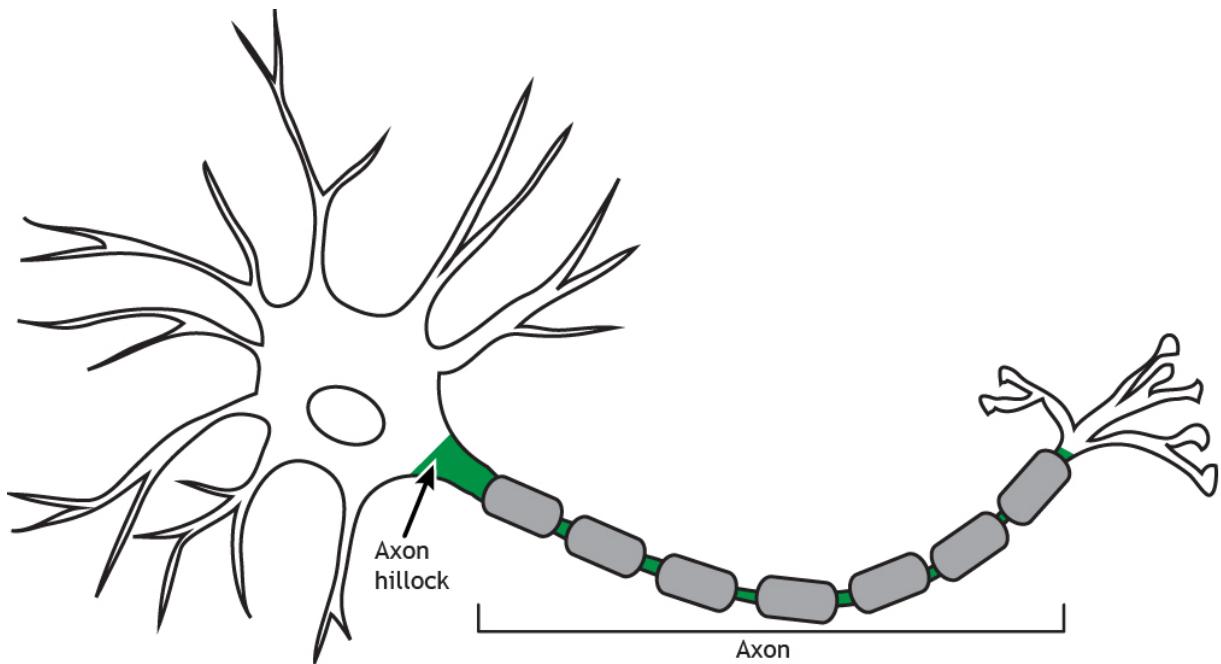


Figure 1.4. The axon is a long single projection that begins at the axon hillock, the region between the cell body and the axon. The axon terminates at the presynaptic terminal. 'Axon' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Action Potential

The axon transmits an electrical signal, called an action potential, from the axon hillock to the presynaptic terminal where the electrical signal will result in a release of chemical neurotransmitters to communicate with the next cell. The action potential is a very brief change in the electrical potential, which is the difference in charge between the inside and outside of the cell. During the action potential, the electrical potential across the membrane moves from a negative value to a positive value and back.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=5>

Animation 1.1. The action potential is a brief but significant change in electrical potential across the membrane. The membrane potential will move from a negative, resting membrane potential, shown here as -65 mV, and will rapidly become positive and then rapidly return to rest during an action potential. The action potential moves down the axon beginning at the axon hillock. When it reaches the synaptic terminal, it causes the release of chemical neurotransmitter. ‘Action Potential Propagation’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License. [View static image of animation.](#)

## Myelin

Many axons are also covered by a myelin sheath, a fatty substance that wraps around portions of the axon and increases action potential speed. There are breaks between the myelin segments called Nodes of Ranvier, and this uncovered region of the membrane regenerates the action potential as it propagates down the axon in a process called saltatory conduction. There is a high concentration of voltage-gated ion channels, which are necessary for the action potential to occur, in the Nodes of Ranvier.

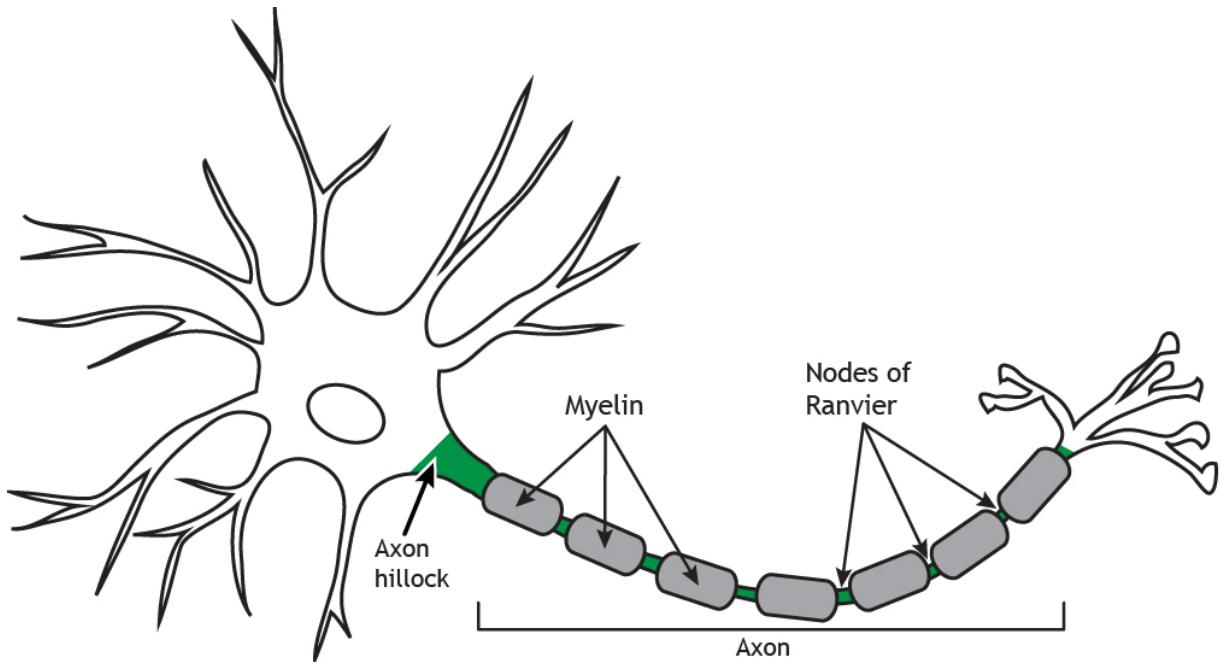


Figure 1.5. Myelin wraps around and insulates the axon. The spaces between the myelin sheath, where the axon is uncovered, are called the Nodes of Ranvier. 'Myelin' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Axon Characteristics

### Axon Length

The length of an axon is variable depending on the location of the neuron and its function. The axon of a sensory neuron in your big toe needs to travel from your foot up to your spinal cord, whereas an interneuron in your spinal cord may only be a few hundred micrometers in length.

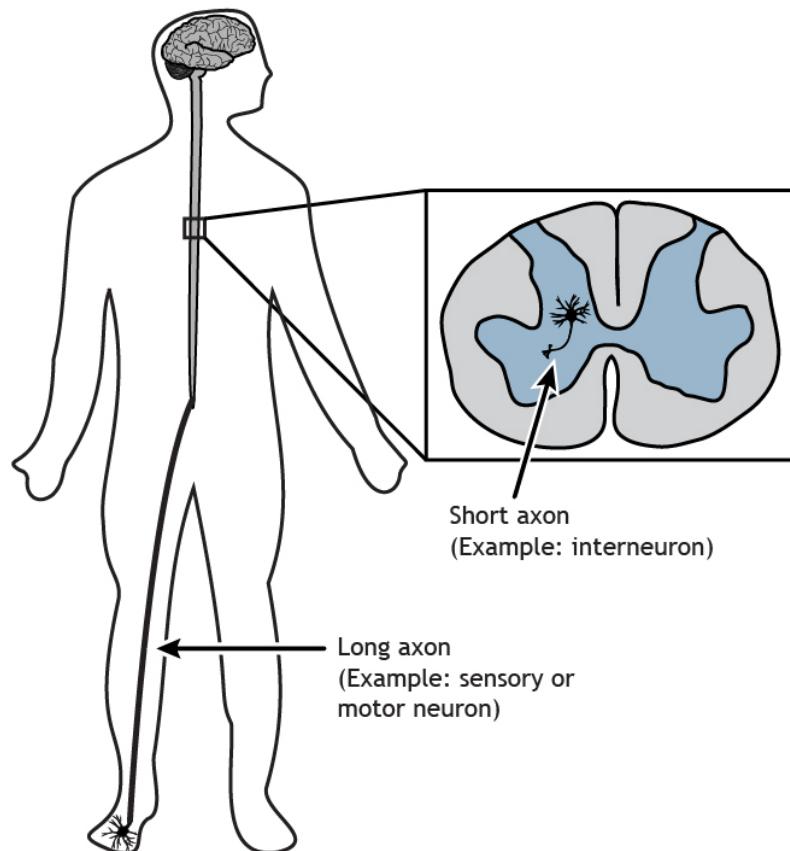


Figure 1.6. Axons vary in length. Spinal interneurons, neurons that fully exist within the spinal cord, can have short axons, whereas sensory or motor neurons, which need to reach from the spinal cord to the appropriate body region, for example the toe, have long axons. 'Axon Length' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Axon Diameter

Axon diameter is also variable and can be used to differentiate different types of neurons. The diameter affects the speed at which the action potential will propagate. The larger the diameter, the faster the signal can travel. Additionally, larger diameter axons tend to have thicker myelin.

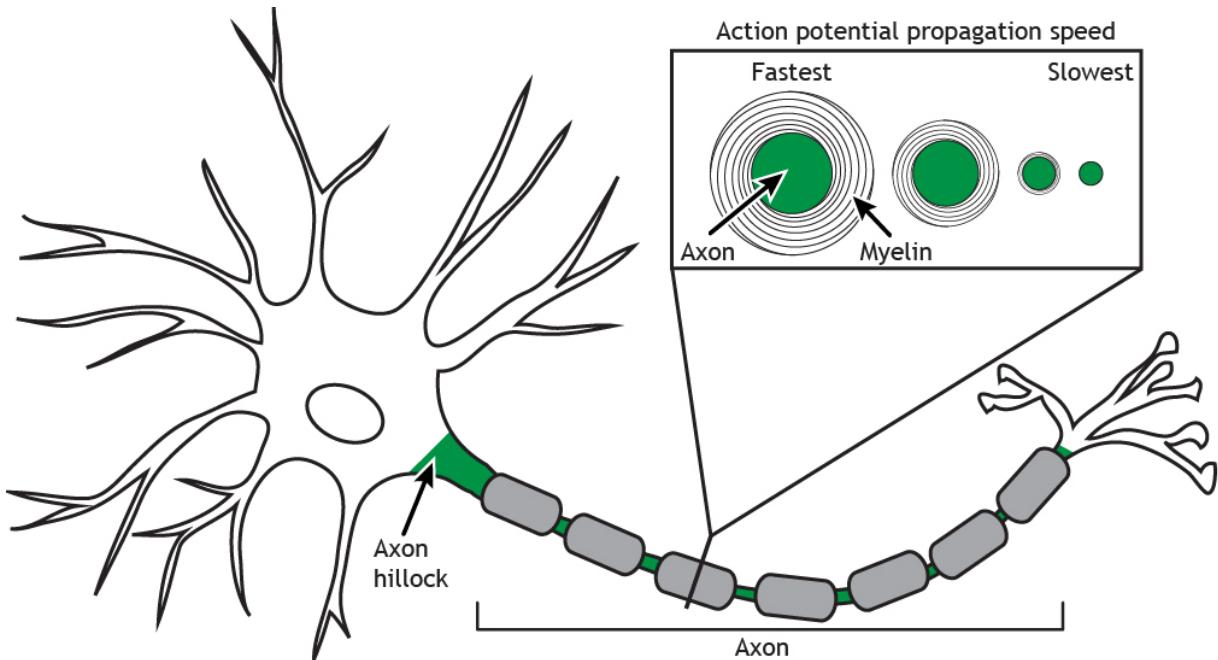


Figure 1.7. The diameter of the axon and the amount of myelination varies. Large diameter axons typically have thicker myelin sheath, which results in fast action potential speed. Small diameter axons may have no myelin present, resulting in slow action potential speed. 'Axon Diameter' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Presynaptic Terminal

The axon terminates at the presynaptic terminal or terminal bouton. The terminal of the presynaptic cell forms a synapse with another neuron or cell, known as the postsynaptic cell. When the action potential reaches the presynaptic terminal, the neuron releases neurotransmitters into the synapse. The neurotransmitters act on the postsynaptic cell. Therefore, neuronal communication requires both an electrical signal (the action potential) and a chemical signal (the neurotransmitter). Most commonly, presynaptic terminals contact dendrites, but terminals can also communicate with cell bodies or even axons. Neurons can also synapse on non-neuronal cells such as muscle cells or glands.

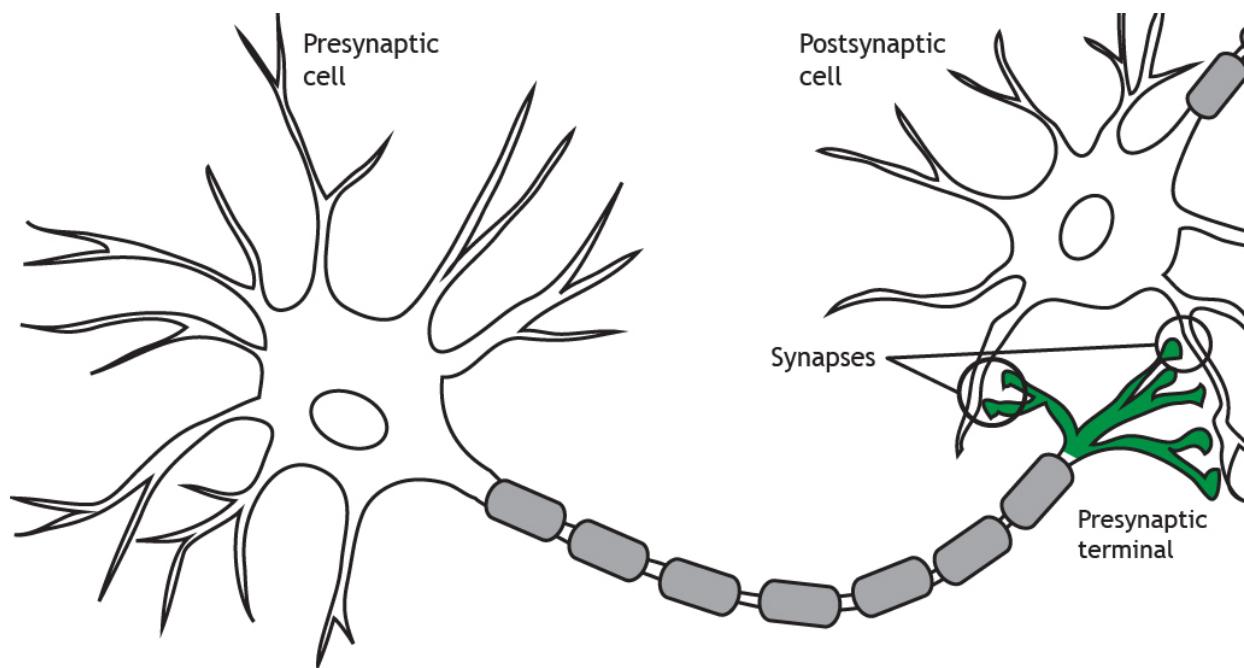


Figure 1.8. The presynaptic terminal forms synaptic contacts with a postsynaptic cell. 'Presynaptic Terminal' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

The terms presynaptic and postsynaptic are in reference to which neuron is releasing neurotransmitters and which is receiving them. Presynaptic cells release neurotransmitters into the synapse and those neurotransmitters act on the postsynaptic cell.

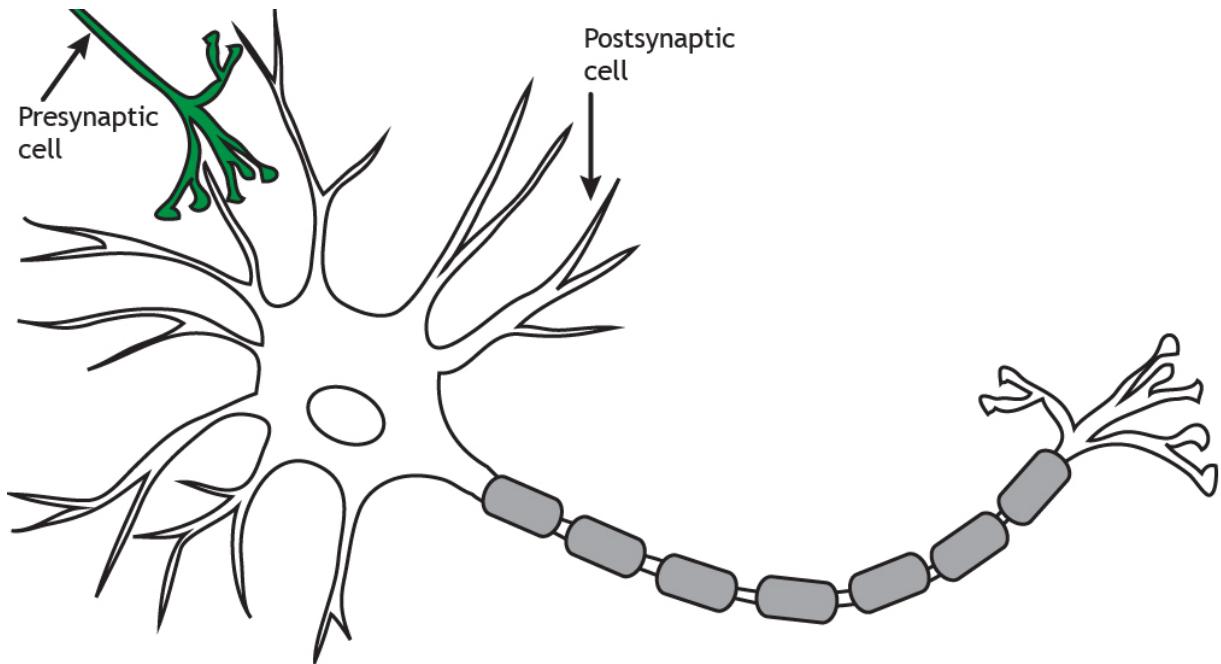


Figure 1.9. The presynaptic cell is the neuron that releases neurotransmitters into the synapse to act upon the postsynaptic cell. 'Postsynaptic Cell' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Variations in Structure

Although these typical structural components can be seen in all neurons, the overall structure can vary drastically depending on the location and function of the neuron. Some neurons, called unipolar, have only one branch from the cell body, and the dendrites and axon terminals project from it. Others, called bipolar, have one axonal branch and one dendritic branch. Multipolar neurons can have many processes branching from the cell body. Additionally, each of the projections can take many forms, with different branching characteristics. The common features of cell body, dendrites, and axon, though, are common among all neurons.

