Foundations of Neuroscience

FOUNDATIONS OF NEUROSCIENCE

Open Edition

CASEY HENLEY

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CONTENTS

Part VI. Behavior

INTRODUCTION

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:

Pain (Fall 2023)
- Auditory (Fall 2023)
- Vestibular (Fall 2023)
- Olfaction (Fall 2023)
- Learning and Memory (Fall 2023)
- Autonomic nervous system (Fall 2023)
- Diseases and disorders for the different systems (2024)
- Cerebellum (2024)

Sleep (2024)
Circadian rhythms (2024)

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
- Video Lecture

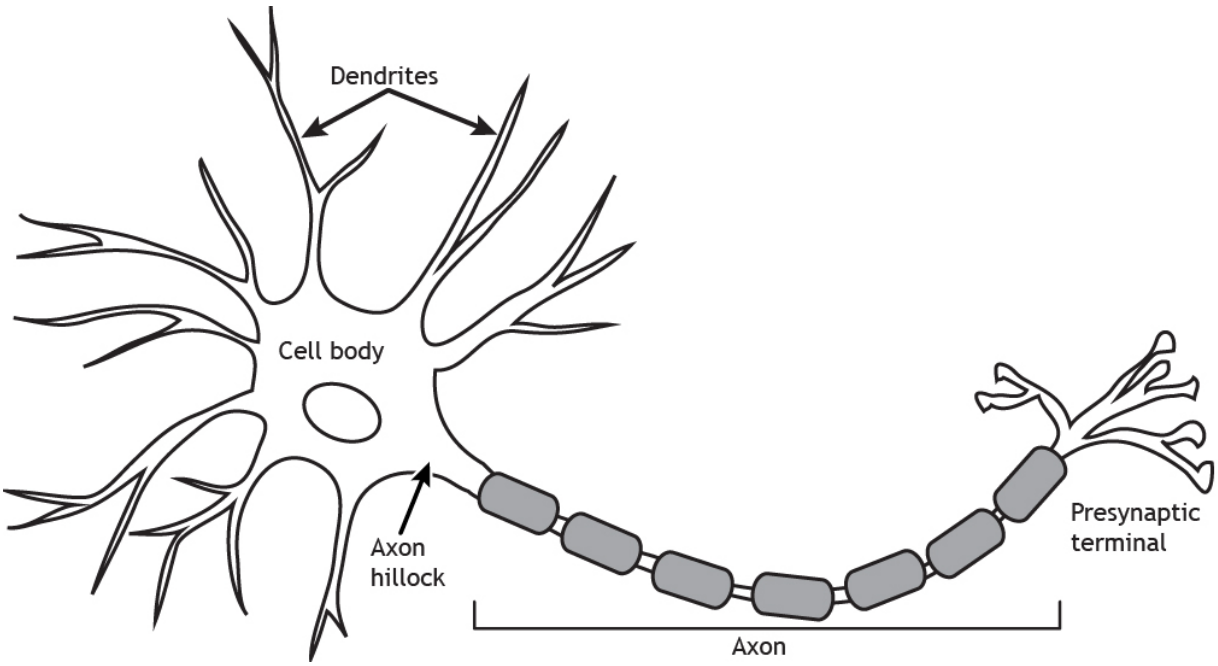

Figure 1.1. A typical neuron. Dendrites branch out from the cell body, where the nucleus is located. The axon hillock is located where the cell body transitions into the axon. The axon begins at the axon hillock and ends at the presynaptic terminal, which can branch into multiple terminals. 'Neuron'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

The structure of the neuron affects how it functions

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.

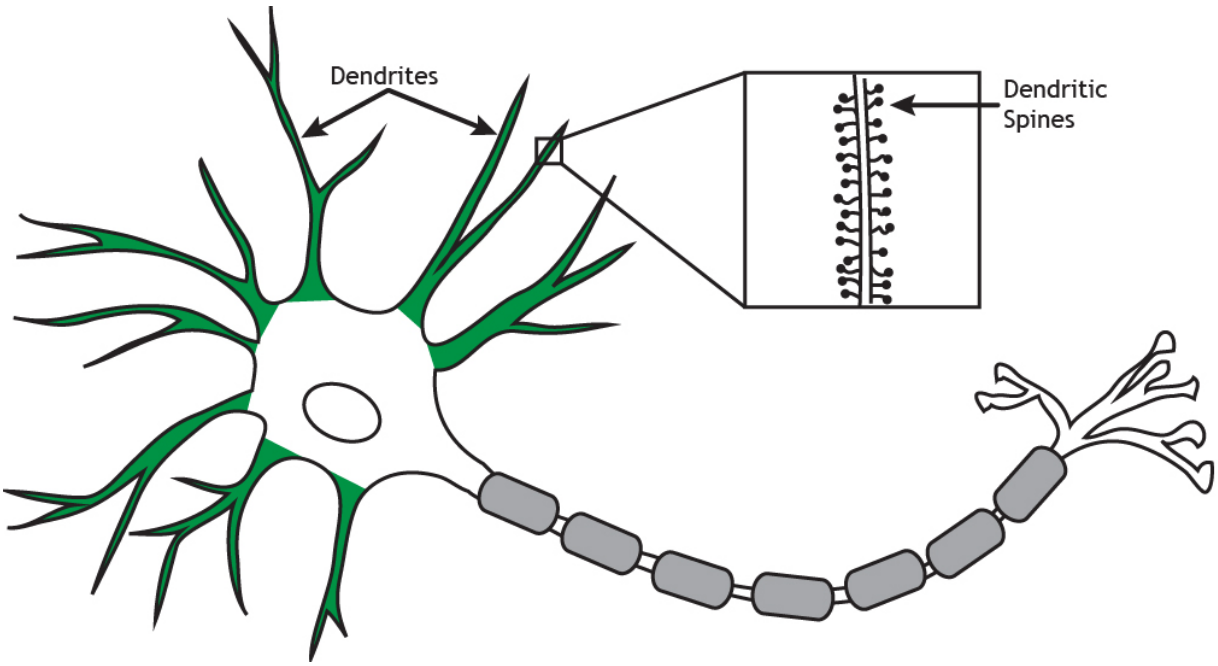

Figure 1.2. Dendrites branch out from the soma. Their function is to receive information from other neurons. Some dendrites have small protrusions called spines that are important for communicating with other neurons. 'Dendrites' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial 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.

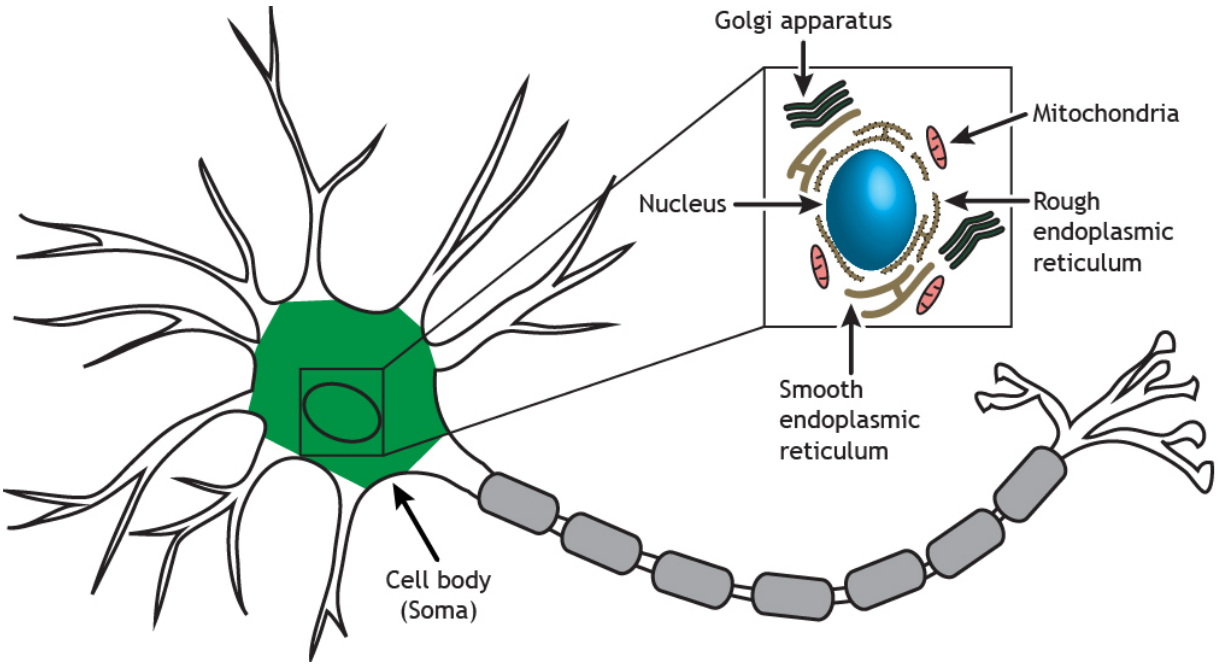

Figure 1.3. The cell body, or soma, of the neuron contains the nucleus and organelles that are commonly found in other cell types and are important for basic cellular functions. These organelles include mitochondria, endoplasmic reticulum, and Golgi apparatus. 'Soma' by Casey Henley is licensed under 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.

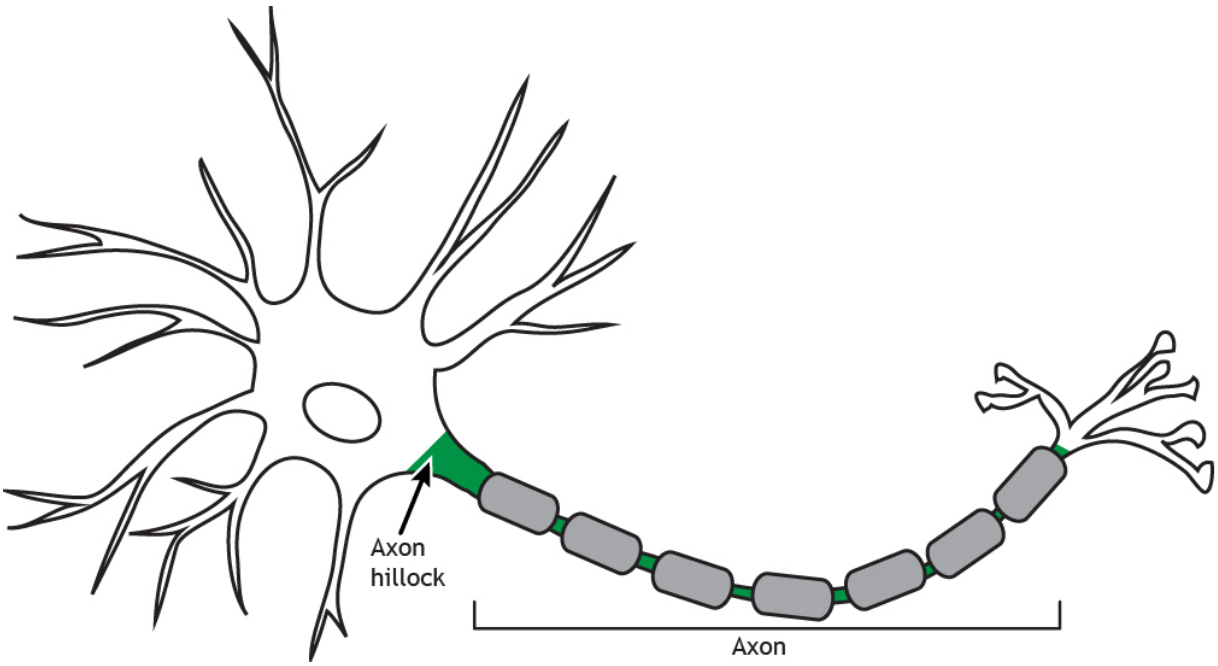

Figure 1.4. The axon is a long single projection that begins at the axon hillock, the region between the cell body and the axon. The axon terminates at the presynaptic terminal. 'Axon' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International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

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=5#video-5-1

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.

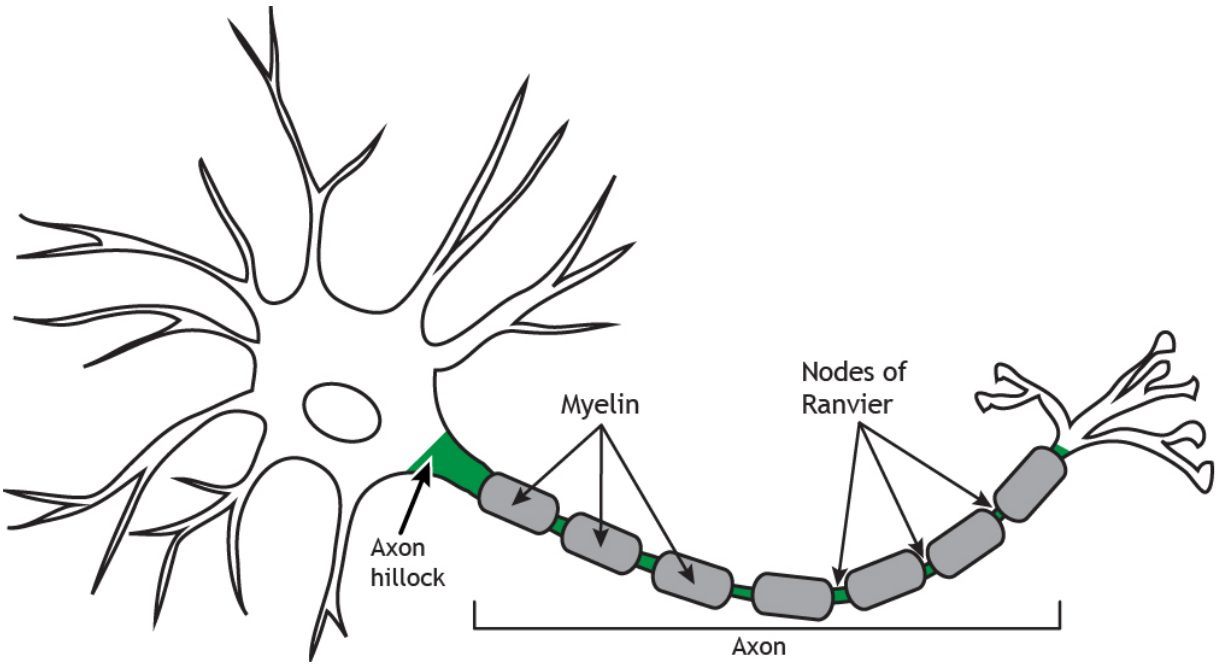

Figure 1.5. Myelin wraps around and insulates the axon. The spaces between the myelin sheath, where the axon is uncovered, are call the Nodes of Ranvier. 'Myelin' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Axon 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.

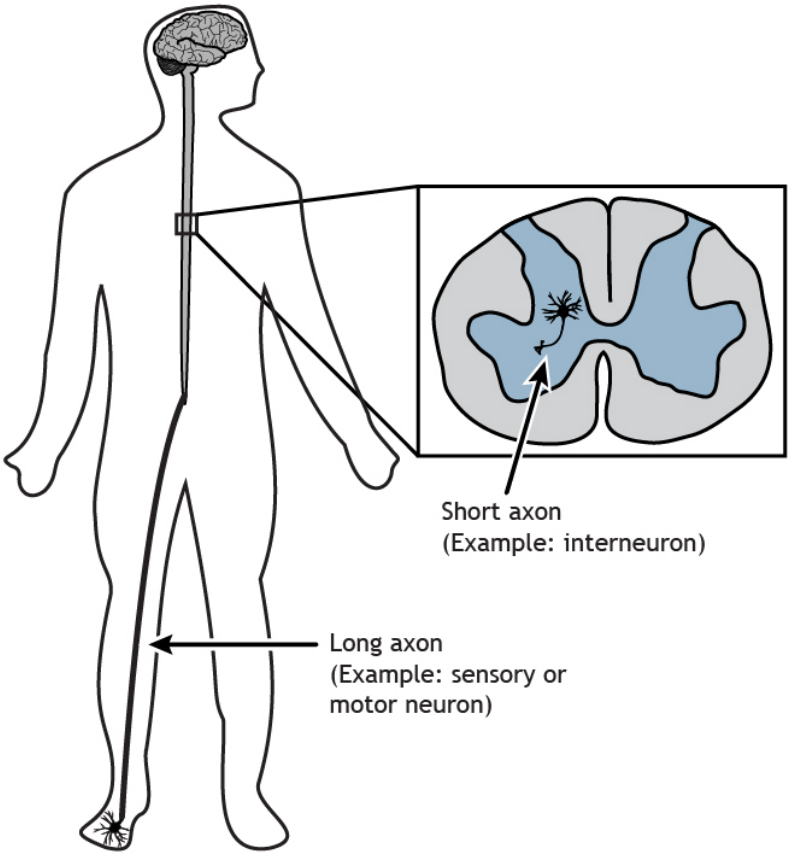

Figure 1.6. Axons vary in length. Spinal interneurons, neurons that fully exist within the spinal cord, can have short axons, whereas sensory or motor neurons, which need to reach from the spinal cord to the appropriate body region, for example the toe, have long axons. 'Axon Length' by Casey Henley 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.

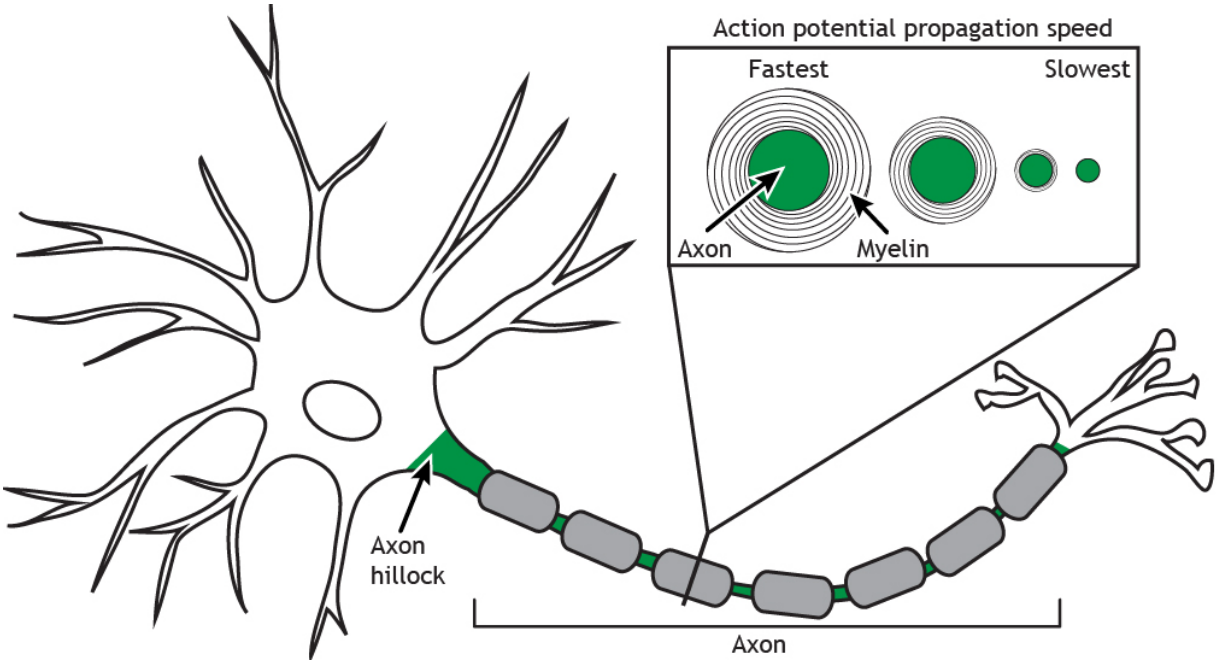

Figure 1.7. The diameter of the axon and the amount of myelination varies. Large diameter axons typically have thicker myelin sheath, which results in fast action potential speed. Small diameter axons may have no myelin present, resulting in slow action potential speed. 'Axon Diameter' by Casey Henley 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.

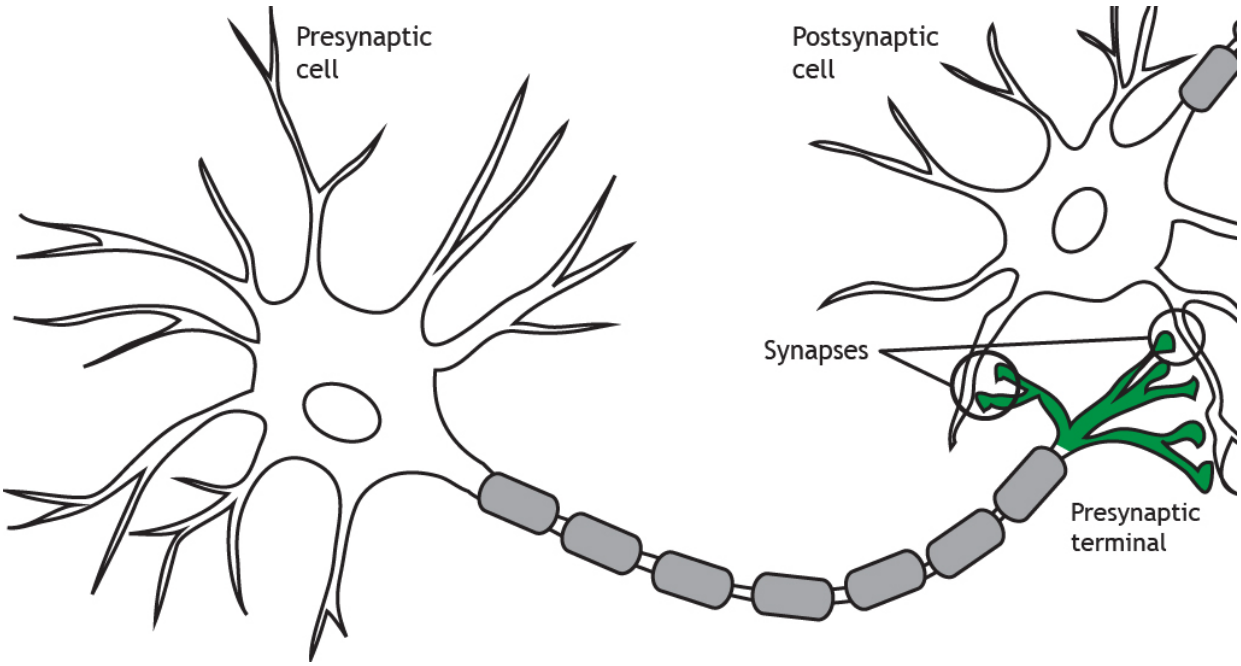

Figure 1.8. The presynaptic terminal forms synaptic contacts with a postsynaptic cell. 'Presynaptic Terminal' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

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.

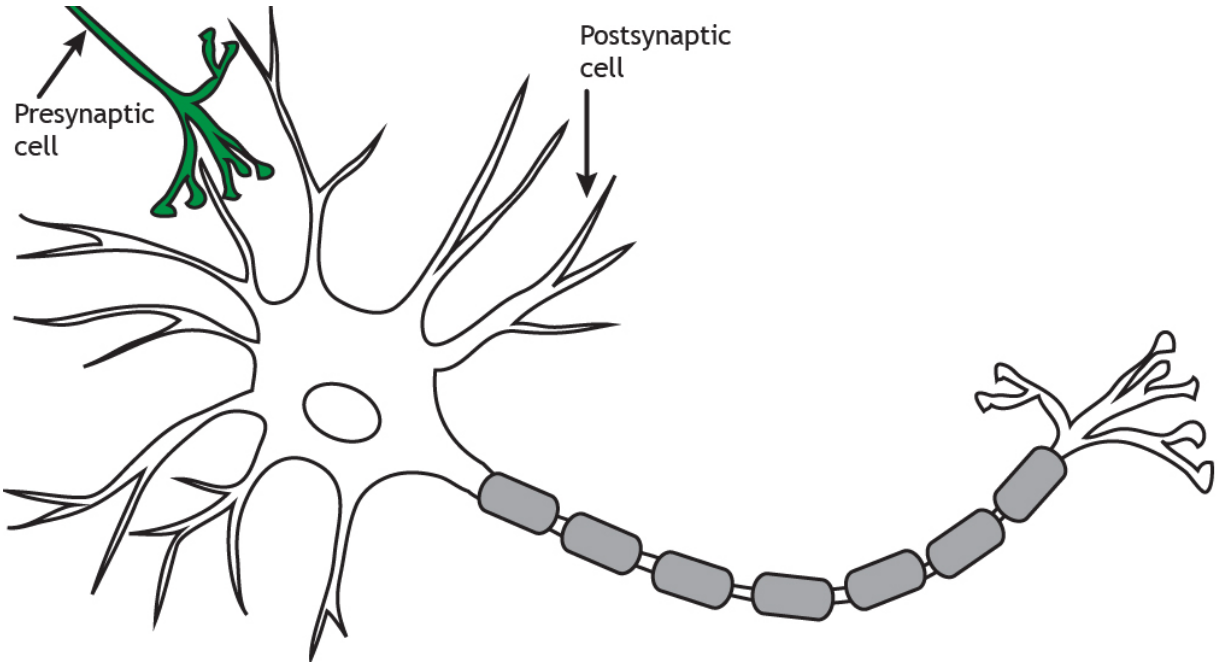

Figure 1.9. The presynaptic cell is the neuron that releases neurotransmitters into the synapse to act upon the postsynaptic cell. 'Postsynaptic Cell' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

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.

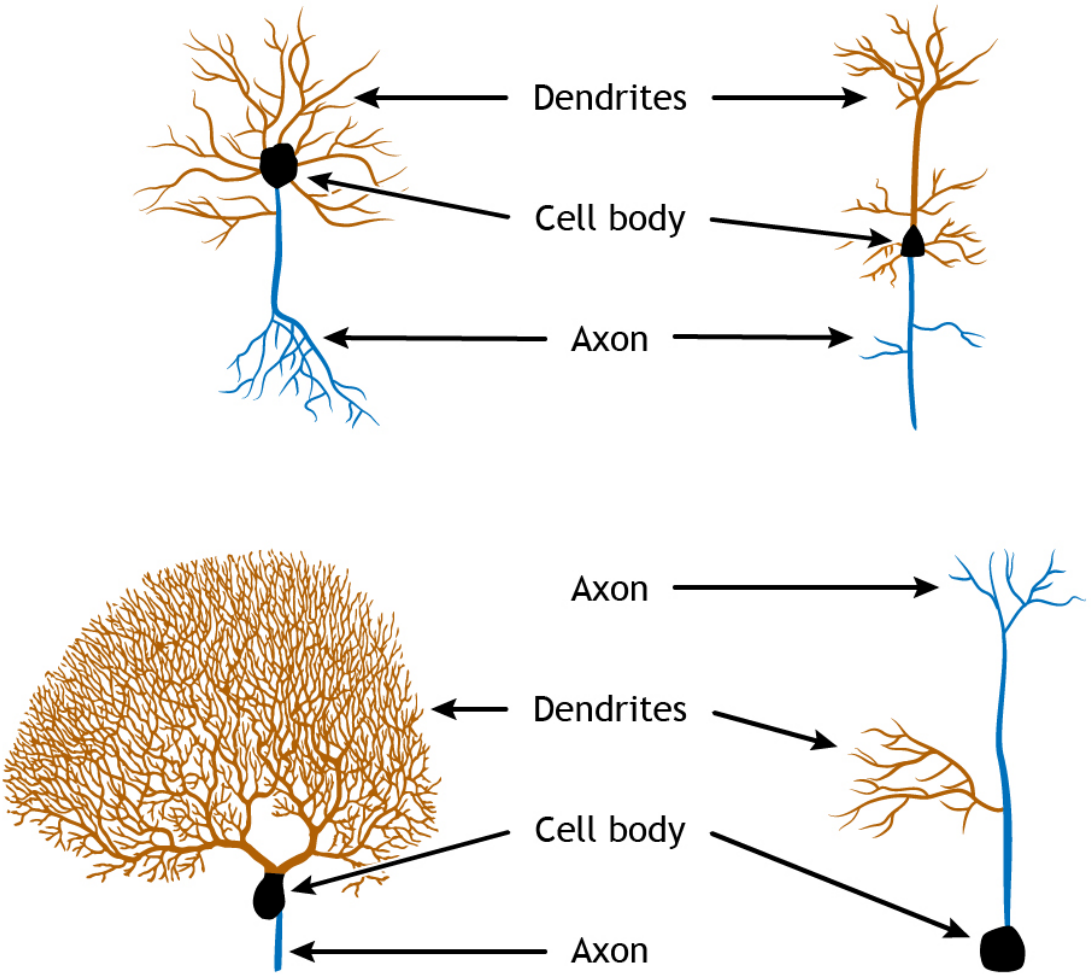

Figure 1.10. Neuron structure is variable, but the main components of cell body (shown in black), dendrites (shown in brown), and axon (shown in blue) are common among all neurons. 'Neuron Types' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA)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

Try the quiz more than once to get different questions!

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

1. From memory, 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 illustration.
3. Predict what would happen to neuron function if myelin was destroyed

Video Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=5#oembed-1

2.

ION MOVEMENT

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

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

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.

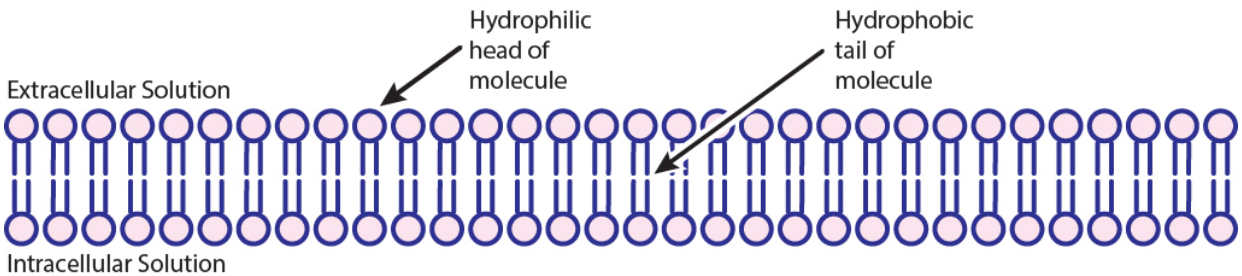

Figure 2.1. The neuronal membrane is composed of two layers of phospholipid molecules that form a barrier to water and water-soluble molecule due to the organization of the hydrophilic heads and hydrophobic ends of the molecules. 'Phospholipid Bilayer' by Casey Henley is licensed under a Creative Commons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

Ions move in predictable ways

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.

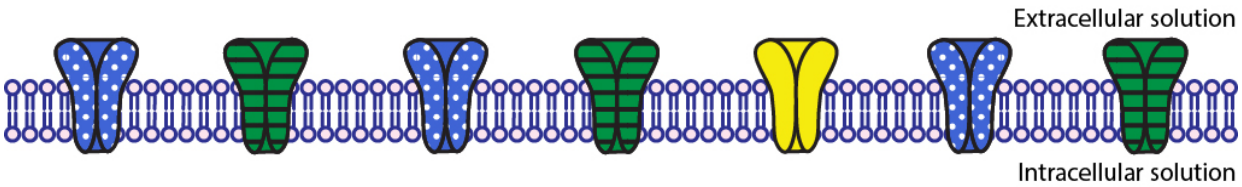

Figure 2.2. The phospholipid bilayer with embedded ion channels. The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the solid yellow channels represent chloride channels. 'Membrane with Channels' by Casey Henley is licensed under a Creative 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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=52#video-52-1

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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=52#video-52-2

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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=52#video-52-3

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

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

Video Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=52#oembed-1

3.

MEMBRANE POTENTIAL

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
- Video Lecture

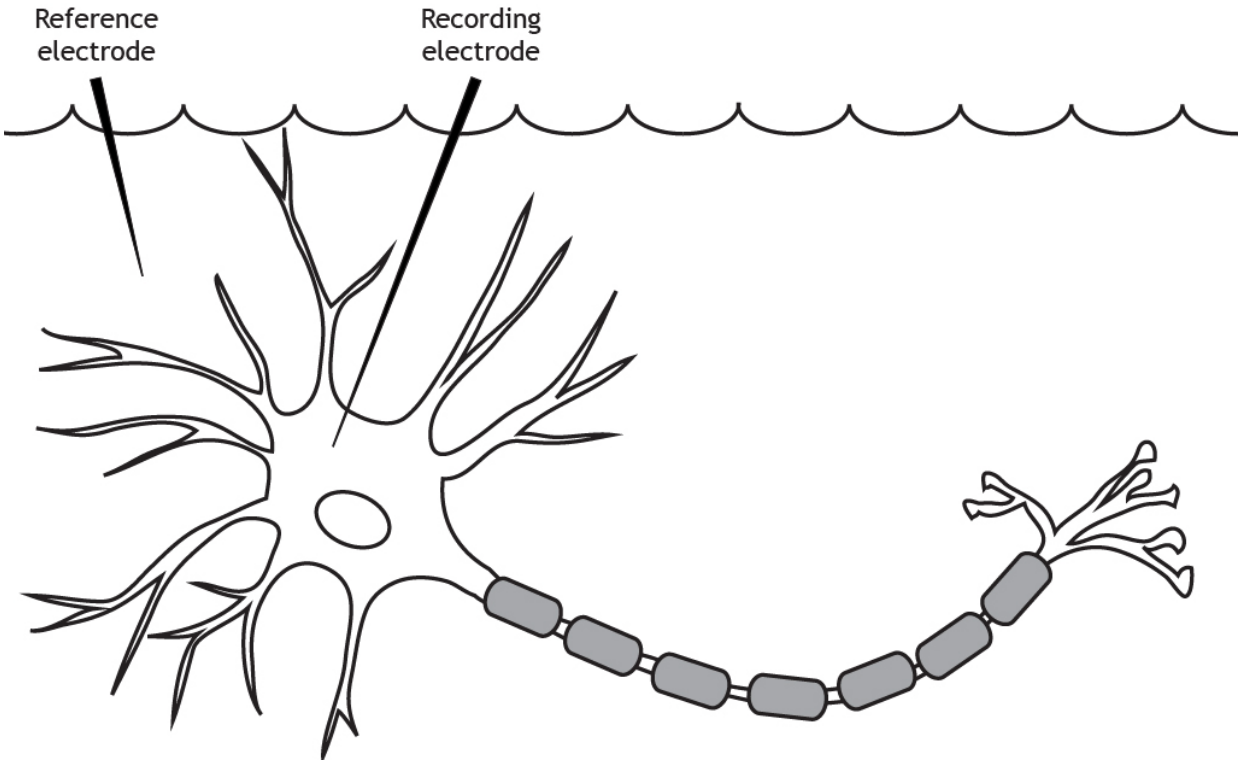

Figure 3.1. The membrane potential is measured using a reference electrode placed in the extracellular solution and a recording electrode placed in the cell soma. The membrane potential is the difference in voltage between these two regions. 'Measuring Membrane Potential' by Casey Henley is licensed 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.