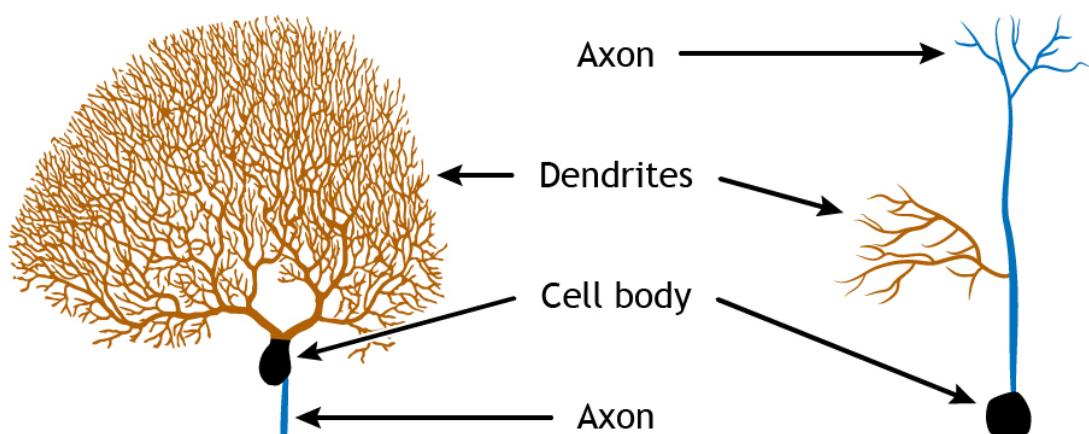
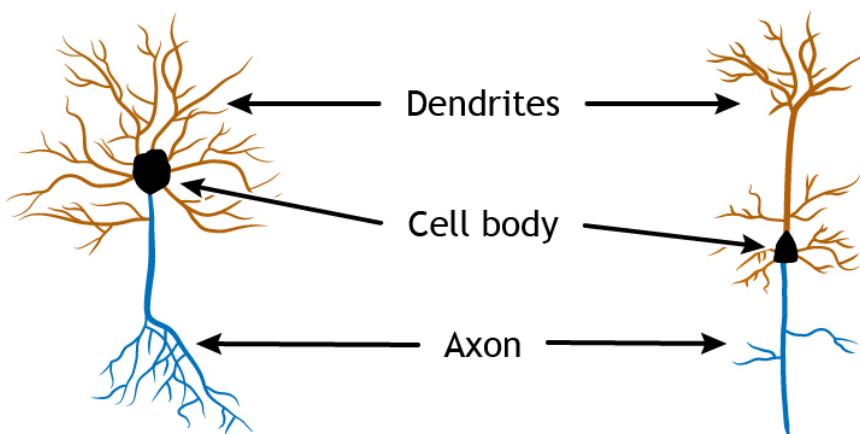


Figure 1.10. Neuron structure is variable, but the main components of cell body (shown in black), dendrites (shown in brown), and axon (shown in blue) are common among all neurons. 'Neuron Types' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

### Key Takeaways

- Each structural component of the neuron has an important function

- Overall structure of the cell can vary depending on location and function of the neuron

## Test Yourself!



An interactive H5P element has been excluded from this version of the text. You can view it online here:

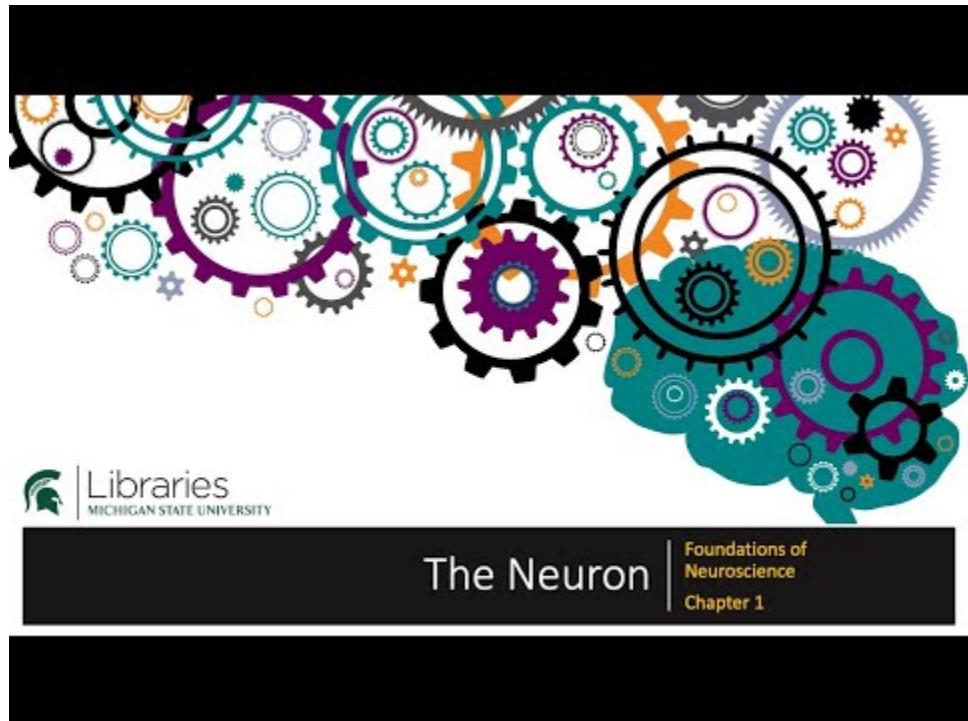
<https://openbooks.lib.msu.edu/neuroscience/?p=5#h5p-2>

### Additional Review

1. Draw a neuron and identify the following structures: dendrites, soma, axon hillock, axon, myelin, nodes of Ranvier, presynaptic terminal
2. Describe functions of each neuronal structure depicted in your model.
3. Predict what would happen to neuron function if myelin was destroyed.

### Answers

## Video Version of Lesson



A YouTube element has been excluded from this version of the text. You can view it online here:

<https://openbooks.lib.msu.edu/neuroscience/?p=5>

## 2.

# ION MOVEMENT

Ion flow into and out of the neuron is a critical component of neuron function. Ions move in predictable ways, and the control of ion movement affects the cell at rest and while sending and receiving information from other neurons.

## Phospholipid Bilayer Prevents Ion Movement

The neuronal membrane is composed of lipid molecules that form two layers. The hydrophilic heads of the molecules align on the outside of the membrane, interacting with the intra- and extracellular solution of the cell, whereas the hydrophobic tails are arranged in the middle, forming a barrier to water and water-soluble molecules like ions. This barrier is critical to neuron function.

### Resources

- Key Takeaways
- Test Yourself
- Additional Review
- Video Version

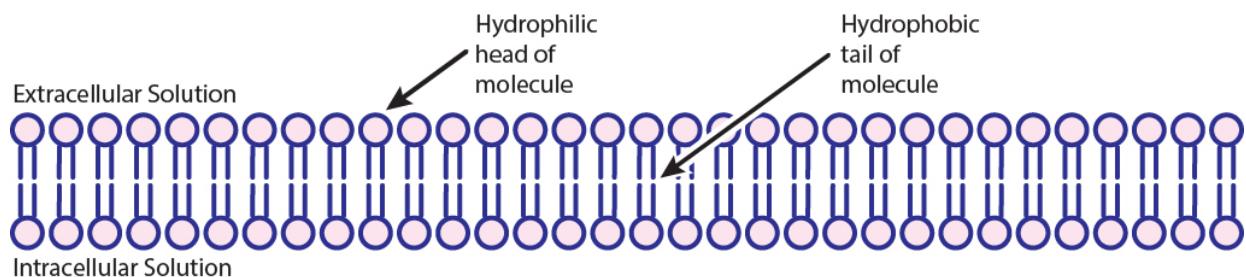


Figure 2.1. The neuronal membrane is composed of two layers of phospholipid molecules that form a barrier to water and water-soluble molecule due to the organization of the hydrophilic heads and hydrophobic ends of the molecules. 'Phospholipid Bilayer' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial (CC-BY-NC) 4.0 International License.

## Ion Channels Allow Ion Movement

Embedded throughout the neuronal membrane are ion channels. Ion channels are proteins that span the width of the cell membrane and allow charged ions to move across the membrane. Ions cannot pass through the phospholipid bilayer without a channel. Channels can be opened in a number of different ways. Channels that open and close spontaneously are called leak or non-gated channels. Channels that open in response to a change in membrane potential are called voltage-gated. Channels that open in response to a chemical binding are called ligand-gated. Other mechanisms like stretch of the membrane or cellular mechanisms can also lead to the opening of channels. Channels can be specific to one ion or allow the flow of multiple ions.

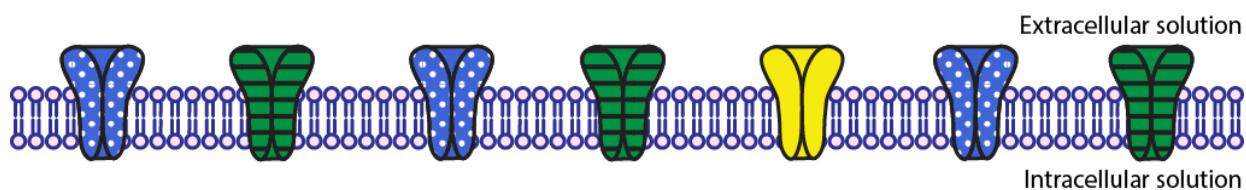


Figure 2.2. The phospholipid bilayer with embedded ion channels. The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. 'Membrane with Channels' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial (CC-BY-NC) 4.0 International License.

Ion channels control ion movement across the cell membrane because the phospholipid bilayer is impermeable to the charged atoms. When the channels are closed, no ions can move into or out of the cell. When ion channels open, however, then ions can move across the cell membrane.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=52>

Animation 2.1. When ion channels in the membrane are closed, ions cannot move into or out of the neuron. Ions can only cross the cell membrane when the appropriate channel is open. For example, only sodium can pass through open sodium channels. The dotted, blue channels represent sodium

channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. ‘Ion Movement’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial (CC-BY-NC) 4.0 International License. View static image of animation.

## Gradients Drive Ion Movement

Ions move in predictable ways. Concentration and electrical gradients drive ion movement. Ions will diffuse from regions of high concentration to regions of low concentration. Diffusion is a passive process, meaning it does not require energy. As long as a pathway exists (like through open ion channels), the ions will move down the concentration gradient.

In addition to concentration gradients, electrical gradients can also drive ion movement. Ions are attracted to and will move toward regions of opposite charge. Positive ions will move toward regions of negative charge, and vice versa.

For discussion of ion movement in this text, the combination of these two gradients will be referred to as the electrochemical gradient. Sometimes the concentration and electrical gradients driving ion movement can be in the same direction; sometimes the direction is opposite. The electrochemical gradient is the summation of the two individual gradients and provides a single direction for ion movement.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=52>

Animation 2.2. Concentration and electrical gradients drive ion movement. Ions diffuse down concentration gradients from regions of high concentration to regions of low concentration. Ions also move toward regions of opposite electrical charge. ‘Gradients’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial (CC-BY-NC) 4.0 International License. View static image of animation.

## When Gradients Balance, Equilibrium Occurs

When the concentration and electrical gradients for a given ion balance, meaning they are equal in strength but in different directions, that ion will be at equilibrium. Ions still move across the membrane through open channels when at equilibrium, but there is no net movement in either direction meaning there is an equal number of ions moving into the cell as there are moving out of the cell.



*A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=52>*

Animation 2.3. When an ion is at equilibrium, which occurs when the concentration and electrical gradients acting on the ion balance, there is no net movement of the ion. The ions continue to move across the membrane through open channels, but the ion flow into and out of the cell is equal . In this animation, the membrane starts and ends with seven positive ions on each side even though the ions move through the open channels. ‘Ion Equilibrium’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial (CC-BY-NC) 4.0 International License. View static image of animation.

### Key Takeaways

- The phospholipid bilayer prevents ion movement into or out of the cell
- Ion channels allow ion movement across the membrane
- Electrochemical gradients drive the direction of ion flow
- At equilibrium, there is no *net* ion movement (but ions are still moving)

## Test Yourself!



An interactive H5P element has been excluded from this version of the text. You can view it online here:

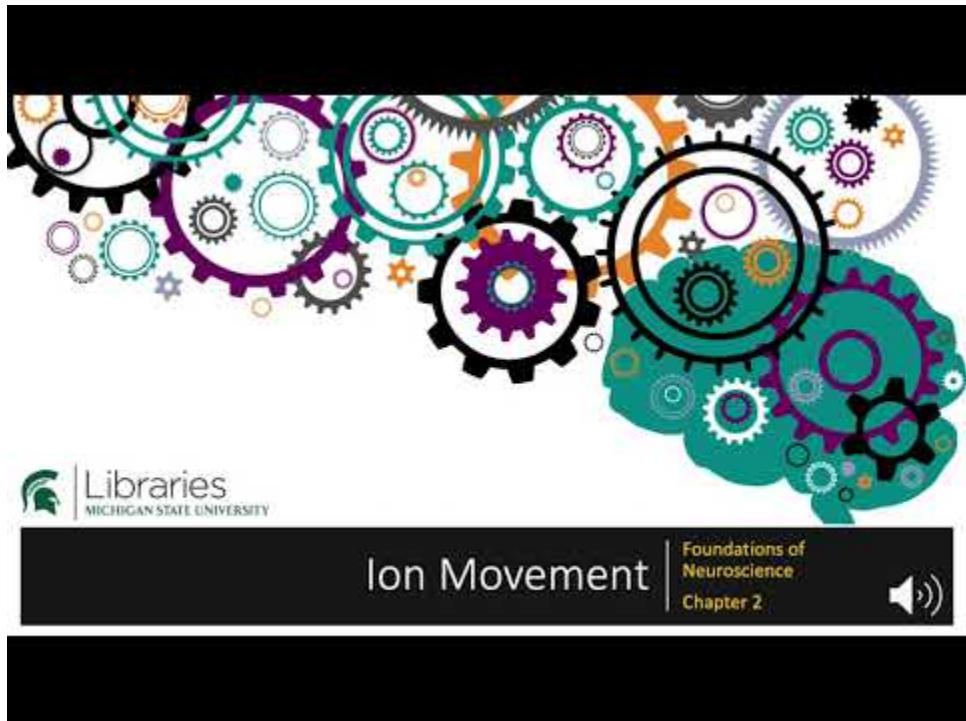
<https://openbooks.lib.msu.edu/neuroscience/?p=52#h5p-10>

### Additional Review

1. Explain how chemical and electrical gradients affect ion flow.
2. Explain ion movement at equilibrium.

### Answers

## Video Version of Lesson



A YouTube element has been excluded from this version of the text. You can view it online here:

<https://openbooks.lib.msu.edu/neuroscience/?p=52>

3.

## MEMBRANE POTENTIAL

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The membrane potential is the difference in electrical charge between the inside and the outside of the neuron. This is measured using two electrodes. A reference electrode is placed in the extracellular solution. The recording electrode is inserted into the cell body of the neuron.

### Resources

- Key Takeaways
- Test Yourself
- Additional Review
- Video Version

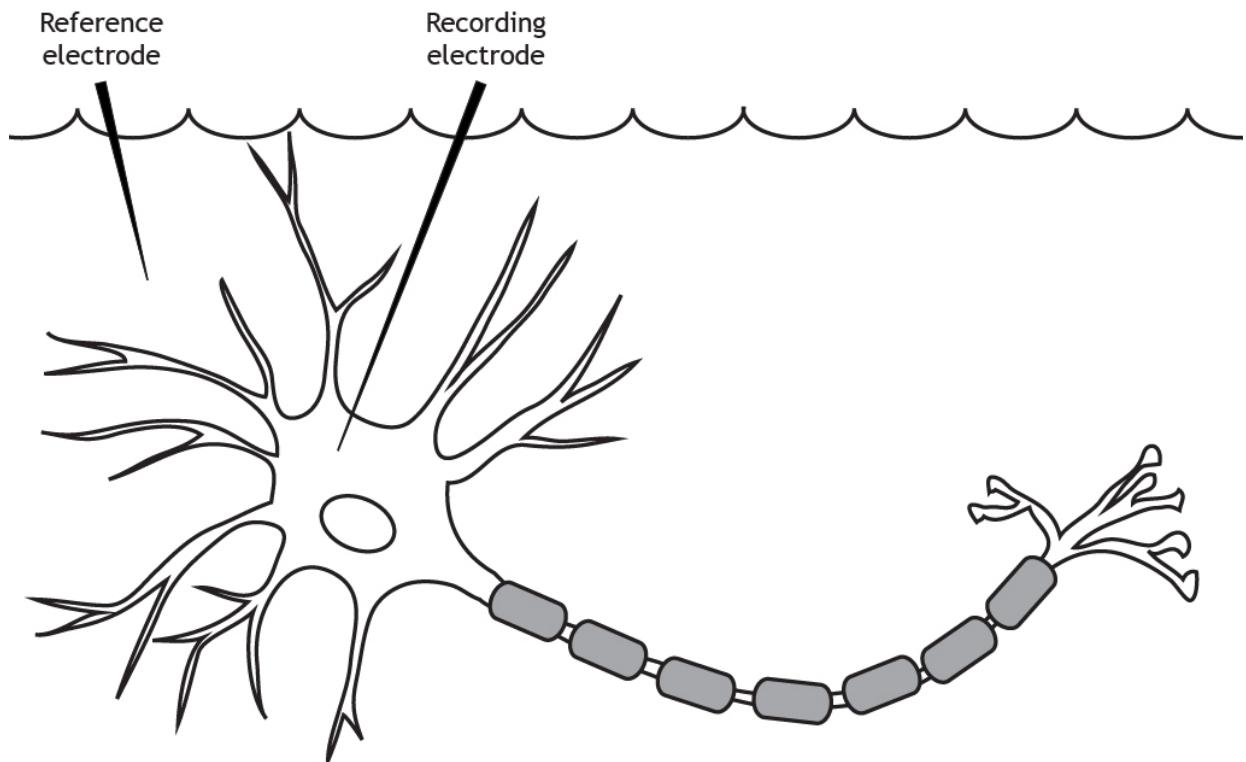


Figure 3.1. The membrane potential is measured using a reference electrode placed in the extracellular solution and a recording electrode placed in the cell soma. The membrane potential is the difference in voltage between these two regions. ‘Measuring Membrane Potential’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

## Terminology

There is more than one way to describe a change in membrane potential. If the membrane potential moves toward zero, that is a *depolarization* because the membrane is becoming less polarized, meaning there is a smaller difference between the charge on the inside of the cell compared to the outside. This is also referred to as a decrease in membrane potential. This means that when a neuron’s membrane potential moves from rest, which is typically around -65 mV, toward 0 mV and becomes more positive, this is a *decrease* in membrane potential. Since the membrane potential is the difference in electrical charge between the inside and outside of the cell, that difference decreases as the cell’s membrane potential moves toward 0 mV.

If the membrane potential moves away from zero, that is a hyperpolarization because the membrane is becoming more polarized. This is also referred to as an increase in membrane potential.

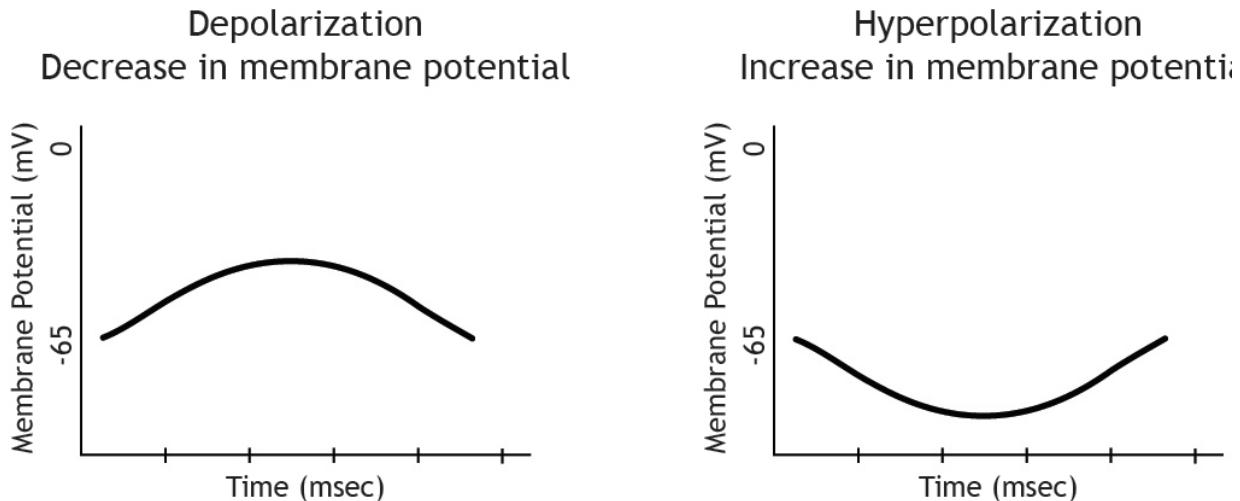


Figure 3.2. A decrease in membrane potential is a change that moves the cell's membrane potential toward 0 or depolarizes the membrane. An increase in membrane potential is a change that moves the cell's membrane potential away from 0 or hyperpolarizes the membrane. 'Membrane Potential Terms' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

## Voltage Distribution

At rest, ions are not equally distributed across the membrane. This distribution of ions and other charged molecules leads to the inside of the cell having a more negative charge compared to the outside of the cell.