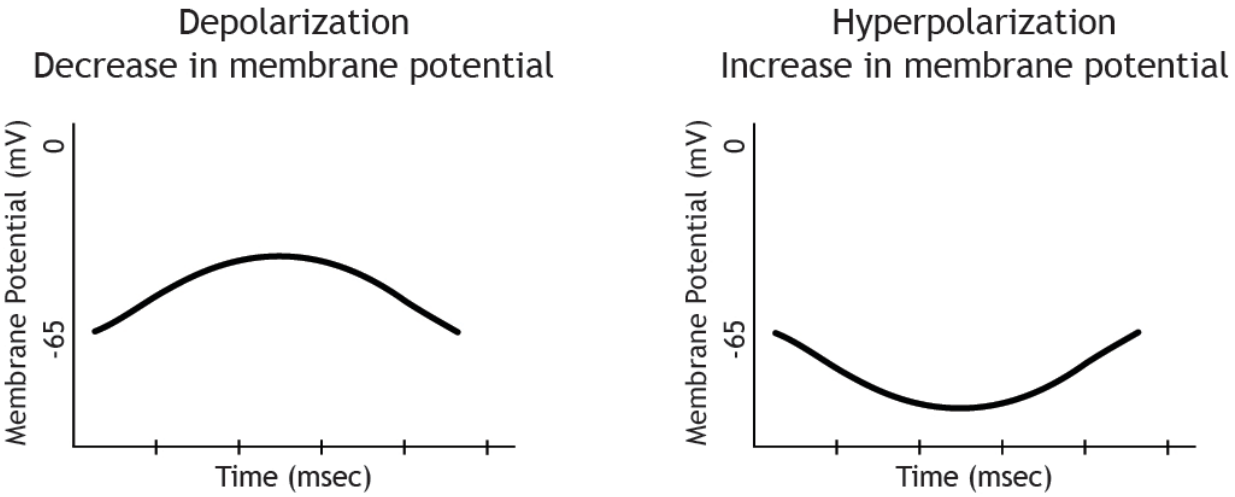

Figure 3.2. A decrease in membrane potential is a change that moves the cell's membrane potential toward 0 or depolarizes the membrane. An increase in membrane potential is a change that moves the cell's membrane potential away from 0 or hyperpolarizes the membrane. 'Membrane Potential Terms' by Casey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

The solution inside of the neuron is more negatively charged than the solution outside

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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.

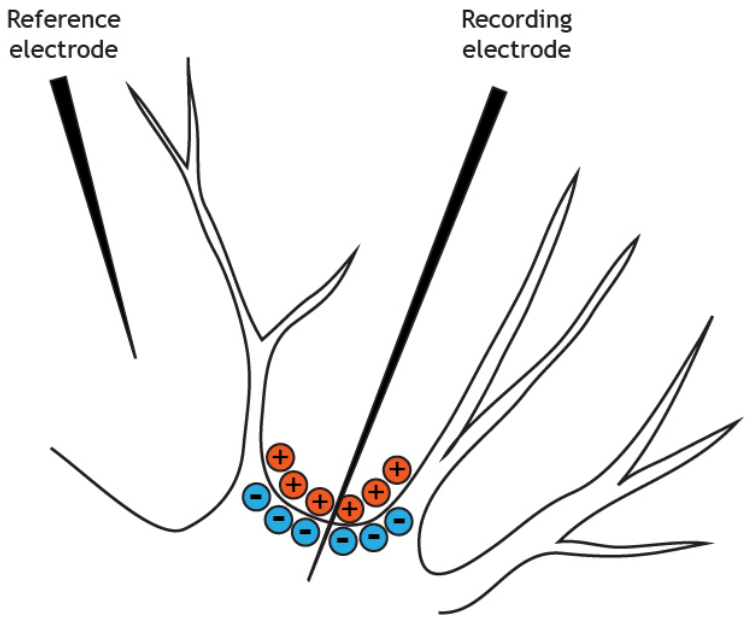

Figure 3.3. The inside of the neuron has a more negative charge than the outside of the neuron. 'Membrane Potential' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

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.

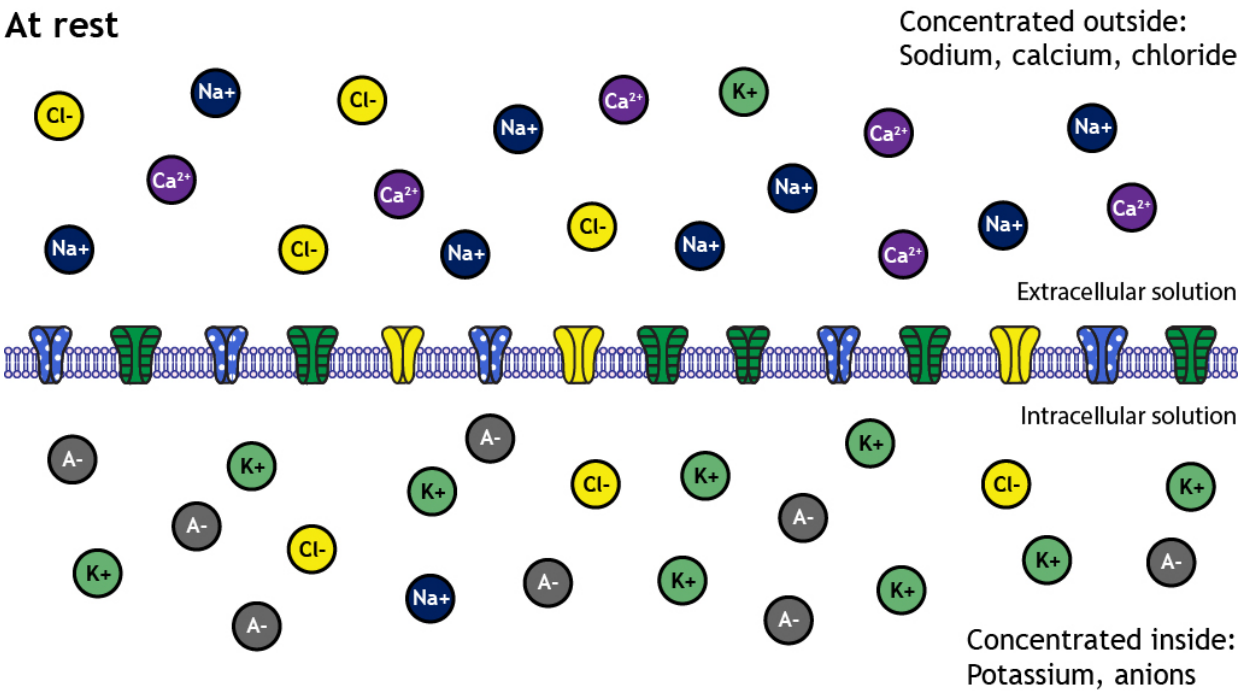

Figure 3.4. For a typical neuron at rest, sodium, chloride, and calcium are concentrated outside the cell, whereas potassium and other anions are concentrated inside. This ion distribution leads to a negative resting membrane potential. The dotted, blue channels represent sodium leak channels; the striped, 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.

The distribution of the different ions across the membrane creates electrochemical gradients that drive ion movement

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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.

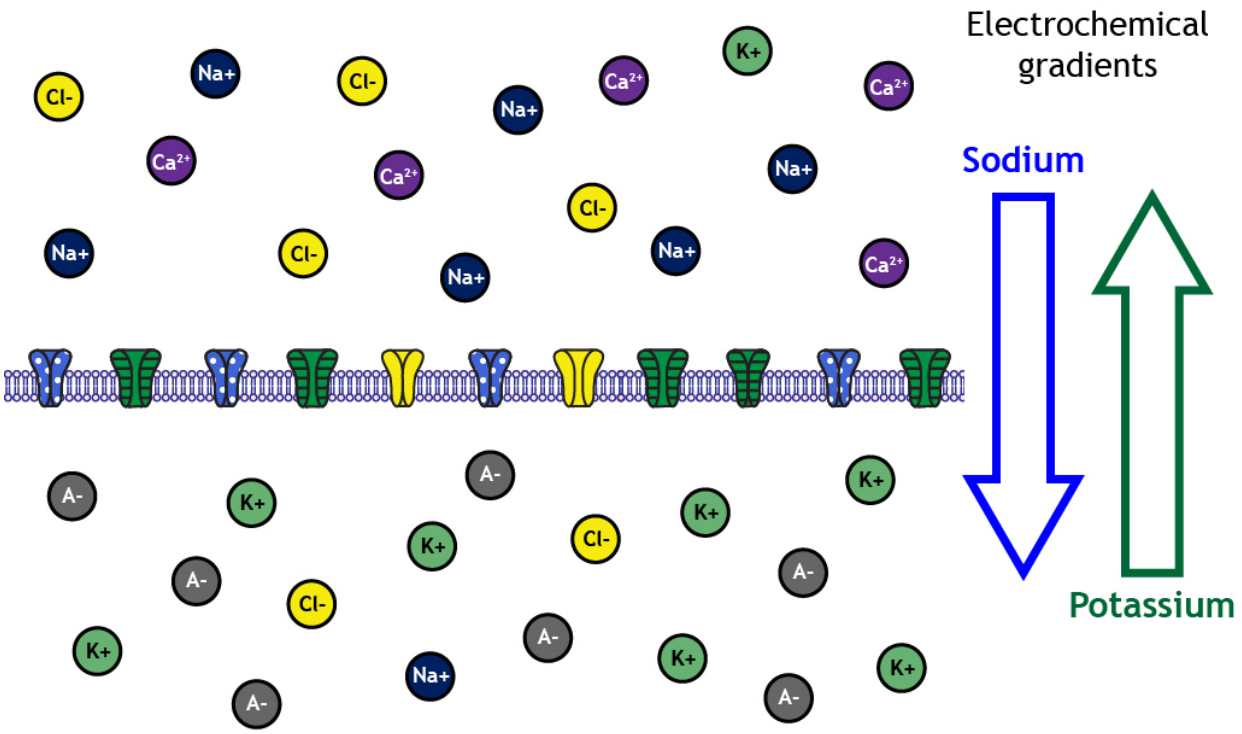

Figure 3.5. The distribution of ions on either side of the membrane lead to electrochemical gradients for sodium and potassium that drive ion flow in different directions. If the membrane is permeable to sodium, ions will flow inward. If the membrane is permeable to potassium, ions will flow outward. 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. The ion is at equilibrium at this membrane potential, meaning there is no *net* movement of the ion in either direction. 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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=752#video-752-1

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

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

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

$[Ion]_{outside}$ 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

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

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

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

It is possible to predict which way an ion will move by comparing the ion's equilibrium potential to the neuron's membrane potential

---

Predict Ion Movement by Comparing Membrane Potential to Equilibrium 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.

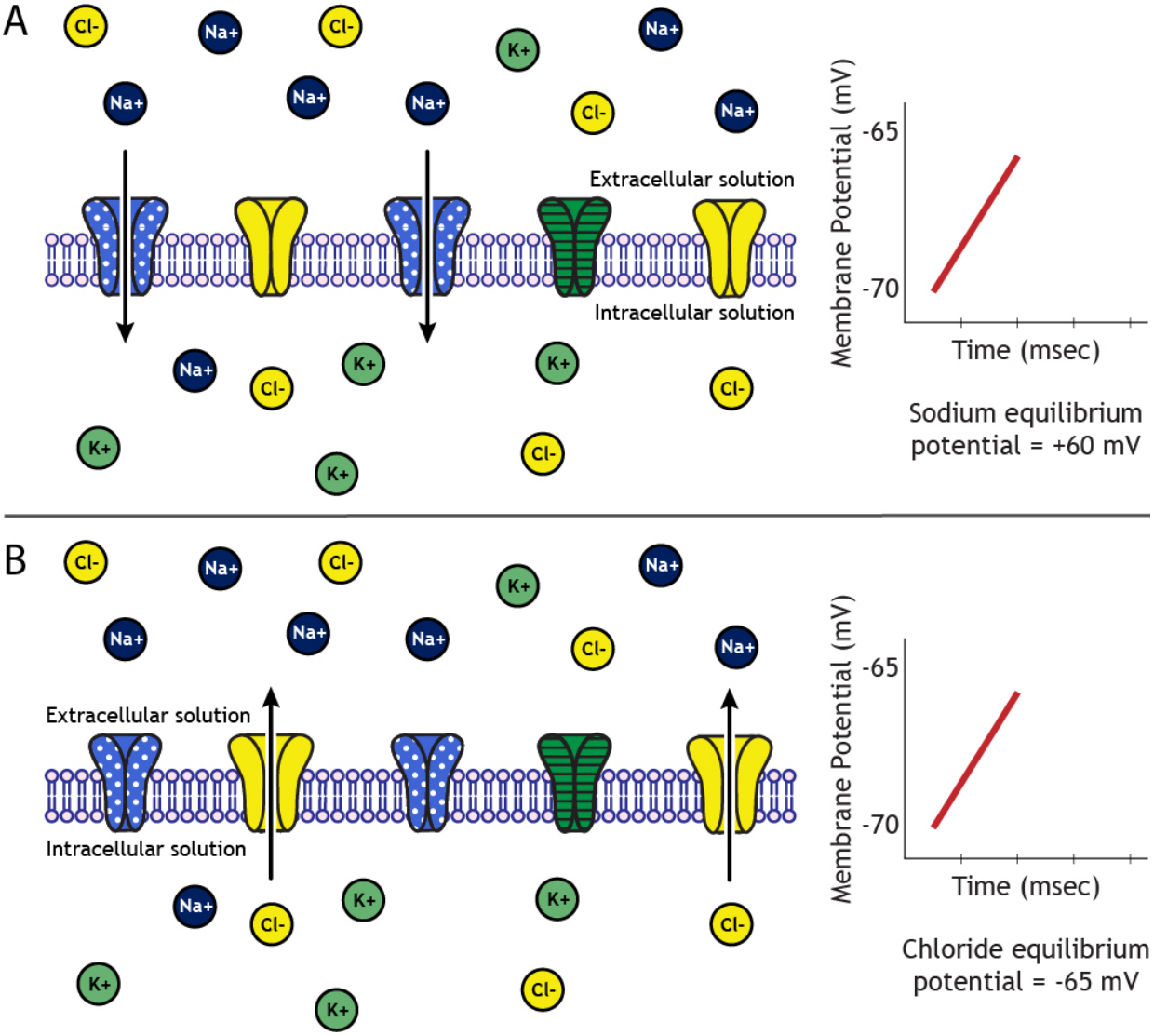

Figure 3.6. A) If a cell is at rest at -70 mV, sodium ions will flow into the cell to move the cell's membrane potential toward sodium's equilibrium potential of +60 mV. B) At the same resting membrane potential, chloride would flow out of the cell, taking away its negative charge, making the inside of the cell more positive and moving toward chloride's equilibrium potential of -65 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:

Ion	Inside concentration (mM)	Outside concentration (mM)	Equilibrium Potential
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!

Try the quiz more than once to get different questions!

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

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-31

1. Define resting membrane potential (Vm) of a cell.
2. Explain the differences between the resting membrane potential and the equilibrium potential.
3. Using the concentration values from the table below, calculate the equilibrium potential of potassium using the Nernst equation. Table A.1. Intra- and extracellular concentration (mM) and equilibrium potential (mV) values for ions present in the Thinking Cell.

Ion	Inside concentration (mM)	Outside concentration (mM)	Equilibrium Potential (mV)
A-	6	125	-65
B+	12	120	+60
D+	125	5	-84
E++	0.00001	1.5	+155

Video Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=752#oembed-1

4.

THE MEMBRANE AT REST

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

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.

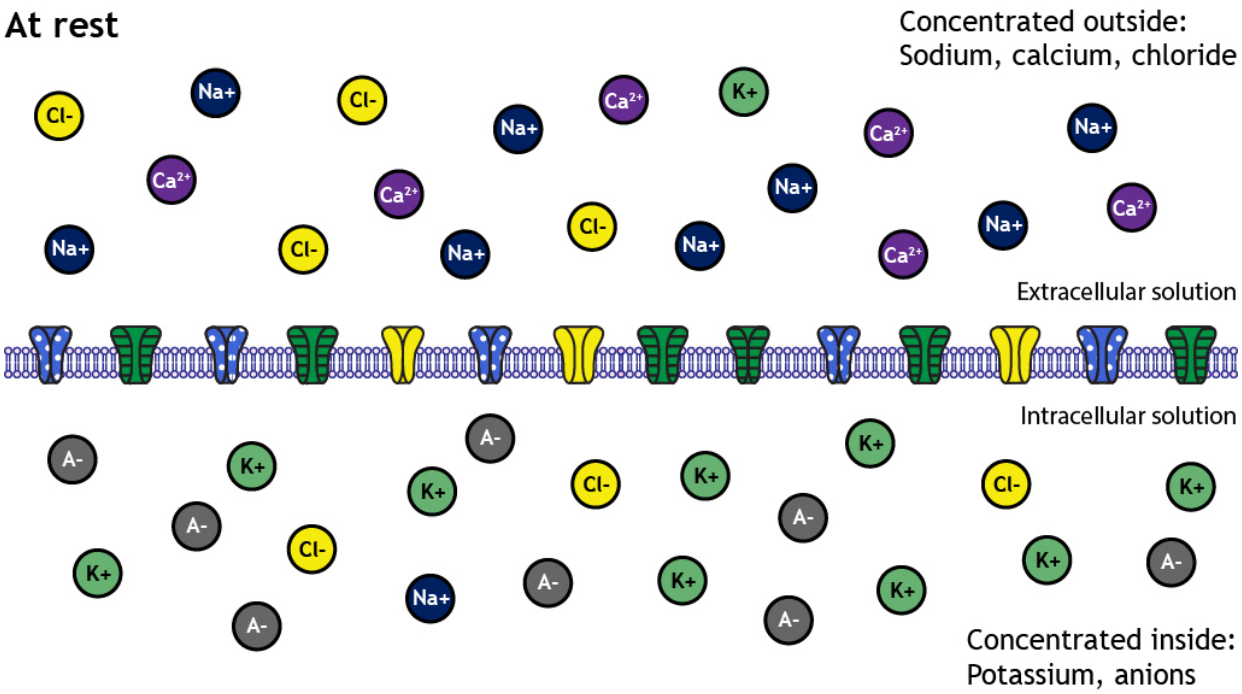

Figure 4.1. For a typical neuron at rest, sodium, chloride, and calcium are concentrated outside the cell, whereas potassium and other anions are concentrated inside. This ion distribution leads to a negative resting membrane potential. The dotted, blue channels represent sodium leak channels; the striped, 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.

Potassium has the highest permeability across the membrane at rest. Other ions, like chloride and sodium, have much lower permeability.

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.

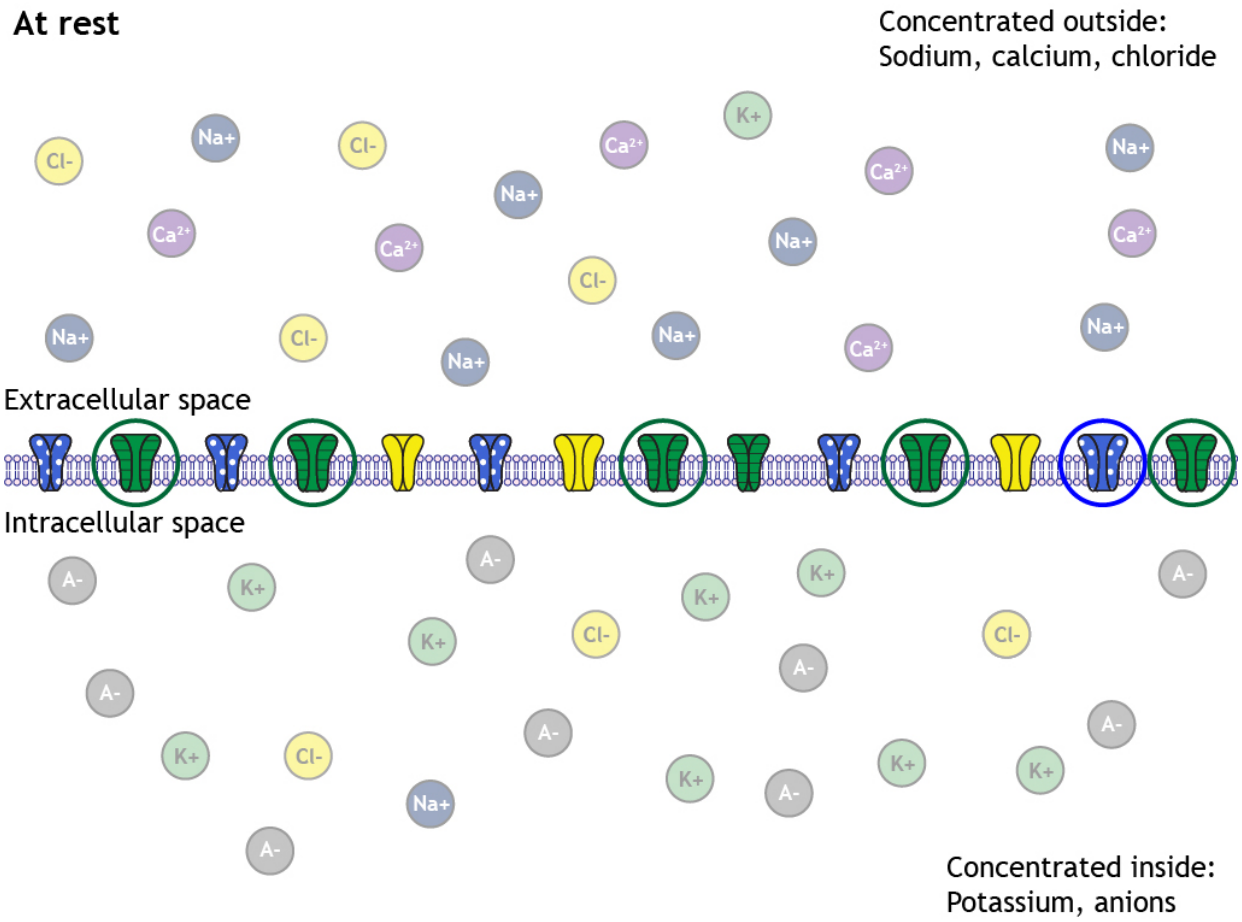

Figure 4.2. At rest, the distribution of ions across the membrane varies for different ions. Additionally, at rest, more potassium non-gated ion channels (emphasized by green circles) are open than sodium channels (emphasized by the blue circle). The dotted, blue channels represent sodium leak channels; 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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=92#video-92-1

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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=92#video-92-2

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.

The sodium-potassium pumps work to keep the ion concentrations stable even as ions cross the membrane at rest.

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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=92#video-92-3

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 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_{ion} is the relative permeability of each ion

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

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

Example: The Neuron at Rest

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

Ion	Inside concentration (mM)	Outside concentration (mM)	Relative permeability
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

- From memory, draw a diagram of a neuronal membrane at rest that includes the non-gated ion channels in their correct state (i.e., open, closed, inactivated).

Video Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=92#oembed-1

5.

POSTSYNAPTIC POTENTIALS

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 Lecture

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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=142#video-142-1

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.

Incoming signals can cause either an excitatory response or an inhibitory response in the neuron

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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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=142#video-142-2

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 not additional stimulation occurs.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=142#video-142-3

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

The direction of ion movement depends on the membrane potential of the cell

---

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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=142#video-142-4

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

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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=142#video-142-5

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. TThe 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

Postsynaptic potentials combine when more than one stimulus is present

---

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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=142#video-142-6

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 that when only on excitatory input occurs.

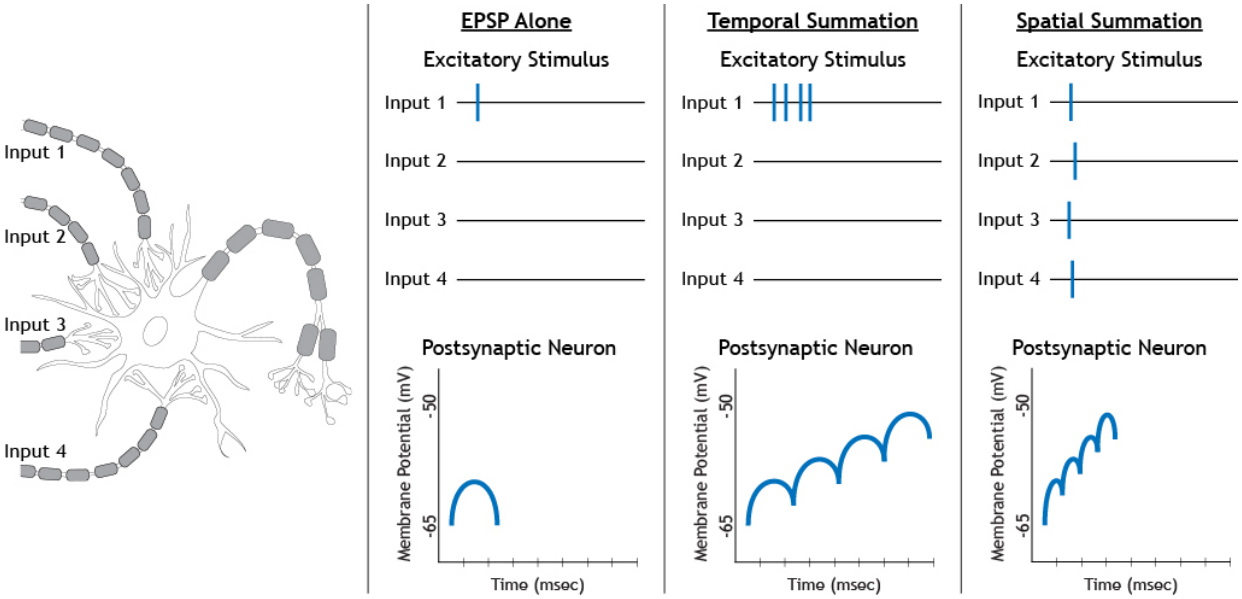

Figure 5.1 EPSPs can summate via temporal or spatial summation. Temporal summation occurs when a presynaptic neuron, Input 1 in the figure, stimulates the postsynaptic neuron multiple times in a row. Spatial summation occurs when more than one presynaptic neuron, Inputs 1 through 4 in the figure, each 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.

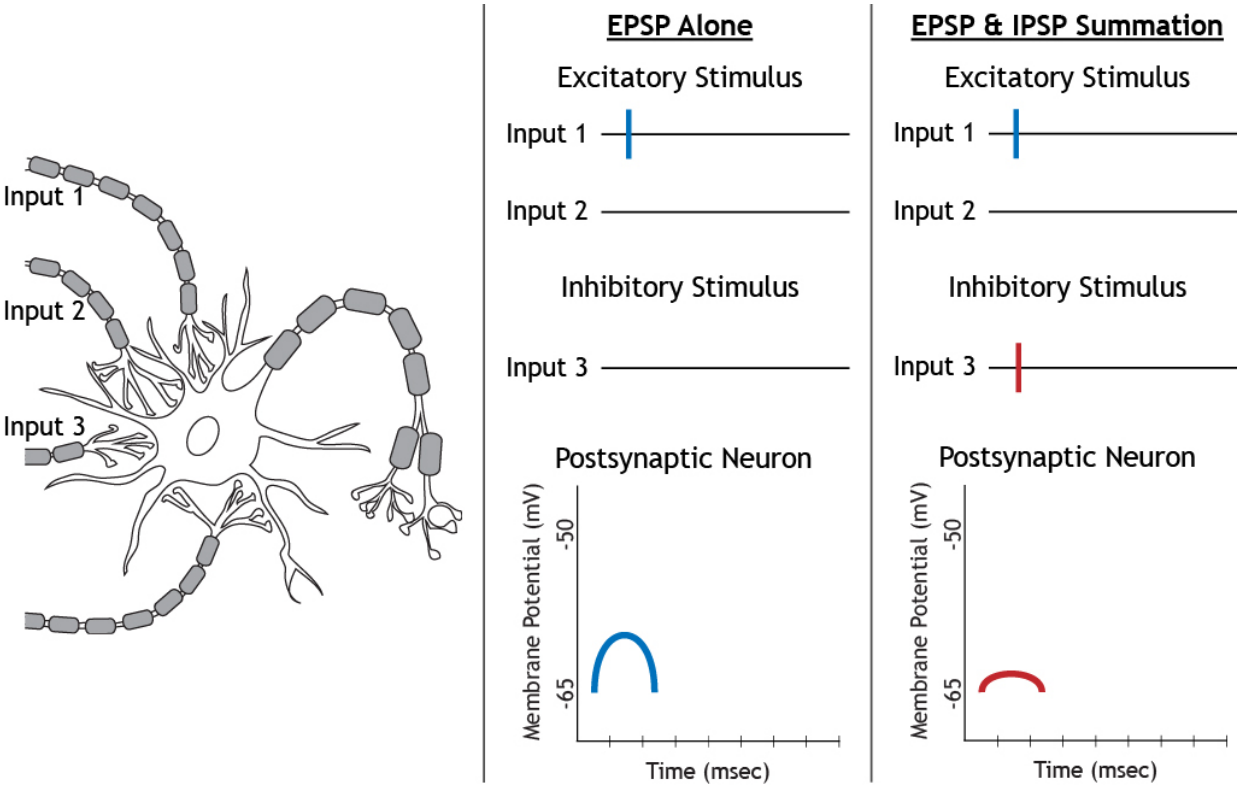

Figure 5.2. If an inhibitory input, Input 3 in the figure, stimulates the postsynaptic neuron at the same time as an excitatory input, Input 1 in the figure, the result is a decrease in the amount of depolarization or the complete prevention of depolarization, depending on the strength of the inhibitory 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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=142#video-142-7

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!

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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 Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=142#oembed-1

6.

ACTION POTENTIALS

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.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

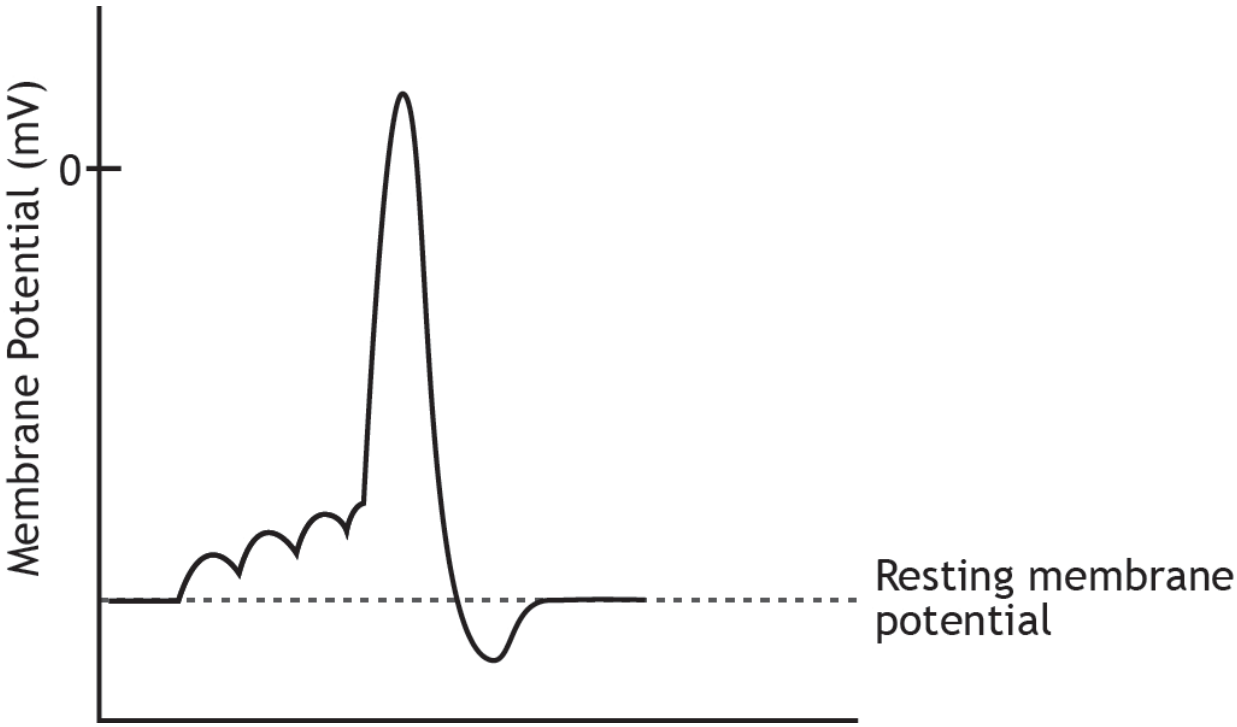

Figure 6.1. The action potential is a brief but significant change in electrical potential across the membrane. The membrane potential will begin at a negative resting membrane potential, will rapidly become positive, and then rapidly return to rest during an action potential. 'Action Potential' by Casey 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.

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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 in 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 of 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.

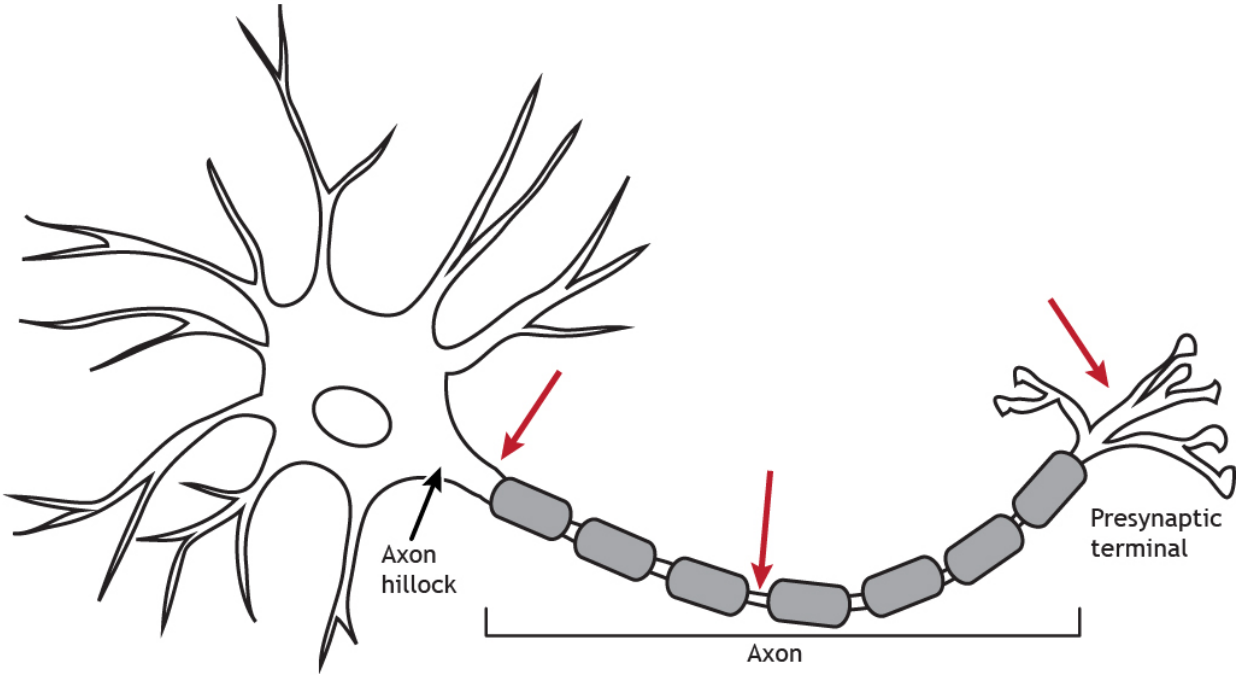

Figure 6.2. Voltage-gated channels critical for the propagation of the action potential are located at the axon hillock, down the axon at the Nodes of Ranvier, and in the presynaptic terminal. 'Voltage-Gated Channel Location' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial 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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=161#video-161-2

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 actions of the voltage-gated channels cause the different phases of the action potential

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The action potential begins when the cell's membrane potential reaches threshold, caused by the summation of EPSPs (Chapter 5). 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.

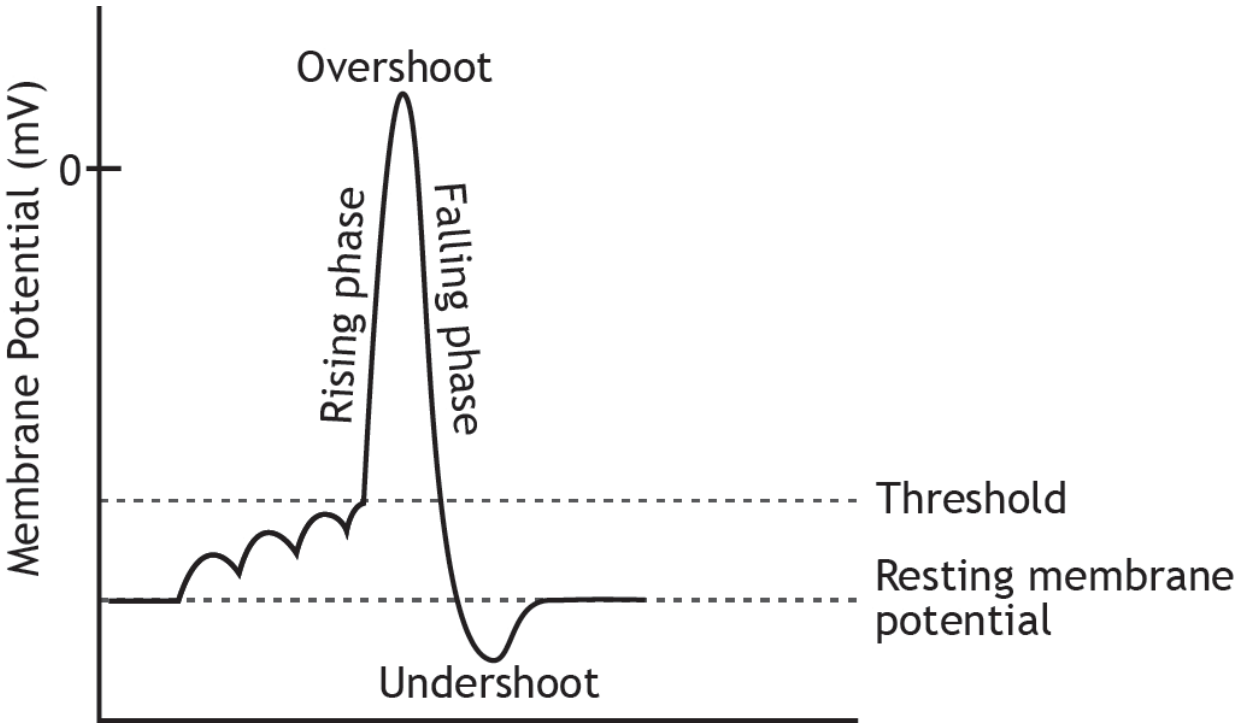

Figure 6.3. EPSPs that summate to reach threshold initiate the action potential. The depolarizing rising phase moves the membrane potential from threshold to above 0 mV. The overshoot is the peak of the action potential where the membrane potential is positive. The falling phase repolarizes the membrane 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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=161#video-161-4

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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=161#video-161-5

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 in the membrane will return the cell to its resting membrane potential, ready to fire another action potential.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=161#video-161-6

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.

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 additional 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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=161#video-161-7

Animation 6.7. 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.

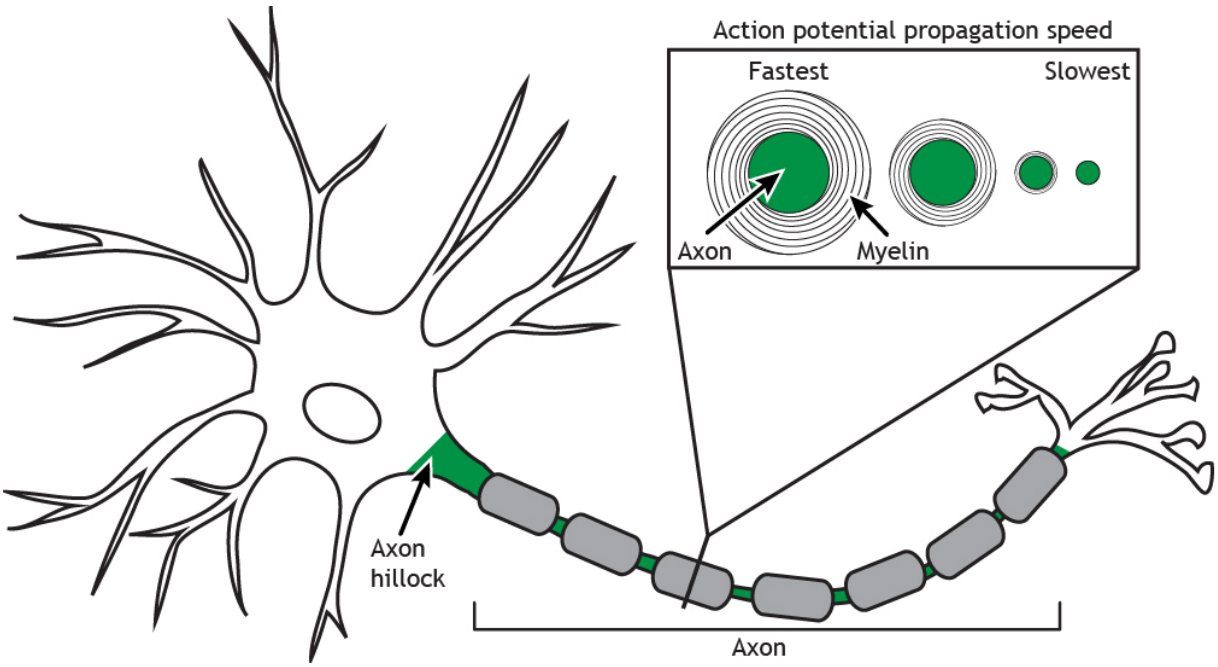

Figure 6.4. The diameter of the axon and the amount of myelination varies. Large diameter axons typically have thicker myelin sheath, which results in fast action potential speed. Small diameter axons may have no myelin present, resulting in slow action potential speed. 'Axon Diameter' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Direction of Propagation

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

> *One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=161#video-161-8*

Animation 6.8. 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.

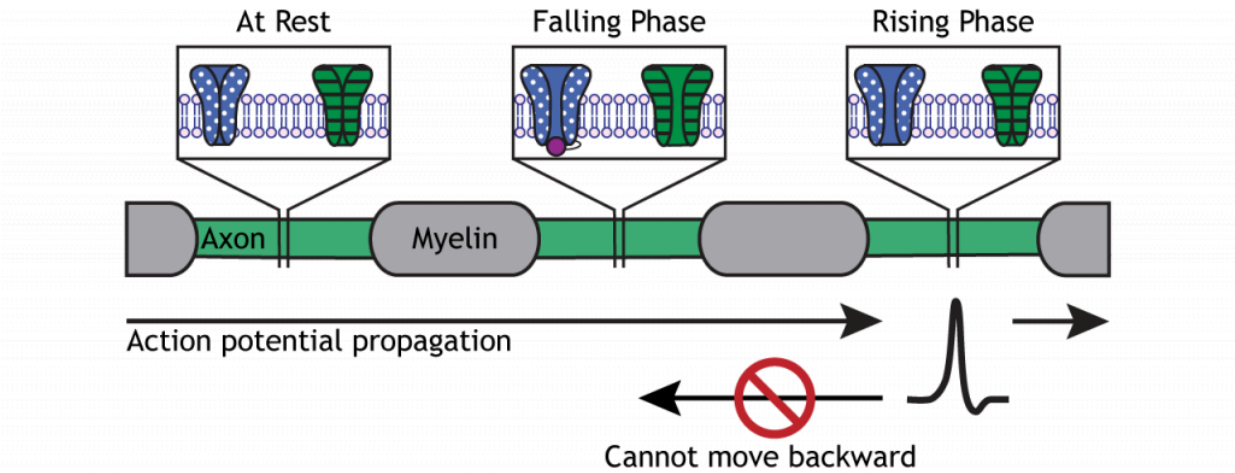

Figure 6.5. Action potentials only travel in one direction. The inactivated sodium channels prevent the action potential from moving backward down the axon. Blue dotted channels: sodium channels; green striped channels: potassium channels. The dotted, blue channels represent voltage-gated sodium channels; 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 Firing Rate

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.

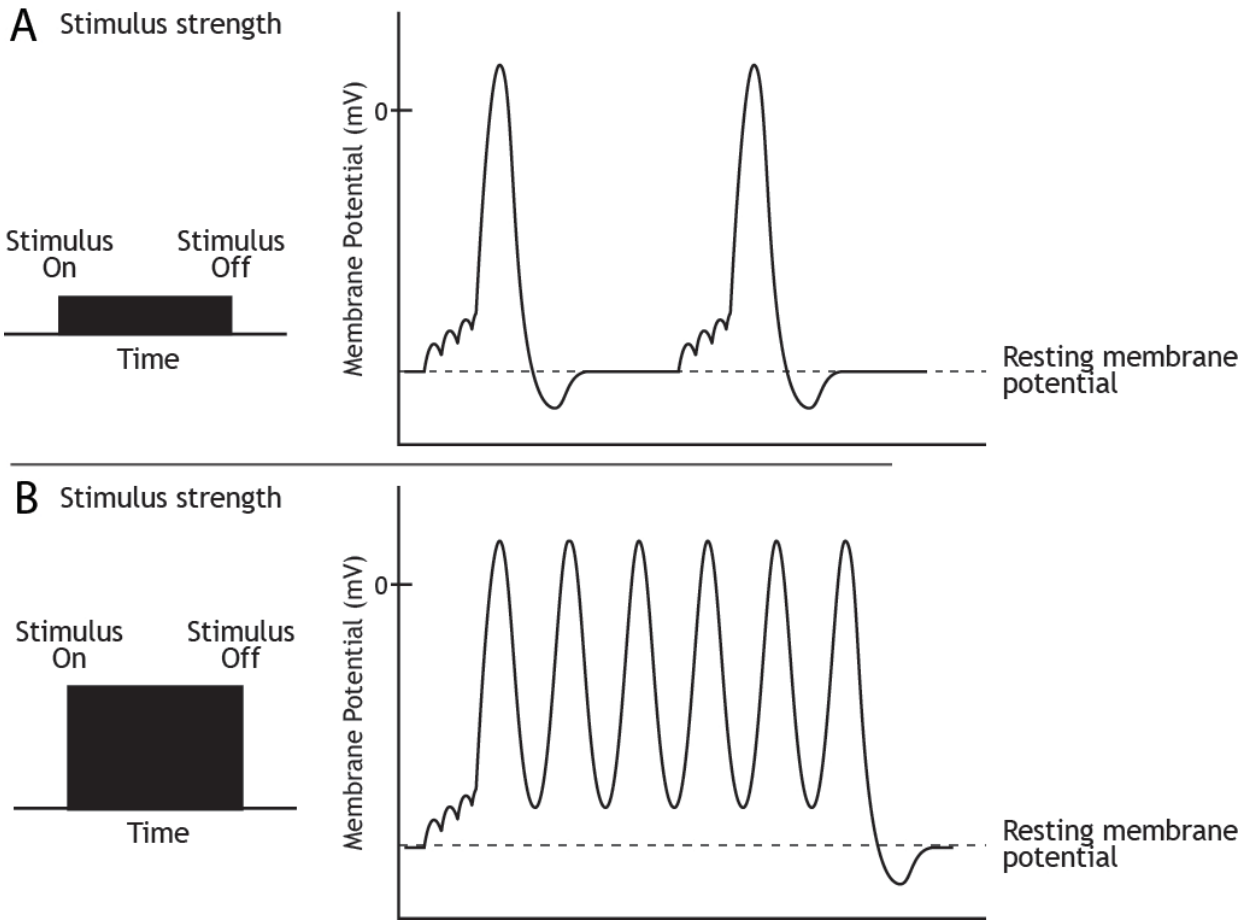

Figure 6.6. Information about the strength of a stimulus is encoded by the rate of action potential firing. A) A weak stimulus results in few action potentials being fired. B) A strong stimulus results in many action potentials firing in a row. 'Stimulus Strength' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

The Absolute Refractory Period

At some point, even if the stimulus continues to increase in strength, the neuron cannot fire at a higher frequency. This is the cell's maximum firing rate. 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). Therefore, the cell cannot fire faster than the time it takes to pass through the absolute refractory period.

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 undershot, 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.

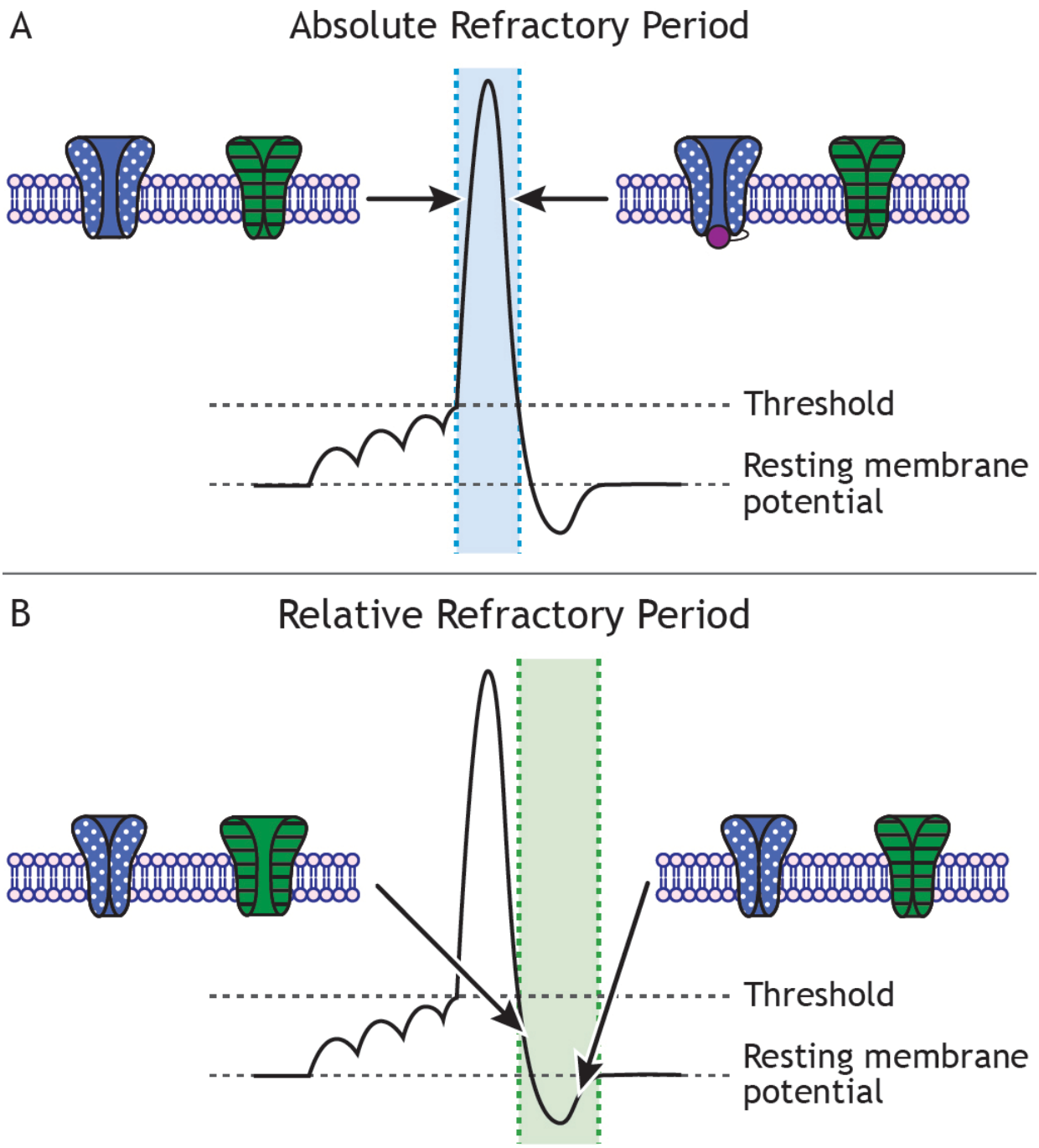

Figure 6.7. The maximum firing rate of a neuron is determined by the refractory periods. A) During the absolute refractory period no additional action potentials can be fired because the voltage-gated sodium channels are either already open (rising phase) or inactivated (falling phase). In these states, 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 open voltage-gated potassium channels cause a hyperpolarization of the membrane. After the potassium

channels close, it takes a short period of time for the membrane potential to return to rest. 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 Can Change

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.

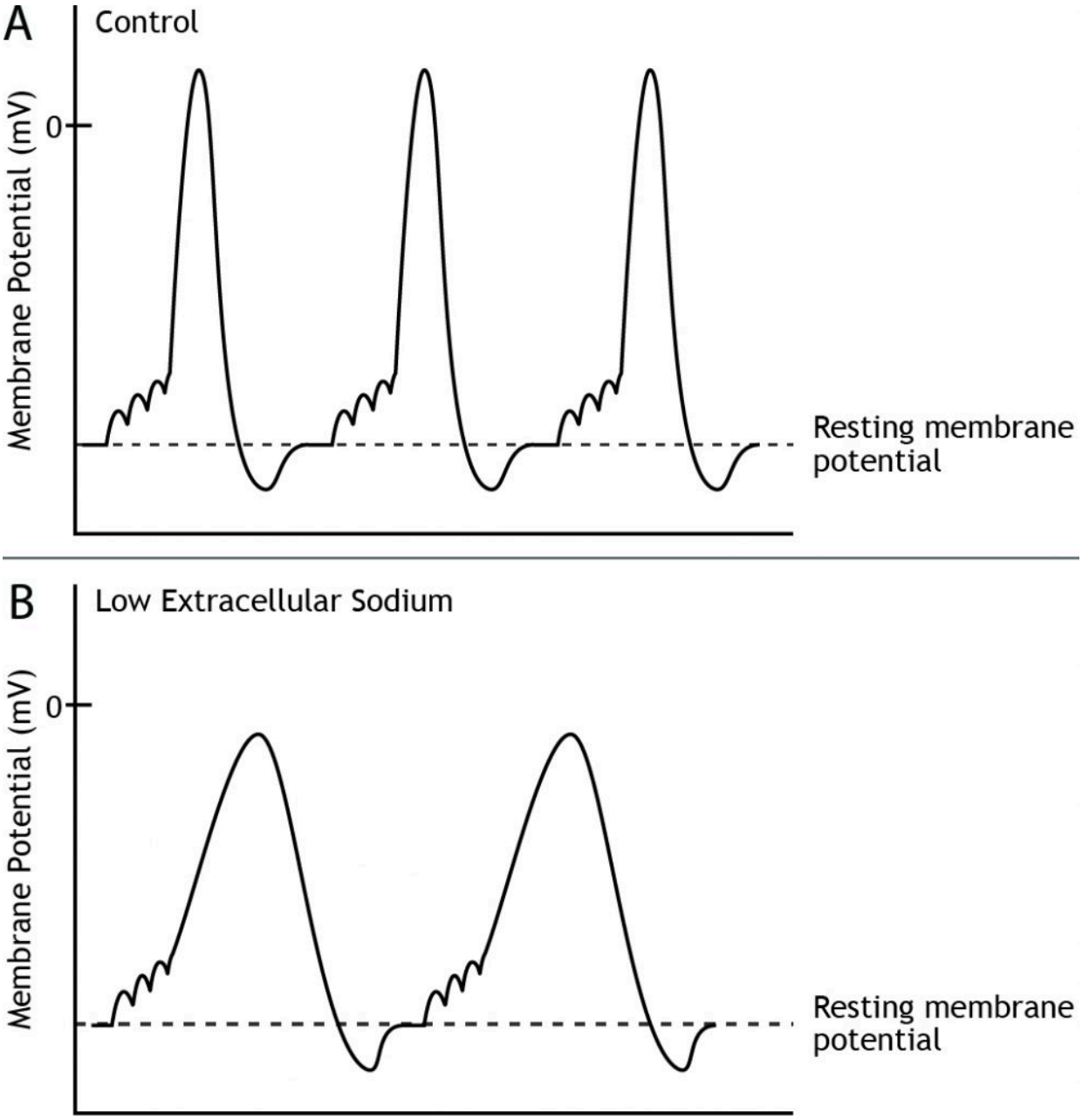

Figure 6.8. A) A neuron kept under the same conditions will display action potentials of similar height and length. B) However, if cellular conditions change, so will the action potential characteristics. If extracellular sodium levels are decreased compared to control levels, the action potential will 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.

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, but can change if extracellular conditions change
- Speed of propagation relies on presence and thickness of myelin and diameter of axon
- Action potential travel in one direction due to the presence of inactivated voltage-gated sodium channels
- Stimulus strength is coded by frequency of action potential firing
- 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

Test Yourself!

Try the quiz more than once to get different questions!

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

- From memory, draw an action potential diagram, label each phase, identify the change in membrane potential (depolarization, repolarization, and hyperpolarization), and label threshold.
- From memory and for each phase of the action potential, draw a diagram of a neuronal membrane that includes the voltage-gated ion channels in their correct state (i.e., open, closed, inactivated).
- Compare and contrast non-gated (leak) channels and voltage-gated channels.

Video Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=161#oembed-1

7.

VOLTAGE CLAMP

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

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.

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.

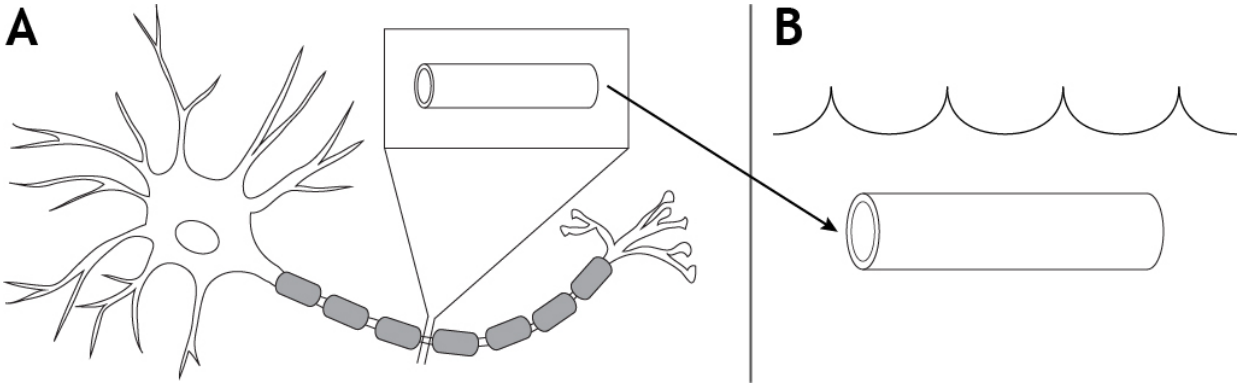

Figure 7.1. To conduct a voltage clamp experiment, a portion of the axon is removed from the neuron. The axon is placed in a special solution that is similar to physiological extracellular solution. '*In Vitro* Axon' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (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.

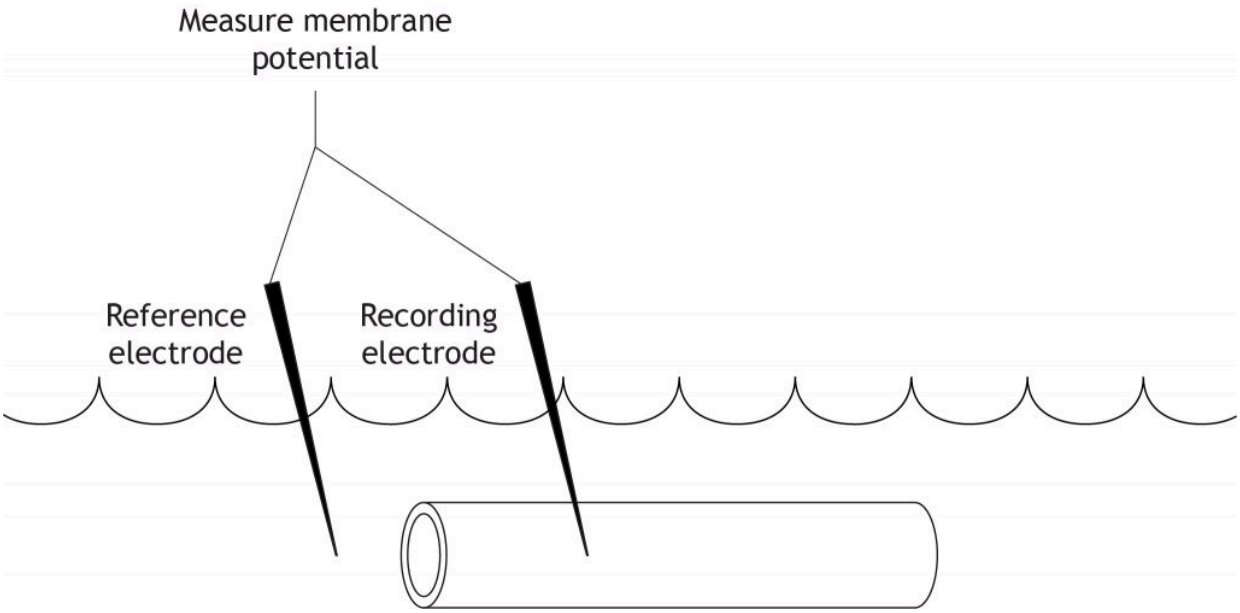

Figure 7.2. Measuring the membrane potential of the axon segment is the first step in the voltage-clamp experiment. The membrane potential is the difference in voltage between the intracellular recording electrode and the extracellular reference electrode. 'Measure Membrane Potential' by Casey Henley 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.

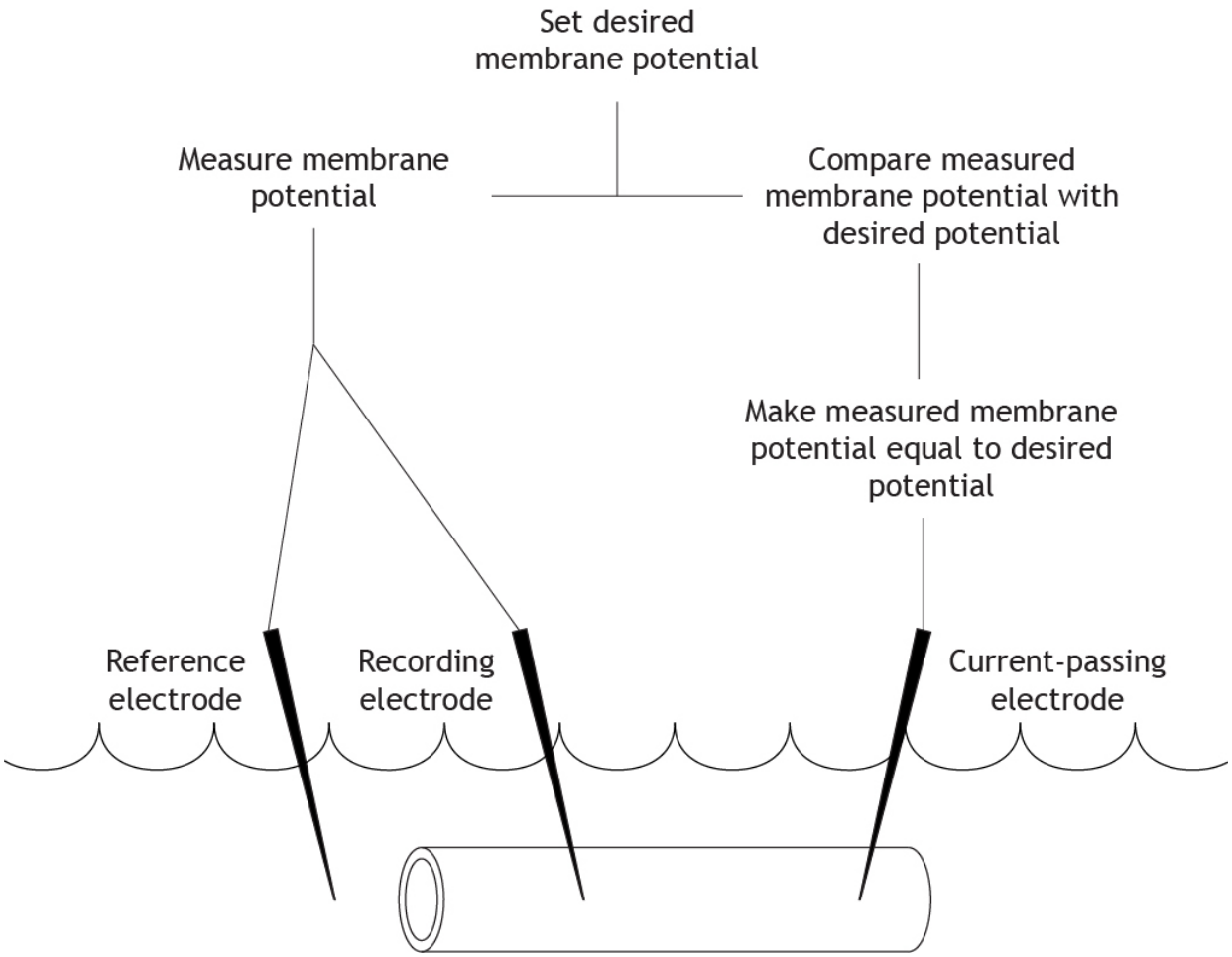

Figure 7.3. A desired membrane potential is set for the experiment. The voltage-clamp experimental equipment then compares the measured membrane potential with the desired potential. Current is then injected into the axon through a current-passing electrode to make the measured membrane potential equal 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.

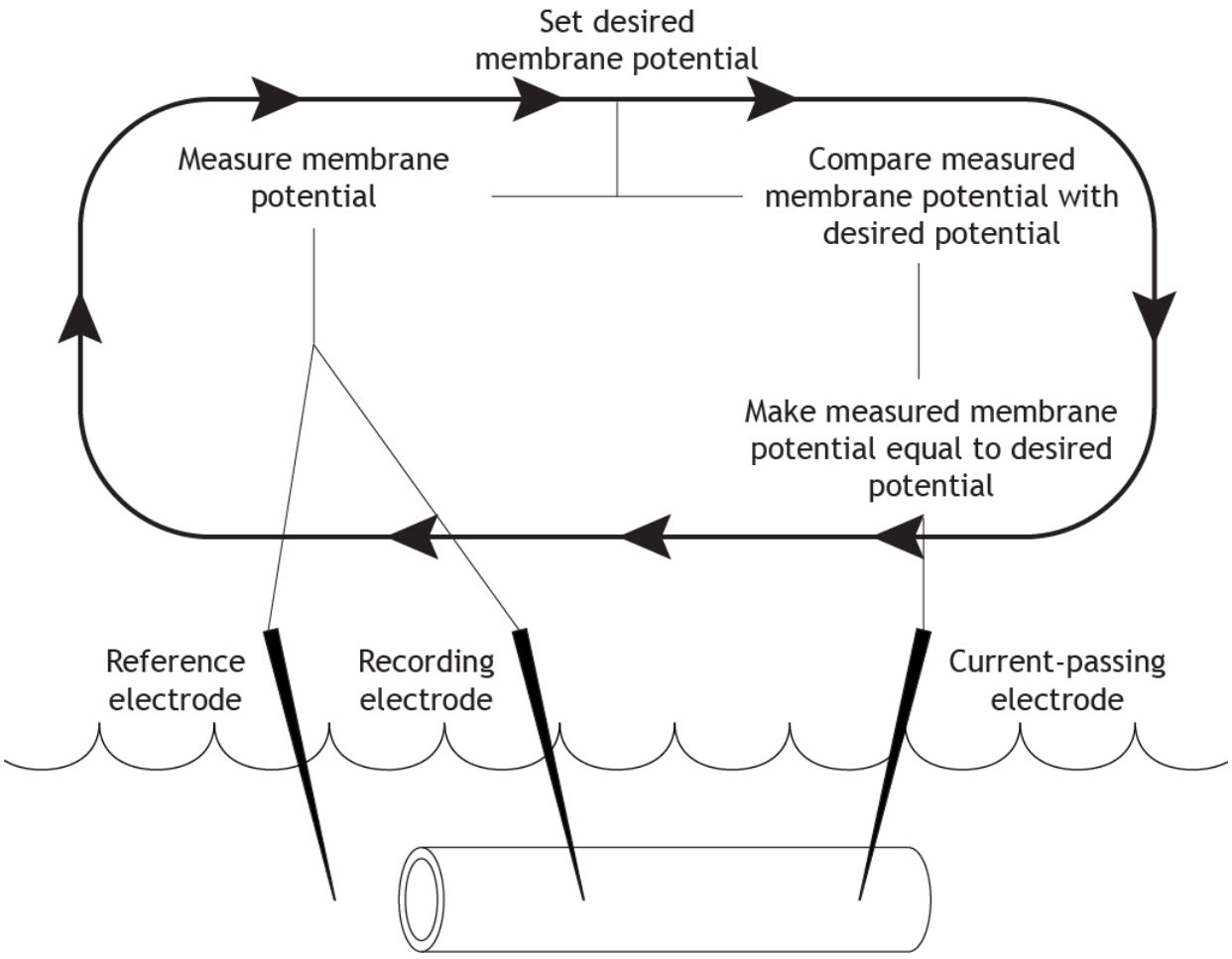

Figure 7.4. The voltage clamp cycle repeats continuously. The actual membrane potential of the axon is measured, compared to the set desired potential value, and then current is passed into the axon to keep the actual membrane potential equal to the desired potential. 'Voltage Clamp Cycle' by Casey Henley 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.