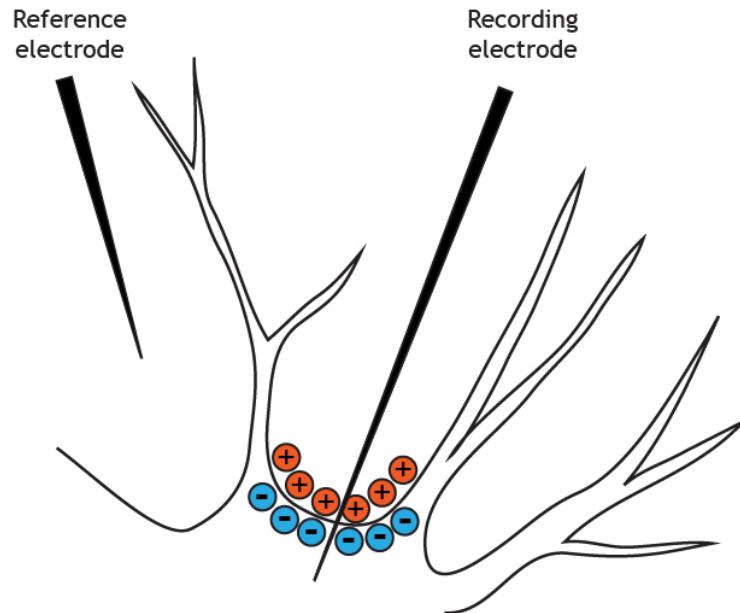


Figure 3.3. The inside of the neuron has a more negative charge than the outside of the neuron.  
‘Membrane Potential’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

A closer look shows that sodium, calcium, and chloride are concentrated outside of the cell membrane in the extracellular solution, whereas potassium and negatively-charged molecules like amino acids and proteins are concentrated inside in the intracellular solution.

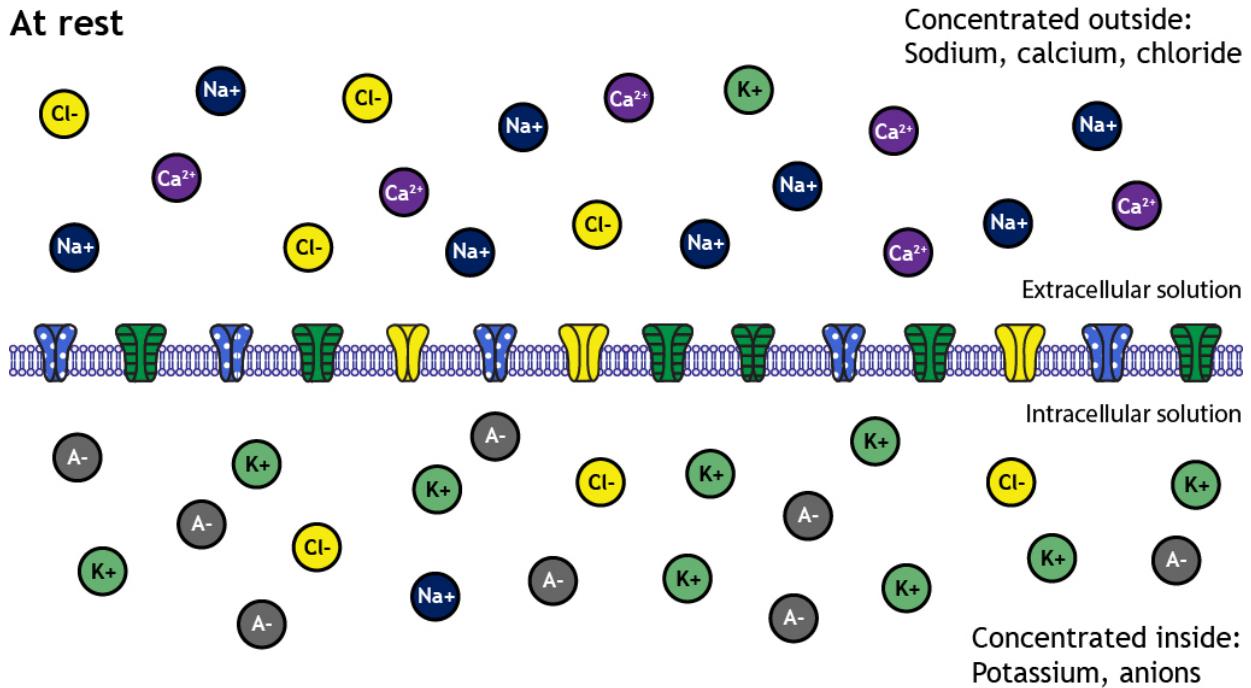
**At rest**

Figure 3.4. For a typical neuron at rest, sodium, chloride, and calcium are concentrated outside the cell, whereas potassium and other anions are concentrated inside. This ion distribution leads to a negative resting membrane potential. The dotted, blue channels represent sodium leak channels; the striped, green channels represent potassium leak channels; the solid yellow channels represent chloride leak channels. ‘Membrane at Rest’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

## Ion Distribution Creates Electrochemical Gradients

These concentration differences lead to varying degrees of electrochemical gradients in different directions depending on the ion in question. For example, the electrochemical gradients will drive potassium out of the cell but will drive sodium into the cell.

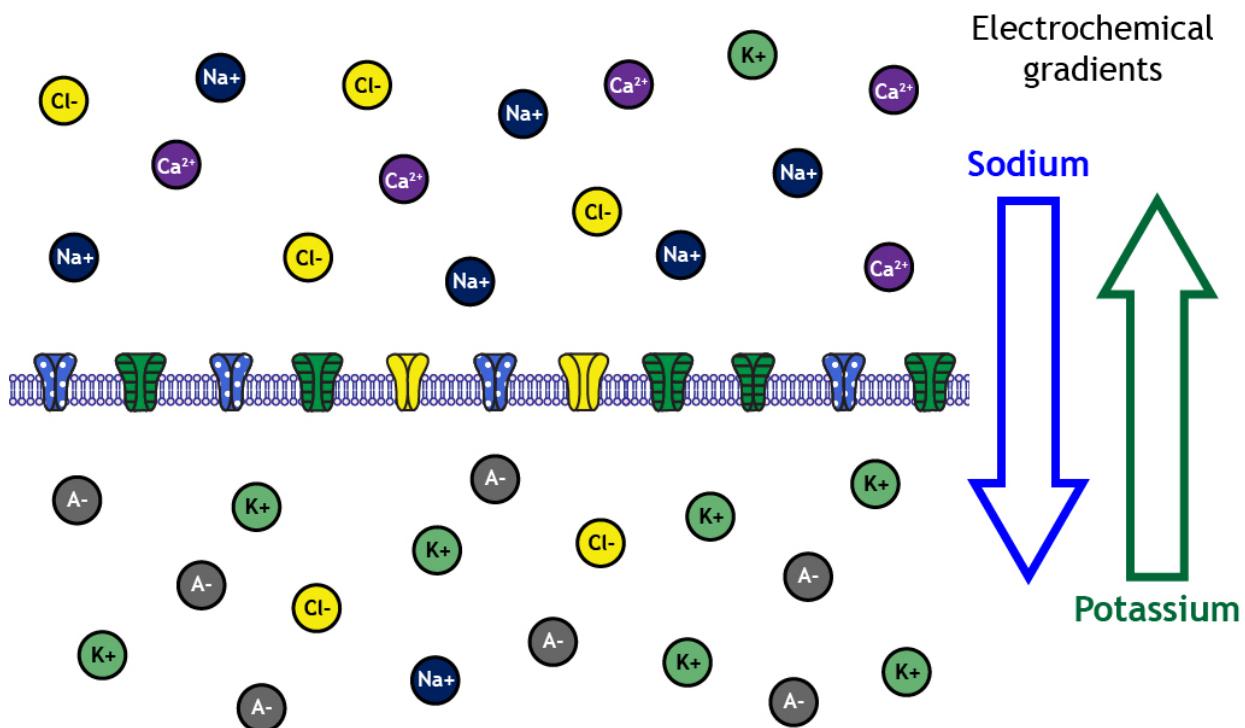


Figure 3.5. The distribution of ions on either side of the membrane lead to electrochemical gradients for sodium and potassium that drive ion flow in different directions. If the membrane is permeable to sodium, ions will flow inward. If the membrane is permeable to potassium, ions will flow outward. The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. 'Gradients Across Membrane' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

## Equilibrium Potential

The neuron's membrane potential at which the electrical and concentration gradients for a given ion balance out is called the ion's equilibrium potential. Let's look at sodium in more detail:

Example: Driving Forces on Sodium Ions

When sodium channels open, the neuron's membrane becomes permeable to sodium, and sodium will begin to flow across the membrane. The direction is dependent upon the electrochemical gradients. The concentration of sodium in the extracellular solution is about 10 times higher than the intracellular solution, so there is a concentration gradient driving sodium into the cell. Additionally, at rest, the inside of the neuron is more negative than the outside, so there is also an electrical gradient driving sodium into the cell.

As sodium moves into the cell, though, these gradients change in driving strength. As the neuron's membrane potential become positive, the electrical gradient no longer works to drive sodium into the cell. Eventually, the concentration gradient driving sodium into the neuron and the electrical gradient driving sodium out of the neuron balance with equal and opposite strengths, and sodium is at equilibrium. The membrane potential of the neuron at which equilibrium occurs is called the equilibrium potential of an ion, which, for sodium, is approximately +60 mV.



*A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=752>*

Animation 3.1. At rest, both the concentration and electrical gradients for sodium point into the cell. As a result, sodium flows in. As sodium enters, the membrane potential of the cell decreases and becomes more positive. As the membrane potential changes, the electrical gradient decreases in strength, and after the membrane potential passes 0 mV, the electrical gradient will point outward, since the inside of the cell is more positively charged than the outside. The ions will continue to flow into the cell until equilibrium is reached. An ion will be at equilibrium when its concentration and electrical gradients are equal in strength and opposite in direction. The membrane potential of the neuron at which this occurs is the equilibrium potential for that ion. Sodium's equilibrium potential is approximately +60 mV. The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. 'Sodium Gradients' by Casey Henley is licensed under a Creative Commons

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## Calculate Equilibrium Potential with Nernst Equation

The gradients acting on the ion will always drive the ion towards equilibrium. The equilibrium potential of an ion is calculated using the Nernst equation:

### The Nernst Equation

$$E_{ion} = \frac{61}{z} \log \frac{[ion]_{outside}}{[ion]_{inside}}$$

The constant 61 is calculated using values such as the universal gas constant and temperature of mammalian cells

Z is the charge of the ion

[ion]<sub>inside</sub> is the intracellular concentration of the ion

[ion]<sub>outside</sub> is the extracellular concentration of the ion

An Example: Sodium's Equilibrium Potential

$$E_{ion} = \frac{61}{z} \log \frac{[ion]_{outside}}{[ion]_{inside}}$$

For Sodium:

$$z = 1$$

$$[\text{Ion}]_{\text{inside}} = 15 \text{ mM}$$

$$[\text{Ion}]_{\text{outside}} = 145 \text{ mM}$$

$$E_{ion} = \frac{61}{1} \log \frac{145}{15} = 60mV$$

## Predict Ion Movement by Comparing Membrane Potential to Equilibrium Potential

It is possible to predict which way an ion will move by comparing the ion's equilibrium potential to the neuron's membrane potential. Let's assume we have a cell with a resting membrane potential of -70 mV. Sodium's equilibrium potential is +60 mV. Therefore, to reach equilibrium, sodium will need to enter the cell, bringing in positive charge. On the other hand, chloride's equilibrium potential is -65 mV. Since chloride is a negative ion, it will need to *leave* the cell in order to make the cell's membrane potential more positive to move from -70 mV to -65 mV.

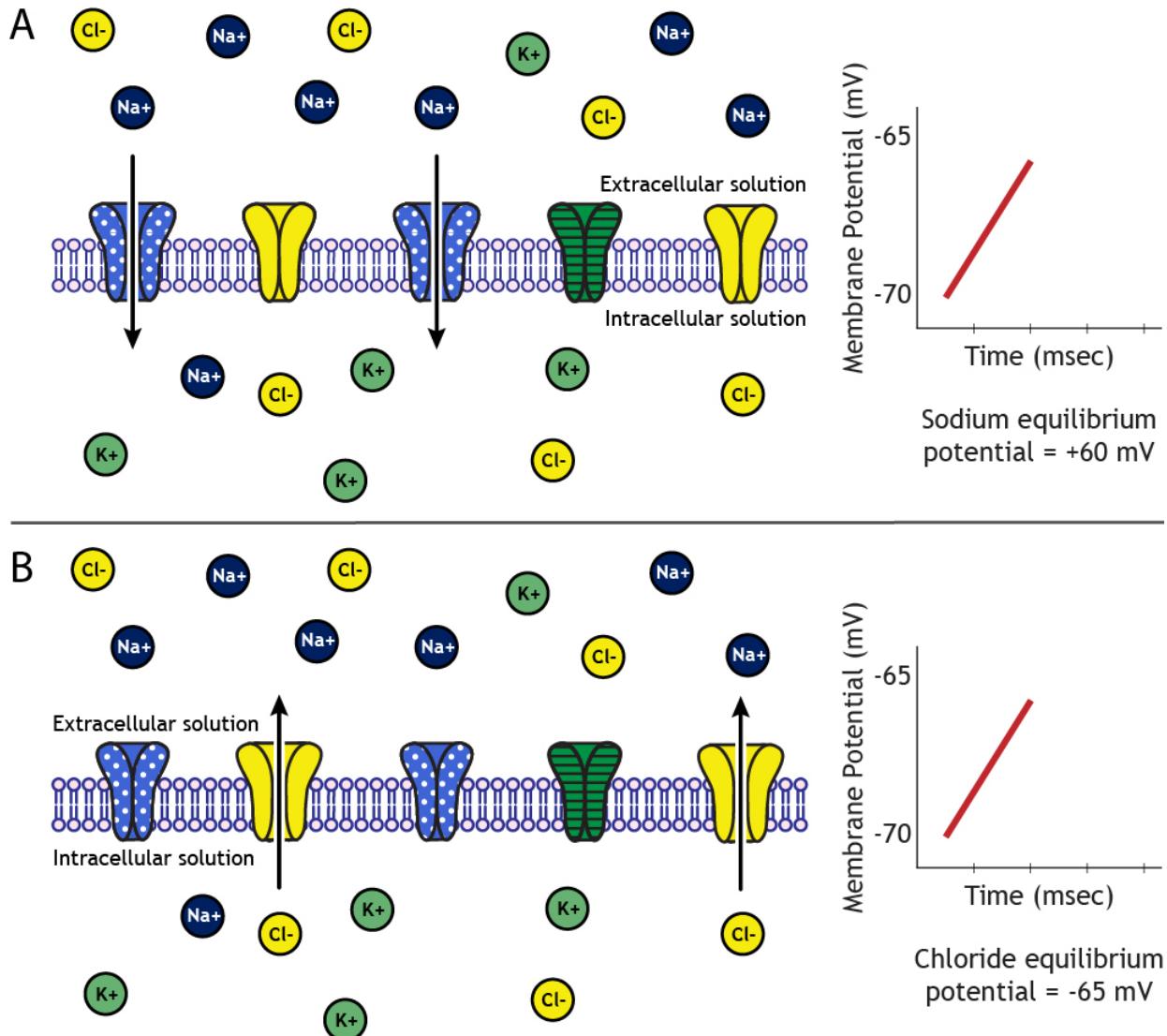


Figure 3.6. A) If a cell is at rest at  $-70 \text{ mV}$ , sodium ions will flow into the cell to move the cell's membrane potential toward sodium's equilibrium potential of  $+60 \text{ mV}$ . B) At the same resting membrane potential, chloride would flow out of the cell, taking away its negative charge, making the inside of the cell more positive and moving toward chloride's equilibrium potential of  $-65 \text{ mV}$ . The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. 'Moving Toward Equilibrium' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

# Concentration and Equilibrium Potential Values

We will use the following ion concentrations and equilibrium potentials:

<b>Ion</b>	<b>Inside concentration (mM)</b>	<b>Outside concentration (mM)</b>	<b>Equilibrium Potential</b>
Sodium	15	145	+60 mV
Potassium	125	5	-85 mV
Chloride	13	150	-65 mV

Table 3.1. Intra- and extracellular concentration and equilibrium potential values for a typical neuron at rest for sodium, potassium, and chloride.

## Key Takeaways

- Moving the membrane potential toward 0 mV is a decrease in potential; moving away from 0 mV is an increase in potential
- The distribution of ions inside and outside of the cell at rest vary among the different ions; some are concentrated inside, some are concentrated outside
- Equilibrium potentials are calculated using the Nernst equation
- To predict ion movement, compare the current membrane potential of the neuron with the ion's equilibrium potential. Determine which way the ion needs to move to cause that membrane potential change (i.e. does the ion need to move into the cell or out of the cell?)

## Test Yourself!



An interactive H5P element has been excluded from this version of the text. You can view it online here:

<https://openbooks.lib.msu.edu/neuroscience/?p=752#h5p-3>

### Additional Review

1. Define resting membrane potential ( $V_m$ ) of a cell.
2. Explain the differences between the resting membrane potential and the equilibrium potential.
3. Using the concentration values from the table above, calculate the equilibrium potential of potassium using the Nernst equation.

### Answers

## Video Version of Lesson



A YouTube element has been excluded from this version of the text. You can view it online here:

<https://openbooks.lib.msu.edu/neuroscience/?p=752>

## 4.

# THE MEMBRANE AT REST

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## Resources

As covered in the previous chapter, at rest there is an uneven distribution of ions on either side of the membrane. The inside of the neuron is more negatively charged than the outside.

- Key Takeaways
- Test Yourself
- Additional Review
- Video Version

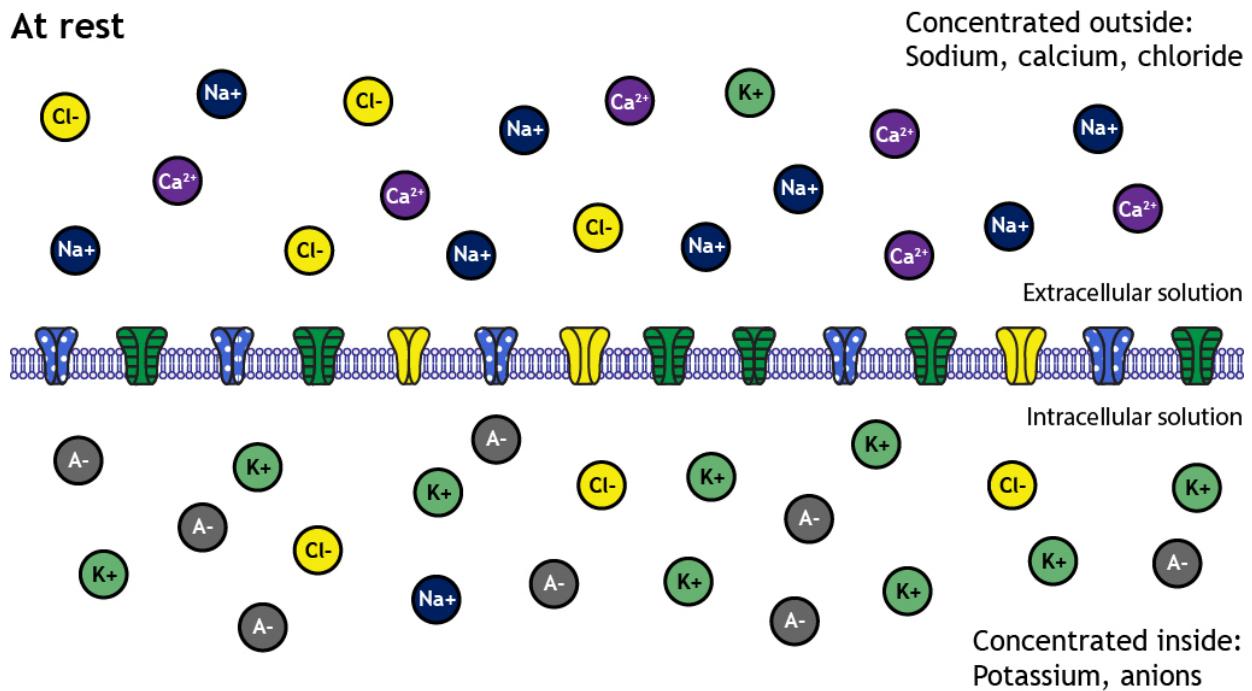
**At rest**

Figure 4.1. For a typical neuron at rest, sodium, chloride, and calcium are concentrated outside the cell, whereas potassium and other anions are concentrated inside. This ion distribution leads to a negative resting membrane potential. The dotted, blue channels represent sodium leak channels; the striped, green channels represent potassium leak channels; the solid yellow channels represent chloride leak channels. ‘Membrane at Rest’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

## Permeability at Rest

How the ions are distributed across the membrane plays an important role in the generation of the resting membrane potential. When the cell is at rest, some non-gated, or leak, ion channels are actually open. Significantly more potassium channels are open than sodium channels, and this makes the membrane at rest more permeable to potassium than sodium.