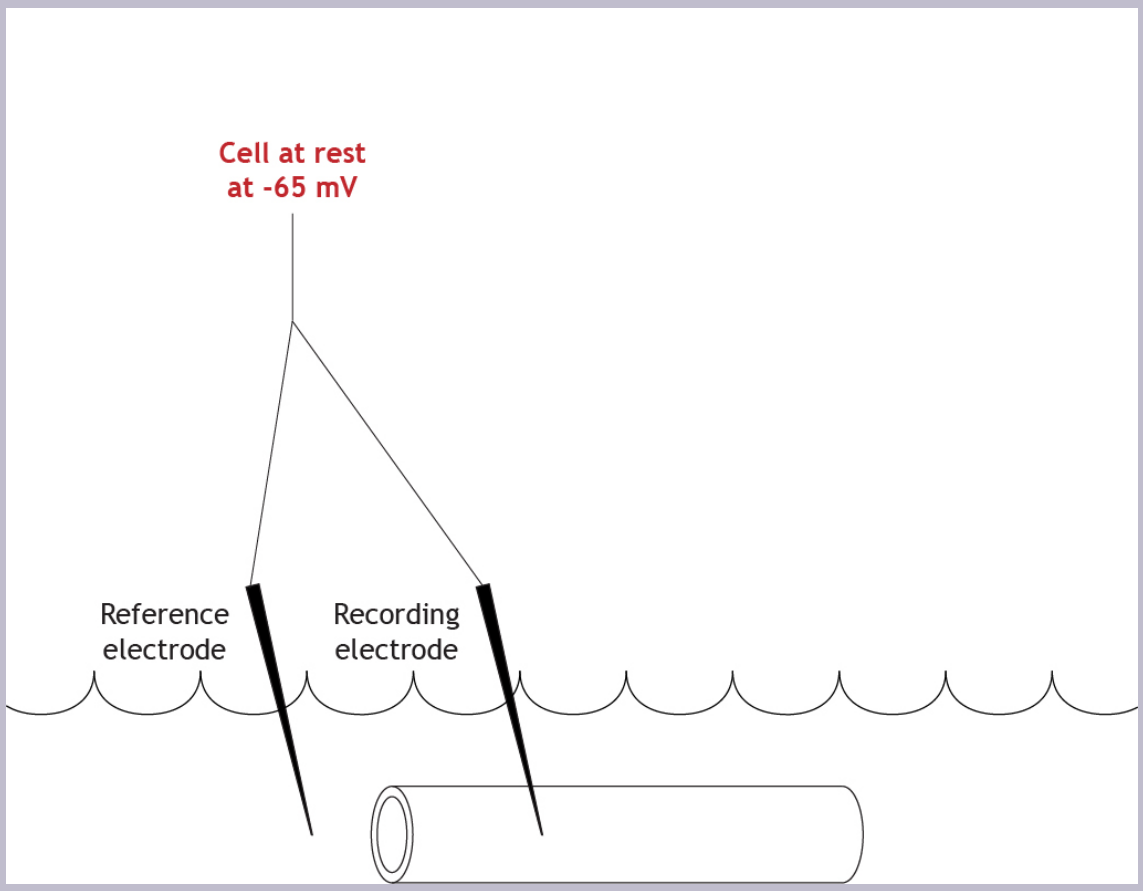

Figure 7.5. Measure the membrane potential. The membrane potential of this axon at rest is -65 mV. 'Voltage Clamp Example at Rest' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Set Clamped Membrane Potential Value

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

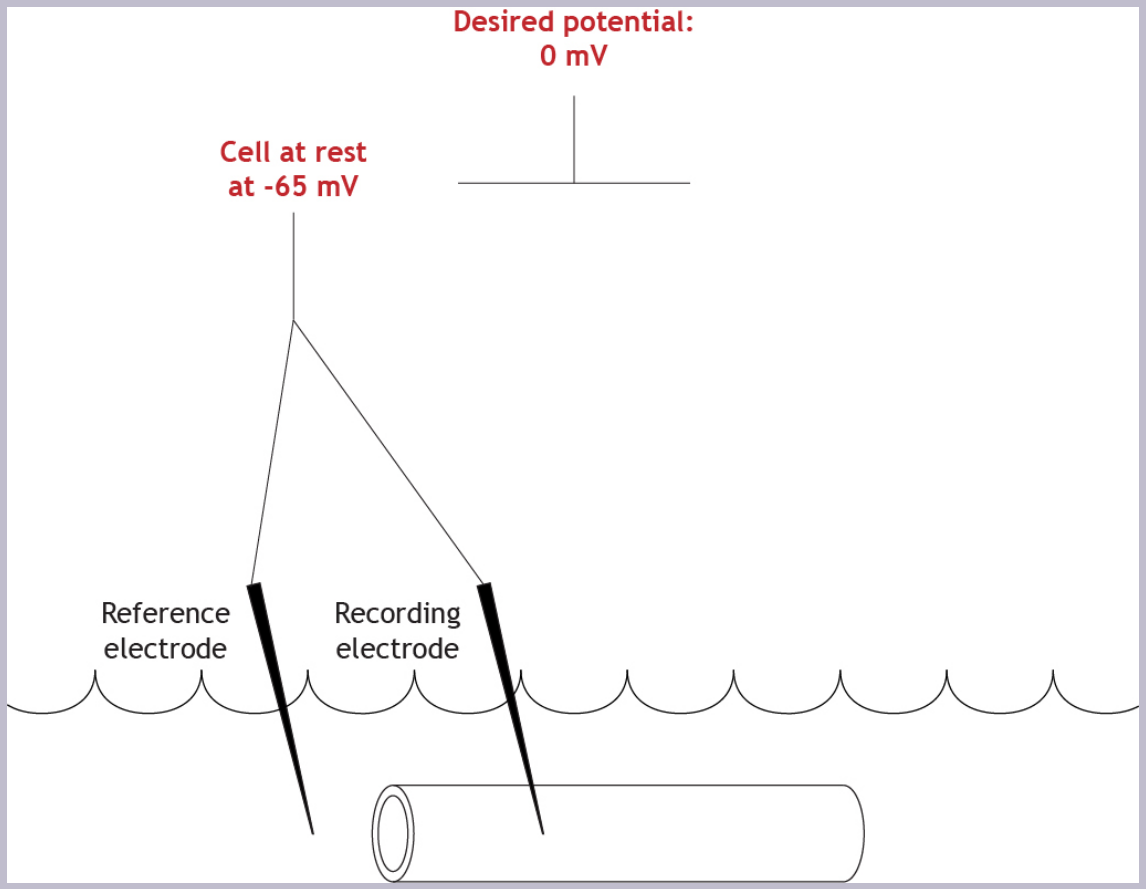

Figure 7.6. Set desired membrane potential. The set value for this experiment is 0 mV. 'Voltage Clamp Example Set Value' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

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.

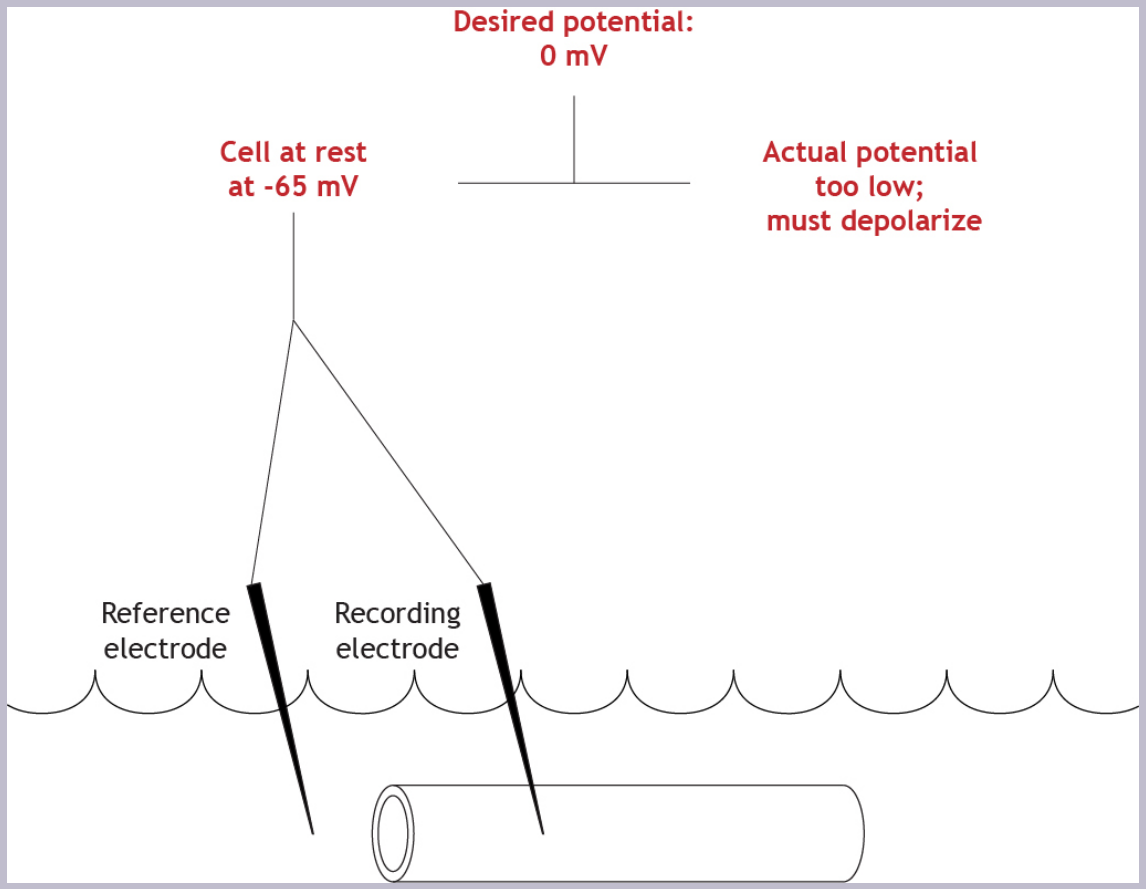

Figure 7.7. Compare measured membrane potential to desired potential. The actual membrane potential of the axon is at -65 mV, so the cell needs to be depolarized to reach the desired potential of 0 mV. 'Voltage Clamp Example Comparison' by Casey Henley is licensed under a Creative Commons Attribution 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.

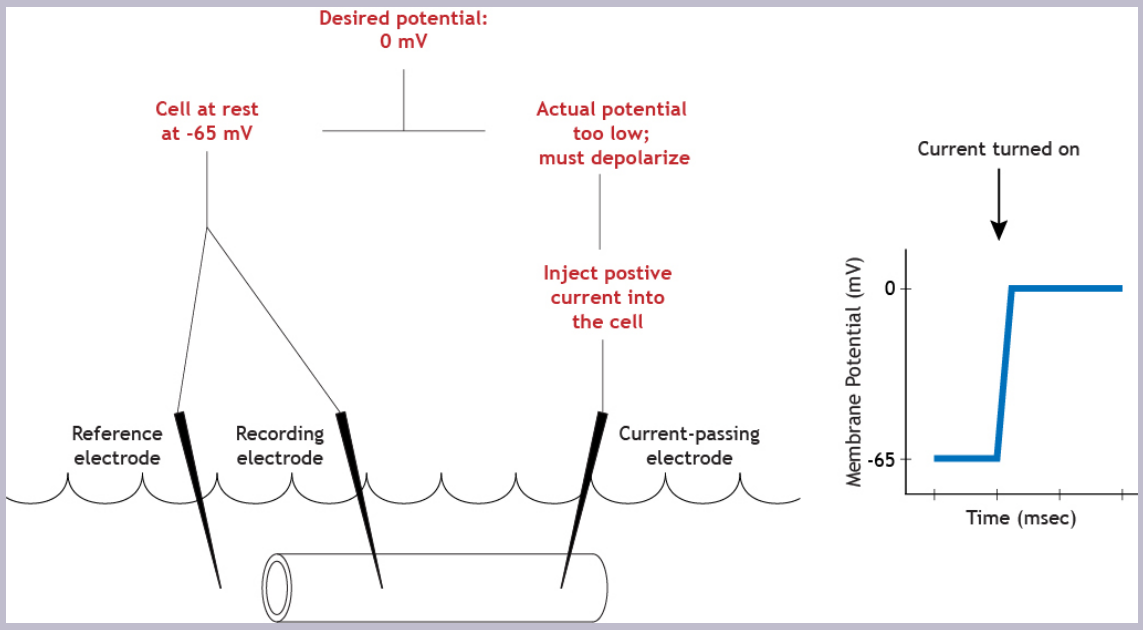

Figure 7.8. Correct actual membrane potential. To depolarize this axon from rest at -65 mV to the desired clamp value of 0 mV, positive current will be injected into the cell. The membrane potential will then depolarize to 0 mV and remain there. 'Voltage Clamp Example Current' by Casey Henley is licensed 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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=193#video-193-1

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.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=193#video-193-2

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 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.

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!

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=193#h5p-7

Video Lecture

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PART II
NEURONAL COMMUNICATION

8.

SYNAPSE STRUCTURE

For the nervous system to function, neurons must be able to communicate with each other, and they do this through structures called synapses. At the synapse, the terminal of a presynaptic cell comes into close contact with the cell membrane of a postsynaptic neuron.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

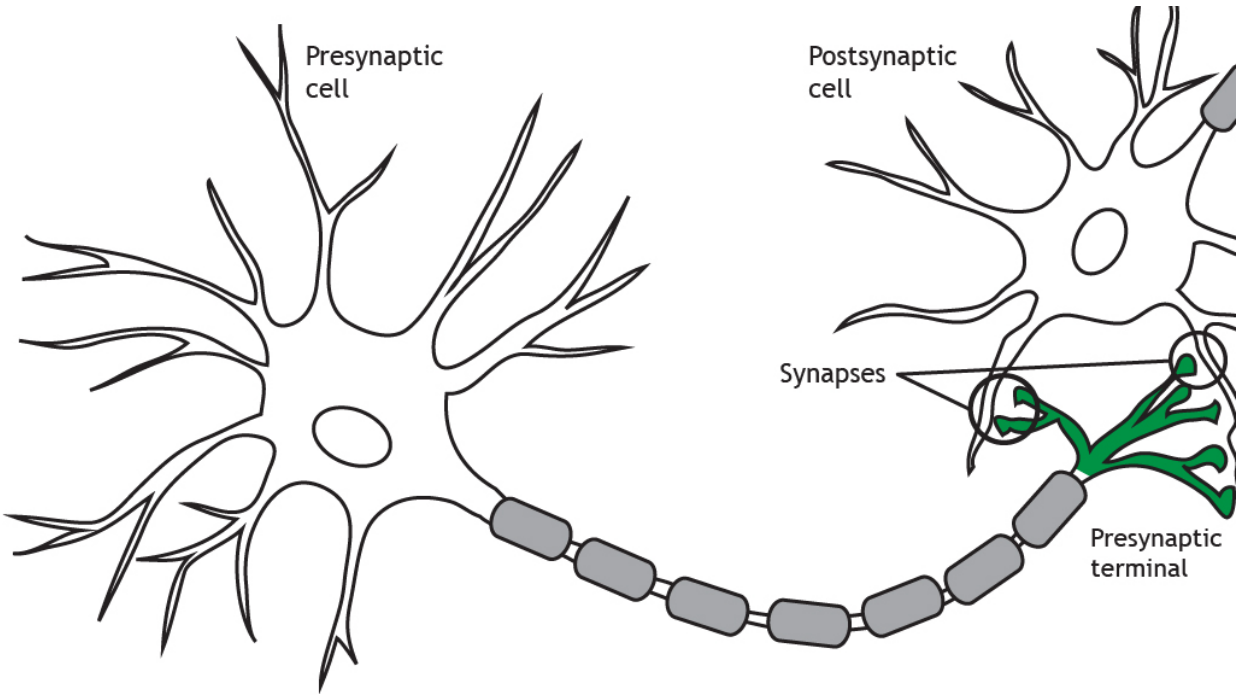

Figure 8.1. The terminal of a presynaptic neuron comes into close contact with a postsynaptic cell at the synapse. 'Synapse' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Synapse Types

There are two types of synapses: electrical and chemical.

Electrical

Electrical synapses outnumber chemical synapses in the developing nervous system

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Electrical synapses are a physical connection between two neurons. Cell membrane proteins called connexons form gap junctions between the neurons. The gap junctions form pores that allow ions to

flow between neurons, so as an action potential propagates in the presynaptic neuron, the influx of sodium can move directly into the postsynaptic neuron and depolarize the cell. The response in the postsynaptic cell is almost immediate, with little to no delay between signaling in the pre- and postsynaptic neurons. Electrical synapses play an important role in the development of the nervous system but are also present throughout the developed nervous system, although in much smaller numbers that chemical synapses.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=307#video-307-1

Animation 8.1. Membrane-bound proteins called connexons form gap junctions between presynaptic and postsynaptic neurons. This allows for direct exchange of ions between neurons. An action potential in the presynaptic neuron will cause an immediate depolarization of the postsynaptic membrane because the sodium ions will cross the membrane through the gap junctions. 'Electrical Synapse – 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.

Since the gap junctions allow diffusion of ions without any obstruction, the signal can flow bidirectionally through an electrical synapse. The electrochemical gradients will drive direction of ion flow.

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Animation 8.2. Since an electrical synapse is a direct, physical connection between two neurons, ions are able to flow either direction across the gap junction. 'Bidirectional Electrical Synapse' 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.

Additionally, small molecules like ATP or second messengers can also move through the gap junctions. These signaling molecules play an important role in cellular mechanisms, which we will see in a later chapter.

> *One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=307#video-307-3*

Animation 8.3. Gap junctions are large enough to allow the flow of small cellular molecules like ATP or second messengers. 'Electrical Synapse – Small Molecules' 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.

Chemical

Chemical synapses outnumber electrical synapses in the fully developed nervous system

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Chemical synapses are the primary synapse type in the developed nervous system and do not form physical connections between the pre- and postsynaptic neurons. Instead, a space called the synaptic cleft exists between the presynaptic terminal and the postsynaptic membrane.

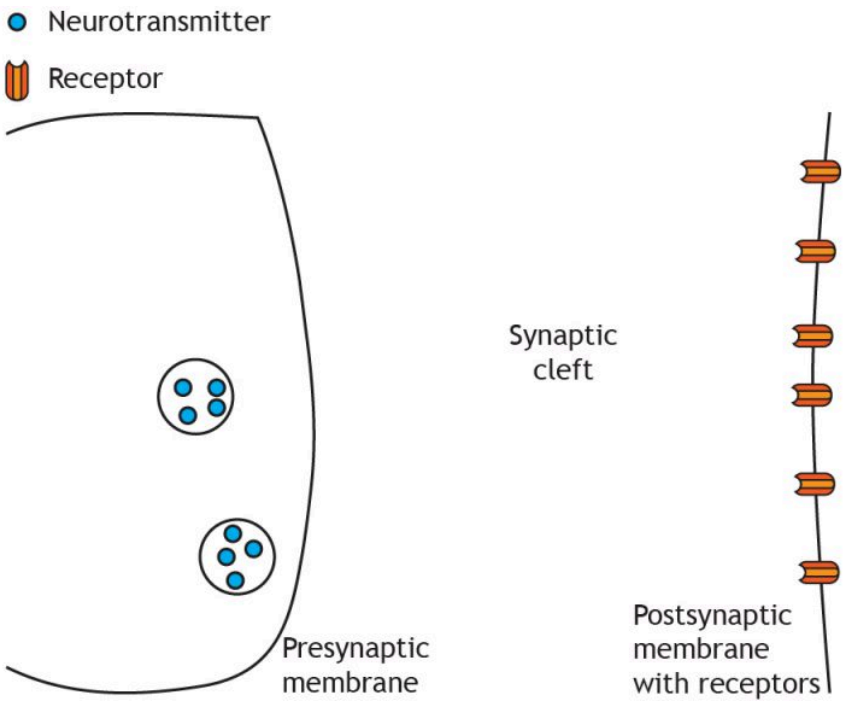

Figure 8.2. A chemical synapse does not make direct contact between the two neurons. The presynaptic terminal and the postsynaptic membrane are separated by the synaptic cleft. Neurotransmitters are stored in the presynaptic cell, and the postsynaptic cell has neurotransmitter receptors in the membrane. 'Chemical Synapse' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

At a chemical synapse, the depolarization of an action potential reaching the presynaptic terminal causes release of neurotransmitters, which act on specialized receptors located in the cell membrane of the postsynaptic neuron. The structure and function of chemical synapses make them slower than electrical synapses and permit signaling in only one direction.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=307#video-307-4

Animation 8.4. An action potential causes release of neurotransmitters from the presynaptic terminal into the synaptic cleft. The transmitters then act on neurotransmitter receptors in the postsynaptic

membrane. 'Chemical Synapse – Neurotransmitter Release' 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.

Synapse Location

As we discuss synaptic transmission, we will focus mainly on axodendritic synapses, in which the presynaptic terminal synapses on the dendrites of the postsynaptic cell. But synapses can also be located between the terminal and the cell body of the postsynaptic cell, called axosomatic, or even between the terminal and the axon of the postsynaptic cell, called axoaxonic.

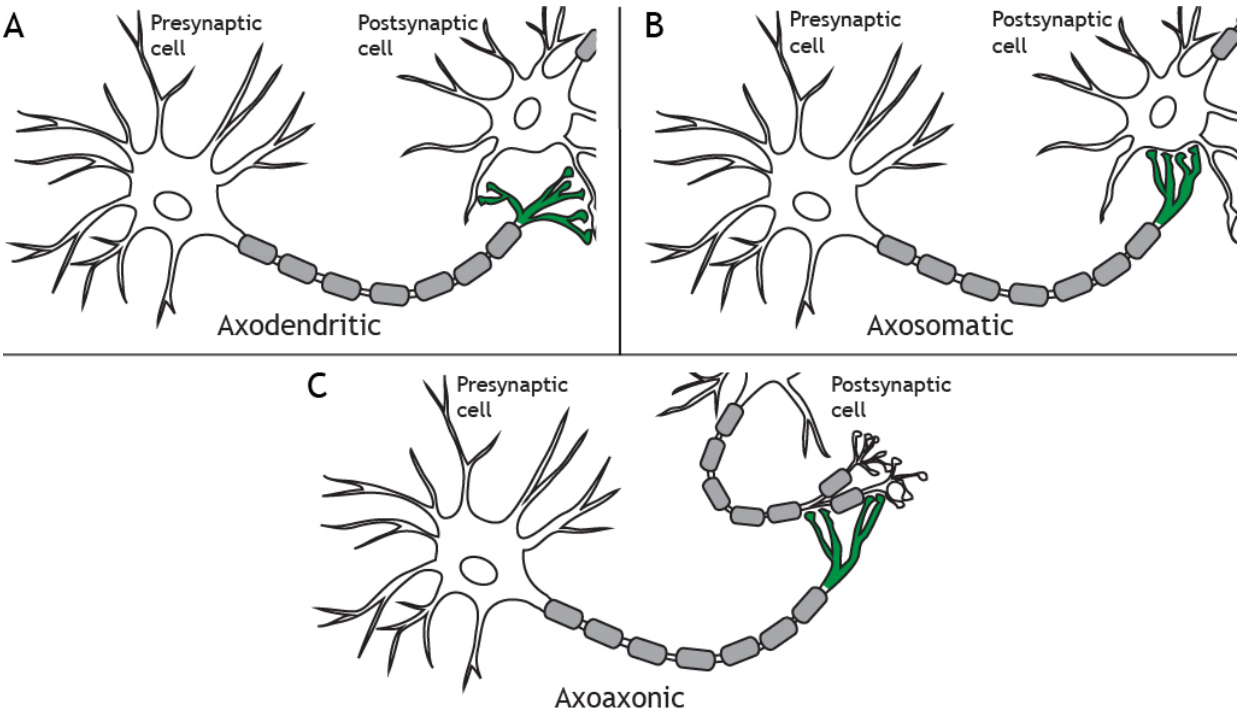

Figure 8.3. A) Axodendritic synapses occur when the presynaptic terminal makes a synaptic connection with the dendrite of a postsynaptic neuron. B) Axosomatic synapses occur when the presynaptic terminal makes a synaptic connection with the cell body of a postsynaptic neuron. C) Axoaxonic synapses occur when the presynaptic terminal makes a synaptic connection with the axon of a postsynaptic neuron. 'Chemical Synapse 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

- Electrical synapses make direct contact between neurons, are faster than chemical synapses, and can be bidirectional
- Chemical synapses form a synaptic cleft between the neurons and are unidirectional
- Synapses can occur between the presynaptic terminal and the postsynaptic dendrites (axodendritic), cell body (axosomatic), or axon (axoaxonic)

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=307#h5p-8

Video Lecture

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9.

NEUROTRANSMITTER SYNTHESIS AND STORAGE

A few criteria must be met for a molecule to be called a neurotransmitter. First, the transmitter must be synthesized within in the presynaptic neuron. Second, the transmitter must be released by the presynaptic neuron in response to stimulation. Third, when a postsynaptic neuron is treated with the transmitter by a researcher, the molecule must cause the same effect in the postsynaptic neuron as when it is released by a presynaptic neuron.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

There are two main categories of neurotransmitters: small molecule transmitters and peptide transmitters. Synthesis and storage of these neurotransmitter groups differ. Small molecule neurotransmitters are synthesized and stored in the terminal for fast release. Neuropeptides are synthesized in the cell body and must be transported to the terminal, which can lead to slower release. Additionally, a neuron typically will synthesize and release only one type of small molecule neurotransmitter but can synthesize and release more than one neuropeptide.

Small Molecule Transmitters

Small molecule transmitters are synthesized in the synaptic terminal

The small molecule transmitters can be divided into two main groups: amino acid neurotransmitters and biogenic amines, also called monoamines. In addition to acting as neurotransmitters, the amino acids glutamate and glycine are used to synthesize proteins in all cell types throughout the body. GABA (γ-Aminobutyric acid) is a metabolite of glutamate but is not used in protein synthesis in the body. The biogenic amines include serotonin and histamine, and the subgroup the catecholamines dopamine, norepinephrine, and epinephrine. Acetylcholine does not fit into either division but is still considered a small molecule neurotransmitter.

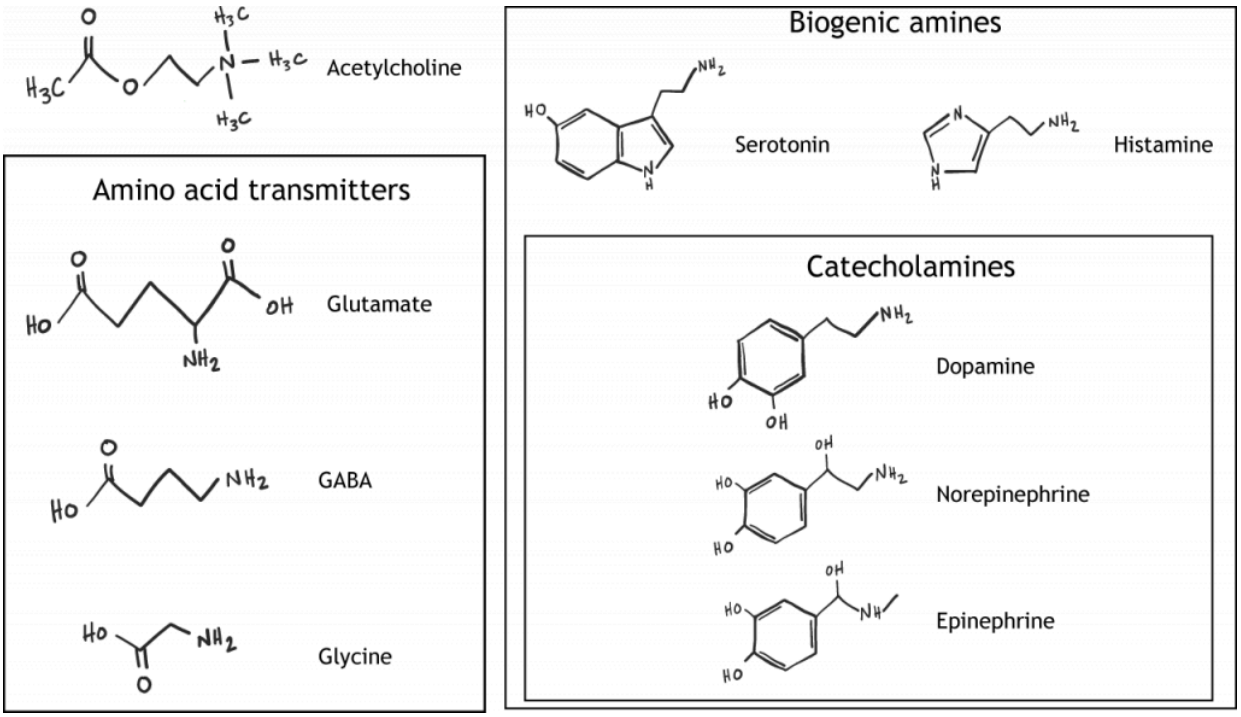

Figure 9.1. Small molecule neurotransmitters can be subdivided into groups based on chemical structure. Amino acid transmitters include glutamate, GABA, and glycine. The biogenic amines include serotonin and histamine, and the catecholamines, a subgroup of the biogenic amines, include dopamine, norepinephrine, and epinephrine. Acetylcholine does not fit into a group. 'Small Molecule Neurotransmitters' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Synthesis and Storage of Small Molecule Transmitters

Most small molecule neurotransmitters are synthesized by enzymes that are located in the cytoplasm (the exception is norepinephrine, see below). This means that small molecule neurotransmitters can

be synthesized and packaged for storage in the presynaptic terminal using enzymes present in the terminal.

Acetylcholine

Acetylcholine is best known for its role at the neuromuscular junction, the synapse between a motor neuron and the muscle fiber. In the presynaptic terminal, acetylcholine is synthesized from acetyl coenzyme A (acetyl CoA) and choline via the enzyme choline acetyltransferase. The level of enzyme activity is the rate-limiting step in the synthesis pathway. Acetylcholine is packaged into vesicles for storage in the terminal via the vesicular acetylcholine transporter (VAChT).

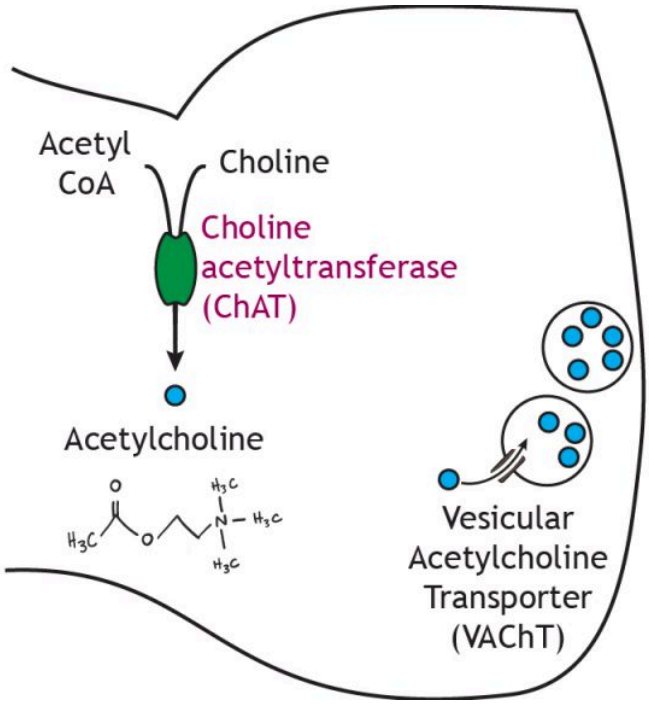

Figure 9.2. Acetylcholine is synthesized from acetyl CoA and choline by choline acetyltransferase, the rate-limiting step in the pathway. Acetylcholine is then packaged into vesicles by vesicular acetylcholine transporter. 'Acetylcholine Synthesis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Glutamate

Glutamate is an amino acid transmitter and is the primary excitatory neurotransmitter in the brain. In

the presynaptic terminal, glutamine is converted into glutamate via the enzyme glutaminase, which is the rate-limiting step in the synthesis pathway. Glutamate is packaged into vesicles for storage via the vesicular glutamate transporter.

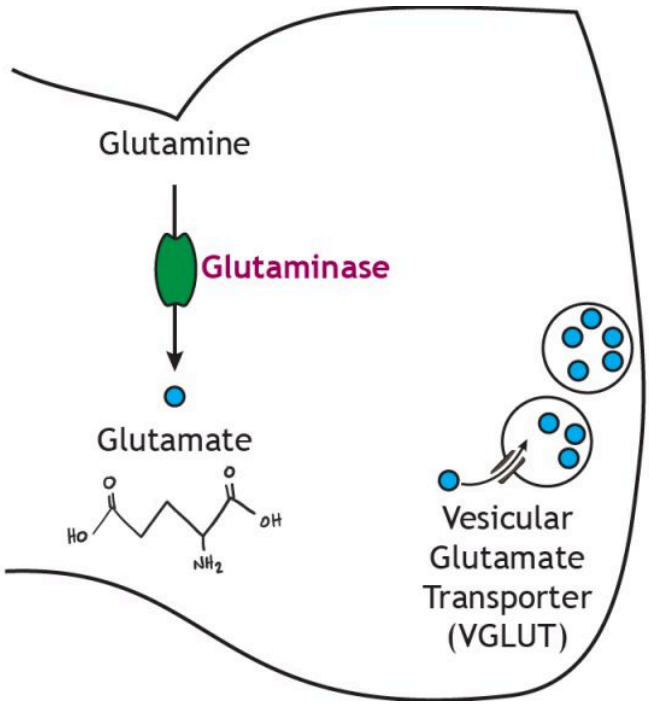

Figure 9.3. Glutamate is synthesized from glutamine by glutaminase, the rate-limiting step in the pathway. Glutamate is then packaged into vesicles by vesicular glutamate transporter. 'Glutamate Synthesis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

GABA

Glutamate is then used to synthesize GABA, another amino acid transmitter and the primary inhibitory neurotransmitter in the brain. In the presynaptic terminal, glutamate is converted into GABA via the enzyme glutamic acid decarboxylase, which like the other synthesis pathways is the rate-limiting step. GABA is packaged into vesicles for storage in the terminal via the vesicular inhibitory amino acid transporter.