**At rest**

Concentrated outside:  
Sodium, calcium, chloride

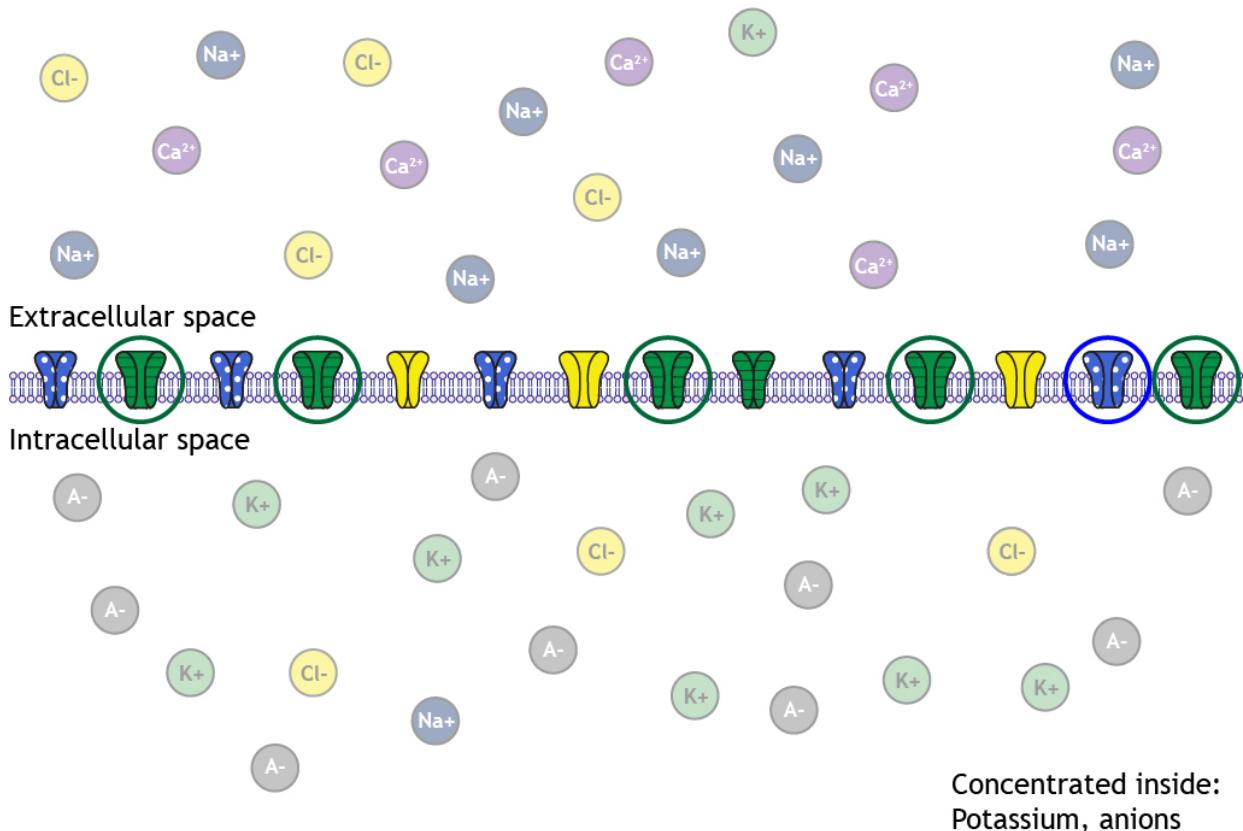


Figure 4.2. At rest, the distribution of ions across the membrane varies for different ions.

Additionally, at rest, more potassium non-gated ion channels (emphasized by green circles) are open than sodium channels (emphasized by the blue circle). The dotted, blue channels represent sodium leak channels; the striped, green channels represent potassium leak channels; the solid yellow channels represent chloride leak channels. 'Channels at Rest' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

## Potassium Can Cross Membrane at Rest

Since the membrane is permeable to potassium at rest due to the open non-gated channels, potassium will be able to flow across the membrane. The electrochemical gradients at work will cause potassium to flow out of the cell in order to move the cell's membrane potential toward potassium's equilibrium potential of -80 mV.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=92>

Animation 4.1. Electrochemical gradients drive potassium out of the cell, removing positive charge, making the cell's membrane potential more negative, in the direction of potassium's equilibrium potential. The dotted, blue channels represent sodium leak channels; the striped, green channels represent potassium leak channels; the solid yellow channels represent chloride leak channels. 'Potassium Flow at Rest' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License. View static image of animation.

## Resting Membrane Potential Value

You might ask, though, if the cell has these open non-gated ion channels, and ions are moving at rest, won't the cell eventually reach potassium's equilibrium potential if the membrane is only permeable to potassium?

If the only structural element involved in ion flow present in the cell membrane were the open non-gated potassium channels, the membrane potential would eventually reach potassium's equilibrium potential. However, the membrane has other open non-gated ion channels as well. There are fewer of these channels compared to the potassium channels, though. The permeability of chloride is about half of that of potassium, and the permeability of sodium is about 25 to 40 times less than that of potassium. This leads to enough chloride and sodium ion movement to keep the neuron at a resting membrane potential that is slightly more positive than potassium's equilibrium potential.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=92>

Animation 4.2. The membrane is most permeable to potassium at rest, and this leads to potassium

efflux. However, the membrane is also permeable to chloride and sodium, and the flow of these ions keep the resting membrane potential more positive than potassium's equilibrium potential. The dotted, blue channels represent sodium leak channels; the striped, green channels represent potassium leak channels; the solid yellow channels represent chloride leak channels. 'Ion Flow at Rest' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License. View static image of animation.

## Maintenance of Gradients

As ions move across the membrane both at rest and when the neuron is active, the concentrations of ions inside and outside of the cell would change. This would lead to changes in the electrochemical gradients that are driving ion movement. What, then, maintains the concentration and electrical gradients critical for the ion flow that allows the neuron to function properly?

The sodium-potassium pump is the key. The pump uses energy in the form of ATP to move three sodium ions out of the cell and two potassium ions in. This moves the ions against their electrochemical gradients, which is why it requires energy. The pump functions to keep the ionic concentrations at proper levels inside and outside the cell.



*A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=92>*

Animation 4.3. The sodium-potassium pump is embedded in the cell membrane and uses ATP to move sodium out of the cell and potassium into the cell, maintaining the electrochemical gradients necessary for proper neuron functioning. Three intracellular sodium ions enter the pump. ATP is converted to ADP, which leads to a conformational change of the protein, closing the intracellular side and opening the extracellular side. The sodium ions leave the pump while two extracellular potassium ions enter. The attached phosphate molecule then leaves, causing the pump to again open toward the inside of the neuron. The potassium ions leave, and the cycle begins again. 'Sodium-Potassium Pump' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License. View static image of animation.

# Calculating Membrane Potential with Goldman Equation

It is possible to calculate the membrane potential of a cell if the concentrations and relative permeabilities of the ions are known. Recall from the last chapter, the Nernst equation is used to calculate one ion's equilibrium potential. Knowing the equilibrium potential can help you predict which way one ion will move, and it also calculates the membrane potential value that the cell would reach if the membrane were only permeable to one ion. However, at rest, the membrane is permeable to potassium, chloride, and sodium. To calculate the membrane potential, the Goldman equation is needed.

## The Goldman Equation

$$V_m = 61 * \log \frac{P_K[K^+]_{\text{outside}} + P_{Na}[Na^+]_{\text{outside}} + P_{Cl}[Cl^-]_{\text{inside}}}{P_K[K^+]_{\text{inside}} + P_{Na}[Na^+]_{\text{inside}} + P_{Cl}[Cl^-]_{\text{outside}}}$$

Like the Nernst equation, the constant 61 is calculated using values such as the universal gas constant and temperature of mammalian cells

$P_{\text{ion}}$  is the relative permeability of each ion

$[\text{Ion}]_{\text{inside}}$  is the intracellular concentration of each ion

$[\text{Ion}]_{\text{outside}}$  is the extracellular concentration of each ion

Example: The Neuron at Rest

$$V_m = 61 * \log \frac{P_K[K^+]_{\text{outside}} + P_{Na}[Na^+]_{\text{outside}} + P_{Cl}[Cl^-]_{\text{inside}}}{P_K[K^+]_{\text{inside}} + P_{Na}[Na^+]_{\text{inside}} + P_{Cl}[Cl^-]_{\text{outside}}}$$

<b>Ion</b>	<b>Inside concentration (mM)</b>	<b>Outside concentration (mM)</b>	<b>Relative permeability</b>
Sodium	15	145	0.04
Potassium	125	5	1
Chloride	13	150	0.4

Table 4.1. Intra- and extracellular concentration and relative permeability values for a typical neuron at rest for sodium, potassium, and chloride.

$$V_m = 61 * \log \frac{1[5] + 0.04[145] + 0.4[13]}{1[125] + 0.04[15] + 0.4[150]} = -65mV$$

## Key Takeaways

- Non-gated (leak) potassium channels are open at rest causing potassium to have the highest permeability at rest
- Other ion channels (chloride and sodium) are also open, but fewer are open than potassium
- The resting membrane potential of a typical neuron is relatively close to the equilibrium potential for potassium

- The sodium-potassium pump is responsible for maintaining the electrochemical gradients needed for neuron functioning

## Test Yourself!



An interactive H5P element has been excluded from this version of the text. You can view it online here:

<https://openbooks.lib.msu.edu/neuroscience/?p=92#h5p-4>

### Additional Review

1. In the example above, we calculated the resting membrane potential of a typical neuron at rest. What would happen to the membrane potential if the extracellular concentration of potassium was changed from 5 mM to 50 mM?
2. What would happen to the membrane potential if the extracellular concentration of potassium returned to 5 mM but the extracellular concentration of sodium was changed from 145 mM to 100 mM?
3. Changing the extracellular concentration of which ion (potassium or sodium) has a significant effect on the membrane potential?
4. Why do you think this is?
5. From memory, draw a neuronal membrane at rest.

- Include structural elements critical for ion movement.
- Label each type of ion channel
- Illustrate appropriate state (open, closed, inactivated) of each channel.

Answers

## Video Version of Lesson



A YouTube element has been excluded from this version of the text. You can view it online here:  
<https://openbooks.lib.msu.edu/neuroscience/?p=92>

## 5.

# POSTSYNAPTIC POTENTIALS

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When the neuron is at rest, there is a baseline level of ion flow through leak channels. However, the ability of neurons to function properly and communicate with other neurons and cells relies on ion flow through channels other than the non-gated leak channels. We will cover how these channels open in a later lesson. This chapter will examine ion flow through these channels after a stimulus and how the membrane potential changes in response.

## Resources

- Key Takeaways
- Test Yourself
- Video Version

## Postsynaptic Potentials

Postsynaptic potentials are changes in membrane potential that move the cell away from its resting state. For our purposes, postsynaptic potentials are measured in the dendrites and cell bodies. Ion channels that are opened by a stimulus allow brief ion flow across the membrane. A stimulus can range from neurotransmitters released by a presynaptic neuron, changes in the extracellular environment like exposure to heat or cold, interactions with sensory stimuli like light or odors, or other chemical or mechanical events. The change in membrane potential in response to the stimulus will depend on which ion channels are opened by the stimulus.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=142>

Animation 5.1. A stimulus can cause ion channels in the membrane of the cell body or dendrites to open, allowing ion flow across the membrane. The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. ‘Postsynaptic Ion Flow’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License. View static image of animation.

## Excitatory Postsynaptic Potentials (EPSPs)

An excitatory postsynaptic potential (EPSP) occurs when sodium channels open in response to a stimulus. The electrochemical gradient drives sodium to rush into the cell. When sodium brings its positive charge into the cell, the cell’s membrane potential becomes more positive, or depolarizes. This change is called a depolarization because the cell’s membrane potential is moving toward 0 mV, and the membrane is becoming less polarized. At 0 mV, there is no potential or polarization across the membrane, so moving toward 0 would be a decrease in potential. This depolarization increases the likelihood a neuron will be able to fire an action potential, which makes this ion flow excitatory. Therefore, an EPSP is an excitatory change in the membrane potential of a postsynaptic neuron.

A postsynaptic potential is typically brief, with ion channels closing quickly after the stimulus occurs. If there is not another stimulus, the cell will return to the resting membrane potential.



*A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=142>*

Animation 5.2. When a stimulus opens sodium channels, sodium rushes into the cell because the equilibrium potential of sodium is +60 mV. This causes an excitatory depolarization called an excitatory postsynaptic potential (EPSP). After the stimulus, the ion channels close, and the membrane potential returns to rest. The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. ‘EPSP’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License. View static image of animation.

## Inhibitory Postsynaptic Potentials (IPSPs)

An inhibitory postsynaptic potential, or IPSP, on the other hand, is caused by the opening of chloride channels. The equilibrium potential of chloride is -65 mV, so if the neuron is at rest at -60 mV, when chloride channels open, the electrochemical gradients drive chloride to flow into the cell. Chloride brings its negative charge into the cell, causing the cell's membrane potential to become more negative, or hyperpolarize. This change is called a hyperpolarization because the cell's membrane potential is moving away from 0 mV, and the membrane is becoming more polarized. An IPSP decreases the likelihood a neuron will be able to fire an action potential, which make this ion flow inhibitory. Therefore, an IPSP is an inhibitory change in the membrane potential of a postsynaptic neuron.

Like an EPSP, an IPSP is also typically brief, and the membrane potential will return to rest if no additional stimulation occurs.



*A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=142>*

Animation 5.3. When a stimulus opens chloride channels, and the resting membrane potential is more positive than chloride's equilibrium potential of -65 mV, chloride rushes into the cell. This causes an inhibitory hyperpolarization called an inhibitory postsynaptic potential (IPSP). After the stimulus, the ion channels close, and the membrane potential returns to rest. The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. 'IPSP' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License. View static image of animation.

## The Resting Membrane Potential is Critical

In the previous example, the resting membrane potential of that cell was -60 mV, so chloride moved into the cell. If the resting membrane potential was instead equal to chloride's equilibrium potential

of  $-65$  mV, then chloride would be at equilibrium and move into and out of the cell, and there would be no net movement of the ion. Even though this would lead to no change in membrane potential, the opening of chloride channels continues to be inhibitory. Increased chloride conductance would make it more difficult for the cell to depolarize and to fire an action potential.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=142>

Animation 5.4. If the cell is at rest at chloride's equilibrium potential, when a stimulus opens the chloride channels, there will be no net movement of chloride in either direction because chloride will be at equilibrium. Since there is no net movement, there will also be no change in membrane potential because there is an equal amount of ion flow into and out of the cell. The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. 'IPSP at Equilibrium' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License. View static image of animation.

If the resting membrane potential of the cell was more negative than chloride's equilibrium potential, for example, at  $-70$  mV, then chloride would *leave* the cell, in order to move the membrane potential toward  $-65$  mV. This would result in a depolarization of the membrane potential. However, the overall effect is still inhibitory because once the cell reaches  $-65$  mV, the driving forces acting on chloride would try to keep the cell at that membrane potential, making it more difficult for the cell to depolarize further and fire an action potential.

A good rule of thumb is to remember that opening of sodium channels is excitatory whereas opening of chloride channels is inhibitory.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=142>

Animation 5.5. If the cell is at rest at chloride's equilibrium potential, when a stimulus opens the

chloride channels, chloride will leave the cell, removing its negative charge. This causes a depolarization in the membrane potential, but it is still inhibitory since chloride movement will try to keep the cell near -65 mV. The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. ‘Inhibitory Depolarization’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License. View static image of animation.

## Summation of Inputs

If an excitatory stimulus is followed by additional excitatory stimuli, the sodium channels will either remain open or additional sodium channels will open. The increased sodium conductance will cause the EPSPs to summate, depolarizing the cell further than one EPSP alone. Each neuron has a threshold membrane potential at which the cell will fire an action potential. The summation of EPSPs causes the neuron to reach that threshold.



*A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=142>*

Animation 5.6. Excitatory stimuli that occur quickly in succession lead to summation of EPSPs. This leads to increased depolarization of the membrane potential compared to a single EPSP. The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. ‘Summated EPSP Ion Flow’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License. View static image of animation.

Summation can occur in two ways. Temporal summation occurs when one presynaptic input stimulates a postsynaptic neuron multiple times in a row. Spatial summation occurs when multiple presynaptic inputs each stimulate the postsynaptic neuron at the same time. Both types of summation result in a depolarization of a higher magnitude than when only one excitatory input occurs.

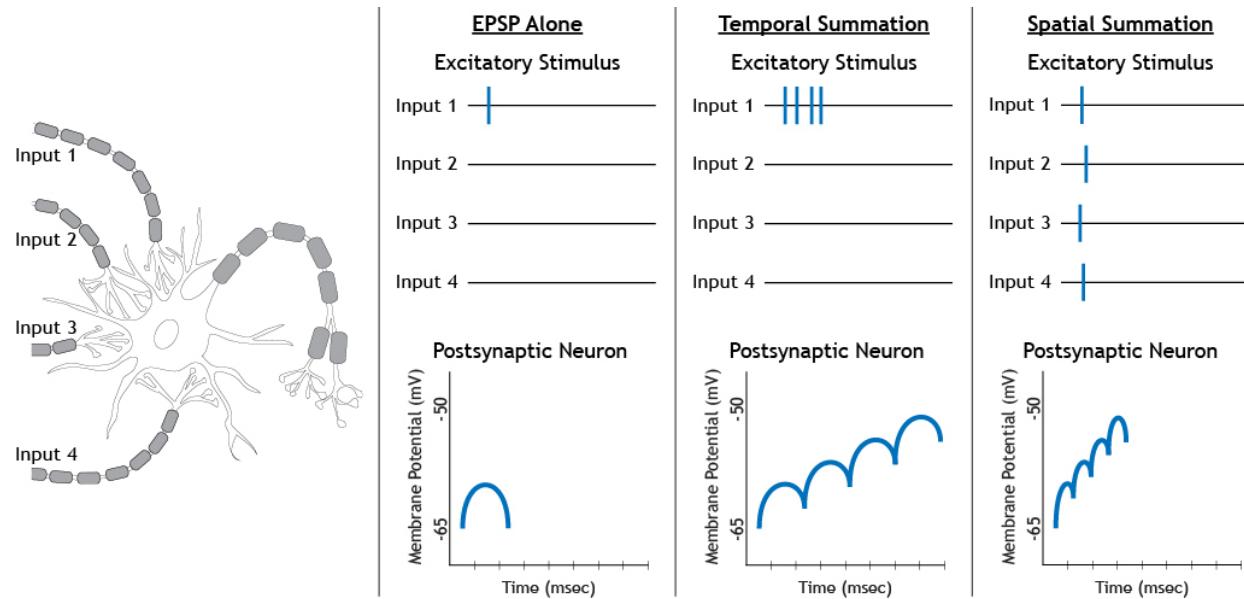


Figure 5.1 EPSPs can summate via temporal or spatial summation. Temporal summation occurs when a presynaptic neuron, Input 1 in the figure, stimulates the postsynaptic neuron multiple times in a row. Spatial summation occurs when more than one presynaptic neuron, Inputs 1 through 4 in the figure, each stimulate the postsynaptic neuron at the same time. The EPSPs of each stimulation will add together to cause a stronger depolarization of the membrane potential of the postsynaptic neuron than one excitatory stimulus alone. "Synaptic Summation" by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

In addition to the summation of excitatory inputs, EPSPs can also summate with inhibitory inputs. The addition of an inhibitory stimulus will result in either a weaker depolarization compared to a single excitatory stimulus or possibly no depolarization at all, depending on the strength of the inhibitory input.