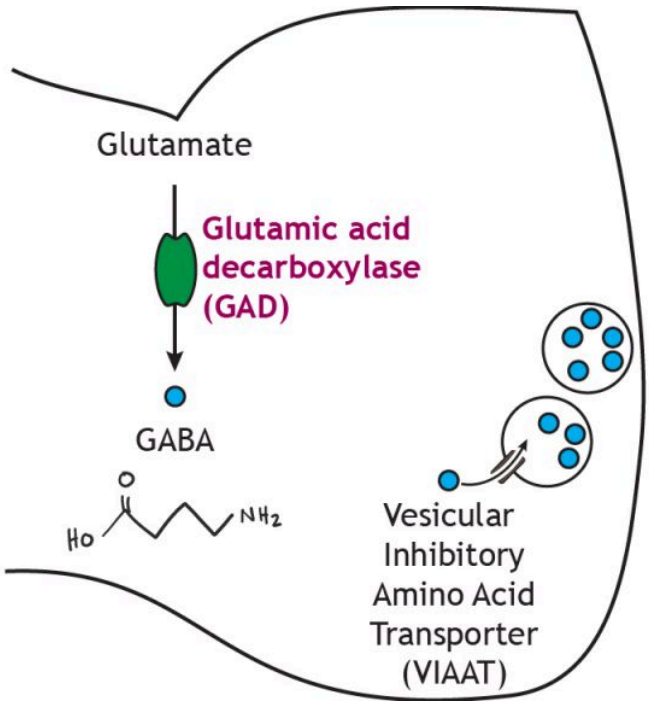

Figure 9.4. GABA is synthesized from glutamate by glutamic acid decarboxylase, the rate-limiting step in the pathway. GABA is then packaged into vesicles by vesicular inhibitory amino acid transporter. 'GABA Synthesis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Glycine

Glycine is another inhibitory amino acid neurotransmitter, but unlike GABA, it is more common in the spinal cord than in the brain. Serine hydroxymethyltransferase converts the amino acid serine into glycine in the presynaptic terminal. The rate limiting step for glycine synthesis occurs earlier in the pathway prior to serine synthesis. Glycine is packaged into vesicles by the vesicular inhibitory amino acid transporter like GABA.

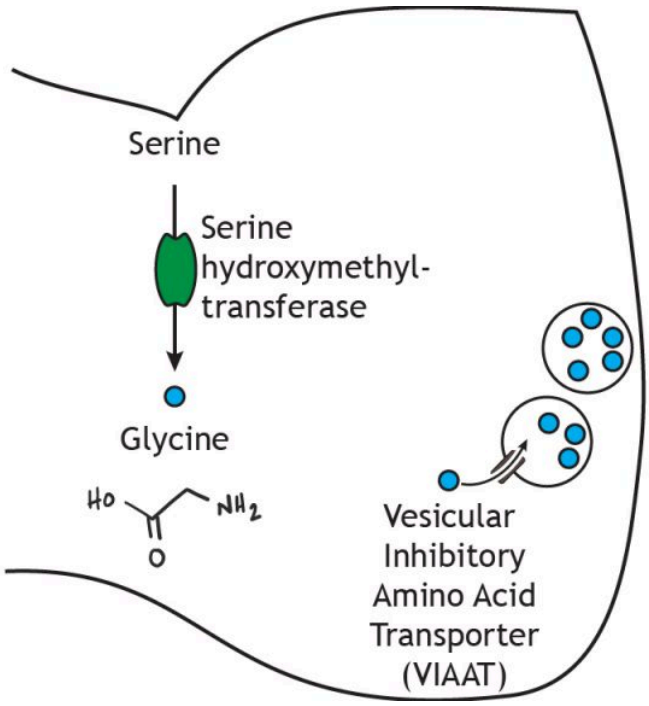

Figure 9.5. Glycine is synthesized from serine by serine hydroxymethyltransferase. Glycine is then packaged into vesicles by vesicular inhibitory amino acid transporter. 'Glycine Synthesis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Dopamine

Dopamine, a catecholamine transmitter, plays many roles in the nervous system, but it is best known for its roles in reward and movement. In the presynaptic terminal, the amino acid tyrosine is converted into DOPA via tyrosine hydroxylase, which is the rate limiting step in the synthesis of all the catecholamines. DOPA is then converted to dopamine by DOPA decarboxylase. Dopamine is packaged into synaptic vesicles by the vesicular monoamine transporter.

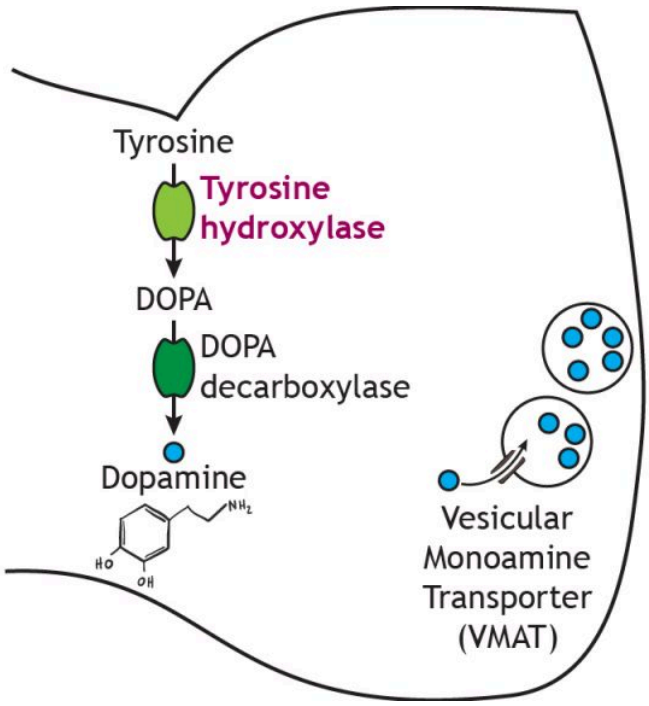

Figure 9.6. Dopamine is synthesized in a two-step process. Tyrosine is converted into DOPA by tyrosine hydroxylase, the rate-limiting step in the pathway. Then dopamine is synthesized from DOPA by DOPA decarboxylase. Dopamine is then packaged into vesicles by vesicular monoamine transporter. 'Dopamine Synthesis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Norepinephrine

In neurons that release norepinephrine, which is another catecholamine transmitter, once dopamine is packaged into the synaptic vesicles, a membrane-bound enzyme called dopamine beta-hydroxylase converts dopamine into norepinephrine. Therefore, unlike the other small molecule neurotransmitters, norepinephrine is synthesized within the vesicles, not in the cytoplasm. Like dopamine, the rate limiting step of this synthesis pathway is the activity of tyrosine hydroxylase.

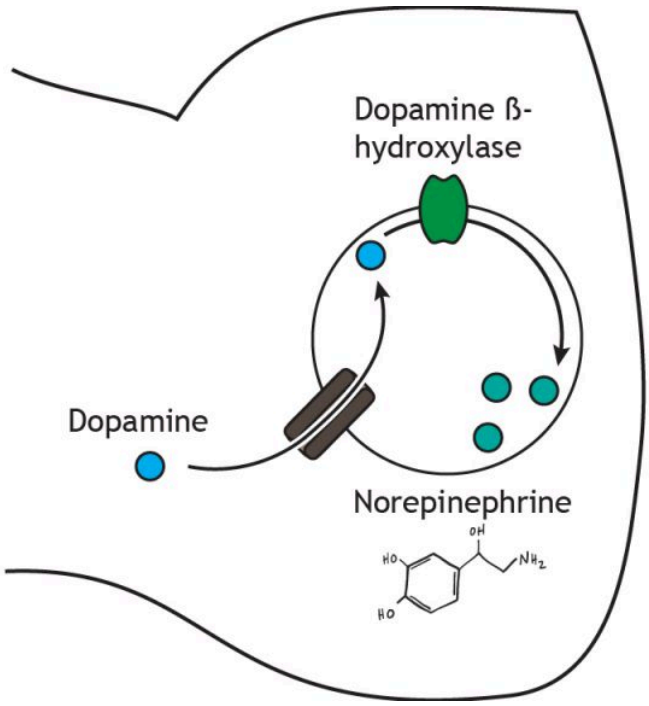

Figure 9.7. Norepinephrine is synthesized from dopamine by dopamine beta-hydroxylase after packaging into vesicles. 'Norepinephrine Synthesis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Epinephrine

Epinephrine, also called adrenaline, is a catecholamine, but it is often considered a hormone instead of a neurotransmitter. Epinephrine is primarily released by the adrenal medulla into the circulation; it is used as a neurotransmitter in only a small number of neurons. Epinephrine is synthesized from norepinephrine in the cytoplasm by the enzyme phenylethanolamine-N-methyltransferase, so epinephrine synthesis requires norepinephrine to exit the vesicles where it was synthesized. After synthesis in the cytoplasm, epinephrine is repackaged into vesicles via the vesicular monoamine transporter.

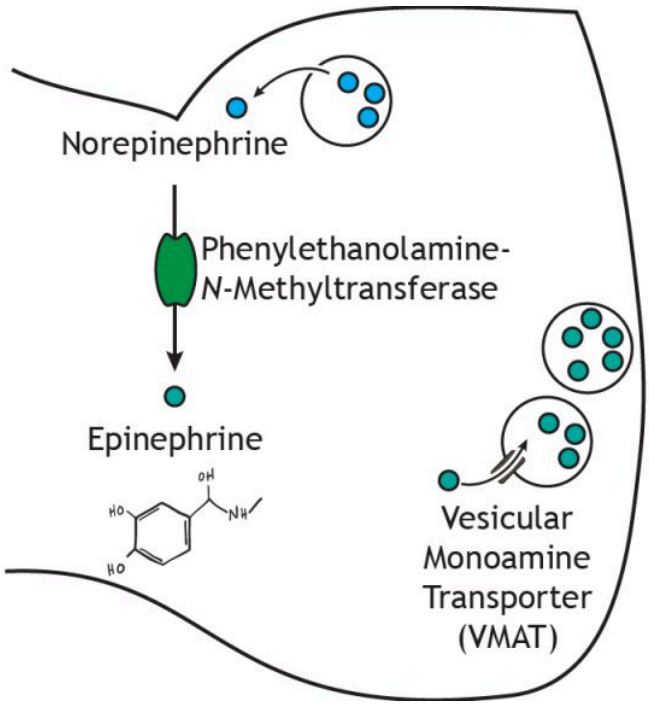

Figure 9.8. Epinephrine is synthesized from norepinephrine by phenylethanolamine-N-methyltransferase in the cytoplasm. Epinephrine is then packaged into vesicles by vesicular monoamine transporter. 'Epinephrine Synthesis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Serotonin

Serotonin, a biogenic amine neurotransmitter, is known for its role in mood. Tryptophan is converted into 5-hydroxytryptophan by tryptophan hydroxylase. This is also the rate-limiting step of the synthesis pathway. Then aromatic L-amino acid decarboxylase converts the 5-hydroxytryptophan into serotonin. Serotonin is packaged into vesicles by the vesicular monoamine transporter similar to the other monoamine neurotransmitters: dopamine and epinephrine.

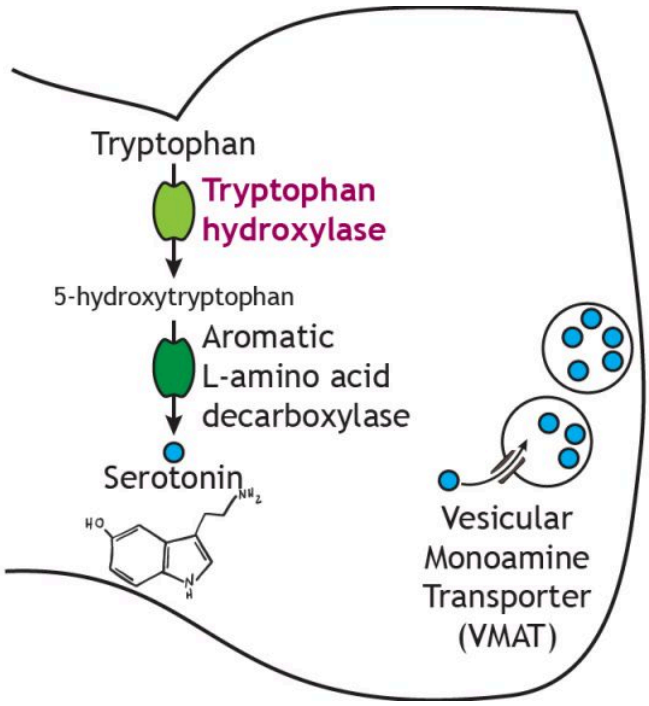

Figure 9.9. Serotonin is synthesized in a two-step process. Tryptophan is converted into 5-hydroxytryptophan by tryptophan hydroxylase, the rate-limiting step in the pathway. Then serotonin is synthesized from 5-hydroxytryptophan by aromatic L-amino acid decarboxylase. Serotonin is then packaged into vesicles by vesicular monoamine transporter. 'Serotonin Synthesis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Histamine

Finally, histamine is another biogenic amine transmitter that is synthesized from histidine through the action of histadine decarboxylase, the rate limiting step of the pathway. Like the other monoamine neurotransmitters, it is packaged into synaptic vesicles via the vesicular monoamine transporter.

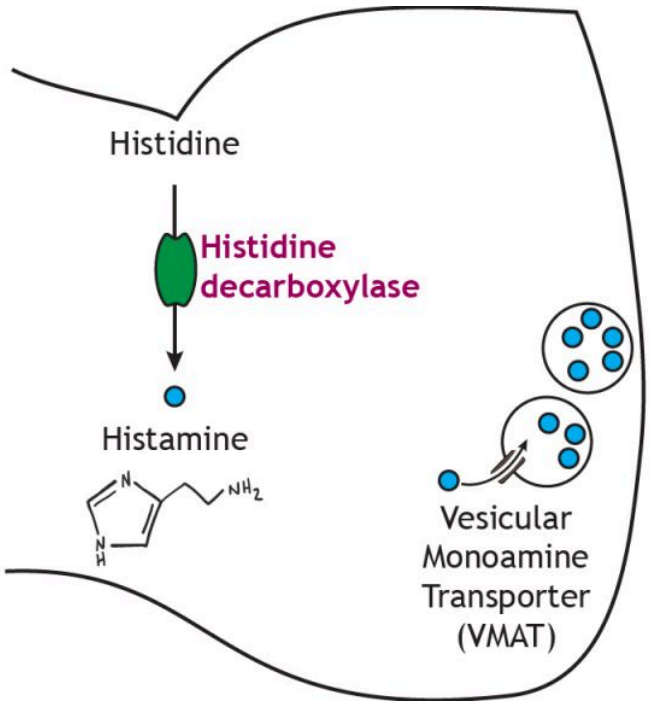

Figure 9.10. Histamine is synthesized from histadine by histadine decarboxylase, the rate-limiting step in the pathway. Histamine is then packaged into vesicles by vesicular monoamine transporter. 'Histamine Synthesis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Synthesis and Storage of Neuropeptides

Neuropeptides are synthesized in the cell body and transported to the synaptic terminal

Neuropeptides are a short string of amino acids and are known to have a wide range of effects from emotions to pain perception. Unlike small molecule neurotransmitters, neuropeptides are synthesized in the cell body and transported to the axon terminal. Like other proteins, neuropeptides are synthesized from mRNA into peptide chains made from amino acids. In most cases, a larger precursor molecule called the prepropeptide is translated into the original amino acid sequence in the

rough endoplasmic reticulum. The prepropeptide is processed further to the propeptide stage. The remaining processing and packaging of the final neuropeptide into a vesicle occurs in the Golgi apparatus. The peptides are packaged into vesicles that are significantly larger that the vesicles that store the small molecule transmitters. These large vesicles must then move from the soma to the terminal.

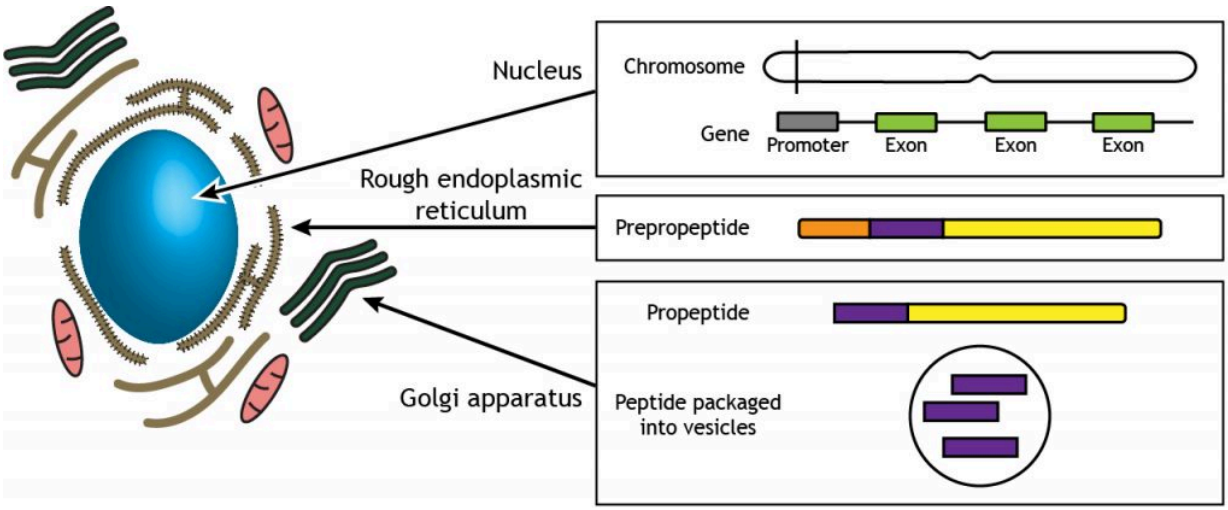

Figure 9.11. Neuropeptide synthesis occurs in the cell body. Each neuropeptide is encoded by a gene on the DNA located in the nucleus. mRNA is translated into an amino acid sequence for a precursor molecule called a prepropeptide in the rough endoplasmic reticulum. Further processing and packaging of the neuropeptide into vesicles occurs in the Golgi apparatus. 'Neuropeptide Synthesis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Axonal Transport

The packaged peptides need to be transported to the presynaptic terminals to be released into the synaptic cleft. Organelles, vesicles, and proteins can be moved from the cell body to the terminal via anterograde transport or from the terminal to the cell body via retrograde transport. Anterograde transport can be either fast or slow.

The packaged neuropeptides are transported to the synaptic terminals via fast anterograde axonal transport mechanisms.

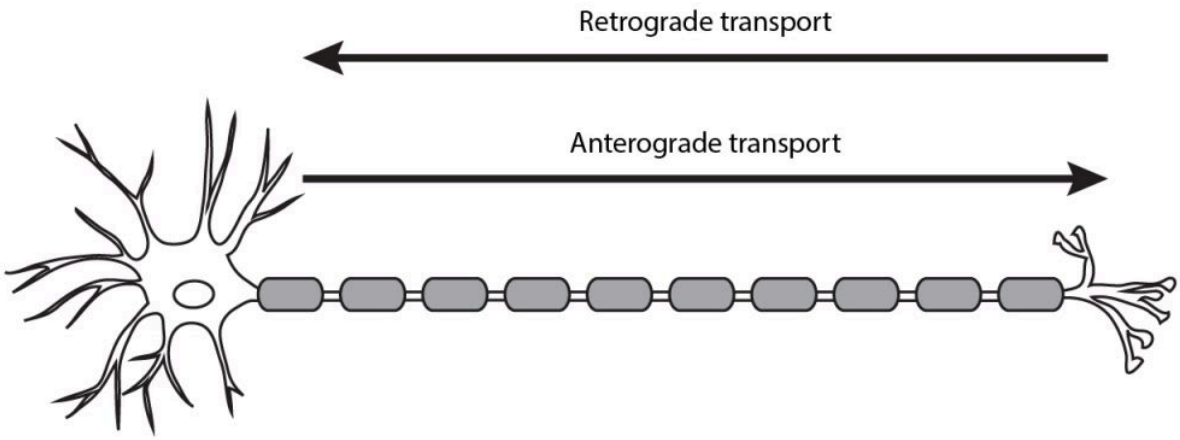

Figure 9.12. Cellular components need to be able to move throughout the cell to have proper functioning. Anterograde transport moves components from the cell body toward the terminal. Retrograde transport moves components from the terminal toward the cell body. 'Axonal Transport' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Key Takeaways

- Small molecules neurotransmitters are synthesized and packaged into vesicles in the presynaptic terminal
- Neuropeptide transmitters are synthesized and packaged into vesicles in the cell body and are transported to the terminal via fast axonal transport
- Each small molecule neurotransmitter has a rate limiting step that controls the rate of synthesis
- Neuropeptides rely on axonal transport mechanisms to move from the soma to the terminal

Test Yourself!

Try the quiz more than once to get different questions!

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=328#h5p-9

- For each neurotransmitter below, which enzyme is responsible for the rate-limiting step in the synthesis pathway, which enzyme is responsible for the final step of the synthesis pathway, and which enzyme is responsible for packaging of the transmitter into vesicles
    - Acetylcholine
    - Glutamate
    - GABA
    - Glycine
    - Dopamine
    - Norepinephrine
    - Epinephrine
    - Serotonin
    - Histamine

Video Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=328#oembed-1

10.

NEUROTRANSMITTER RELEASE

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

Action Potential

As we have covered, when an action potential propagates down the axon to the presynaptic terminal, the electrical signal will result in a release of chemical neurotransmitters that will communicate with the postsynaptic cell.

One or more interactive elements has been excluded from this version of the text. You can view them online here:
https://openbooks.lib.msu.edu/neuroscience/?p=356#video-356-1

Animation 10.1. 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

Ion flow in Terminal

Depolarization of the terminal causes voltage-gated calcium channels to open

When the action potential reaches the terminal, there is an influx of sodium ions, just like when the action potential moves down the axon. This inward current causes a depolarization of the terminal, and that depolarization activates voltage-gated calcium channels. There is a strong electrochemical gradient that moves calcium into the terminal.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=356#video-356-2

Animation 10.2. An action potential causes an influx of sodium in the terminal. The depolarization opens voltage-gated calcium channels, and calcium ions flow into the terminal down their electrochemical gradient. The blue, dotted channels represent voltage-gated sodium channels, and the purple, striped channels represent voltage-gated calcium channels. 'Terminal Calcium Influx' 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.

Active Zones

The voltage-gated calcium channels are concentrated in the presynaptic terminal at active zones, the regions of the membrane where small molecule neurotransmitters are released. At active zones, some synaptic vesicles are docked and are ready for immediate release upon arrival of the action potential. Other neurotransmitter-filled vesicles remain in a reserve pool outside of the active zone.

Vesicles filled with neuropeptides do not dock at active zones. They are located outside of the active zone, further away from the membrane and the high density of voltage-gated calcium channels and are therefore slower to release than the small molecule transmitters.

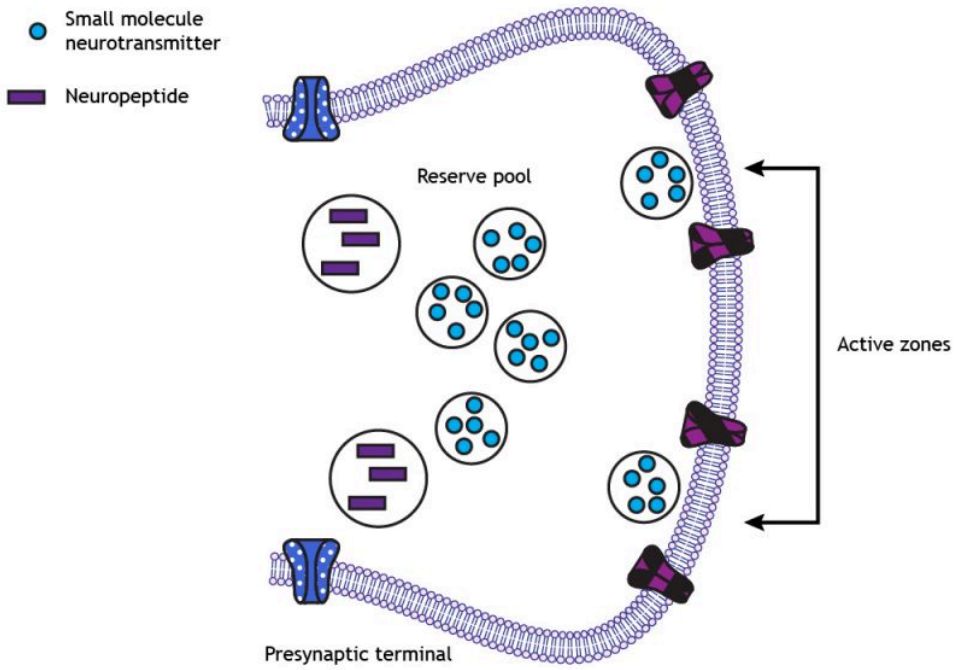

Figure 10.1. Some synaptic vesicles filled with small molecule neurotransmitters dock at active zones on the presynaptic membrane, ready for immediate release. Other synaptic vesicles remain nearby in reserve pools, ready to move into empty active zones. Neuropeptide-filled vesicles do not dock at active zones. The blue, dotted channels represent voltage-gated sodium channels, and the purple, striped channels represent voltage-gated calcium channels. 'Active Zones' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Vesicle Docking

Docking of synaptic vesicles packaged with small molecule neurotransmitters occurs through the interaction of three membrane-bound proteins called SNARE proteins. Synaptobrevin is called a v-SNARE because it is located on the Vesicular membrane. Syntaxin and SNAP-25 are called t-SNARES because they are located on the terminal membrane, which is the Target membrane. The interaction of these three proteins leads to vesicle docking at the active zone.

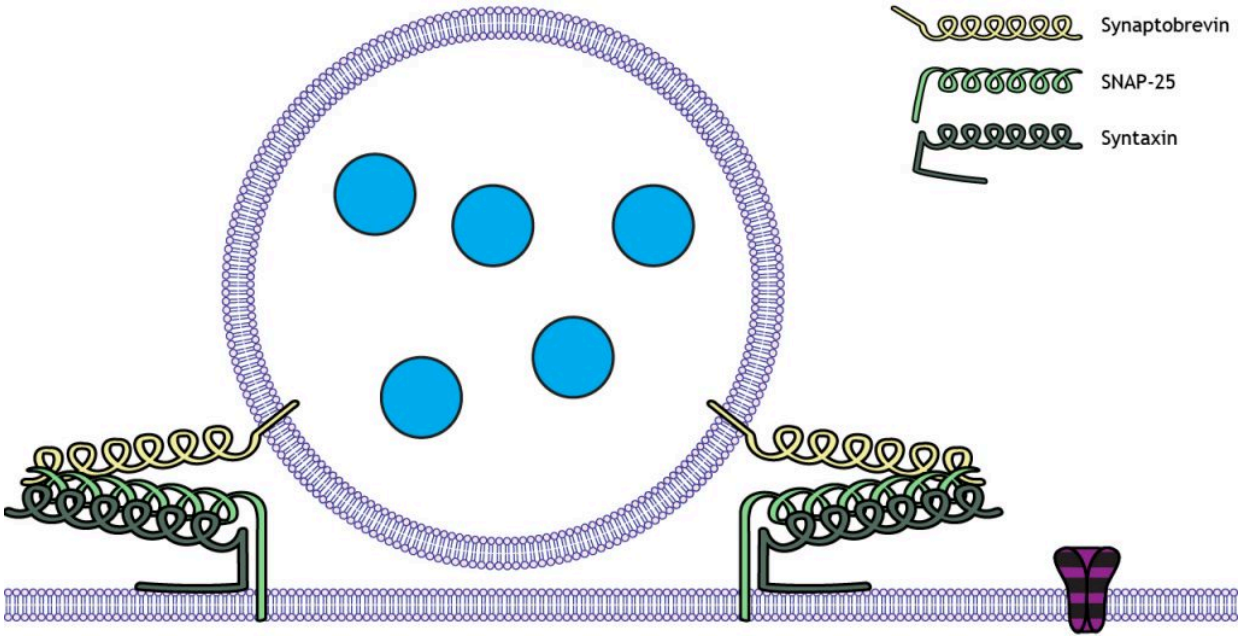

Figure 10.2. Synaptic vesicles filled with small molecule neurotransmitters are able to dock at active zones by the interaction of v- and t-SNARE proteins. Synaptobrevin is embedded in the membrane of the vesicle whereas SNAP-25 and Syntaxin are embedded in the presynaptic terminal membrane. The purple, striped channels represent voltage-gated calcium channels. 'SNARE proteins' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Exocytosis

Exocytosis of neurotransmitters is dependent on calcium

The influx of calcium through the voltage-gated calcium channels initiates the exocytosis process that leads to neurotransmitter release. Calcium enters the cell and interacts with another vesicle-bound protein called synaptotagmin. This protein is a calcium sensor, and when calcium is present at the active zone, synaptotagmin interacts with the SNARE proteins. This is the first step toward exocytosis of the synaptic vesicle.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=356#video-356-3

Animation 10.3. Calcium enters the cell when the voltage-gated channels open. In the presence of calcium, synaptotagmin, a protein bound to the vesicular membrane interacts with the SNARE proteins. The purple, striped channels represent voltage-gated calcium channels. 'Synaptotagmin' 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

Once synaptotagmin interacts with the SNARE proteins, the synaptic vesicle membrane fuses with the presynaptic terminal membrane, exocytosis occurs, and the neurotransmitters released.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=356#video-356-4

Animation 10.4. Once the synaptotagmin-SNARE protein complex forms, the synaptic vesicle membrane fuses with the terminal membrane, and the neurotransmitters are released into the synaptic cleft through exocytosis. The purple, striped channels represent voltage-gated calcium channels. 'Transmitter Exocytosis' 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.

Neurotransmitter Action

After exocytosis of the transmitter molecules, they enter the synaptic cleft and bind to receptors on the postsynaptic membrane. Receptors fall into two main categories: ligand-gated channels and G-protein coupled receptors. The next two chapters cover these receptors.

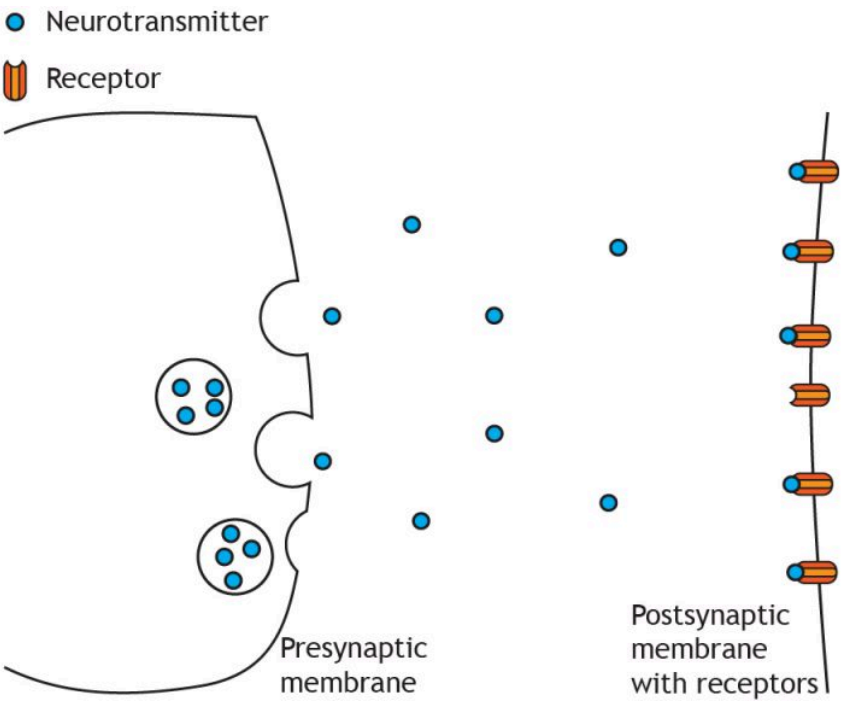

Figure 10.4. After exocytosis of the neurotransmitters into the synaptic cleft, the transmitters bind to receptors present on the postsynaptic membrane. 'Neurotransmitter in Synapse' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Key Takeaways

- Neurotransmitter release is dependent on the influx of calcium into the terminal
- SNARE proteins are important for vesicle docking at active zones and exocytosis
- Synaptotagmin is a calcium sensor

Test Yourself!

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https://openbooks.lib.msu.edu/neuroscience/?p=356#h5p-11

- Describe the events that occur in the presynaptic terminal when an action potential arrives. Include the role of Ca2+.

Video Lecture

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11.

NEUROTRANSMITTER ACTION: IONOTROPIC RECEPTORS

Ionotropic receptors, also called neurotransmitter-gated or ligand-gated channels, are ion channels that open in response to the binding of a neurotransmitter. They are primarily located along the dendrites or cell body, but they can be present anywhere along the neuron if there is a synapse. Ligand-gated channels are important for receiving incoming information from other neurons.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

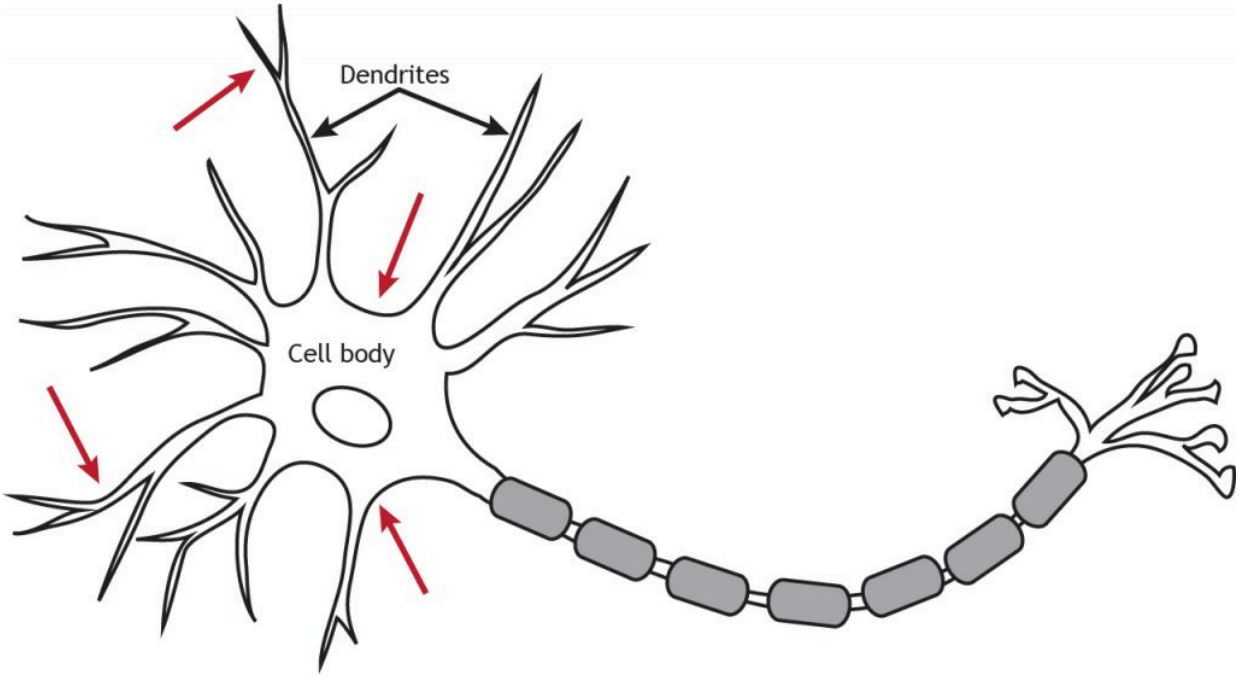

Figure 11.1. Ligand-gated channels critical for receiving incoming synaptic information are primarily located along the dendrites and cell body. 'Receptor Location' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Although ionotropic receptors are ion channels, they open in a different way than the voltage-gated ion channels needed for propagation of the action potential. The ionotropic receptors are ligand-gated, which means that a specific molecule, such as a neurotransmitter, must bind to the receptor to cause the channel to open and allow ion flow. As seen in previous chapters, the voltage-gated channels open in response to the membrane potential reaching threshold.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=368#video-368-1

Animation 11.1. Ionotropic receptors, also called ligand-gated channels, are ion channels that are opened by the binding of neurotransmitters. Voltage-gated channels are opened by the membrane

potential of the cell reaching threshold. Both types of channels allow ions to diffuse down their electrochemical gradient. The lined, teal channels represent glutamate receptors; the solid yellow channels represent GABA receptors; the dotted, blue channels represent voltage-gated sodium channels. 'Ion Channel Gating' 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 receptors can only be opened by a specific ligand. Neurotransmitters and receptors fit together like a lock and key; only certain neurotransmitters are able to bind to and open certain receptors.