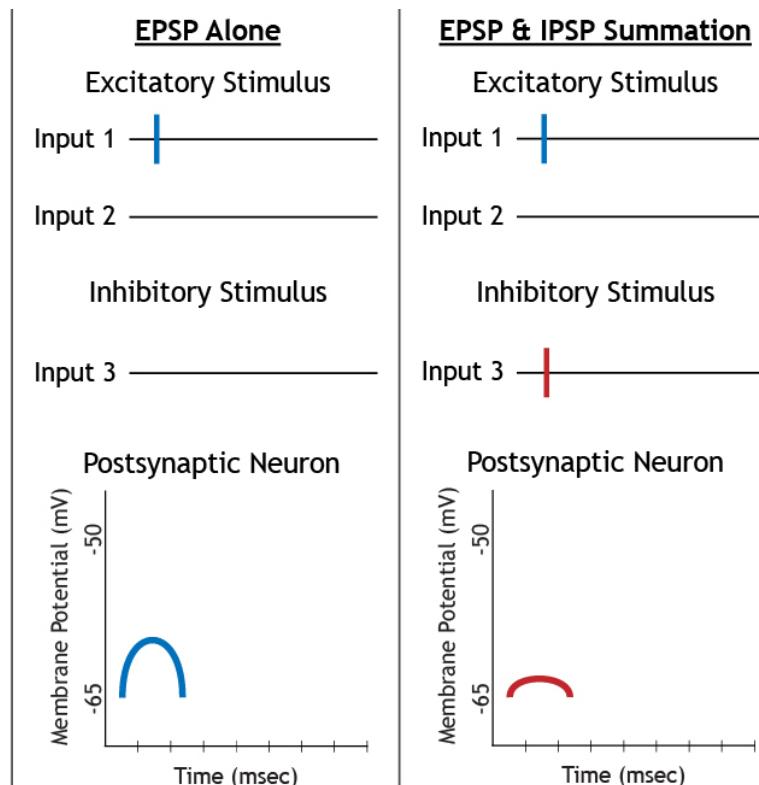
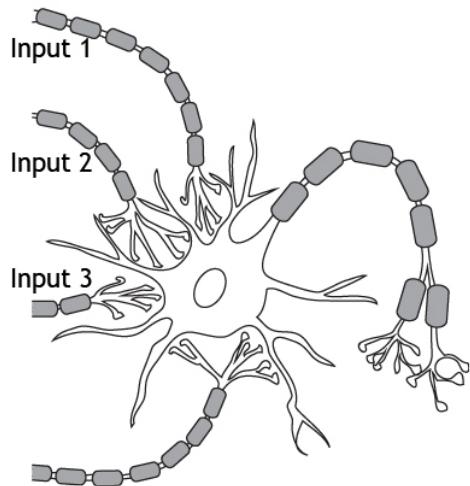


Figure 5.2. If an inhibitory input, Input 3 in the figure, stimulates the postsynaptic neuron at the same time as an excitatory input, Input 1 in the figure, the result is a decrease in the amount of depolarization or the complete prevention of depolarization, depending on the strength of the inhibitory input. ‘EPSP and IPSP Summation’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

In the case of combined inhibitory and excitatory stimuli, both chloride and sodium channels will open. As sodium enters the cell trying to move the membrane potential to +60 mV, the equilibrium potential of sodium, chloride will also enter, trying to keep the cell near -65 mV, the equilibrium potential of chloride.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=142>

Animation 5.7. When an inhibitory input and an excitatory input stimulate a postsynaptic neuron at

the same time, chloride and sodium channels open. Due to the equilibrium potentials of the two ions, both will flow into the cell. Sodium tries to depolarize the cell, whereas chloride tries to keep the cell near rest. The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. ‘EPSP and IPSP Ion Flow’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License. View static image of animation.

### Key Takeaways

- Postsynaptic potentials occur in the dendrites or cell body
- Excitatory postsynaptic potentials are caused by sodium channels opening
- Inhibitory postsynaptic potentials are caused by chloride channels opening
- Since the resting membrane of a typical neuron is usually very close to chloride's equilibrium potential, knowing and comparing these two values is important for determining direction of ion flow when chloride channels open
- Input effects, whether excitatory or inhibitory, can summate and affect the postsynaptic neuron's membrane potential

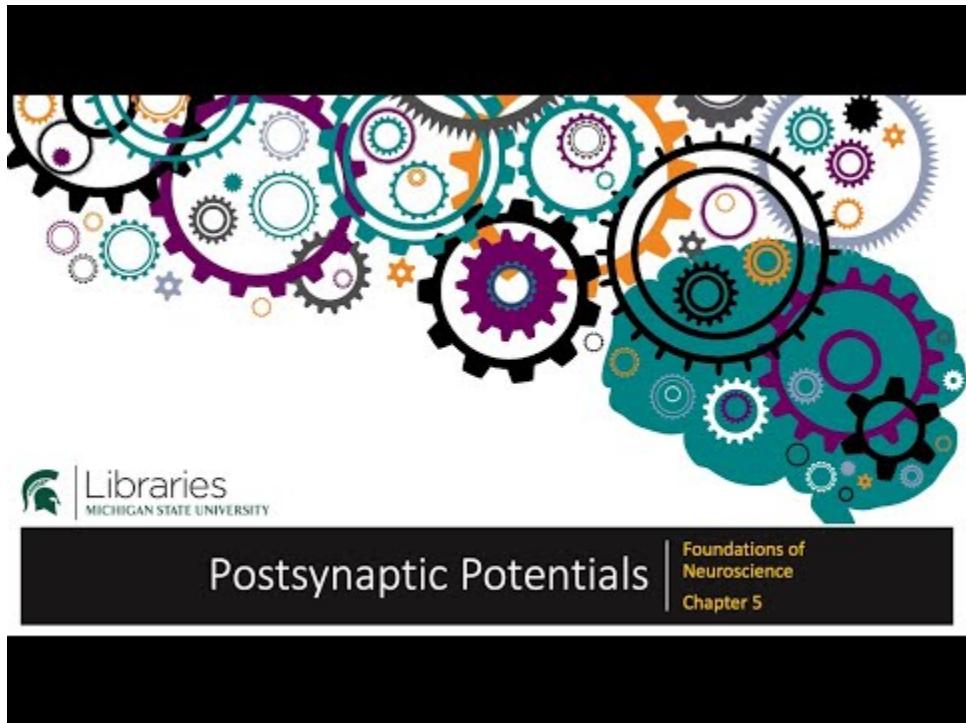
## Test Yourself!



An interactive H5P element has been excluded from this version of the text. You can view it online here:

<https://openbooks.lib.msu.edu/neuroscience/?p=142#h5p-5>

## Video Version of Lesson



A YouTube element has been excluded from this version of the text. You can view it online here:

<https://openbooks.lib.msu.edu/neuroscience/?p=142>

## 6.

# ACTION POTENTIALS

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## Resources

- Key Takeaways
- Test Yourself
- Additional Review
- Video Version

As covered in Chapter 1, the action potential is a very brief change in the electrical potential, which is the difference in charge between the inside and outside of the cell. During the action potential, the electrical potential across the membrane moves from a negative resting value to a positive value and back.

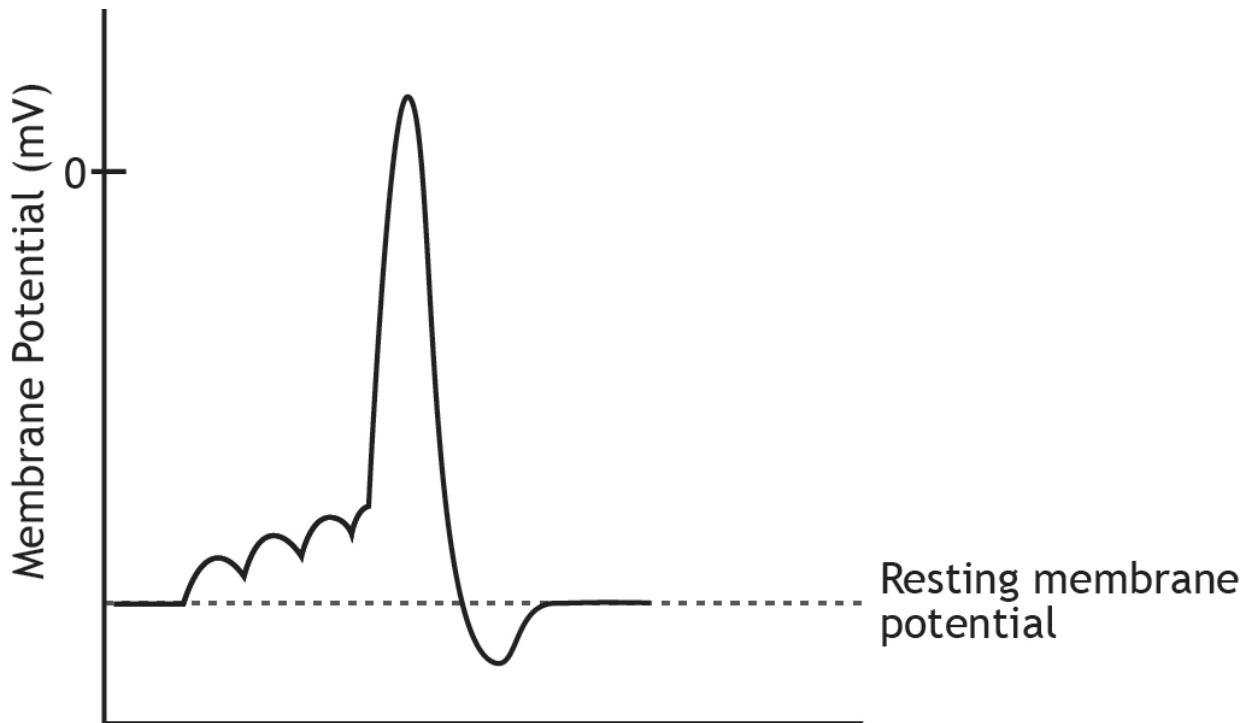


Figure 6.1. The action potential is a brief but significant change in electrical potential across the membrane. The membrane potential will begin at a negative resting membrane potential, will rapidly become positive, and then rapidly return to rest during an action potential. 'Action Potential' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Propagation

The propagation of the action potential from the axon hillock down the axon and to the presynaptic terminal results in release of chemical neurotransmitters that communicate with a postsynaptic neuron.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=161>

Animation 6.1. The action potential moves down the axon beginning at the axon hillock. The action

potential moving down a myelinated axon will jump from one Node of Ranvier to the next. This saltatory conduction leads to faster propagation speeds than when no myelin is present. When the action potential reaches the synaptic terminal, it causes the release of chemical neurotransmitter. ‘Action Potential Propagation’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License. View static image or animation.

## Voltage-Gated Ion Channels

The change in membrane potential during the action potential is a function of ion channels in the membrane. In the previous lessons, we have learned about the principles of ion movement and have discussed non-gated (leak) channels at rest, as well as ion channels involved in the generation of postsynaptic potentials. In this chapter, we will examine a different type of ion channel: voltage-gated ion channels. For our purposes, these channels are located primarily at the axon hillock, along the axon and at the terminal. They are necessary for the propagation of the action potential.

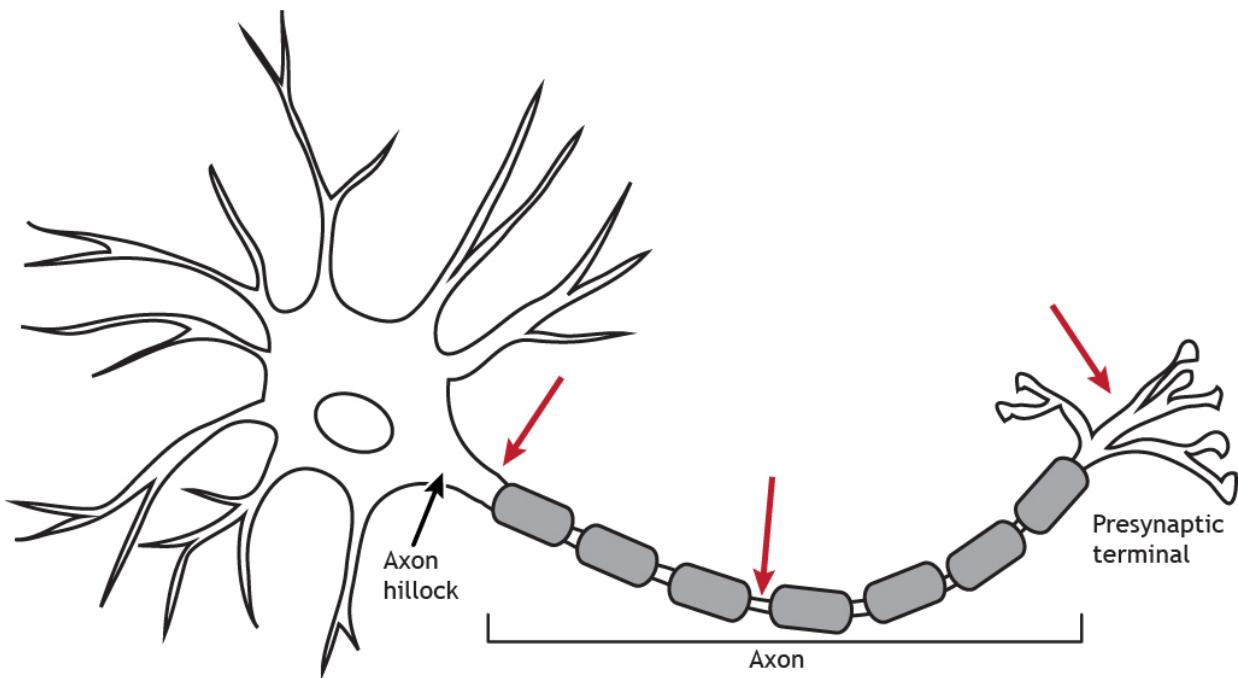


Figure 6.2. Voltage-gated channels critical for the propagation of the action potential are located at the axon hillock, down the axon at the Nodes of Ranvier, and in the presynaptic terminal.

'Voltage-Gated Channel Location' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Voltage-gated channels allow ions to cross the membrane using the same ion movement principles covered in previous lessons. The main difference between voltage-gated channels and leak channels are how they are opened or “gated”. Voltage-gated channels open when the cell’s membrane potential reaches a specific value, called threshold. The neuron reaches threshold after enough EPSPs summate together.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=161>

Animation 6.2. As EPSPs summate, a result of ion movement not shown in the animation, the cell’s membrane potential will depolarize. Reaching threshold causes voltage-gated ion channels to open.

Once the channels are open, ions will move toward equilibrium. In the animation, sodium ions flow inward. The dotted, blue channels represent voltage-gated sodium channels; the striped, green channels represent voltage-gated potassium channels; the solid yellow channels represent chloride channels. ‘Voltage-Gated Channel’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License. View static image of animation.

## The Action Potential

The action potential begins when the cell’s membrane potential reaches threshold. Once initiated in a healthy, unmanipulated neuron, the action potential has a consistent structure and is an all-or-nothing event. It will run through all the phases to completion.

The rising phase is a rapid depolarization followed by the overshoot, when the membrane potential becomes positive. The falling phase is a rapid repolarization followed by the undershoot, when the membrane potential hyperpolarizes past rest. Finally, the membrane potential will return to the resting membrane potential.

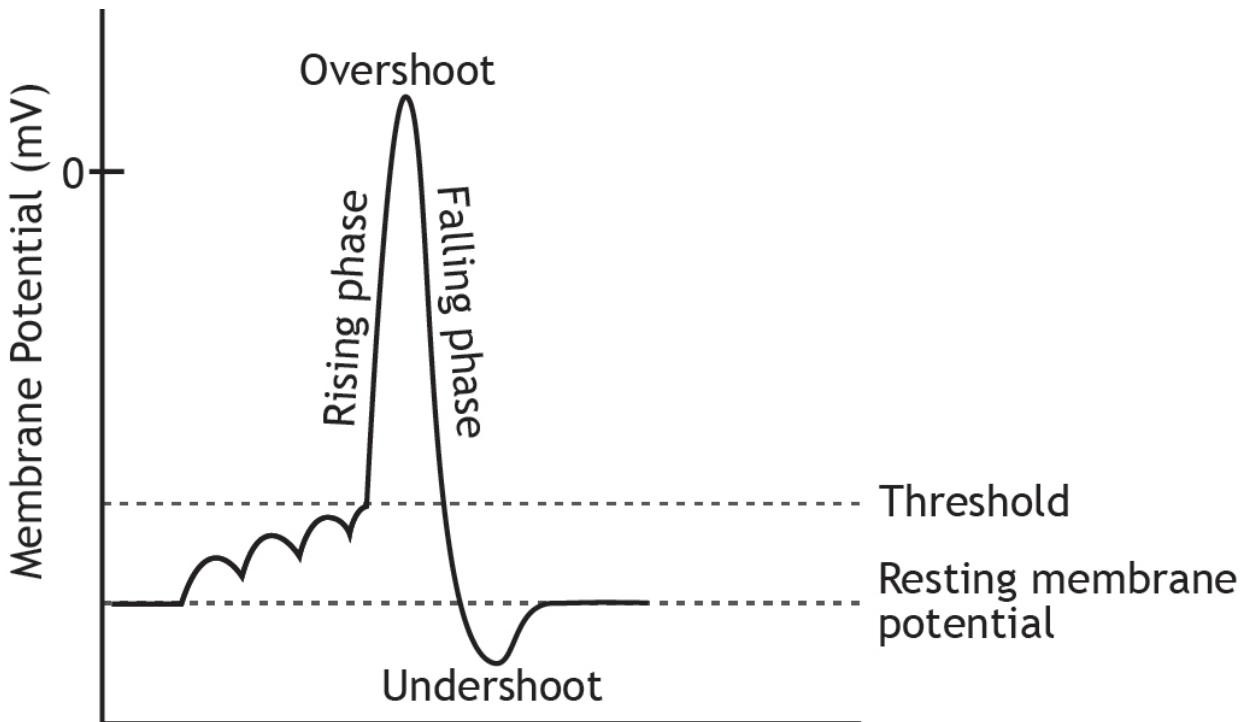


Figure 6.3. EPSPs that summate to reach threshold initiate the action potential. The depolarizing rising phase moves the membrane potential from threshold to above 0 mV. The overshoot is the peak of the action potential where the membrane potential is positive. The falling phase repolarizes the membrane potential, and the undershoot takes the membrane potential more negative than the resting membrane potential. After the undershoot, the membrane potential returns to rest. 'Action Potential Phases' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Rising Phase

The rising phase is caused by the opening of voltage-gated sodium channels. These ion channels are activated once the cell's membrane potential reaches threshold and open immediately. The electrochemical gradients drive sodium into the cell causing the depolarization.



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Animation 6.3. Voltage-gated sodium channels open once the cell's membrane potential reaches threshold. The rapid influx of sodium results in a large depolarization called the rising phase. The dotted, blue channels represent voltage-gated sodium channels; the striped, green channels represent voltage-gated potassium channels; the solid yellow channels represent chloride channels. ‘Rising Phase’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License. View static image of animation.

## Falling Phase

The falling phase of the action potential is caused by the inactivation of the sodium channels and the opening of the potassium channels. After approximately 1 msec, the sodium channels inactivate. The channel becomes blocked, preventing ion flow. At the same time, the voltage-gated potassium channels open. This allows potassium to rush out of the cell because of the electrochemical gradients, taking its positive charge out of the cell, and repolarizing the membrane potential, returning the cell’s membrane potential back near rest.

Like the voltage-gated sodium channels, the voltage trigger for the potassium channel is when the cell’s membrane potential reaches threshold. The difference is that the sodium channels open immediately, whereas the potassium channels open after a delay.



*A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=161>*

Animation 6.4. After approximately 1 msec, the voltage-gated sodium channels inactivate, which prevents any further ion flow into the cell. Although the voltage-gated potassium channels are activated in response to the cell reaching threshold, their opening is delayed and occurs alone with the sodium channel inactivation. This allows an efflux of potassium ions, which causes the repolarization of the falling phase. The dotted, blue channels represent voltage-gated sodium channels; the striped, green channels represent voltage-gated potassium channels; the solid yellow channels represent chloride channels. ‘Falling Phase’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License. View static image of animation.

## Undershoot

As the membrane potential returns to resting level, the sodium channels will de-inactivate, returning to the closed position, ready to be opened by a voltage change again. The potassium channels will also close, but they remain open long enough to cause a hyperpolarizing undershoot as potassium continues to move toward its equilibrium potential of -80 mV.



*A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=161>*

Animation 6.5. Once the cell's membrane potential repolarizes, the voltage-gated sodium channels de-inactivate and return to their closed state. The voltage-gated potassium channels remain open long enough for the undershoot to occur as potassium continues to flow out of the cell. The dotted, blue channels represent voltage-gated sodium channels; the striped, green channels represent voltage-gated potassium channels; the solid yellow channels represent chloride channels. 'Undershoot' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License. View static image of animation.

## Return to Rest

Once the voltage-gated channels close, the sodium-potassium pumps will reestablish the proper ionic concentrations needed for the electrochemical gradients. This action along with open leak channels will return the cell to its resting membrane potential.



*A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=161>*

Animation 6.6. Once the voltage-gated potassium channels close, the sodium-potassium pump will

work to re-establish the electrochemical gradients and return the cell to its resting membrane potential. ‘Return to Rest’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License. View static image of animation.

## Refractory Periods

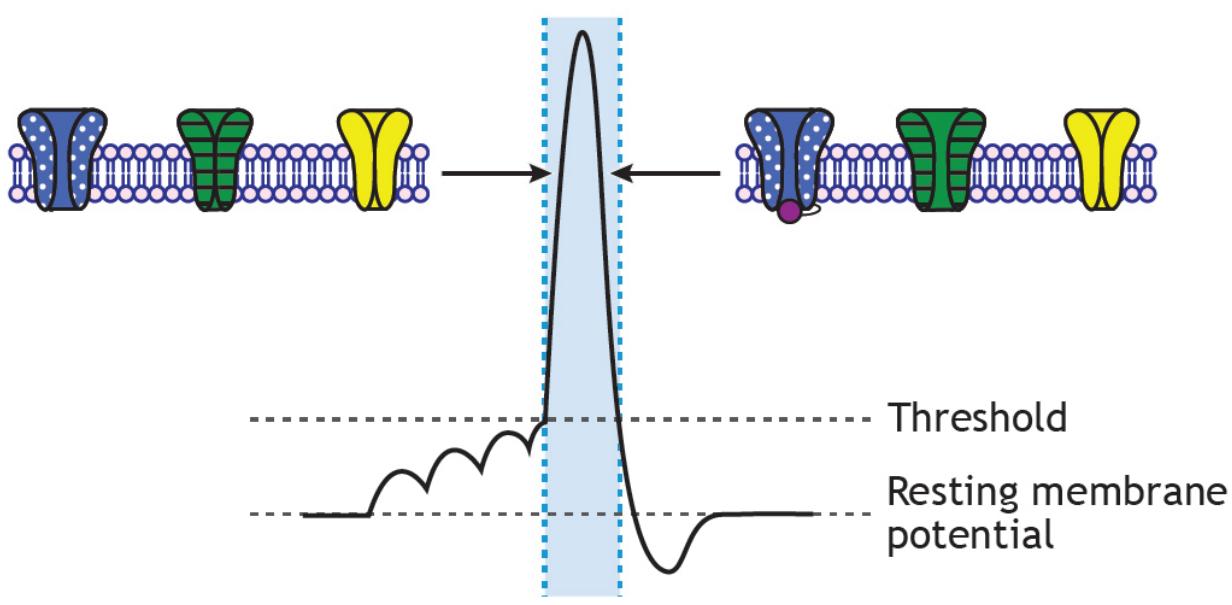
### The Absolute Refractory Period

Each neuron does have a maximum firing rate. And even if the stimulus continues to increase in strength, the neuron cannot fire at a higher frequency. The maximum firing rate of a cell is determined by the status of the ion channels in the neuronal membrane during the different phases of the action potential. During the absolute refractory period, a second action potential cannot be fired under any circumstances regardless of the strength of the stimulus. The voltage-gated sodium channels are either open (during the rising phase) or inactivated (during the falling phase).

### The Relative Refractory Period

When the cell repolarizes and the voltage-gated sodium channels de-inactivate and return to a closed state, the cell is again able to fire another action potential. However, during the end of the falling phase and the during the undershoot, voltage-gated potassium channels are still open. During the undershoot, while the neuron is hyperpolarized, a larger-than-normal stimulus is needed to make the cell reach threshold again. This segment of the action potential is called the relative refractory period. Action potentials can be fired, but a stronger stimulus is needed than when the cell is at rest.

A

**Absolute Refractory Period**

B

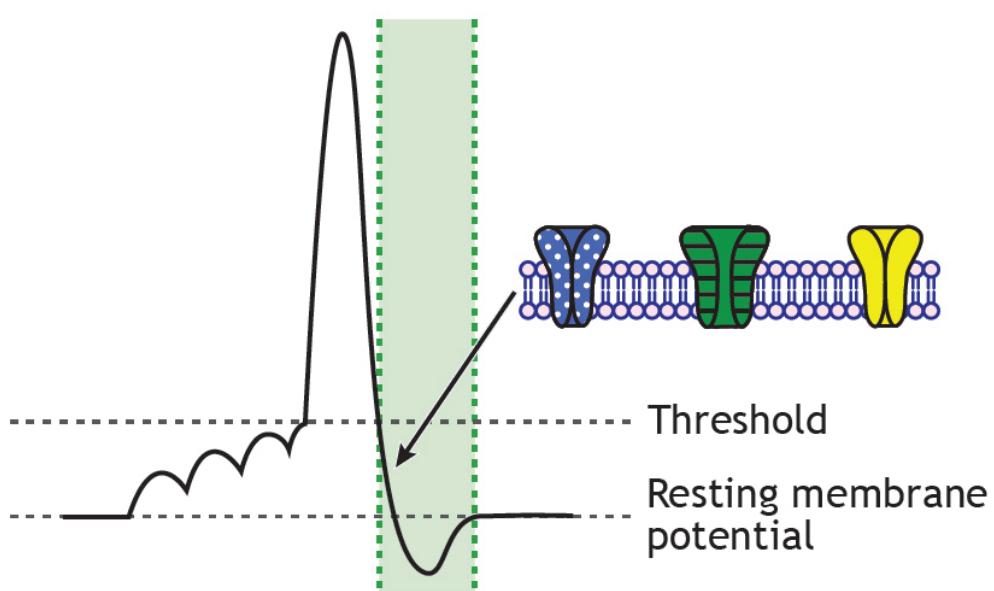
**Relative Refractory Period**

Figure 6.6. The maximum firing rate of a neuron is determined by the refractory periods. A) During the absolute refractory period no additional action potentials can be fired because the voltage-gated sodium channels are either already open (rising phase) or inactivated (falling phase). In these states, they cannot be opened again to begin a second action potential. B) The relative refractory period occurs when the voltage-gated sodium channels are closed, but the voltage-gated potassium channels remain open, causing a hyperpolarization of the membrane. Action potentials

can be fired during this time, but a stronger stimulus is required to reach threshold compared to when the cell is at rest. The dotted, blue channels represent voltage-gated sodium channels; the striped, green channels represent voltage-gated potassium channels; the solid yellow channels represent chloride channels. ‘Refractory Periods’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Action Potential Characteristics

For a given cell, all action potentials have the same characteristics; they depolarize to the same membrane potential value and take the same amount of time. However, different neurons may exhibit different action potential characteristics. Likewise, if a neuron has a change in its environment, like altered extracellular ion concentrations, the shape of the action potential would change due to a change in the electrochemical gradients. For example, if the external concentration of sodium is decreased, the equilibrium potential of sodium, as well as the strength of the electrochemical gradients will change, which will result in a slower rate of rise and a lower amplitude of the action potential.

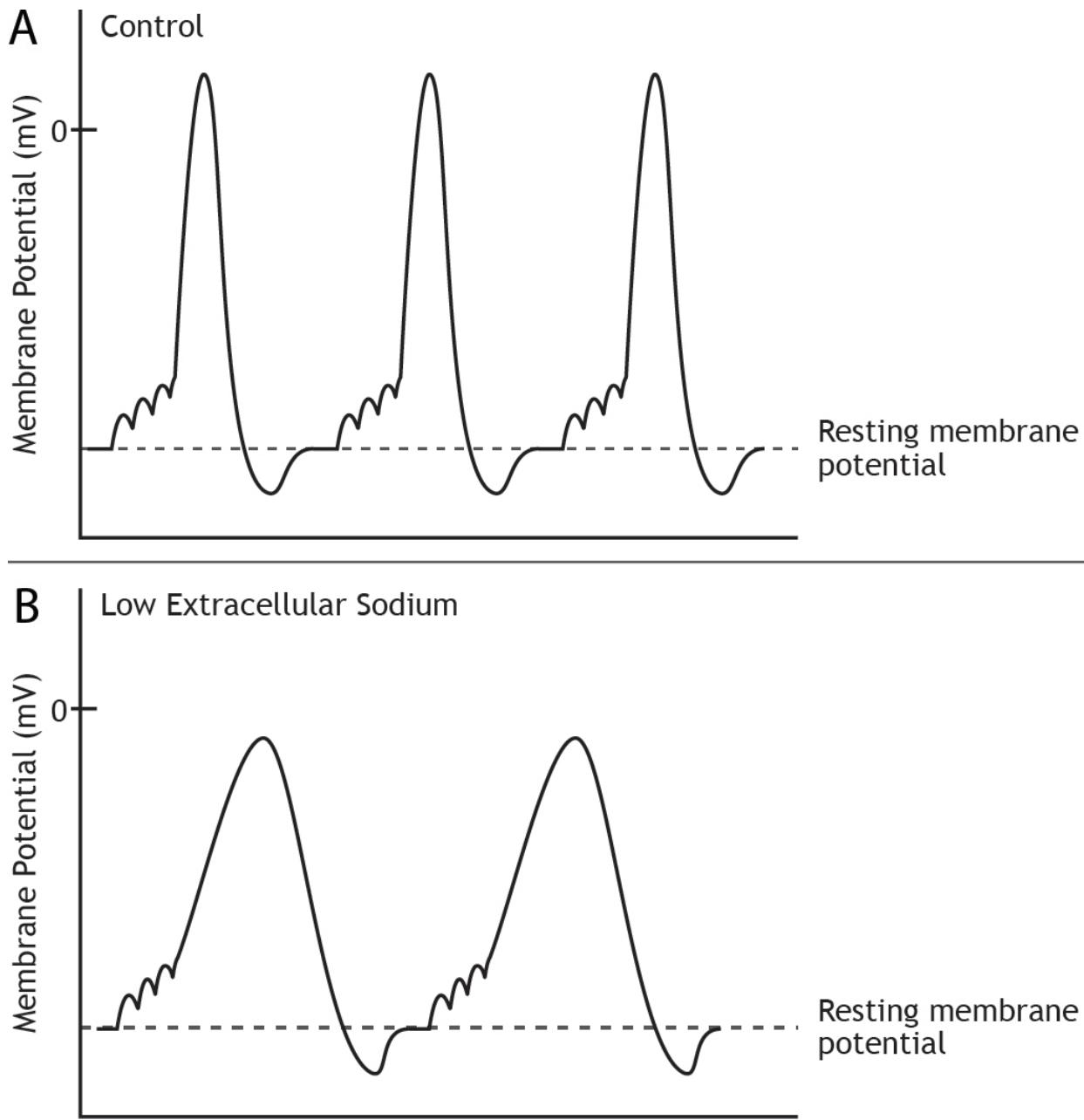


Figure 6.4. A) A neuron kept under the same conditions will display action potentials of similar height and length. B) However, if cellular conditions change, so will the action potential characteristics. If extracellular sodium levels are decreased compared to control levels, the action potential will show a slower rate of rise and a decreased height. 'Low Sodium Action Potential' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Stimulus Strength

The strength of a stimulus needs to be encoded by the neurons. We need to be able to perceive the difference, for example, between a dim light and a bright one. The frequency or rate of action potential firing informs the nervous system of stimulus strength.

Since the height of the action potential is always the same for a given neuron, the strength of the stimulus is determined by the frequency of action potential firing. A weak stimulus would cause fewer action potentials to be fired than a strong stimulus.

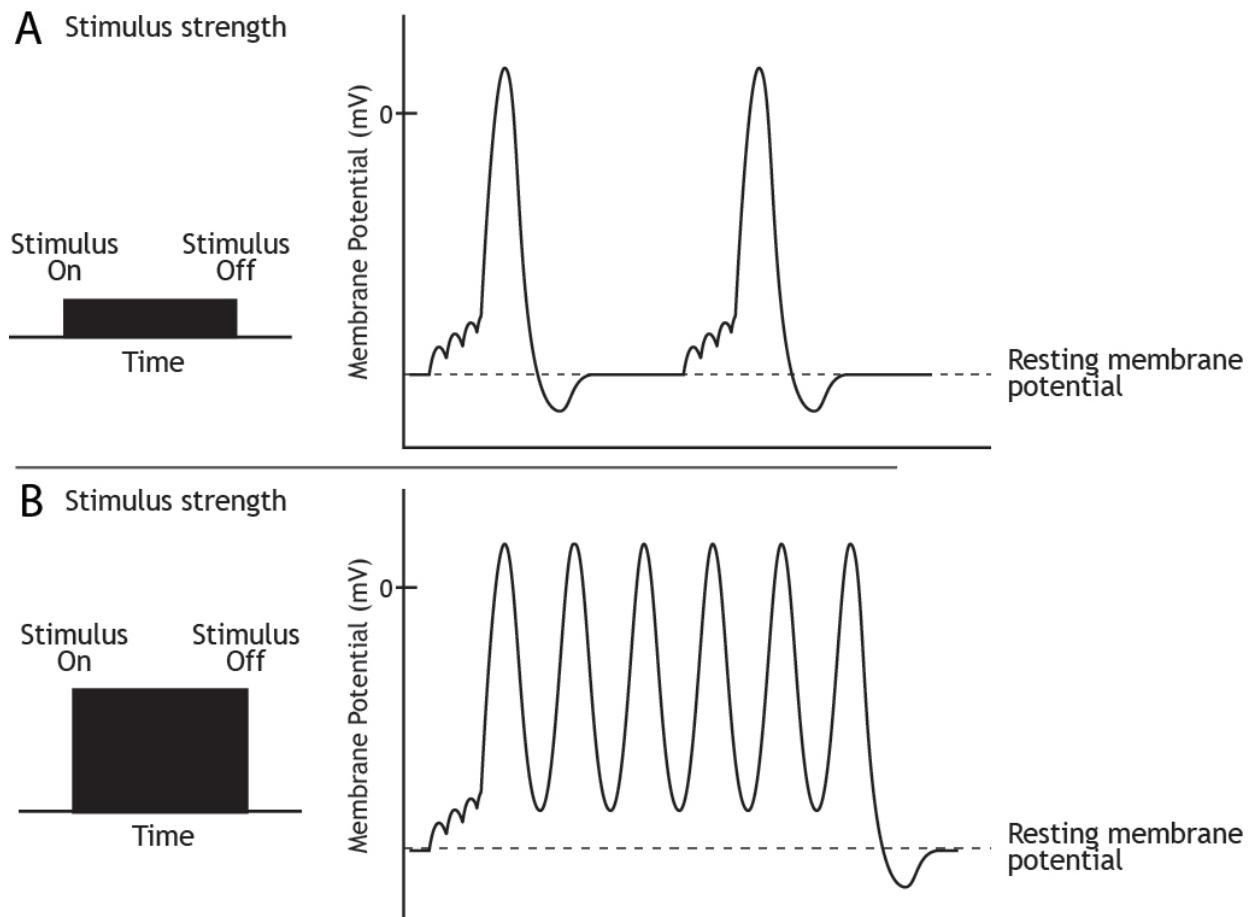


Figure 6.5. Information about the strength of a stimulus is encoded by the rate of action potential firing. A) A weak stimulus results in few action potentials being fired. B) A strong stimulus results in many action potentials firing in a row. 'Stimulus Strength' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Direction of Propagation

The action potential moves down the axon due to the influx of sodium depolarizing nearby segments of axon to threshold.



*A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=161>*

Animation 6.7. A voltage change that reaches threshold will cause voltage-gated sodium channels to open in the axonal membrane. The influx of sodium causes the rising phase of the action potential, but the ion flow also depolarizes nearby axon regions. As the depolarization reaches threshold, the action potential moves down the axon. The dotted, blue channels represent voltage-gated sodium channels; the striped, green channels represent voltage-gated potassium channels. ‘Action Potential Movement’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License. View static image of animation.

Action potentials only move in one direction, though, from the cell body to the presynaptic terminal. The refractory period keeps the action potential from moving backward down the axon. As the action potential moves from one Node of Ranvier to the next, the inactivated sodium channels in the previous axon segment prevent the membrane from depolarizing again. Therefore, the action potential can only move forward toward axon segments with closed sodium channels ready for rising phase depolarization.

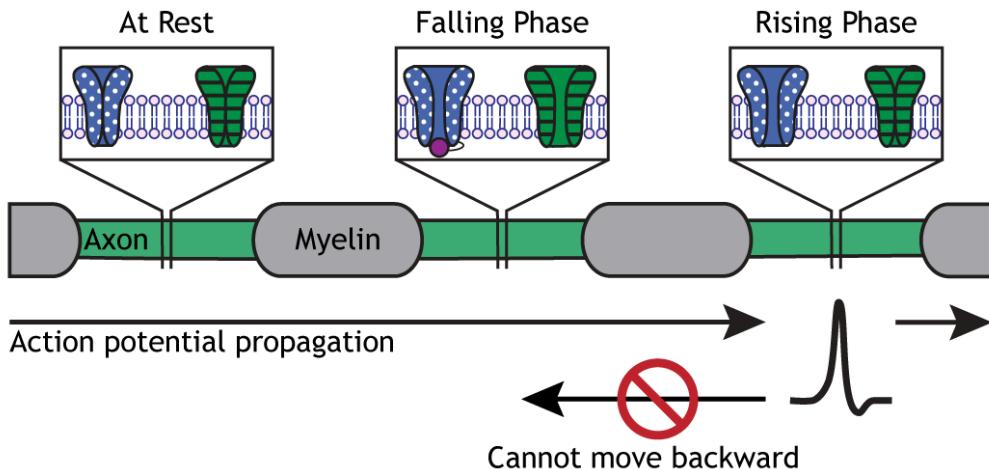


Figure 6.7. Action potentials only travel in one direction. The inactivated sodium channels prevent the action potential from moving backward down the axon. Blue dotted channels: sodium channels; green striped channels: potassium channels. The dotted, blue channels represent voltage-gated sodium channels; the striped, green channels represent voltage-gated potassium channels. 'No Backward Propagation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Speed of Propagation

### Presence of Myelin

The presence of myelin leads to a significant increase in action potential conduction speed compared to an unmyelinated axon. For a myelinated axon, the action potential “jumps” between Nodes of Ranvier in a process called saltatory conduction. The nodes have a high density of voltage-gated channels, and the action potential is able to skip the axon segments covered by the myelin. In an unmyelinated axon, the action potential moves in a continuous wave. In addition to the saltatory conduction process, the presence of myelin also insulates the axon, preventing charge loss across the membrane, which also increases speed of the action potential.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=161>

Animation 6.8. The action potential moves down an unmyelinated axon like a wave, opening voltage-gated channels along the length of the axon. In a myelinated axon, though, the action potential is able to skip portions of the axon that are covered by the myelin; the action potential jumps from node to node and travels further down the axon in the same amount of time. The dotted, blue channels represent voltage-gated sodium channels; the striped, green channels represent voltage-gated potassium channels. ‘Action Potential Speed’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License. View static image of animation.

## Diameter of Axon

The diameter of the axon also affects speed. The larger the diameter of the axon, the faster the propagation of the action potential down the axon. A larger axon leads to less resistance against the flow of ions, so the sodium ions are able to move more quickly to cause the regeneration of the action potential in the next axon segment.