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Animation 11.2. Since neurotransmitter receptors can only bind specific neurotransmitters, glutamate binds to and opens glutamate receptors but has no effect on GABA receptors. The lined, teal channels represent glutamate receptors; the solid yellow channels represent GABA receptors. 'Ligand and Receptor' 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.

Ion movement through ligand-gated ion channels follows the same principles covered in previous chapters

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Glutamate Receptors

Glutamate causes EPSPs by opening cation channels that increase sodium permeability across the membrane

Glutamate is the primary excitatory neurotransmitter in the central nervous system and opens non-selective cation channels. There are three subtypes of glutamate receptors. The AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) and kainate receptors allow both sodium and potassium to cross the membrane. Although potassium can leave the cell when the receptors open, the electrochemical gradient driving sodium ion movement is stronger than the gradient driving potassium movement, resulting in a depolarization of the membrane potential.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=368#video-368-3

Animation 11.3. AMPA and kainate glutamate receptors are non-selective ion channels that allow both sodium and potassium to flow across the membrane. When glutamate binds, sodium flows in and potassium flows out. The lined, teal channel represent sAMPA receptors; the checkered, teal channel represents kainate receptors. 'AMPA and Kainate' 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 NMDA (N-methyl-D-aspartate) receptor requires the binding of glutamate to open, but it is also dependent on voltage. When the membrane potential is below, at, or near rest, a magnesium ion blocks the open NMDA receptor and prevents other ions from moving through the channel. Once the cell depolarizes, the magnesium block is expelled from the receptor, which allows sodium, potassium, and calcium to cross the membrane. The voltage change needed to open the NMDA receptor is usually a result of AMPA receptor activation. Released glutamate binds to both AMPA and NMDA receptors, sodium influx occurs through open AMPA channels, which depolarizes the cell enough to expel the magnesium ion and allow ion flow through the NMDA receptors.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=368#video-368-4

Animation 11.4. NMDA receptors are opened by a combination of glutamate binding and a voltage trigger. At low levels of stimulation, when the the membrane potential is near rest, a magnesium ion blocks the open NMDA receptor channel preventing ion flow. Ions can flow through open AMPA receptors, which begins to depolarize the membrane. The voltage change eventually expels the magnesium ion from the channel, allowing sodium, potassium, and calcium to cross the membrane. The lined, teal channel represents AMPA receptors; the dotted, violet channel represents NMDA receptors. 'AMPA and NMDA' 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.

Nicotinic Acetylcholine Receptors

Like glutamate receptors, nicotinic acetylcholine receptors are non-selective cation channels. Nicotinic receptors, though, are located primarily outside of the central nervous system and are primarily used at the neuromuscular junction.

GABA and Glycine Receptors

GABA and Glycine cause IPSPs by opening chloride channels that increase chloride permeability across the membrane

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GABA and glycine receptors are chloride channels. Since an increase chloride permeability across the membrane is inhibitory, the binding of GABA or glycine to their respective ionotropic receptor will cause inhibition.

> *One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=368#video-368-5*

Animation 11.5. GABA and glycine are inhibitory receptors that are selective to chloride. The solid yellow channel represents a GABA receptor; the patterned, yellow channel represents a glycine receptor. 'GABA and Glycine' 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.

Ionotropic Receptors Cause Postsynaptic Potentials

Postsynaptic potentials (Chapter 5) are a result of ionotropic receptors opening. Excitatory ionotropic receptors increase sodium permeability across the membrane, whereas inhibitory ionotropic receptors increase chloride permeability. Ion flow through the ionotropic receptors follows the same principles as other ion channels covered so far.

Equilibrium Potential Review

Previously, we covered ion movement through voltage-gated channels and discussed that electrochemical gradients will drive ion movement toward equilibrium. The neuron's membrane potential at which the chemical and electrical gradients balance and equilibrium occurs is the ion's equilibrium potential.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=368#video-368-6

Animation 11.6. Ions move through open voltage-gated channels trying to reach equilibrium. As the ions cross the membrane, the neuron's membrane potential moves closer to the ion's equilibrium potential. In the animation, a voltage-gated sodium channel opens, and sodium flows in until the membrane potential equals approximately +60 mV, sodium's equilibrium potential. The blue, dotted channel represents a voltage-gated sodium channel. 'Equilibrium Potential' 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.

Reversal Potential

This same principle is used for ion movement through ionotropic receptors. The membrane potential at which ion flow through a receptor is at equilibrium is called the reversal potential of the receptor. The direction of ion movement can be predicted if the reversal potential of the receptor is known.

You can think of a reversal potential as being the equilibrium potential for a receptor, which may allow more than one ion to move across the membrane

---

GABA and Glycine – Receptors Selective to One Ion

When an ionotropic receptor that is selective to only one ion opens, the reversal potential of the receptor is the same as the equilibrium potential of the ion. GABA and glycine receptors only allow chloride ions to cross the membrane. Therefore, the reversal potential of a GABA or glycine receptor

is equal to the equilibrium potential of chloride, and the binding of GABA or glycine to their respective ionotropic receptor will cause an inhibitory postsynaptic potential (IPSP).

> *One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=368#video-368-7*

Animation 11.7. Ions move through open ligand-gated channels trying to reach equilibrium. As the ions cross the membrane, the neuron's membrane potential moves closer to the receptor's reversal potential. When the ionotropic receptor only increases permeability for one ion, the receptor's reversal potential is the same as the ion's equilibrium potential. In the animation, a GABA receptor open, and chloride flows in until the membrane potential equals approximately -65 mV, GABA's reversal potential and chloride's equilibrium potential. Increased chloride permeability causes an IPSP and inhibits the neuron. The yellow, checkered channel represents a GABA receptor. 'GABA Reversal Potential' 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.

Glutamate – Reversal Potential for Receptors that are Non-Selective

However, if the ionotropic receptor allows the flow of more than one ion, or is non-selective, the reversal potential of the receptor does not equal the equilibrium potential of either ion but is somewhere in between. The equilibrium potential of sodium is approximately +60 mV, and the equilibrium potential of potassium is approximately -80 mV. A glutamate receptor is a non-selective cation channel that allows the flow of both ions, and the reversal potential of the receptor is 0 mV. This means that if the neuron's membrane potential is negative, the driving forces acting on sodium are stronger than the driving forces acting on potassium, so more sodium will flow in than potassium will flow out, and the membrane potential will depolarize, causing an excitatory postsynaptic potential (EPSP).

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=368#video-368-8

Animation 11.8. The reversal potential of an ionotropic receptor that is not selective to one ion will fall between the equilibrium potentials of the permeable ions. Glutamate receptors allow the flow of both sodium and potassium ions, so the reversal potential for the receptor is approximately 0 mV. More sodium will flow into the cell than potassium flows out, resulting in a depolarization of the membrane. The line, teal channel represents a glutamate receptor. 'Glutamate Reversal Potential – 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.

If the membrane potential reached the reversal potential of the glutamate receptor, the electrochemical gradients acting on sodium and potassium would balance, so overall ion flow in both directions would be equal, and the membrane potential would not change.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=368#video-368-9

Animation 11.9. At the reversal potential, there is no net ion flow in either direction. An equal number of sodium ions enter the cell as potassium ions leave. Since there is no change in voltage at the reversal potential, if the receptor remained open, the membrane potential would stay at 0 mV. 'Glutamate Reversal Potential – 0 mV' 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

- Ionotropic receptors are ligand-gated ion channels that open when a specific neurotransmitter binds
- For receptors selective to one ion, the reversal potential equals the ion's equilibrium potential
- For receptors not selective for only one ion, the reversal potential is a value between the ions' equilibrium potentials
- Glutamate is an excitatory neurotransmitter that opens non-selective cation channels that allow the influx of sodium, causing an EPSP
- GABA and glycine are inhibitory neurotransmitters that open chloride channels, causing an IPSP

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=368#h5p-12

The following questions refer to a mythical cell, the Thinking Cell. The properties for this cell are given in the table. In all cases, the postsynaptic membrane is a dendrite. Use the information in the table to answer the following questions.

Table A.1. Intra- and extracellular concentration (mM) and equilibrium potential (mV) values for ions present in the Thinking Cell.

Ion	Inside concentration (mM)	Outside concentration (mM)	Equilibrium Potential (mV)
A-	6	125	-65
B+	12	120	+60
D+	125	5	-84
E++	0.00001	1.5	+155

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=368#h5p-33

Video Lecture

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12.

NEUROTRANSMITTER ACTION: G-PROTEIN-COUPLED RECEPTORS

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

G-protein-coupled receptors (GPCRs), also called metabotropic receptors, are membrane-bound proteins that activate G-proteins after binding neurotransmitters. Like ionotropic receptors, metabotropic receptors are primarily located along the dendrites or cell body, but they can be present anywhere along the neuron if there is a synapse. Metabotropic receptors are also important for receiving incoming information from other neurons. GPCRs have slower effects than ionotropic receptors, but they can have long-lasting effects, unlike the brief action of a postsynaptic potential.

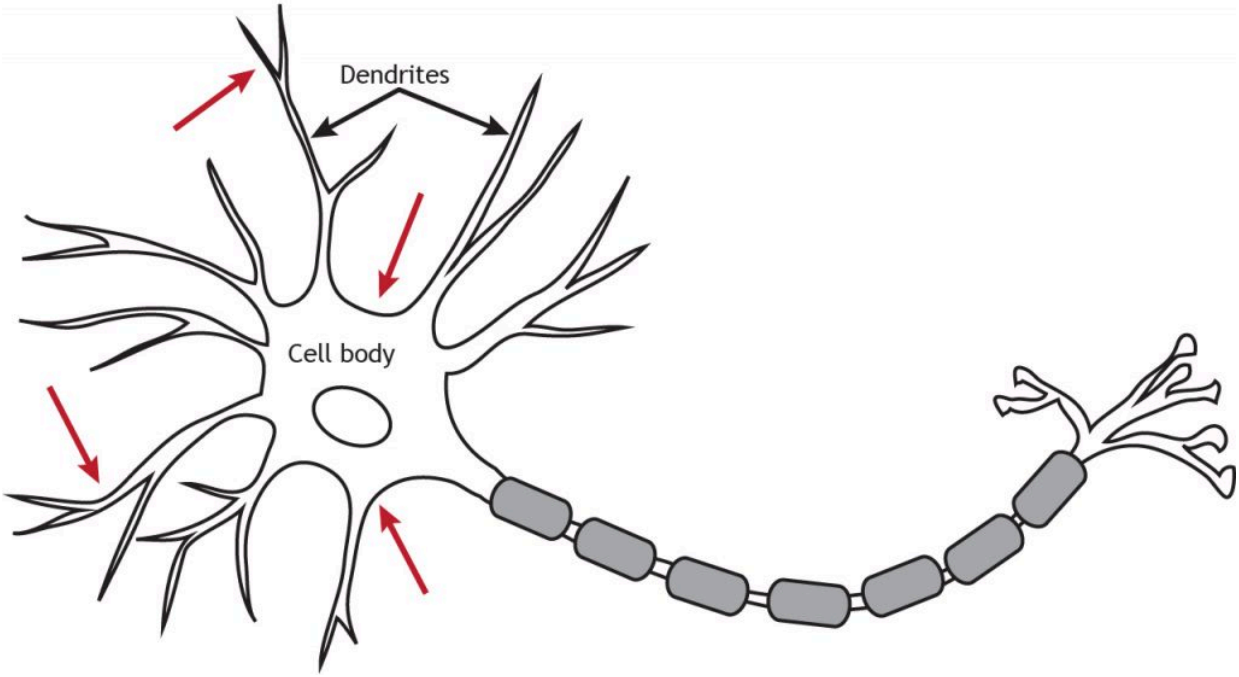

Figure 12.1. Metabotropic receptors critical for receiving incoming synaptic information are primarily located along the dendrites and cell body. 'Receptor Location' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

G-Proteins

G-proteins are enzymes with three subunits: alpha, beta, and gamma. In the resting state of the G-protein complex, the alpha subunit is bound to a GDP molecule. There are multiple types of alpha subunits, and each initiate different cellular cascades in the neuron.

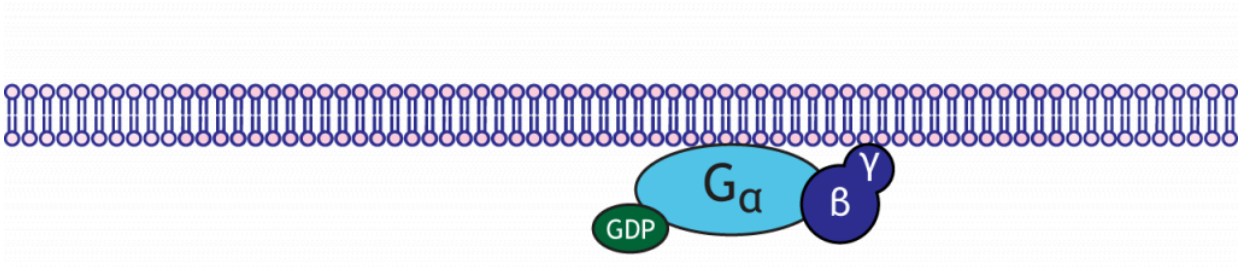

Figure 12.2. The unactivated G-protein complex in the cell consists of three subunits (alpha, beta, and gamma) and a bound GDP molecule. 'G-protein Complex' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

G-Protein Coupled Receptors

When a neurotransmitter binds to a GPCR, the receptor is able to interact with an inactivated G-protein complex. The complex that binds is specific to the receptor; different metabotropic receptors for the same neurotransmitter can have different effects in the cell due to which G-protein binds. Once coupled to the receptor, the GDP molecule is exchanged for a GTP molecule, and the G-protein becomes activated.

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Animation 12.1. Neurotransmitter binding to a G-protein-coupled receptor causes the inactivated G-protein complex to interact with the receptor. The GDP molecule is then exchanged for a GTP molecule, which activates the G-protein complex. 'G-protein Binding' 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.

After activation, the G-protein complex will separate into the alpha-GTP subunit and the beta-gamma subunit. Both components can alter the function of effector proteins in the cell. Effector protein functions can range from altering ion permeability across the membrane by opening ion

channels to initiating second messenger cascades. Second messenger cascades can have long-term, widespread, and diverse cellular effects including activation of cellular enzymes or altering gene transcription.

> *One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=397#video-397-2*

Animation 12.2. Once activated, the G-protein complex will separate into the alpha-GTP subunit and the beta-gamma subunit. These subunits can stimulate or inhibit effector proteins within the cell. 'G-protein Effects' 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.

Cellular Effects of G-Proteins

Open Ion Channels – Beta Gamma Subunit

Metabotropic receptors can indirectly open ion channels; this process is slower than ionotropic receptors

---

In certain situations, the activated beta-gamma subunit can open or close ion channels and change membrane permeability. Muscarinic acetylcholine receptors in the heart use this pathway. When acetylcholine binds to a muscarinic receptor in the heart muscle fiber, the activated beta-gamma subunit opens a type of potassium channel called G-protein-coupled inwardly-rectifying potassium (GIRK) channel, hyperpolarizing the cell. This inhibitory effect explains why acetylcholine or an agonist like atropine slow the heart rate.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=397#video-397-3

Animation 12.3. Some GPCRs, like the muscarinic acetylcholine receptors in the heart, alter cellular permeability by opening ion channels. The activated beta-gamma subunit of the muscarinic receptor opens GIRK potassium channels and allows the efflux of potassium. 'Beta-Gamma Ion Channels' 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.

Second Messenger Cascades

Metabotropic receptors can alter protein function in the cell through second messenger cascades; these cascades may lead to changes in gene transcription

In addition to direct effects like the activated beta-gamma subunit opening ion channels, G-proteins can have many indirect actions in the cell through the use of second messenger cascades. The specific second messenger pathway that is activated or suppressed by G-protein action depends on the type of alpha subunit.

For example, norepinephrine can act on either alpha- or beta-adrenergic receptors. Beta-adrenergic GPCRs couple to a stimulatory G-protein, or G_s, which initiates the cyclic AMP (cAMP) second messenger system by activating the enzyme adenylyl cyclase. Alpha 2-adrenergic receptors, however, couple to an inhibitory G-protein, or G_i, and suppress the activity of adenylyl cyclase. Alpha 1-adrenergic receptors couple to a third type of G-protein, G_q, which activates the phospholipase C pathway. One neurotransmitter can, therefore, cause a wide range of cellular effects after binding to

GPCRs, unlike the single function of ion flow through the ionotropic receptors. The pathway initiated by norepinephrine will depend on the type of receptor a specific cell expresses.

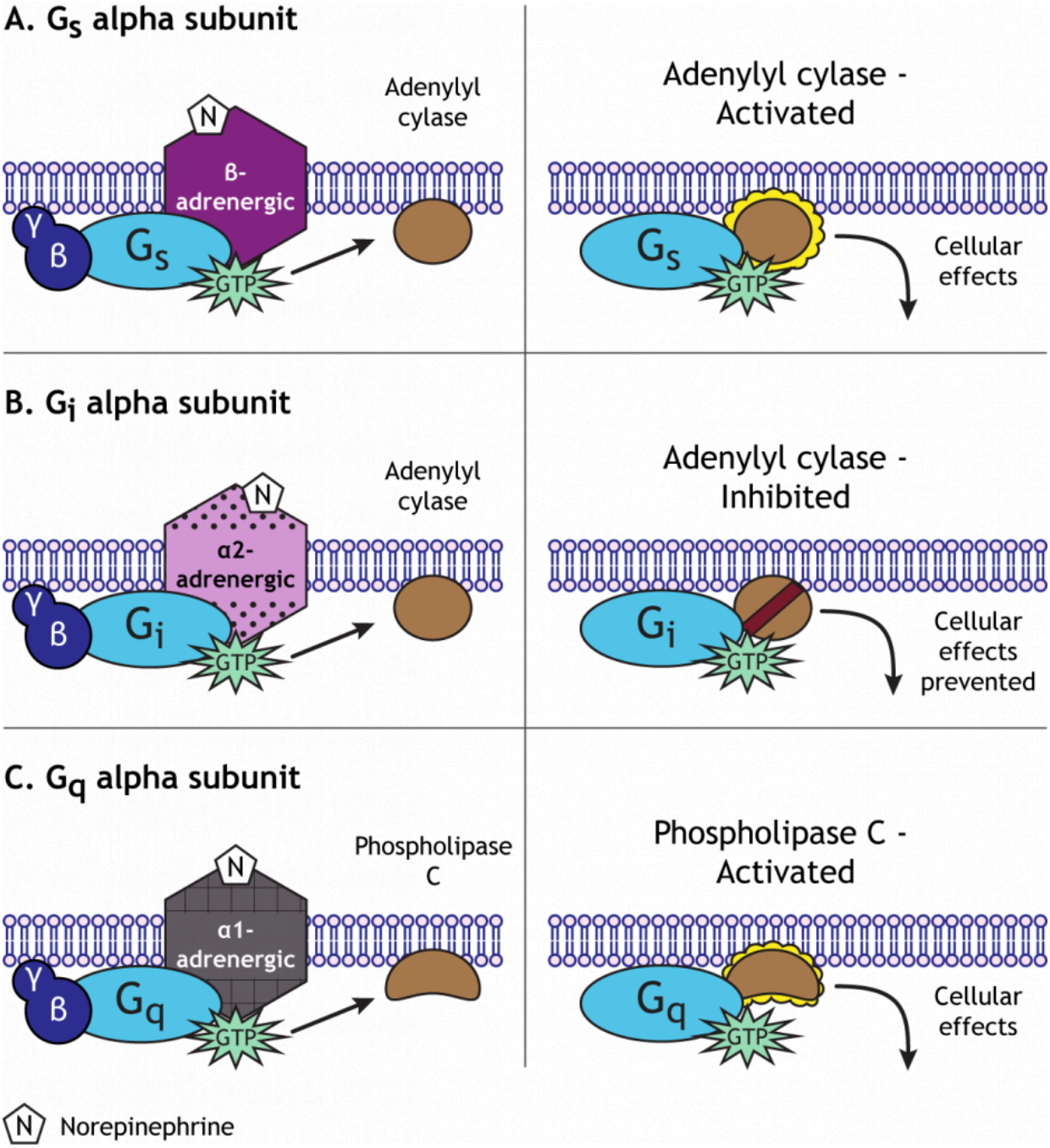

Figure 12.3. The second messenger pathway use and whether that pathway is stimulated or inhibited depends on the type of alpha subunit in the G-protein complex. Different receptors couple to different G-protein complexes. This allows one neurotransmitter to initiate multiple types of signaling cascades. A) The norepinephrine beta-adrenergic receptor couples to the G_s subunit and activates adenylyl cyclase, which initiates downstream cellular effects. B) The norepinephrine alpha 2-adrenergic receptor couples to the G_i subunit and inhibits adenylyl cyclase, which prevents

downstream cellular effects. C) The norepinephrine alpha 1-adrenergic receptor couples to the G_q subunit and activates phospholipase C, which initiates downstream cellular effects. 'Alpha Subunit Effects' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Adenylyl Cyclase / cAMP Second Messenger Cascade

The cyclic AMP (cAMP) second messenger pathway is used by many GPCRs. Activation of the pathway is caused by the G_s alpha subunit and inhibition of the pathway is caused by the G_i alpha subunit. When activated, adenylyl cyclase converts ATP to cAMP in the cytoplasm. cAMP then activates another enzyme called protein kinase A (PKA) by binding to the regulatory subunits, allowing the catalytic (functional) subunits to separate and become active. Protein kinases add a phosphate molecule to proteins, a mechanism called phosphorylation. The addition of the phosphate changes the activity of the protein and how it functions in the cell.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=397#video-397-4

Animation 12.4. GPCRs that couple to the G_s alpha subunit initiate the adenylyl cyclase / cAMP pathway. The G_s subunit activates adenylyl cyclase, which then converts ATP to cAMP. cAMP binds to and activates protein kinase A (PKA), which phosphorylates proteins in the cell. 'Adenylyl Cyclase Pathway' 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 end effects of this pathway will depend on which proteins are targeted. For example, cAMP can gate ion channels and PKA can phosphorylate ion channels altering permeability and membrane potential. Phosphorylation can open the channel, or it may modulate the activity of the channel, making the channel easier to open or remain open longer.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=397#video-397-5

Animation 12.5. The adenylyl cyclase / cAMP pathway can alter many cellular functions. One example is that both cAMP and PKA can open ion channels. Like ligand-gated channels, there are also cAMP-gated channels, which open after cAMP binding. PKA is able to phosphorylate and modulate ion channel function by converting ATP to ADP. 'Second Messenger Ion Channel Action' 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.

In addition to altering ion channel function, PKA can phosphorylate other proteins important for neuron function, such as proteins involved with neurotransmitter synthesis and release. One other critical target of PKA phosphorylation is the transcription factor CREB (cAMP response element binding-protein). Transcription factors bind to DNA in the nucleus and change the rate of gene transcription. Phosphorylation by PKA can cause CREB to initiate transcription of genes, creating new proteins for the neuron. Depending on which genes are transcribed, the effects on the neuron can be long-lasting.

Overall, neurotransmitters working through GPCRs and second messenger cascades like the adenylyl cyclase pathway can cause a diverse range of cellular effects: from opening ion channels, to changing protein activity via phosphorylation, to altering the proteins synthesized in the neuron.

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Animation 12.6. PKA can phosphorylate a number of proteins involved with neuron function. It can target proteins involved with neurotransmitter synthesis, packing, and release, or it can enter the nucleus and phosphorylate CREB, a transcription factor that can initiate gene transcription and

protein synthesis. 'PKA Targets' 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.

Phospholipase C / IP_3 / DAG Second Messenger Cascade

The Gq alpha subunit initiates a separate signaling pathway in the cell by activating phospholipase C. Phospholipase C targets PIP_2 (phosphatidylinositol 4,5-bisphosphate), which is a phospholipid present in the plasma membrane of the cell. PIP_2 is split into two cellular molecules: IP_3 (inositol 1,4,5-trisphosphate) and DAG (diacylglycerol). DAG remains in the membrane and interacts with protein kinase c (PKC). IP_3 moves to the endoplasmic reticulum where it opens calcium channels and allows calcium to flow into the cytosol.

Calcium is also a second messenger in the cell. One important effect is the binding of calcium to calmodulin protein. This complex can then activate another kinase, the calcium/calmodulin-dependent protein kinase (CaMK). Both PKC and CaMK can phosphorylate specific cellular and nuclear proteins like PKA.

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Animation 12.7. The G_q G-protein subunit activates phospholipase C, which converts the phospholipid PIP_2 in the cell membrane into DAG, another membrane-bound molecule, and IP_3, a cytoplasmic molecule. DAG can interact with PKA, initiating phosphorylation of cellular proteins. IP_3 opens calcium channels in the endoplasmic reticulum, allowing calcium to flow into the cytoplasm. Calcium, another second messenger can have many cellular effects. It can bind to calmodulin, which then activates CaMK, causing phosphorylation of more protein targets. 'IP_3-DAG Pathway' 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.

Signal Amplification

One characteristic of GPCR activation is the signal amplification that takes place. One receptor is able to activate more than one G-protein complex. The effector protein activated by the G-protein can create many second messengers, and the activated protein kinases can each phosphorylate multiple cellular proteins. This means that one neurotransmitter can have a significant effect on cellular function.

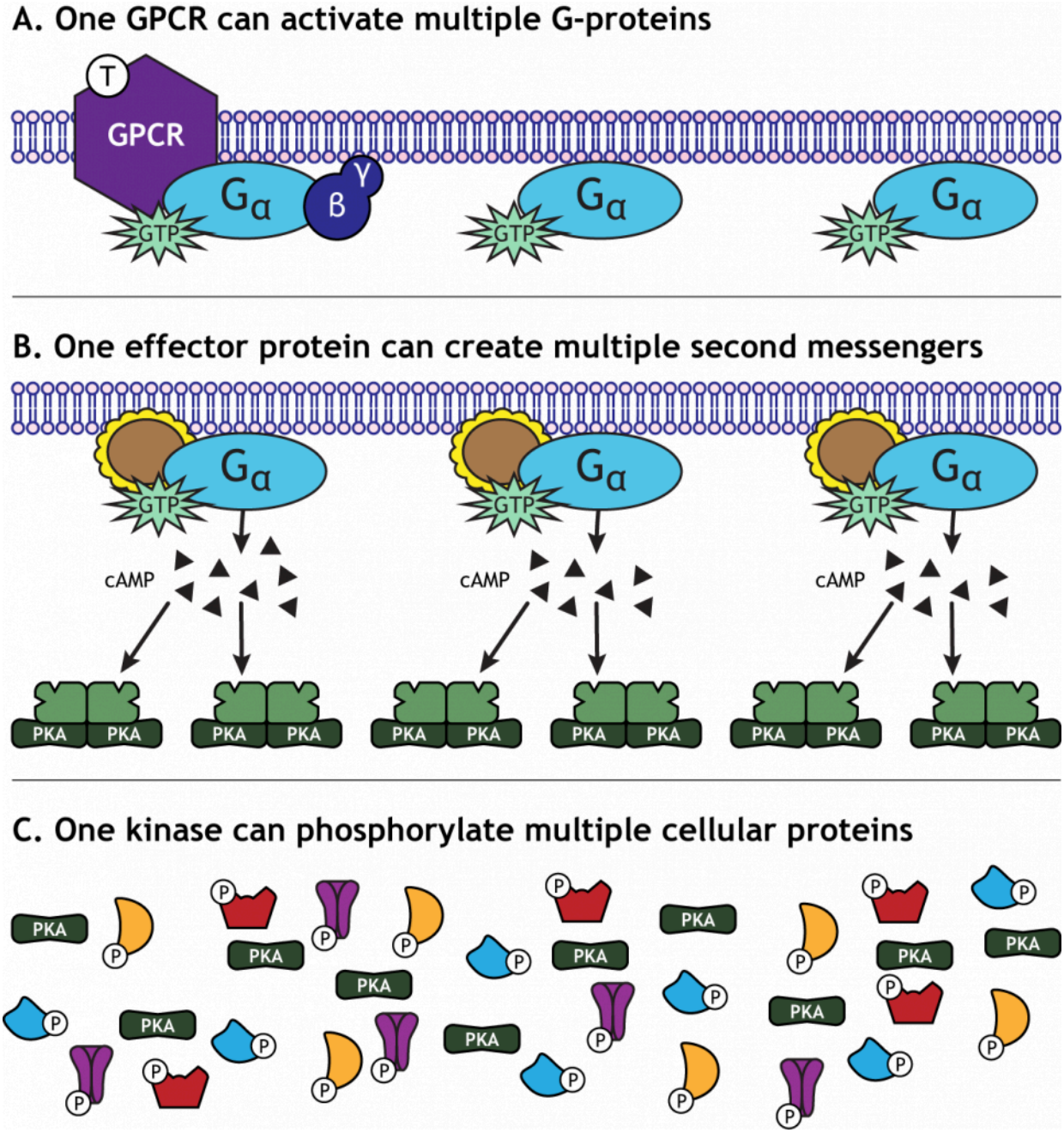

Figure 12.4. The second messenger cascades initiated by GPCRs undergo significant signal amplification. A) Multiple G-proteins can be activated by a GPCR. B) Each effector protein is able to synthesize numerous second messenger molecules. C) Each protein kinase activated by the second messengers can phosphorylate various cellular proteins. 'Signal Amplification' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Signal Termination

Eventually, the cascade initiated by binding of the neurotransmitter to the GPCR needs to end. The alpha subunit of the G-protein is able to convert the bound GTP back to GDP after a short period of time, inactivating the G-protein. The alpha subunit will then interact with a beta-gamma subunit and stay in the resting state until activated by another GPCR. Enzymes in the cell called protein phosphatases find and remove the phosphate groups added to cellular proteins by the protein kinases. And finally, other cellular mechanisms exist to remove calcium from the cytoplasm and degrade other second messengers.

Key Takeaways

- G-protein-coupled receptors rely on the activation of G-proteins to cause cellular changes
- G-protein-coupled receptors have slower effects than ligand-gated receptors
- G-proteins can open ion channels, alter protein function via phosphorylation, and alter gene transcription
- The G_s subunit initiates the adenylyl cyclase / cAMP signaling pathway
- The G_i subunit inhibits the adenylyl cyclase / cAMP signaling pathway
- The G_q subunit initiates the phospholipase C / IP_3 / DAG signaling pathway

Test Yourself!

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https://openbooks.lib.msu.edu/neuroscience/?p=397#h5p-13

- What are some differences between ionotropic and metabotropic neurotransmitter receptors?

Video Lecture

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13.

NEUROTRANSMITTER CLEARANCE

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

After neurotransmitters have been released into the synaptic cleft, they act upon postsynaptic receptors, as covered in the previous chapters. That action must be terminated in order for proper neuronal communication to continue. This is accomplished mainly through two processes: neurotransmitter transport and/or degradation. Transport physically removes the neurotransmitter molecule from the synaptic cleft. Degradation breaks down the neurotransmitter molecule by enzyme activity.

Neurotransmitters can be degraded by enzymes in the synapse

Acetylcholine

Acetylcholine action is terminated by acetylcholinesterase, an enzyme present in the synaptic cleft. Acetylcholinesterase degrades acetylcholine into choline and acetate molecules. Choline is then transported back into the presynaptic terminal and used in the synthesis of new acetylcholine.