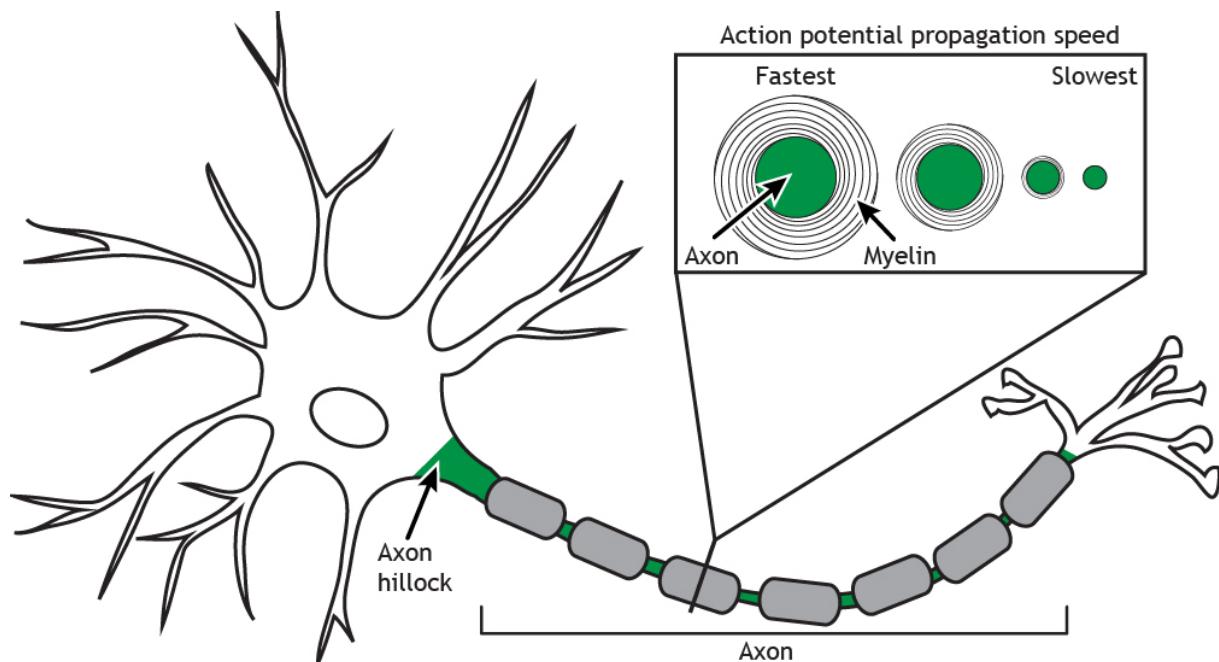


Figure 6.8. The diameter of the axon and the amount of myelination varies. Large diameter axons typically have thicker myelin sheath, which results in fast action potential speed. Small diameter axons may have no myelin present, resulting in slow action potential speed. ‘Axon Diameter’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

### Key Takeaways

- The voltage-gated ion channels are located along the axon hillock and axon; they open in response to the membrane potential reaching a threshold value
- The rising phase of the action potential is a result of sodium influx
- The falling phase of the action potential is a result of potassium efflux
- Action potentials are all-or-none (postsynaptic potentials are graded)
- Action potential have the same height of depolarization for a given cell under typical conditions
- The neuron cannot fire a second action potential during the absolute refractory phase
- The neuron can fire a second action potential during the relative refractory phase, but it requires a stronger stimulus than when the neuron is at rest
- Stimulus strength is coded by frequency of action potential firing
- Action potential travel in one direction due to the presence of inactivated voltage-gated sodium channels
- Speed of propagation relies on presence and thickness of myelin and diameter of axon

## Test Yourself!



An interactive H5P element has been excluded from this version of the text. You can view it online here:

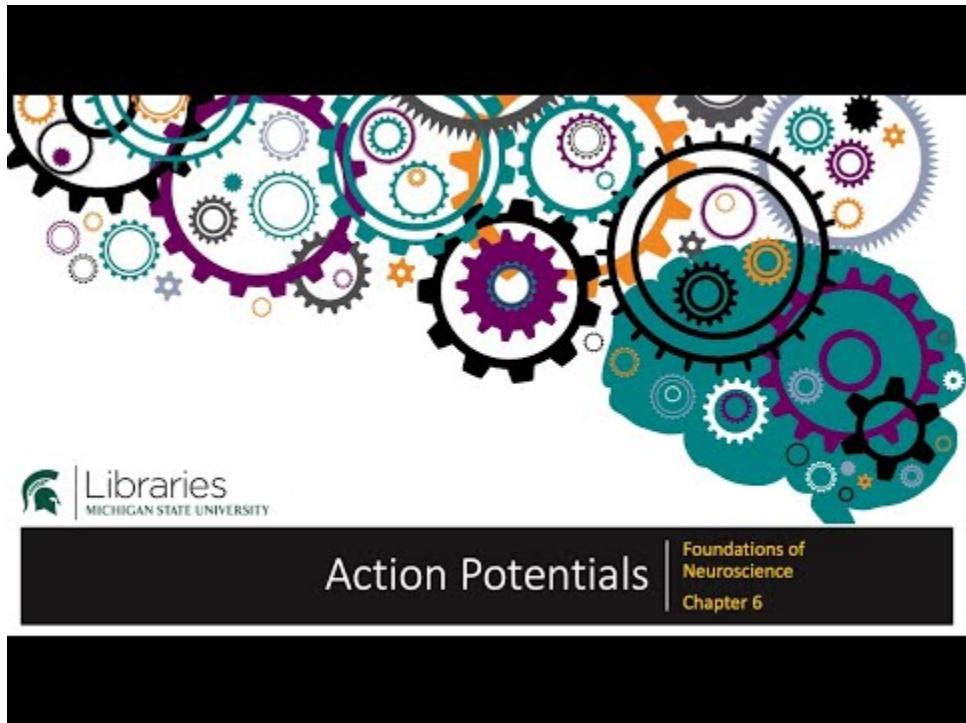
<https://openbooks.lib.msu.edu/neuroscience/?p=161#h5p-6>

## Additional Review

1. From memory, draw an action potential.
  - Label the main phases (rising, falling, etc...) and include threshold
  - Identify the change in potential (depolarization, repolarization, hyperpolarization)
  - Describe the state (open, closed, inactivated) of the ion channels at each phase
2. From memory, draw the neuronal membrane during each refractory period.
3. In comparison to being at rest, how likely is the neuron to fire an action potential during the two refractory periods?

## Answers

## Video Version of Lesson



A YouTube element has been excluded from this version of the text. You can view it online here:

<https://openbooks.lib.msu.edu/neuroscience/?p=161>

7.

# VOLTAGE CLAMP

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In the previous chapter, we covered ion flow and membrane potential changes that occur during the action potential in the neuron. We have this level of understanding about how ions move during the action potential because of a special technique called a voltage clamp experiment that was used in the 1950s. The voltage clamp method allows researchers to study voltage-gated ion channels by controlling the membrane potential of a neuron.

## Resources

- Key Takeaways
- Test Yourself
- Additional Review
- Video Version

## The Voltage Clamp Experiment

### Initial Set-Up

To conduct a voltage clamp experiment, a portion of the axon, which would include the cell membrane and all the voltage-gated ion channels located there, is removed from a neuron and placed into a solution that mimics that of physiological extracellular solution. The ion concentrations across the membrane, as well as the electrochemical gradients, would remain the same.

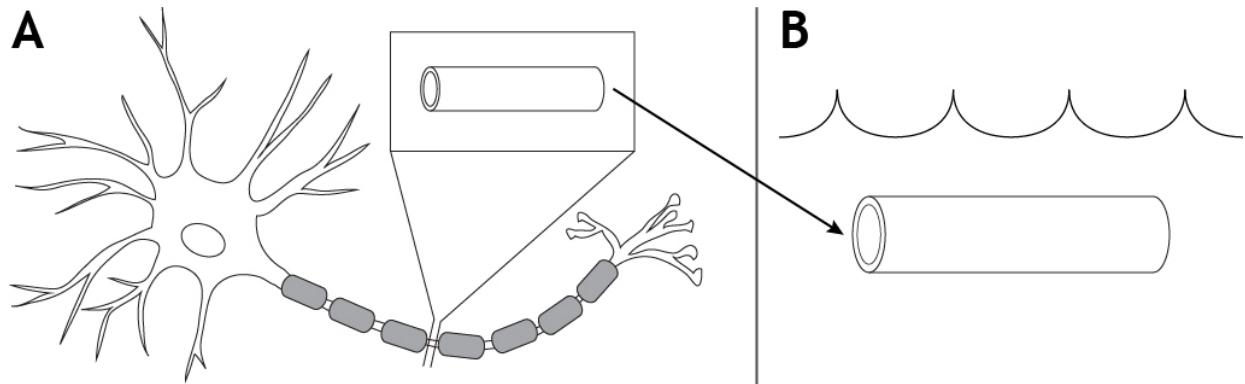


Figure 7.1. To conduct a voltage clamp experiment, a portion of the axon is removed from the neuron. The axon is placed in a special solution that is similar to physiological extracellular solution. ‘In Vitro Axon’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Measuring the Membrane Potential

The initial step in the voltage clamp method is to measure the membrane potential of the axon. A recording electrode is placed into the axon, and a reference electrode is placed into the extracellular solution. The voltage difference between these two electrodes is the membrane potential of the axon.

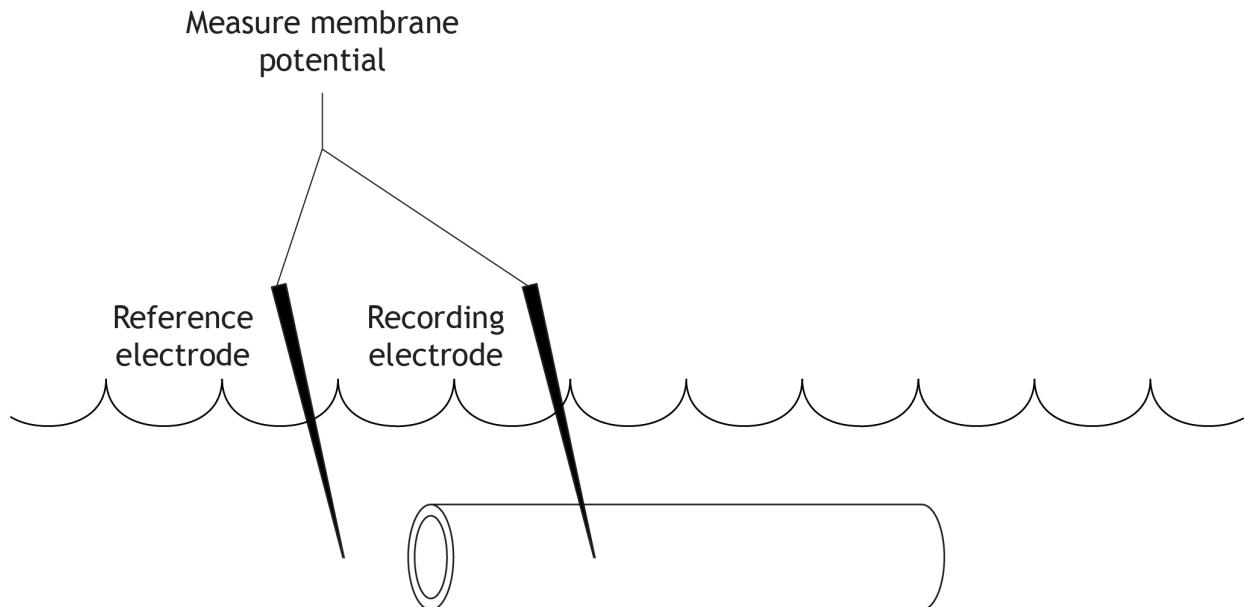


Figure 7.2. Measuring the membrane potential of the axon segment is the first step in the voltage-clamp experiment. The membrane potential is the difference in voltage between the intracellular recording electrode and the extracellular reference electrode. 'Measure Membrane Potential' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Clamping the Voltage

The researchers running the experiment can set a desired membrane potential for the cell. The equipment then compares the desired membrane potential with the measured membrane potential from the electrodes. If these values differ, current is injected into the cell to change the measured membrane potential and make it equal to the desired potential.

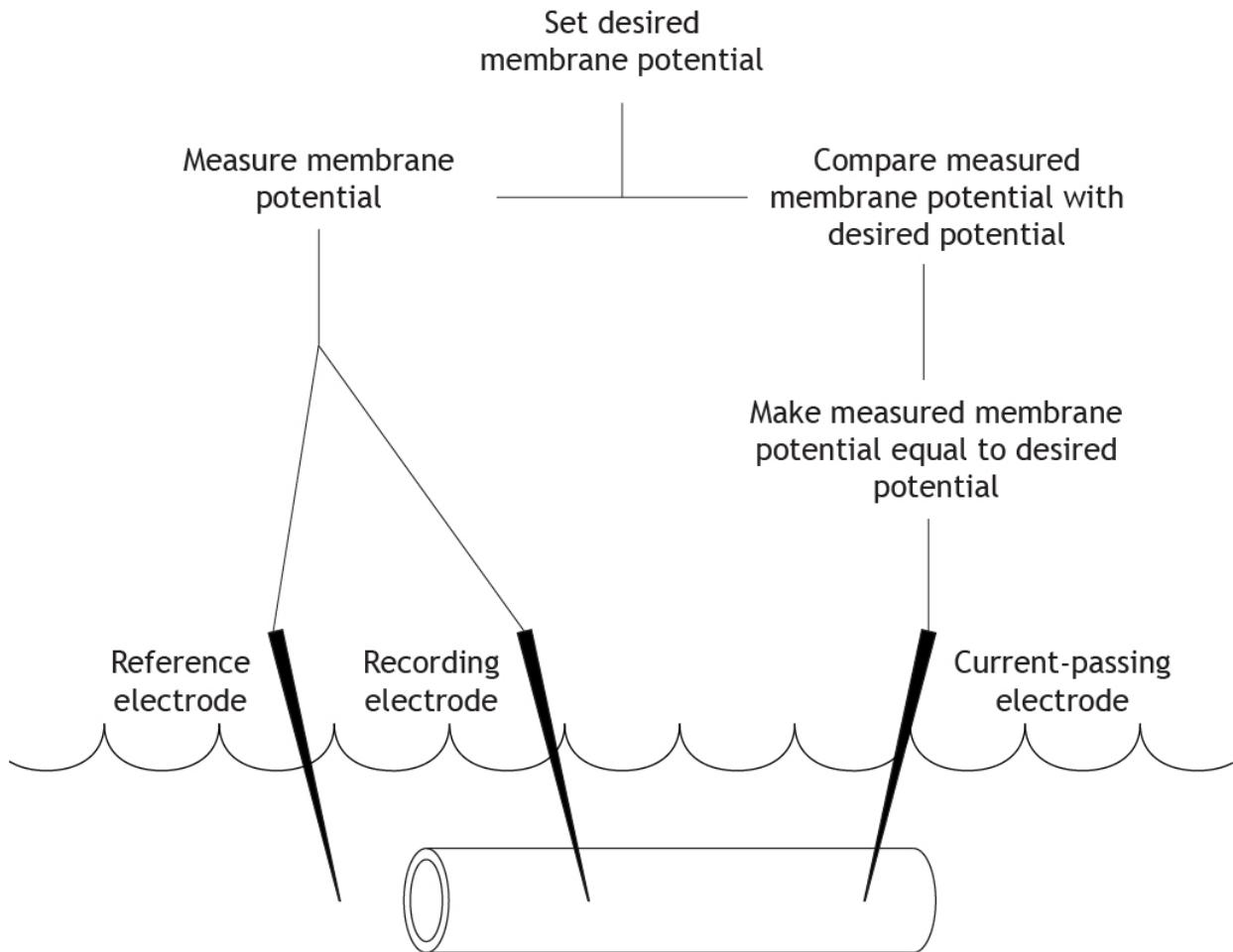


Figure 7.3. A desired membrane potential is set for the experiment. The voltage-clamp experimental equipment then compares the measured membrane potential with the desired potential. Current is then injected into the axon through a current-passing electrode to make the measured membrane potential equal to the desired potential. 'Clamping Voltage' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Repeat

The equipment continues this cycle for the length of the experiment. It constantly measures and compares the actual membrane potential with the desired potential, and then uses current to correct any changes, “clamping” the potential at one value.

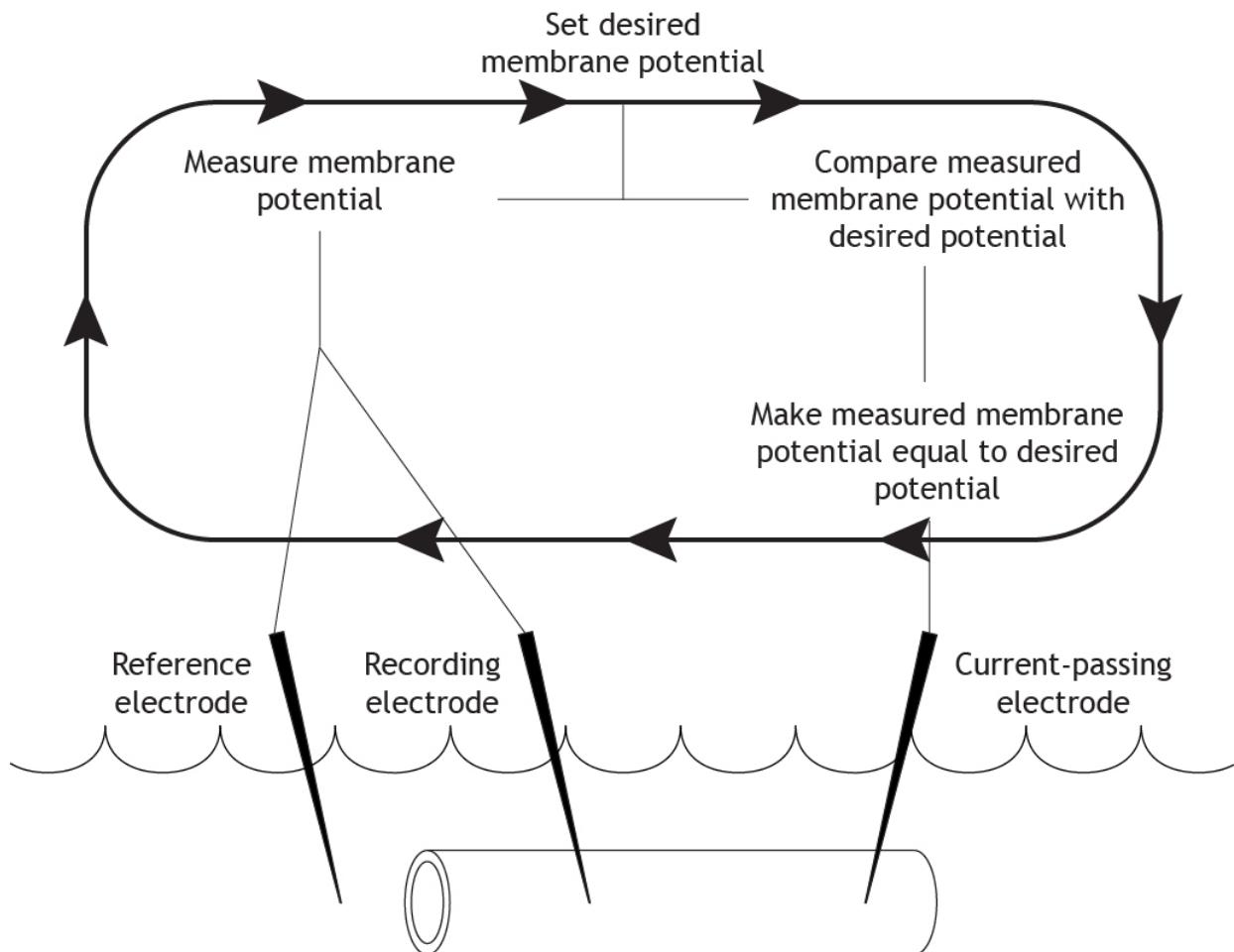


Figure 7.4. The voltage clamp cycle repeats continuously. The actual membrane potential of the axon is measured, compared to the set desired potential value, and then current is passed into the axon to keep the actual membrane potential equal to the desired potential. 'Voltage Clamp Cycle' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

#### Voltage Clamp Experiment Example

## At Rest

Let's work through the system with an example. Here is an axon bathed in the extracellular solution. The resting membrane potential is measured at -65 mV.