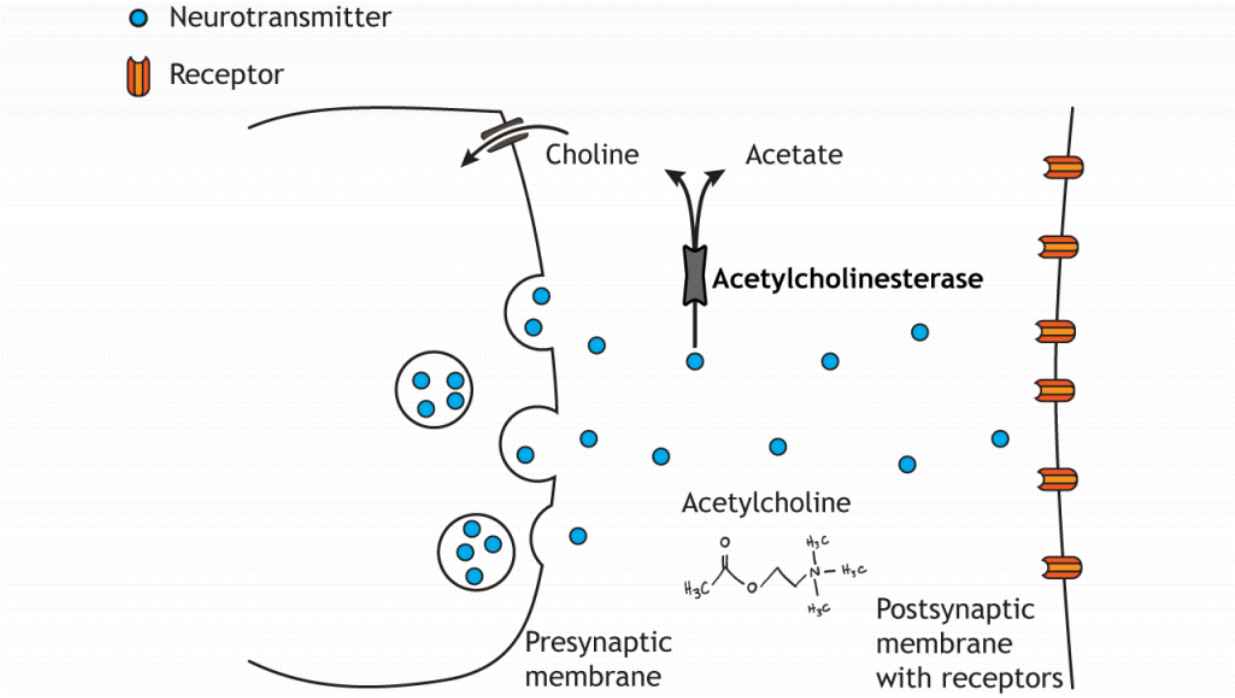

Figure 13.1. Acetylcholine is degraded into choline and acetate within the synaptic cleft via acetylcholinesterase. Choline is then transported back into the presynaptic terminal. 'Acetylcholine Degradation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Neurotransmitters can be transported into glial cells and degraded by enzymes

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Glutamate

Glutamate action is terminated by two mechanisms. Reuptake of glutamate molecules into the presynaptic terminal can occur, or glutamate can be transported into nearby glial cells. The excitatory amino acid transporters are sodium co-transporters and use the sodium electrochemical gradient to drive neurotransmitter transport. Within glial cells, glutamate is converted into glutamine by glutamine synthetase. Glutamine is then transported out of the glial cell and back into the presynaptic

terminal for use in future glutamate synthesis. If glutamate is transported back into the presynaptic terminal, it can be repackaged in synaptic vesicles.

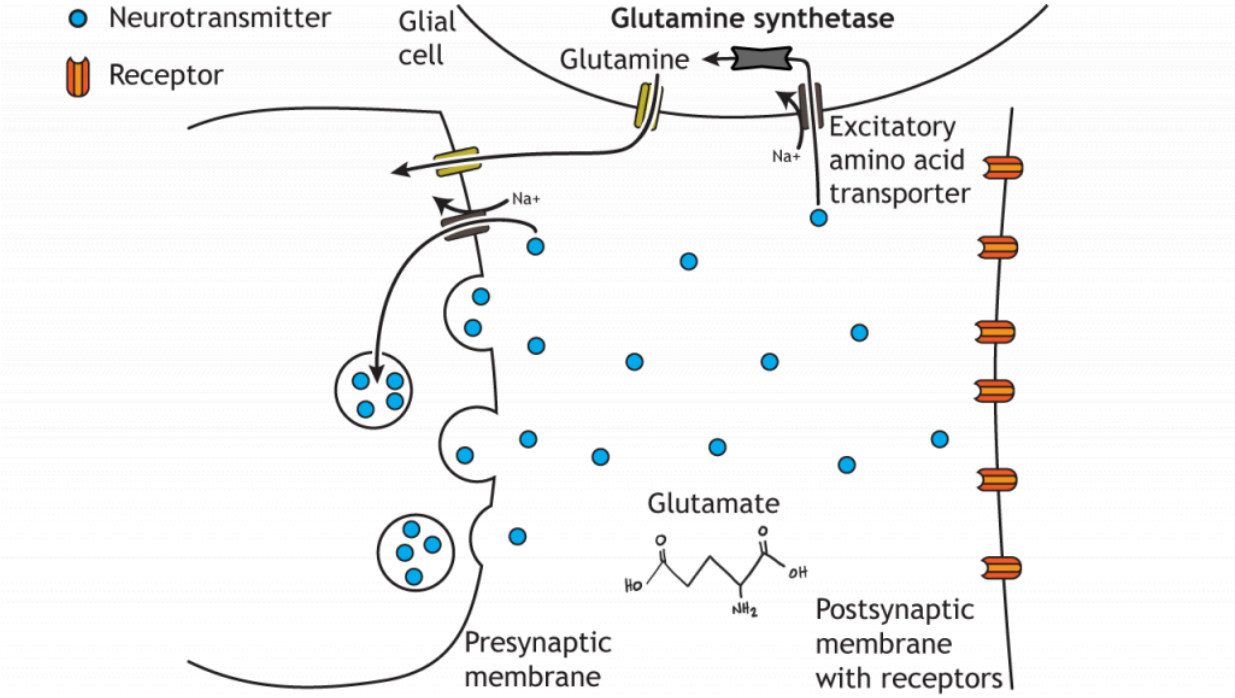

Figure 13.2. Glutamine needs to removed from the synapse. The excitatory amino acid transporter that uses sodium to drive glutamate movement across the membrane can move glutamate into glial cells or back into the presynaptic terminal. In the terminal, glutamate is repackaged into synaptic vesicles. In the glial cells, glutamate is broken down into glutamine by glutamine synthetase. 'Glutamate Degradation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

GABA and Glycine

Like glutamate, GABA and glycine action are terminated by either reuptake into the presynaptic terminal and packaging in synaptic vesicles or through transport into glial cells where breakdown can occur. The GABA and glycine transporter also use the sodium electrochemical gradient to drive the movement of the transmitter across the membrane.

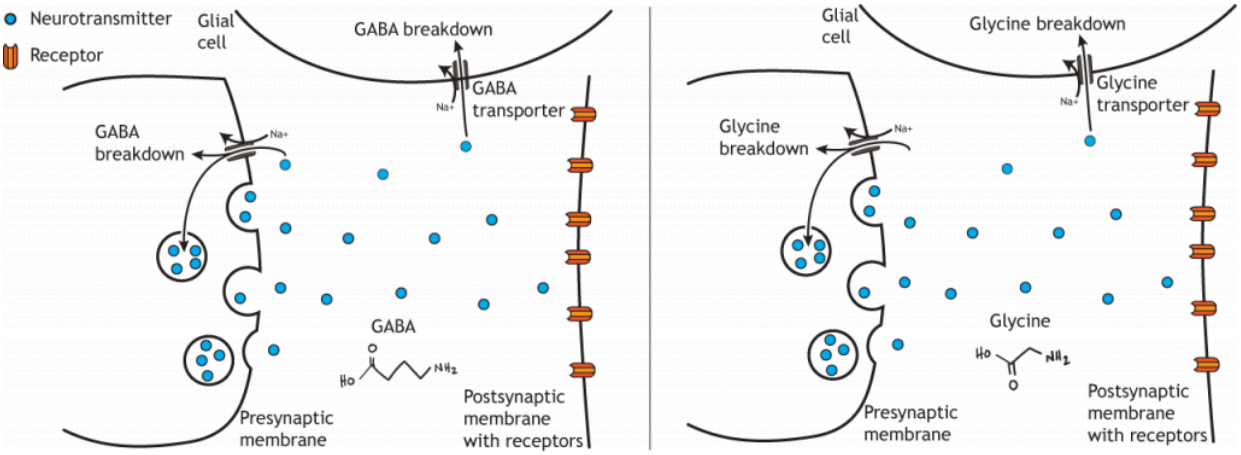

Figure 13.3. GABA and glycine action is terminated by reuptake by sodium co-transporters into either glial cells or back into the presynaptic terminal. In both locations, the neurotransmitters can be broken down by enzymes, whereas in the presynaptic terminal, the transmitters can be repackaged in synaptic vesicles. 'GABA and Glycine Degradation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Neurotransmitters can be transported back into the terminal and either degraded or repackaged

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Dopamine

Dopamine action is terminated by reuptake into the presynaptic terminal via the dopamine transporter (DAT). Once inside the cell, dopamine is either degraded via the actions of either monoamine oxidase (MAO) or catechol-O-methyltransferase (COMT), or it is repackaged into vesicles.

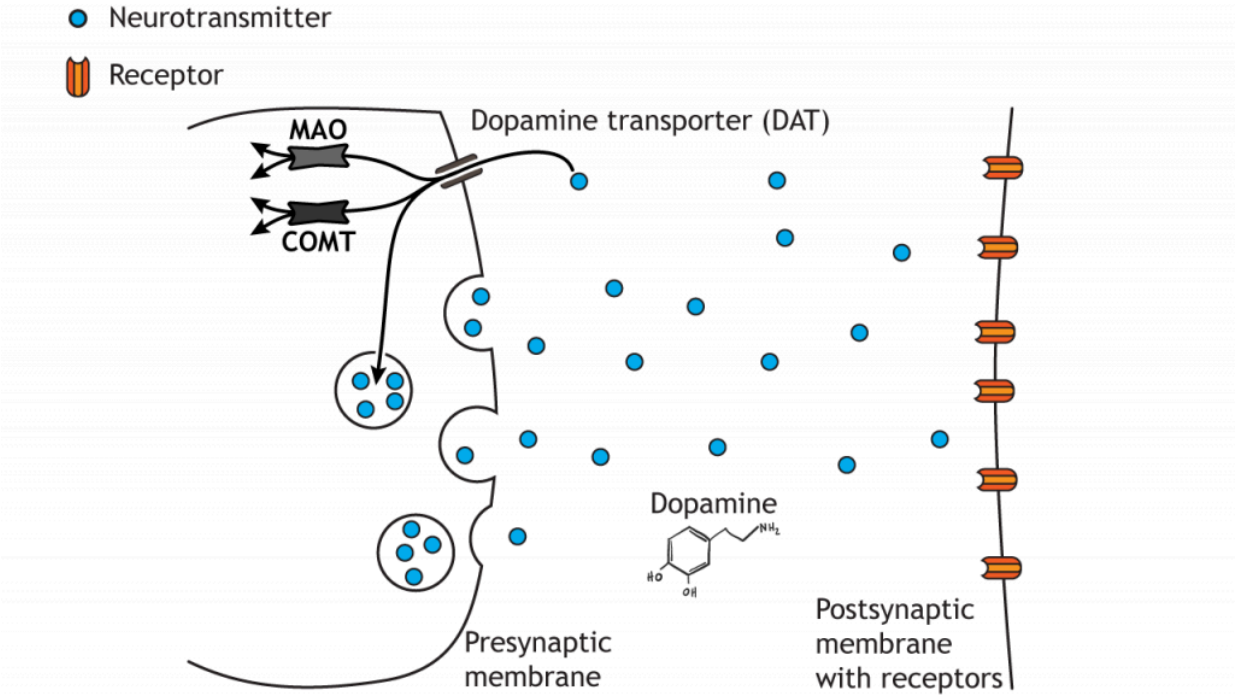

Figure 13.4. Dopamine action is terminated by reuptake into the presynaptic terminal via DAT. Dopamine is then either degraded by MAO or COMT or repackaged into synaptic vesicles. 'Dopamine Degradation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Norepinephrine

Norepinephrine follows the same pathway as dopamine. Reuptake into the presynaptic terminal occurs via the norepinephrine transporter (NET), and then the transmitter is either degraded within the cell by MAO or COMT or repackaged into synaptic vesicles.

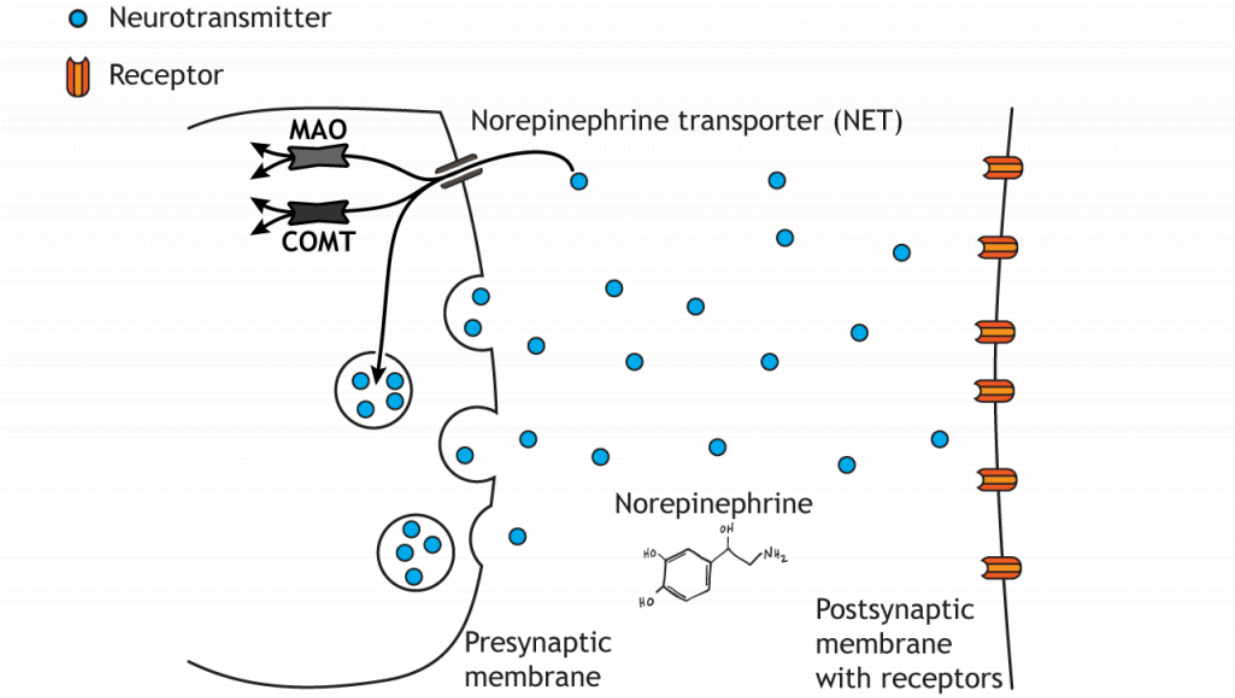

Figure 13.5. Norepinephrine action is terminated by reuptake into the presynaptic terminal via NET. Norepinephrine is then either degraded by MAO or COMT or repackaged into synaptic vesicles. 'Norepinephrine Degradation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Serotonin

Like the other monoamines, serotonin is transported back into the presynaptic terminal via the serotonin transporter (SERT). The difference between serotonin and the catecholamines dopamine and norepinephrine is that monoamine oxidase is the only enzyme used for degradation.

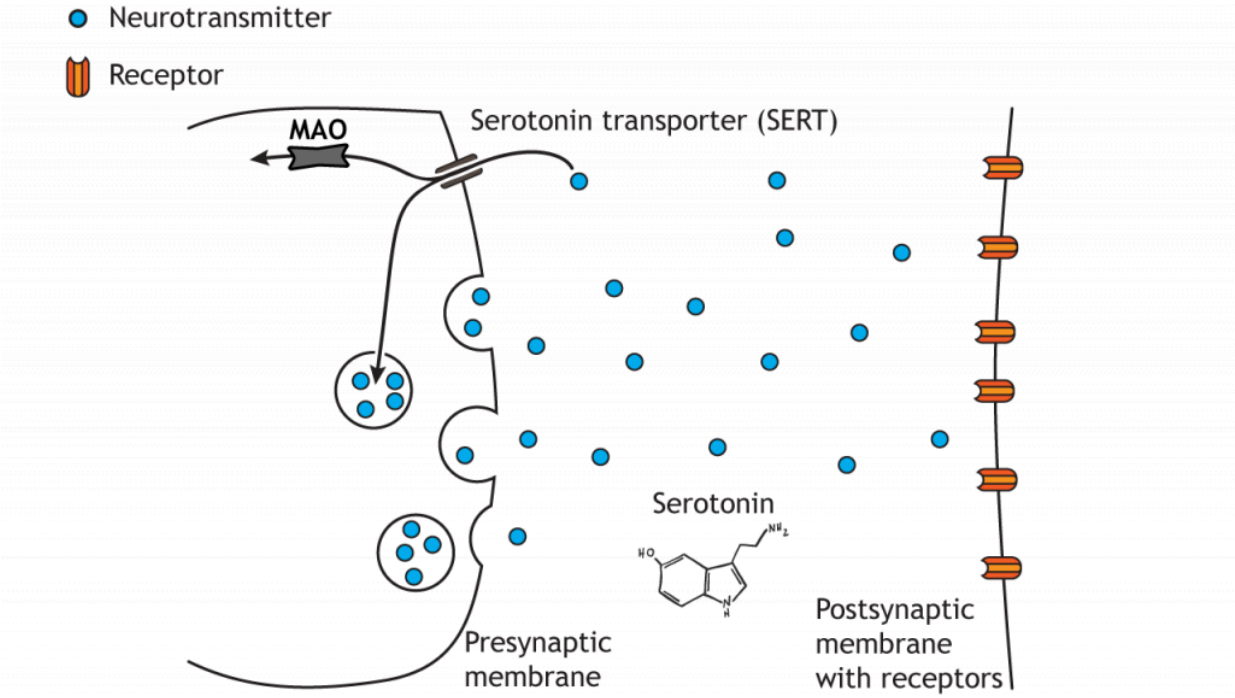

Figure 13.6. Serotonin action is terminated by reuptake into the presynaptic terminal via SERT. Serotonin is then either degraded by MAO or repackaged into synaptic vesicles. 'Serotonin Degradation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Key Takeaways

- Neurotransmitter action in the synapse must be terminated
- This occurs by either
  - reuptake into the presynaptic terminal where enzymatic degradation or repackaging into vesicles occurs
  - transport into glial cells where enzymatic degradation occurs
  - enzymatic degradation in the synapse

Test Yourself!

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

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14.

DRUG AND TOXIN EFFECTS

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

Drugs and toxins can alter neuron functioning in a range of ways, from activation to inhibition and all levels of modulation. Although many drugs exist that alter molecular process typical of many cells, this lesson will focus on neuron-specific targets.

Drug and toxin effects can be excitatory, inhibitory, or modulatory

Synaptic Effects

As we have seen, the synapse is an incredibly complex structure, and for small molecule neurotransmitters, the entire "lifecycle" of the transmitter occurs in this space – synthesis, packaging, release, action, and termination. This means there are numerous targets upon which drugs and toxins can act and alter synaptic communication.

Drug Effects on Neurotransmitter Release

Drugs can alter neurotransmitter synthesis pathways, either increasing or decreasing the amount of neurotransmitter made in the terminal, affecting how much transmitter is released. An example of this is administration of L-DOPA, a dopamine precursor molecule that results in increased dopamine production; it is used as a treatment for Parkinson's Disease.

Neurotransmitter packaging is another site of possible drug action. Reserpine, which has been used to treat high blood pressure, blocks the transport of the monoamine transmitters into vesicles by inhibiting the vesicular monoamine transporter (VMAT). This decrease the amount of neurotransmitter stores and the amount of neurotransmitter released in response to an action potential.

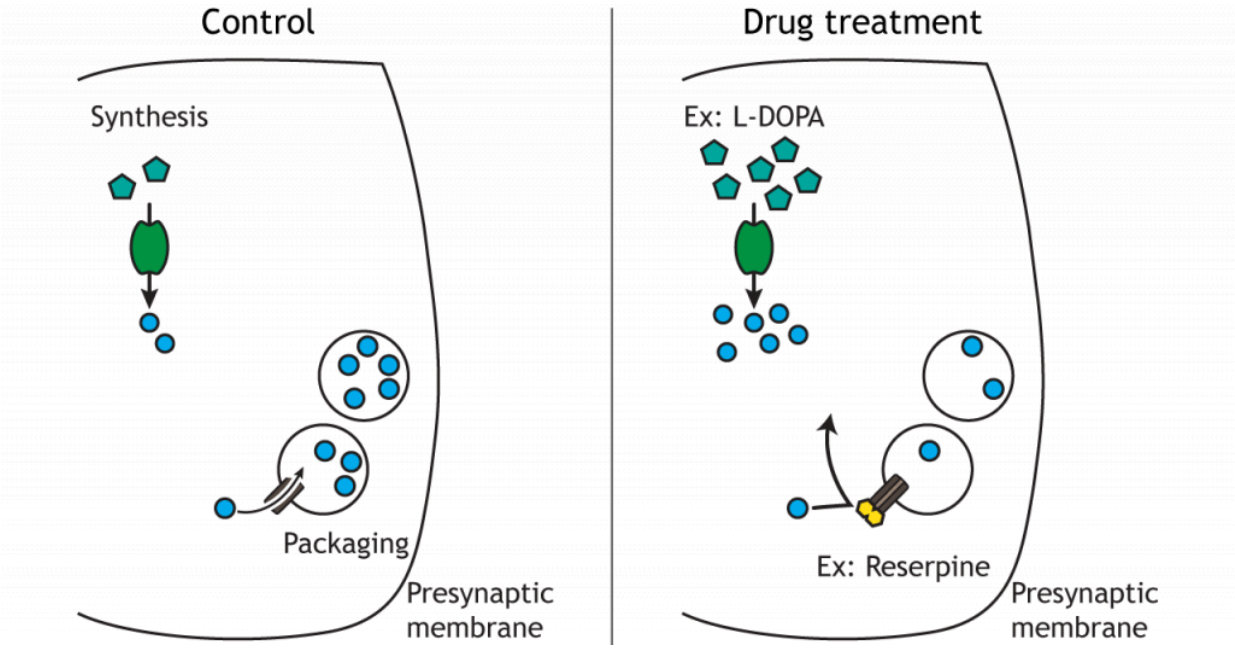

Figure 14.1. Drugs and toxins can alter neurotransmitter synthesis and packaging into synaptic vesicles. L-DOPA increases the synthesis of dopamine in the terminal. Reserpine prevents packaging of the biogenic amines, resulting in low concentrations of transmitter stored in synaptic vesicles. 'Drug Effects on Neurotransmitter Release' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Drug Effects on the Postsynaptic Membrane

The neurotransmitter receptors are another critical location for drug and toxin action. Agonists mimic neurotransmitter effects, whereas antagonists block neurotransmitter effects. Muscimol, a component of some mushrooms, is an agonist for the ionotropic GABA receptor. Bicuculine, a component of some plants, is an antagonist to this receptor and blocks the action of GABA. Additionally, many chemicals are able to modulate receptors in either a positive or negative fashion. Alcohol binds to the GABA receptor and increases the time the receptor is open when GABA binds.

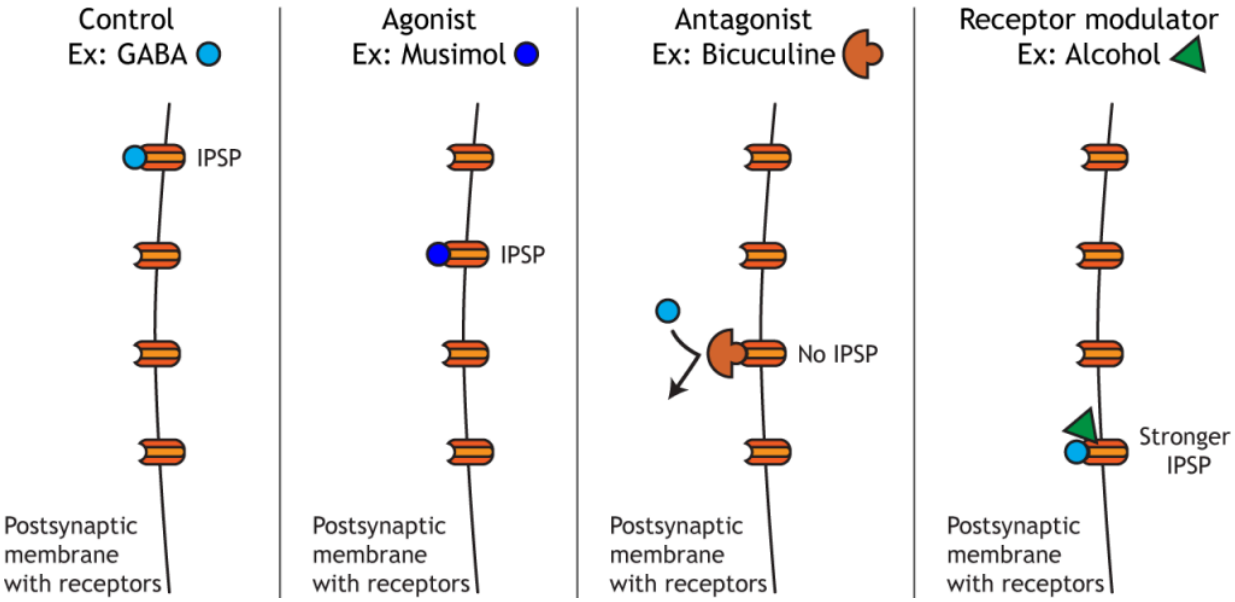

Figure 14.2. Drugs and toxins can alter neurotransmitter receptors on the postsynaptic neuron. A GABA agonist, muscimol, would replicate the actions of GABA and cause an IPSP. A GABA antagonist, bicuculine, would prevent GABA actions resulting in no IPSP. Modulators such as alcohol, alter how the receptor works, so when GABA binds the response is a stronger IPSP than when alcohol is not present. 'Postsynaptic Drug Effects' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Drug Effects on Neurotransmitter Clearance

Finally, neurotransmitter degradation and reuptake can also be altered by drugs and toxins. Depending on the neurotransmitter, enzymes located in either the synapse or in the terminal are responsible for degradation of the transmitter, and these enzyme can be blocked by drugs.

Organophosphates are found in many pesticides and prevent the action of acetylcholinesterase, the enzyme that breaks down acetylcholine in the synapse. This inhibition increases acetylcholine action on the postsynaptic neuron. Monoamine oxidase inhibitors (MAOIs) prevent monoamine oxidase from degrading the biogenic amine neurotransmitters. MAOIs have been used as antidepressants since they increase the amount of transmitter available. Additionally, drugs can prevent the reuptake of neurotransmitters into the presynaptic terminal. Cocaine blocks the dopamine transporter, which results in increased action of dopamine in the synapse.

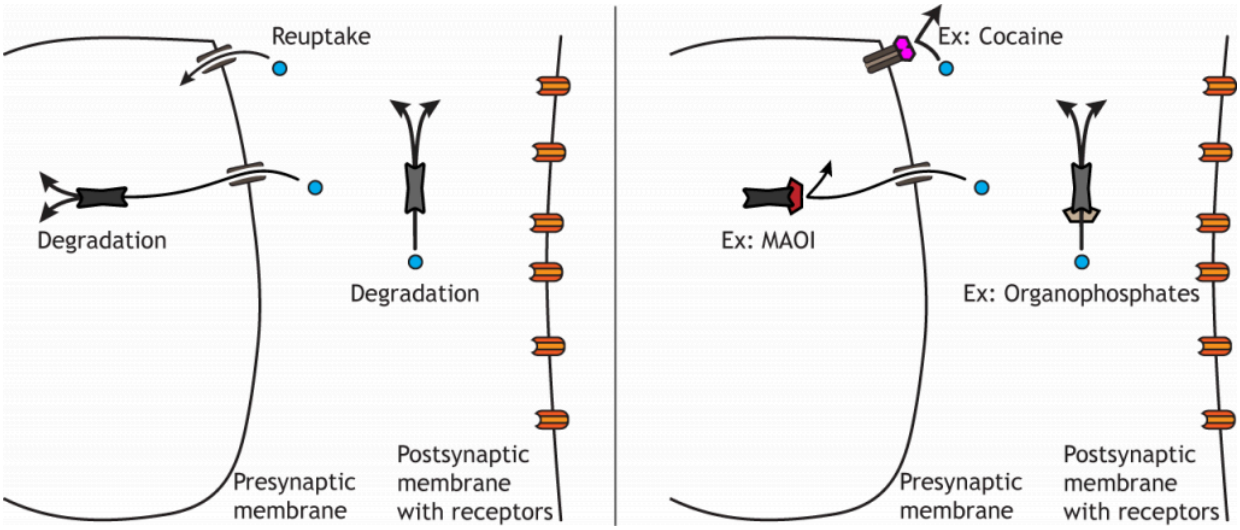

Figure 14.3. Drugs and toxins can alter neurotransmitter degradation and reuptake into the presynaptic terminal. Organophosphates prevent the degradation of acetylcholine in the synapse. MAOIs prevent the degradation of monoamine transmitters in the terminal. Cocaine prevents dopamine from being transported into the presynaptic terminal. All of these effects lead to increased neurotransmitter action and availability. 'Drug Effects on Neurotransmitter Clearance" by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Non-Synaptic Effects

Drugs and toxins can also affect neuron function by acting outside of the synapse. For example, some chemicals change voltage-gated ion channel dynamics. Veratridine, a compound found in plants from the lily family, prevents voltage-gated sodium channels from inactivating. Initially, this causes an increase in neurotransmitter release, but it can quickly lead to excitotoxicity.

Key Takeaways

- There are many ways in which drugs and toxins can alter neuron function
- Effects can be excitatory, inhibitory, or modulatory

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=567#h5p-15

Video Lecture

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15.

EPIGENETICS

We have seen how neurotransmitter action can alter gene transcription and translation through binding to G-protein coupled receptors. The effectiveness of the signaling cascade on new protein synthesis does depend on some DNA-specific factors. This chapter will briefly cover how genes are transcribed and then how non-sequence, molecular changes to DNA can affect transcription rates.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

Central Dogma

DNA to RNA to protein. The central dogma of genetics. It may look simple, but many complex steps must occur for the process to be successful.

DNA

Doubled-stranded DNA (deoxyribonucleic acid) is comprised of four nucleotide bases: adenosine (A), thymine (T), guanine (G), and cytosine (C). Adenosine and thymine form base pairs whereas guanine and cytosine form pairs. The pairs cause the two strands to coil around each other and form a double helix.

RNA

The single-stranded messenger RNA (ribonucleic acid) is created from the DNA sequence via

complementary base pairing. Like DNA, there are four bases, but in RNA the thymine base is replaced by uracil (U). Messenger RNA (mRNA) leaves the nucleus and interacts with ribosomes to synthesize proteins in a process called translation. The ribosomes pair amino acids to specific three-base sequences called codons. For example, the codon sequence AUG is the start codon and it codes for methionine. The ribosomes will move down the mRNA to find the start codon of the protein and begin translation there, adding a new amino acid for each codon until a stop codon is reached.

Protein

Proteins are synthesized by the linking of amino acids together by the ribosomes. There are 20 amino acids that are each encoded by one or more mRNA codon sequences.

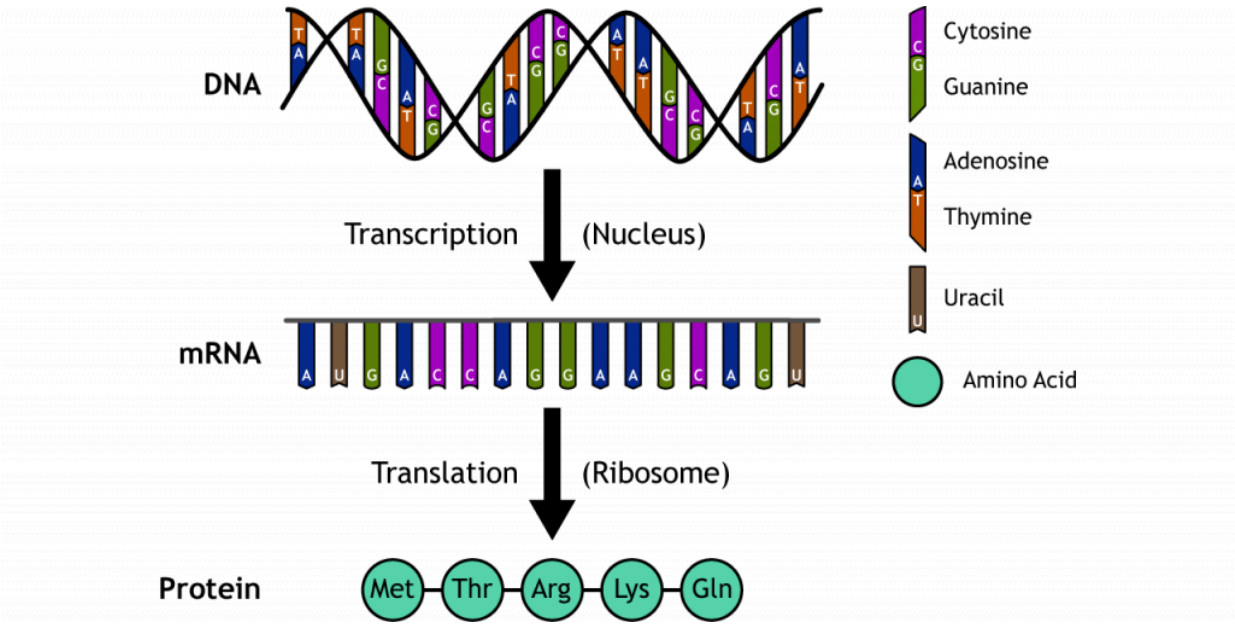

Figure 15.1. The central dogma of genetics. DNA is transcribed into RNA, which is translated into protein. DNA is composed of the nucleotides cytosine, guanine, adenosine, and thymine. RNA is composed of the nucleotides cytosine, guanine, adenosine, and uracil. Protein is composed of amino acids. 'Central Dogma' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Gene Transcription

In the nucleus, proteins called transcription factors and an RNA polymerase attach to the DNA. The DNA unwinds, the proteins bind, and an mRNA strand is synthesized using the DNA as a template. The mRNA is a complementary sequence to the DNA strand being transcribed.

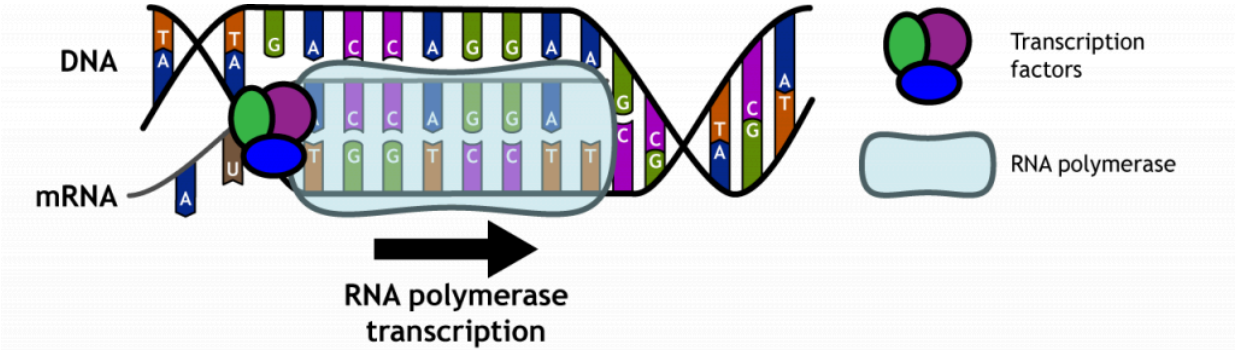

Figure 15.2. The double helix of the DNA unwinds, and proteins including transcription factors and RNA polymerase bind. The mRNA strand is synthesized by the proteins that use the DNA as a template for the nucleotide sequence. 'Transcription' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

DNA must be unwound from its condensed form to allow for gene transcription

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DNA Packaging

DNA is not always accessible to those transcription proteins, though. There is so much DNA in each cell, that in order to save space, it is highly condensed in the nucleus. The double helix is wrapped around proteins called histones. The histones are then wrapped into nucleosome strands. The nucleosomes are compacted into denser structures called chromatin. Finally, the chromatin is condensed more and creates chromosomes.