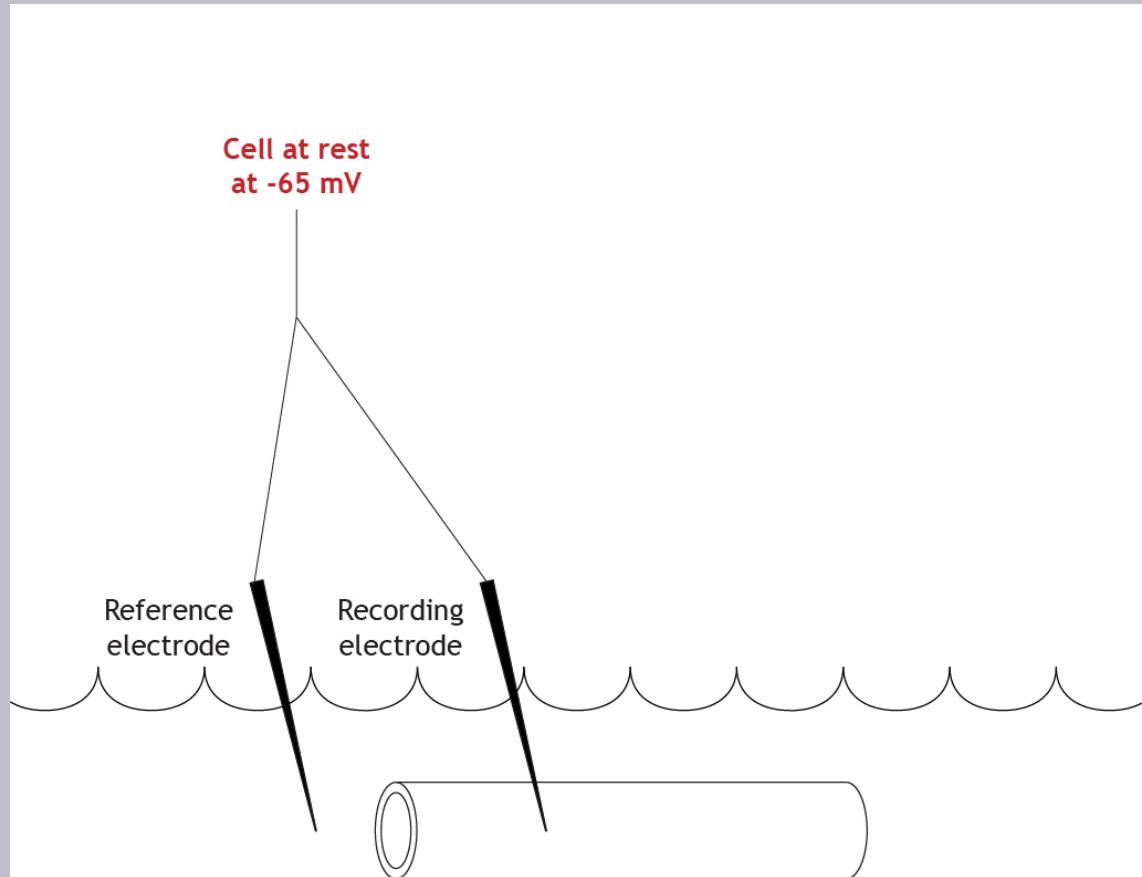


Figure 7.5. Measure the membrane potential. The membrane potential of this axon at rest is -65 mV. 'Voltage Clamp Example at Rest' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Set Clamped Membrane Potential Value

For this experiment, the desired membrane potential value is 0 mV.

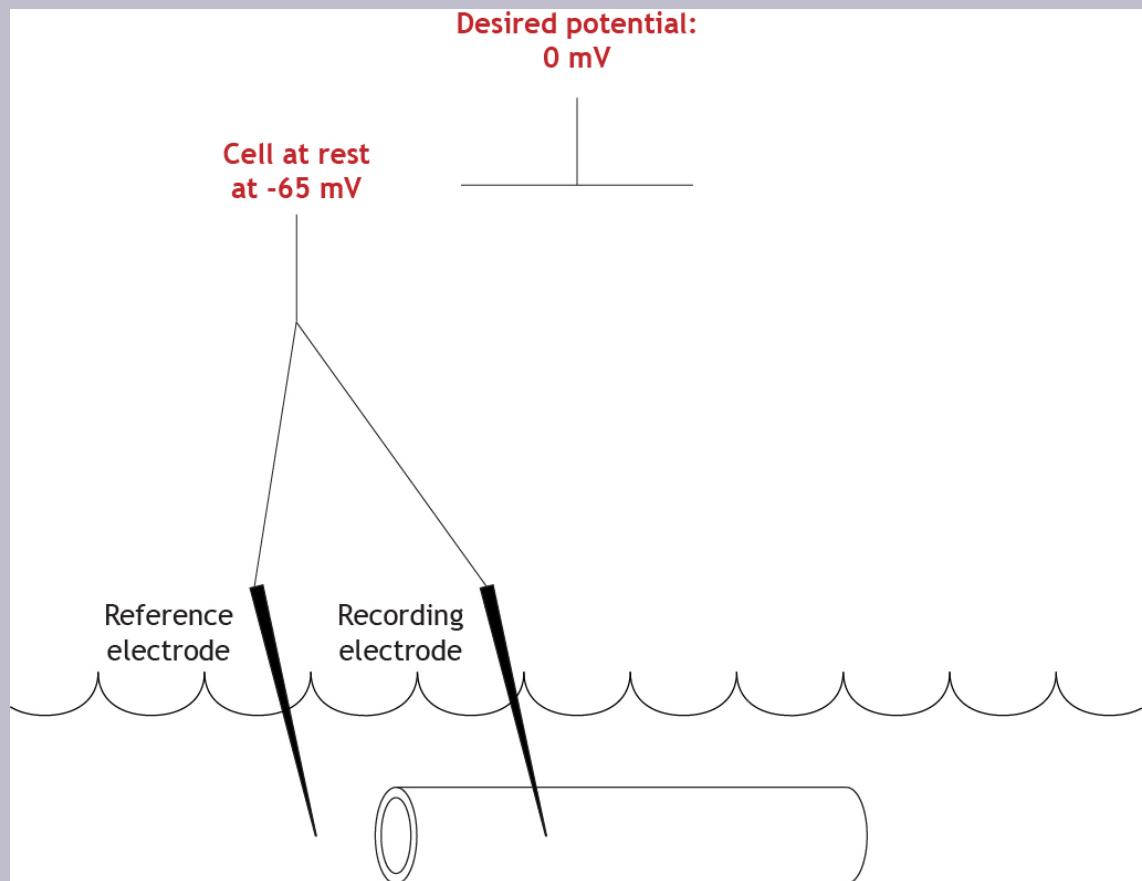


Figure 7.6. Set desired membrane potential. The set value for this experiment is 0 mV. 'Voltage Clamp Example Set Value' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Compare Actual and Set Membrane Potential Values

The equipment will determine that the actual membrane potential of the cell is not correct (-65 mV compared to 0 mV), so the cell must depolarize to reach the set value.

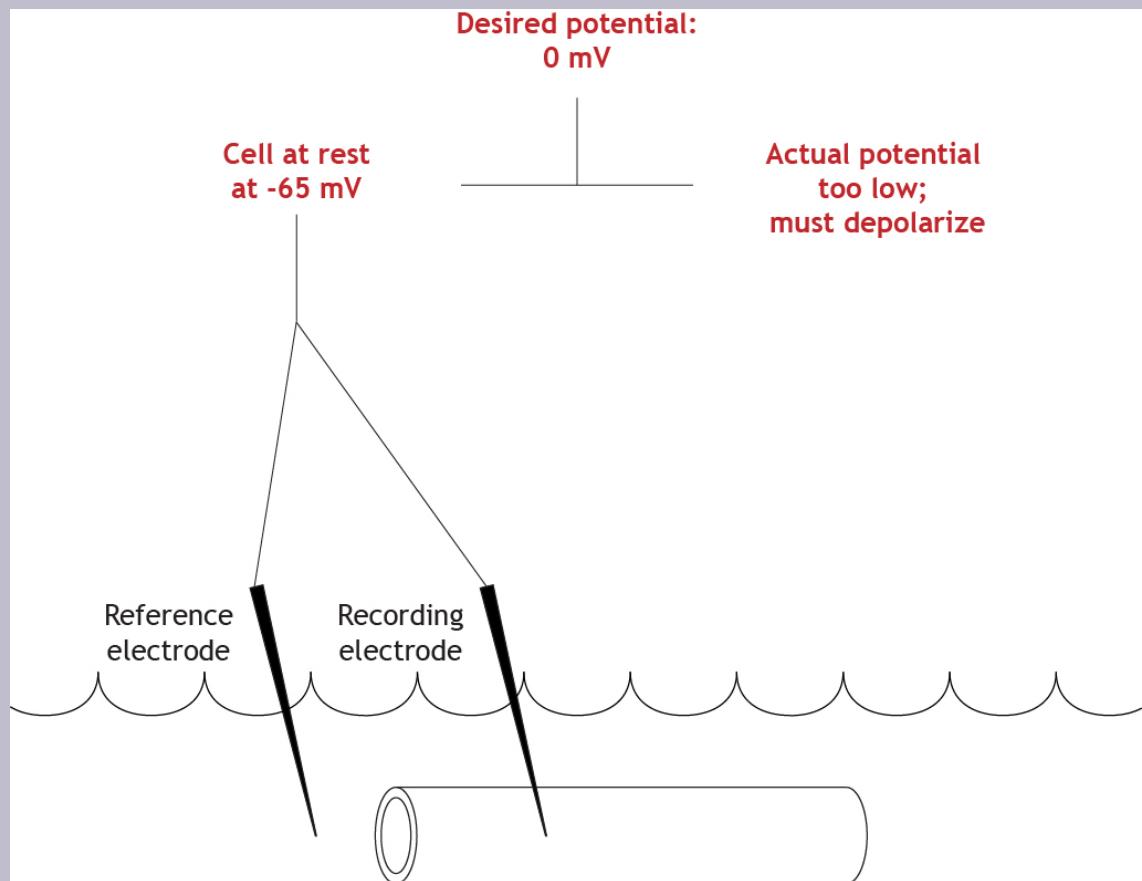


Figure 7.7. Compare measured membrane potential to desired potential. The actual membrane potential of the axon is at -65 mV, so the cell needs to be depolarized to reach the desired potential of 0 mV. 'Voltage Clamp Example Comparison' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Adjust Membrane Potential

To make the axon move from its resting membrane potential to 0 mV, the current electrode will pass positive current into the cell, depolarizing the cell until the membrane potential reaches the set value.

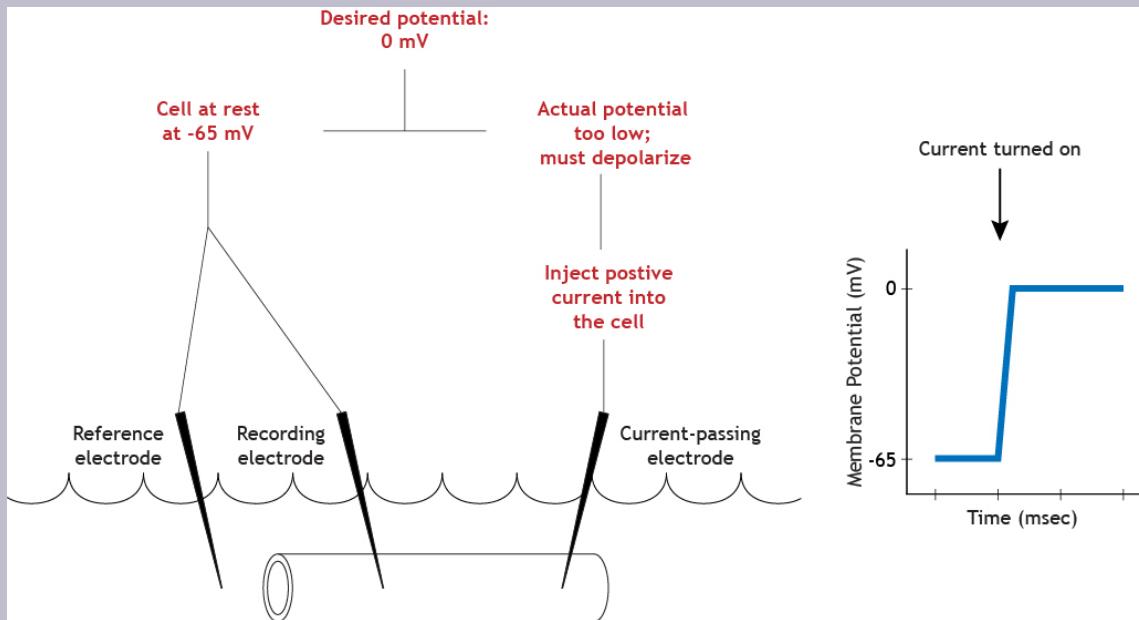


Figure 7.8. Correct actual membrane potential. To depolarize this axon from rest at -65 mV to the desired clamp value of 0 mV, positive current will be injected into the cell. The membrane potential will then depolarize to 0 mV and remain there. ‘Voltage Clamp Example Current’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

## Ion Channels Continue to Function During Voltage Clamp

The important aspect of the depolarization seen in the example is that it is above threshold. Moving the membrane potential above threshold will activate the voltage-gated ion channels. Sodium channels will open immediately, and sodium will begin rushing into the cell. This influx of positive ions would normally cause change the membrane potential to depolarize, but the voltage clamp equipment will measure the ion flow and inject a current of equal strength and opposite charge into the axon to maintain the membrane potential at 0 mV. This happens almost instantly and is a constant process, so as the ion flow changes, so does the injected current.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=193>

Animation 7.1. Clamping the cell at 0 mV will result in current being passed into the axon to depolarize the membrane potential. This depolarization is above threshold, so the voltage-gated ion channels in the membrane will be activated. Sodium will enter the axon through the open sodium channels. The voltage clamp equipment will inject current equal in strength and opposite in charge to the sodium influx in order to keep the membrane potential of the axon at 0 mV. The membrane potential will remain at 0 mV because the injected current offsets any change that would normally occur due to ion flow. ‘Voltage Clamp Sodium Flow’ by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License. View static image of animation.

Since the ion channels function as expected during the voltage clamp experiment, the voltage-gated sodium channels will inactivate, and the delayed voltage-gated potassium channels will open because, like the sodium channels, they are also activated when the membrane potential reaches threshold. This causes the ion flow to change from inward to outward. Normally, potassium efflux would cause a repolarization of the membrane potential, but the voltage clamp equipment will again inject a current that is equal in strength and opposite in charge to the potassium flow to keep the membrane potential steady at 0 mV.



A video element has been excluded from this version of the text. You can watch it online here: <https://openbooks.lib.msu.edu/neuroscience/?p=193>

Animation 7.2. The voltage-gated sodium channels will inactivate, and the potassium channels will open. Potassium will then flow out of the axon. Similar to the sodium influx, the voltage clamp equipment will inject current equal in strength and opposite in charge to the potassium efflux in order to keep the membrane potential of the axon at 0 mV. ‘Voltage Clamp Potassium Flow’ by Casey

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## Data Collection

Researchers can determine how much current is moving through the voltage-gated ion channels by observing how much current the equipment must inject into the cell to keep the membrane potential steady. If the equipment has to inject negative current in for 2 milliseconds, then the researchers know that positive ions were flowing in for 2 milliseconds. So the voltage-clamp set up allowed researchers in the 1950s to learn about how the voltage-gated ion channels were functioning during an action potential.

### Key Takeaways

- The membrane potential does not change during a voltage clamp experiment
- Voltage-gated ion channels are still able to function normally and allow ion flow
- If the clamped membrane potential is above threshold, the voltage-gated channels will act as if the cell is firing an action potential
- The equipment must compensate for the neuron's ion flow by injecting current into the axon. The amount of current needed to keep the membrane potential steady is equal and opposite to the current actually flowing in the cell

## Test Yourself!

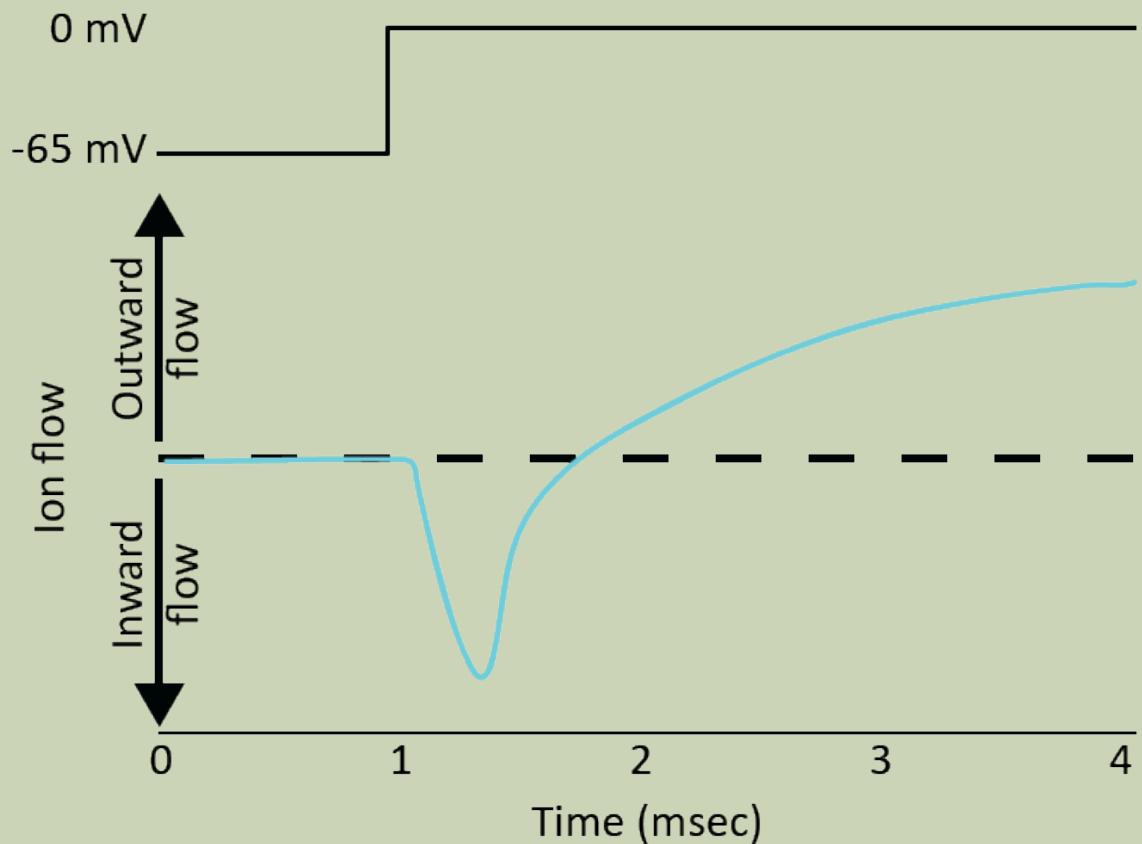


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<https://openbooks.lib.msu.edu/neuroscience/?p=193#h5p-7>

### Additional Review

You conduct a voltage clamp experiment where you move the membrane potential from rest at -65 mV to 0 mV. You collect the following data:

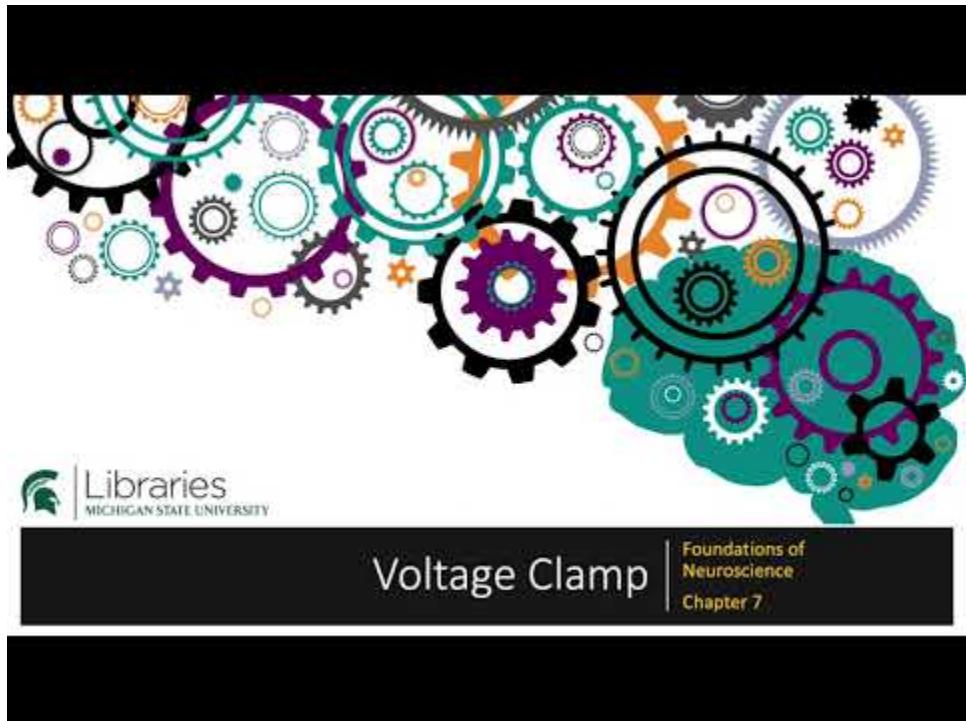


The membrane potential of a neuron is clamped at 0 mV. An initial inward current is seen, followed by an outward current.

Describe what causes the observed ion flow, including information about which ion(s) is/are moving and in which direction.

Answers

## Video Version of Lesson



A YouTube element has been excluded from this version of the text. You can view it online here:

<https://openbooks.lib.msu.edu/neuroscience/?p=193>