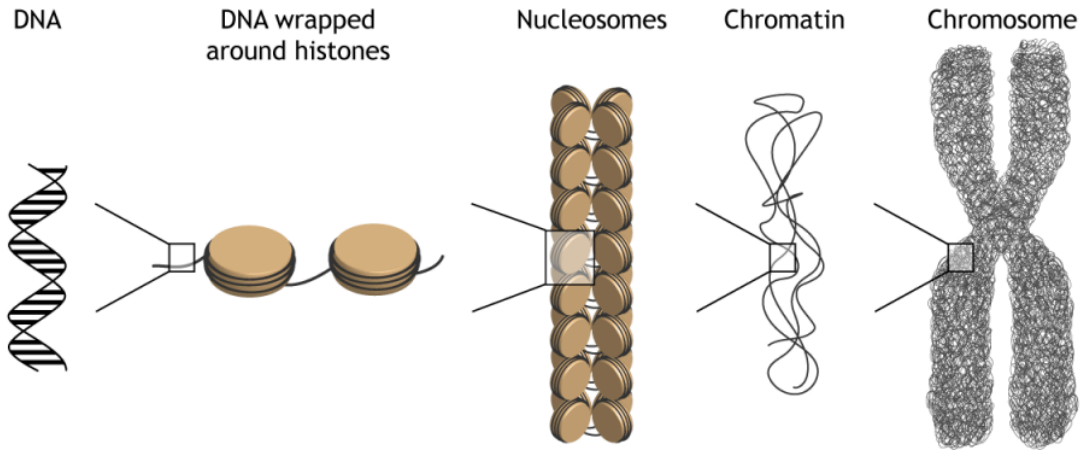

Figure 15.3. DNA is highly condensed within the cell. DNA is wrapped around histone proteins in a structure called nucleosomes. The nucleosomes are compacted into chromatin which is further compacted into chromosomes. 'DNA Packaging' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

In order for gene transcription to occur, the strands of DNA must uncoil from the histone bodies to become accessible to the transcriptional machinery.

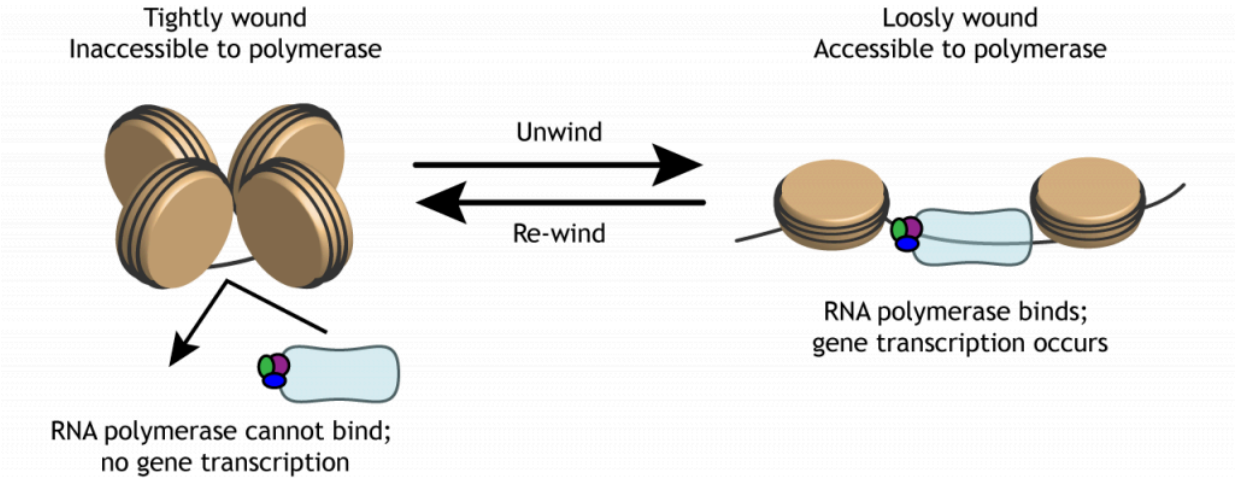

Figure 15.4. When the DNA is wound tightly around histones, the strands are inaccessible to the polymerase proteins and transcription factors. Since these proteins cannot bind, no gene transcription can occur. If the histones unwind, the DNA then becomes accessible to the transcription proteins. RNA polymerase can bind, and gene transcription can take place. 'RNA Polymerase Binding' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Molecular modifications to the DNA (the epigenome) can alter the ability for gene transcription

Epigenetics

Molecules such as methyl groups can be attached to DNA or on the histones. These epigenetic tags can affect how tightly the DNA is wound around the histones. Since gene expression can be altered by modifying how easily the histones unwind and how accessible DNA strands are, epigenetic tags are able to have an indirect effect on gene transcription.

Methyl groups make it more difficult for the polymerase to access the DNA by keeping the DNA coiled around the histones, reducing transcription. When the methyl groups are removed, called demethylation (not to be confused with dimethylation, the addition of two methyl groups), gene expression can increase because the DNA uncoils and is accessible to the transcriptional machinery.

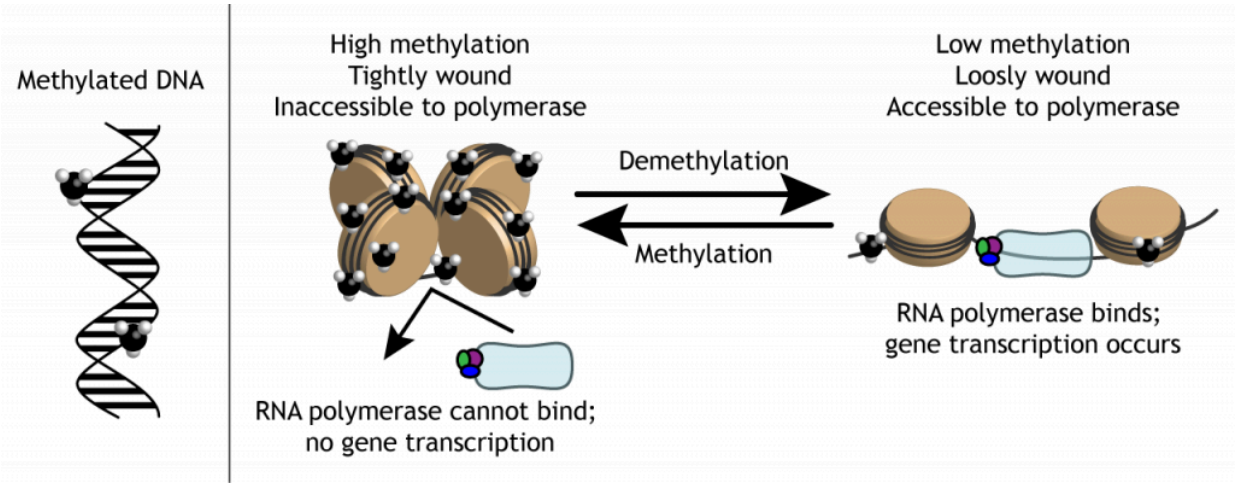

Figure 15.5. Methyl groups attached to DNA affect how accessible genes are to transcription proteins. Highly methylated DNA stays tightly wound around histones, preventing RNA polymerase binding and gene transcription. Low methylation loosens the coils and make the DNA accessible to RNA polymerase, allowing gene transcription. 'DNA methylation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Epigenome is Flexible

An individual's DNA sequence is fixed (excluding mutations that occur due to damage or errors in cell replication), but the epigenome is flexible and can change throughout life. An individual's life experiences, especially during development or other critical periods, are able to alter the epigenome.

Some experiences will increase methylation, sometimes for only certain genes, sometimes genome-wide, whereas other experiences will decrease it. For example, early life stress can increase the amount of methylation found on the gene that encodes for the receptor that is activated by stress hormones. Increased methylation leads to reduced transcription which has downstream effects on the negative feedback loop on the stress response. Scientists are starting to realize how important the epigenome is in regulating our brain and behavior.

Inherited Epigenome

Additionally, epigenetic modifications are heritable. Recent research is starting to show that experiences of mothers, fathers, and even grandparents can have transgenerational effects. And these effects, once thought only to be inherited from the maternal side, have now been shown to be paternally inherited as well. This means an animal that had early life stress may have increased methylation and changes in gene transcription that is then passed down for generations even if the offspring do not experience the same stressors.

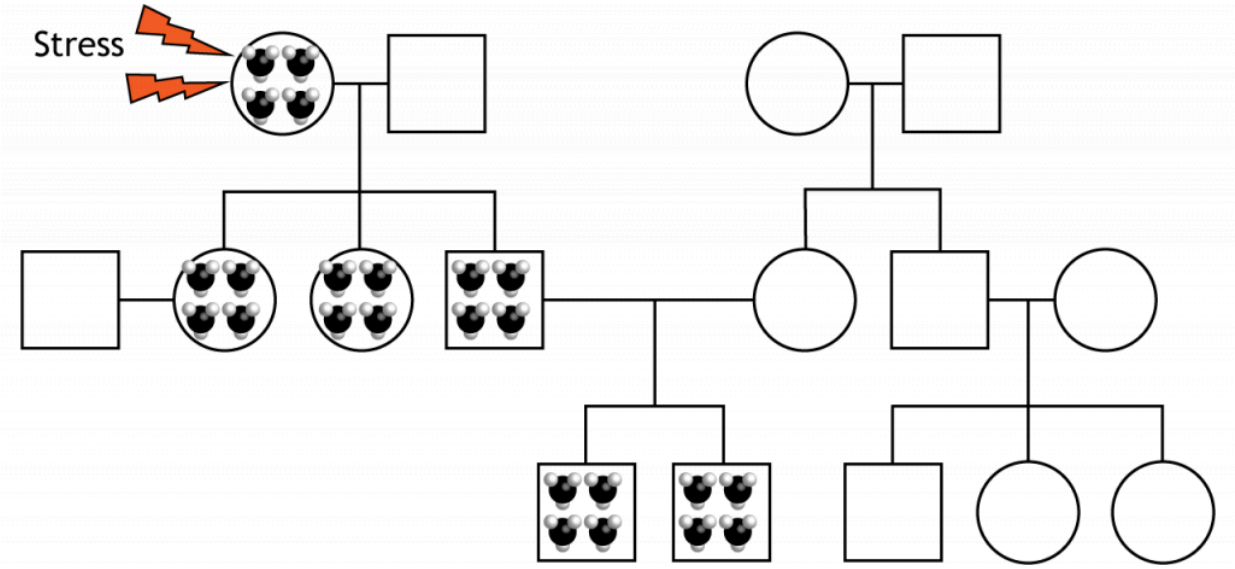

Figure 15.6. Epigenetic factors can be inherited. Stress experienced by a grandparent can increase DNA methylation and that effect can be found in first- and second-generation offspring. 'Transgenerational Methylation Effects' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Key Takeaways

- DNA is highly condensed in the nucleus
- The DNA must unwind for transcription to take place
- Epigenetic modifications can alter how easily the DNA can unwind
- Epigenetic modifications can be inherited

Test Yourself!

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Video Lecture

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PART III

NERVOUS SYSTEM ORGANIZATION

16.

ANATOMICAL TERMINOLOGY

Familiarity with the terminology used to describe location and relationships within the nervous system is critical as we move forward into examining brain systems.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

Directional Terms

Directional terms are used to locate one structure, usually in relation to another structure. Some terms, like dorsal or ventral, are relative to the axis of the central nervous system, so the direction these terms define changes if used for brain regions versus other body regions. Other terms, like superior or inferior, keep their meaning across the entire body.

- Anterior: In front of; toward the face
- Posterior: Behind; toward the back
- Superior: Above; toward the head
- Inferior: Below; toward the feet
- Medial: Toward the middle
- Lateral: Toward the edge
- Dorsal: Toward the top of the brain or the back of the spinal cord
- Ventral: Toward the bottom of the brain or the front of the spinal cord
- Rostral: Toward the front of the brain or the top of the spinal cord
- Caudal: Toward the back of the brain or the bottom of the spinal cord

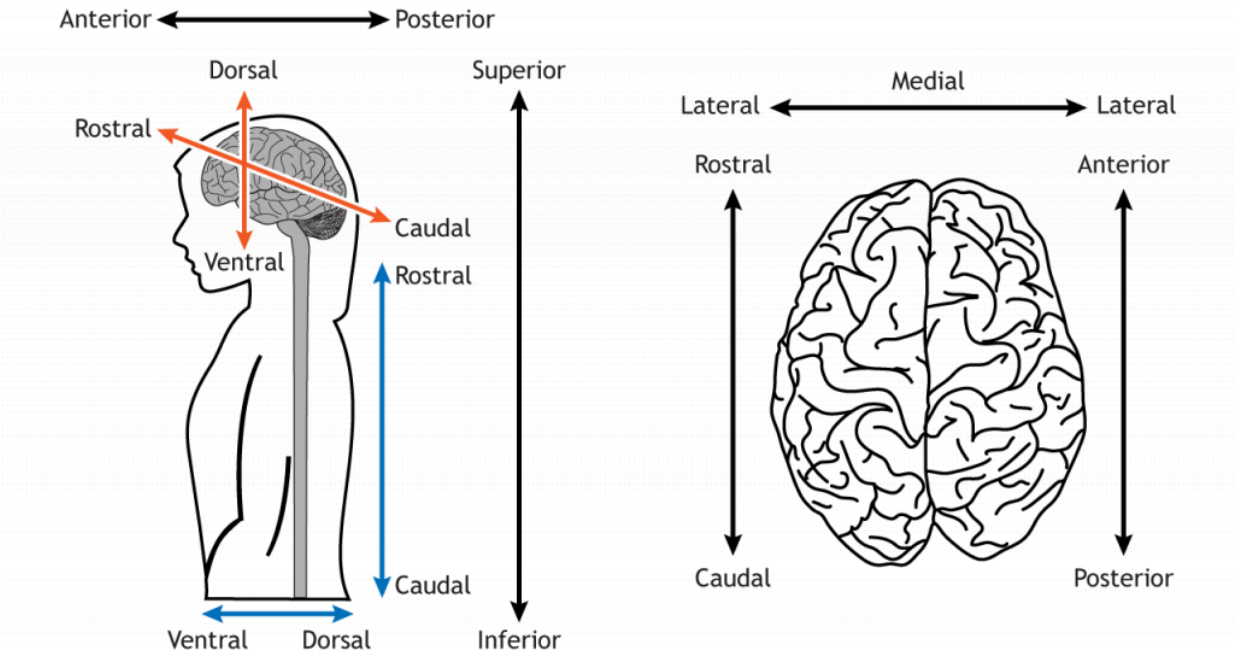

Figure 16.1. Directional terms used to locate nervous system structures. The dorsal / ventral and rostral / caudal pairs point in different directions depending on if they are referring to the axis of the brain (orange arrows) or the axis of the spinal cord (blue arrows). The definitions of each term are described in the text. 'Anatomical Directions' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Anatomical Planes

There are planes or axes that can be used to examine the nervous system. The frontal or coronal plane is a vertical plane in a medial to lateral direction, dividing objects into front and back pieces. The sagittal plane is also a vertical plane but in a rostral-caudal direction, meaning it divides objects into right and left regions. Finally, the horizontal plane divides objects into top and bottom regions.

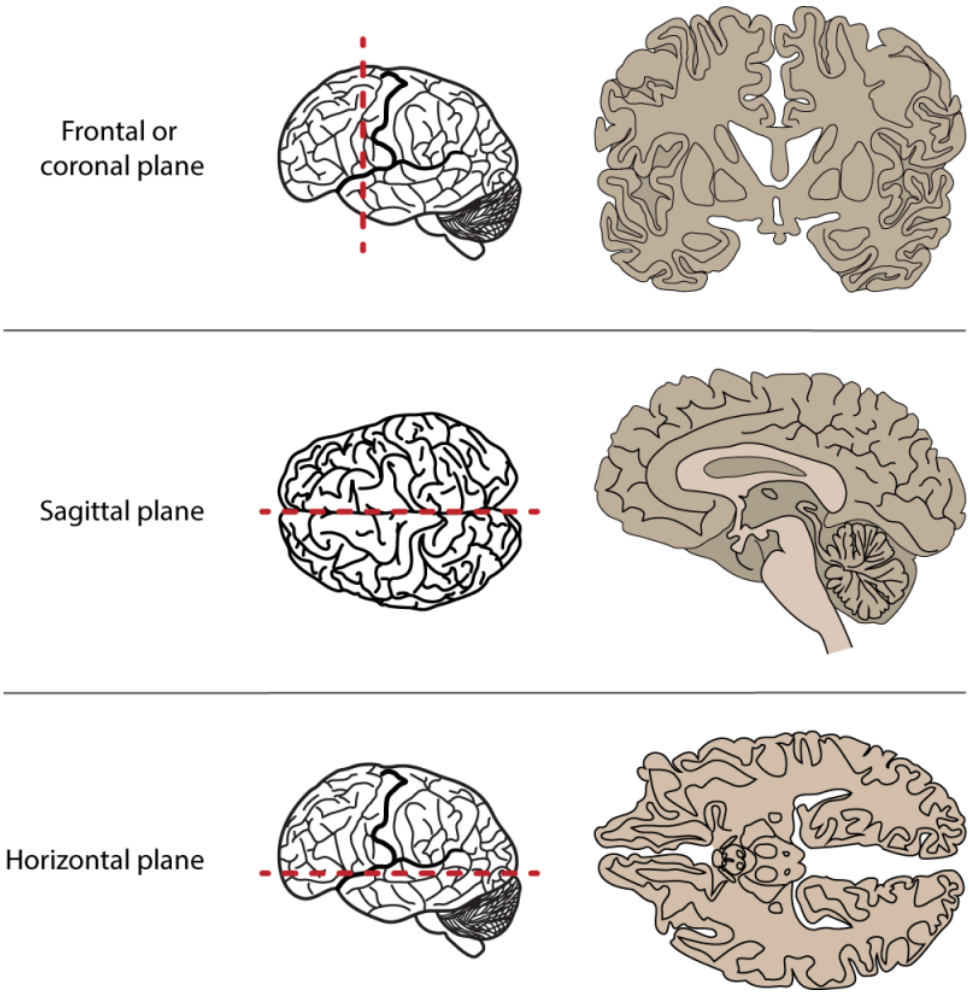

Figure 16.2. Three anatomical planes are used to divide the nervous system to be able to view internal regions and structures. The frontal or coronal plane is a vertical plane that runs parallel to the eyes or ears and will divide the body into front and back regions. The sagittal plane is a vertical plane that runs perpendicular to the eyes or ears and will divide the body into left and right regions. The horizontal plane runs parallel to the ground and will divide the body into top and bottom regions. 'Anatomical Planes' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Nervous System Divisions

The nervous system is divided into two primary components. The central nervous system (CNS) is comprised of the brain and the spinal cord. The peripheral nervous system (PNS) is comprised of the cranial and spinal nerves. When information flow is described in the nervous system, it can either be

afferent communication, meaning it is moving from the periphery to the brain, or efferent communication, meaning it is moving from the brain to the periphery.

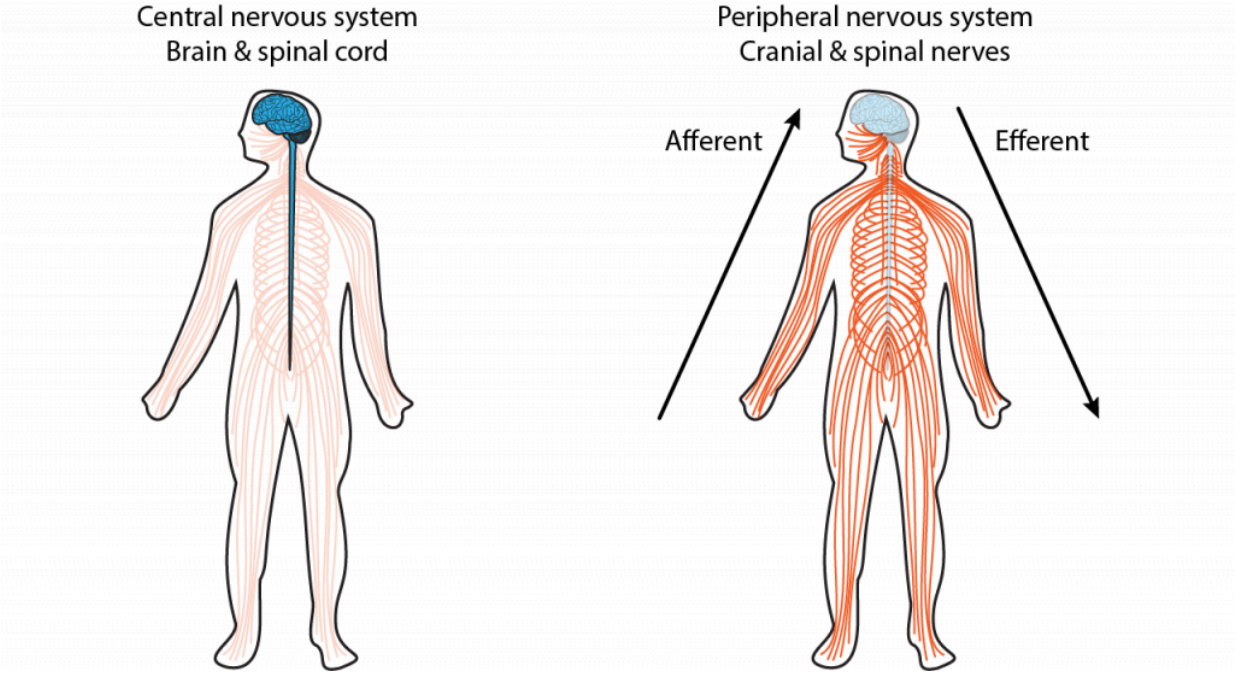

Figure 16.3. The nervous system is divided into the central nervous system, which includes the brain and spinal cord, and the peripheral nervous system, which includes the cranial and spinal nerves. Information traveling toward the brain is called afferent, whereas information traveling from the brain is called efferent. 'CNS and PNS' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Tissue in the central nervous system can be further divided into either white matter or gray matter. White matter regions are comprised of axons. It appears white due to the myelin sheath on the axons. Gray matter regions are comprised of cell bodies and dendrites. Gray matter is the location of most synapses.

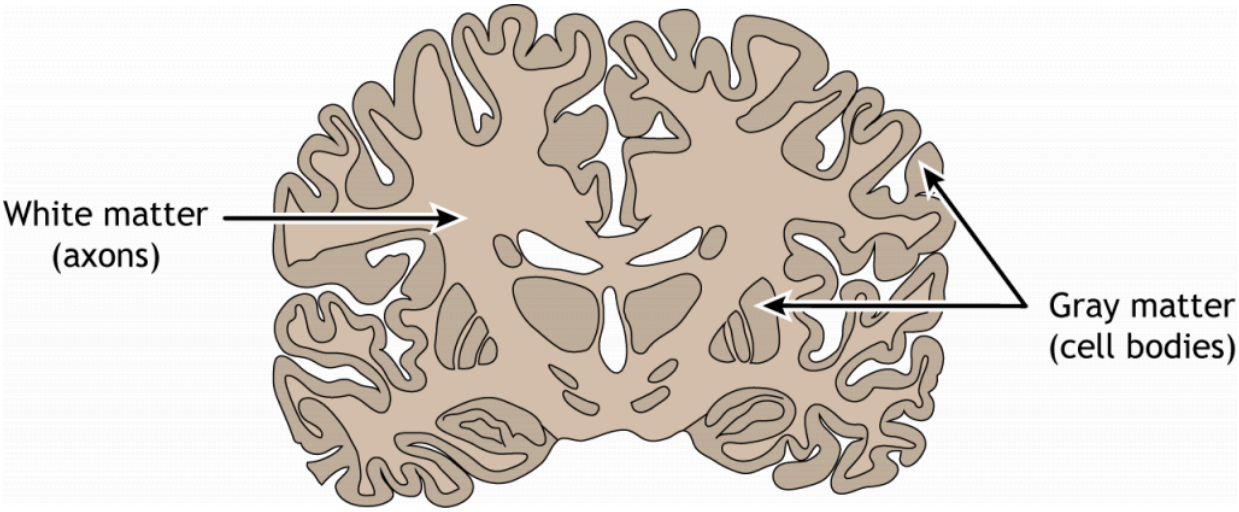

Figure 16.4. The central nervous system tissue can be divided into white and gray matter. White matter is primarily myelinated axons. Gray matter is primarily neuronal cell bodies and dendrites. In the brain, the surface of the cerebral cortex is a layer of gray matter. White matter can be found below the gray matter layer and is the location of the axons traveling to and from the cortical cell layer. Gray matter can also be found deep in the brain in subcortical regions that play critical roles in behavior. 'White and Gray Matter' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Key Takeaways

- Anatomical terminology is critical for determining neurological landmarks

Test Yourself!

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Video Lecture

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17.

EXTERNAL BRAIN ANATOMY

The brain is comprised of the cerebrum, cerebellum, and brainstem. The cerebrum is the most prominent region of the brain. It is divided into left and right hemispheres. The hemispheres have many of the same functions, for example, each perceives touch on one side of the body, but some functions, like language, demonstrate laterality, meaning they are primarily controlled on one side of the brain. The cerebral hemispheres in humans have many folds to increase the surface area of the brain. The ridges are called gyri and the grooves are called sulci. Large sulci are often called fissures.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

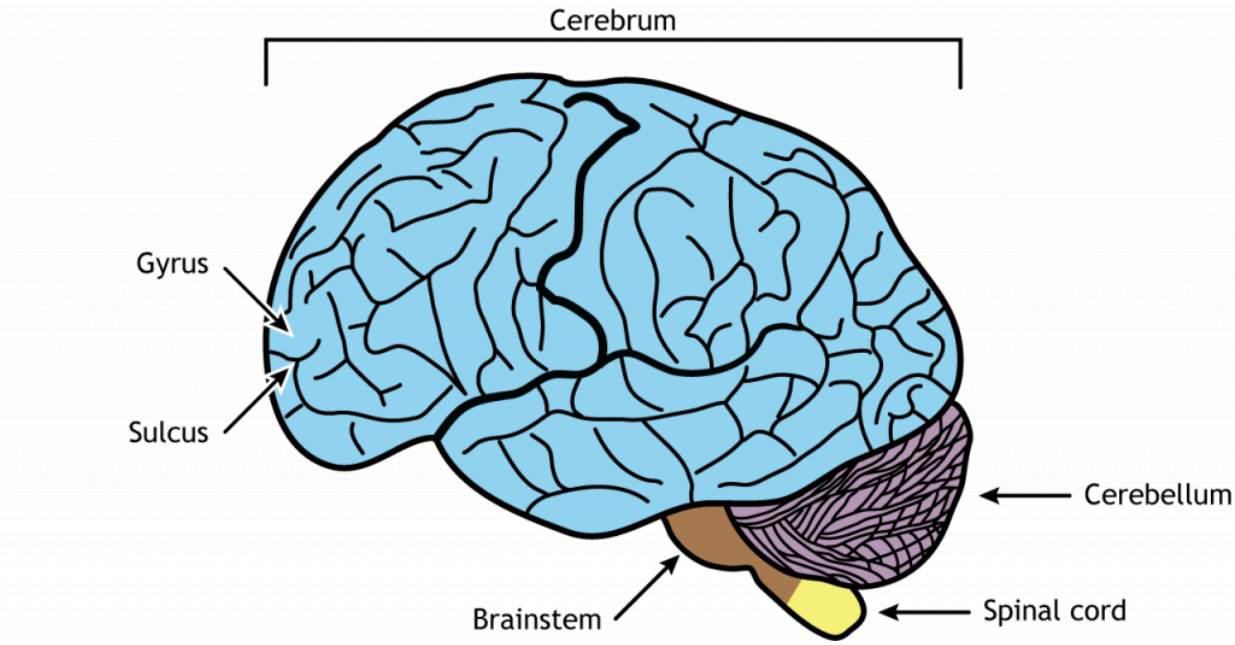

Figure 17.1 An external, side view of the parts of the brain. The cerebrum, the largest part of the brain, is organized into folds called gyri and grooves called sulci. The cerebellum sits behind (posterior) and below (inferior) the cerebrum. The brainstem connects the brain with the spinal cord and exits from the ventral side of the brain. 'External Brain Regions' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The four lobes of the brain are each responsible for specific functions

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Frontal Lobe

The cerebral hemispheres of the brain are divided into four lobes. The frontal lobes are the most rostral, located in the front of the brain and are responsible for higher level executive functions, like attention, critical thinking, and impulse control. They are the last brain region to fully develop, not completing development until individuals reach their 20s. The frontal lobes are also the location of

the primary motor cortex, the region of the brain responsible for planning and executing movement. The primary motor cortex is located in the precentral gyrus.

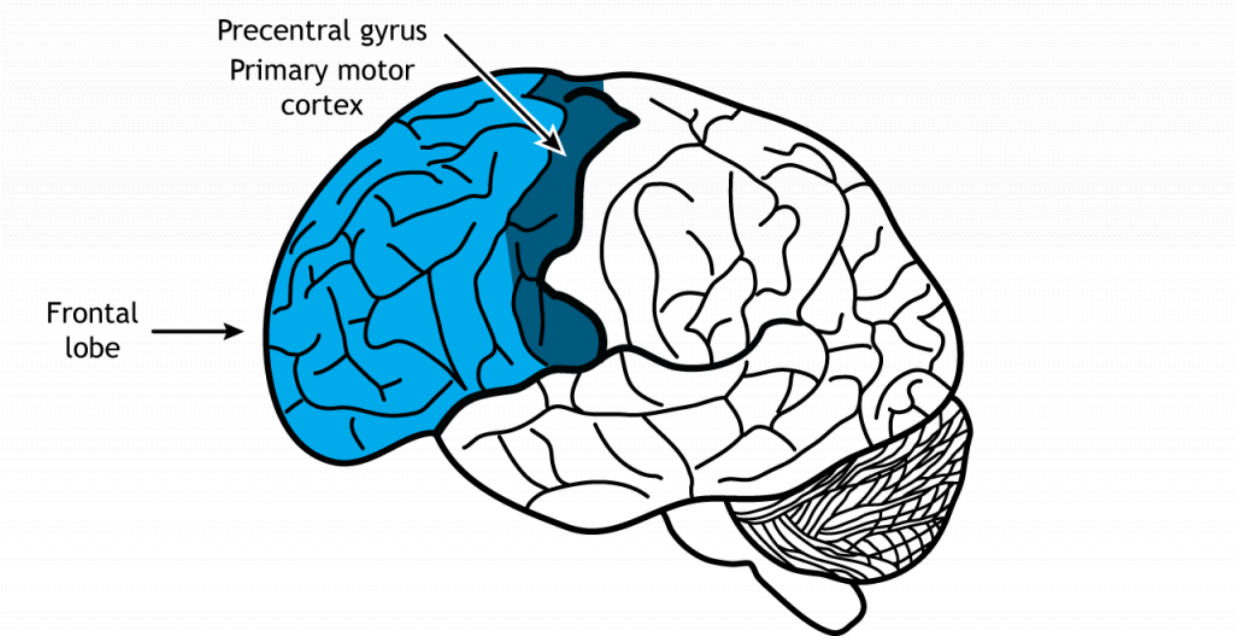

Figure 17.2. The frontal lobe is located in the front of the brain. It includes the precentral gyrus, the location of the primary motor cortex. 'Frontal Lobe' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the frontal lobe using the BrainFacts.org 3D Brain

Parietal Lobe

The central sulcus lies caudal to the frontal lobe and divides the frontal lobes from the parietal lobes. The parietal lobes are important for processing sensory information. The primary somatosensory cortex is located in the postcentral gyrus of the parietal lobe and is responsible for the perception of touch and pain. The parietal lobes also perform higher-level visual processing.

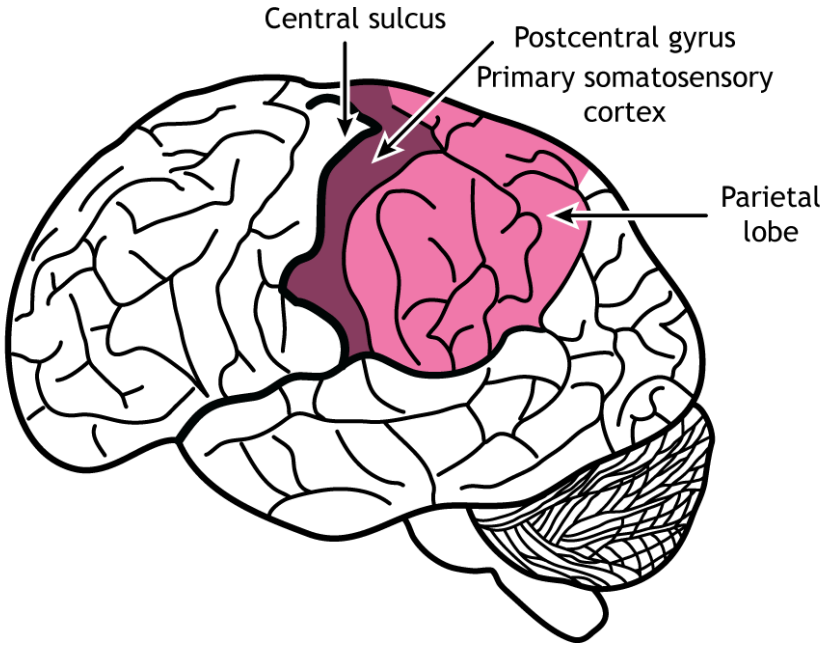

Figure 17.3. The parietal lobe is located on the top of the brain. It includes the postcentral gyrus, the location of the primary somatosensory cortex. The central sulcus divides the parietal lobe from the frontal lobe. 'Parietal Lobe' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the parietal lobe using the BrainFacts.org 3D Brain

Temporal Lobe

The temporal lobes are located on the side of the brain, separated from the frontal and parietal lobes by the lateral fissure. Like the parietal lobe, the temporal lobe plays a role in sensory processing, specifically with hearing, smell, taste, and higher-level visual processing. The temporal lobe is also important for speech and memory. Beneath the cerebral cortex, deep in the temporal lobes, lie the hippocampus and amygdala, two regions of the limbic system, a circuit important for emotion and memory.

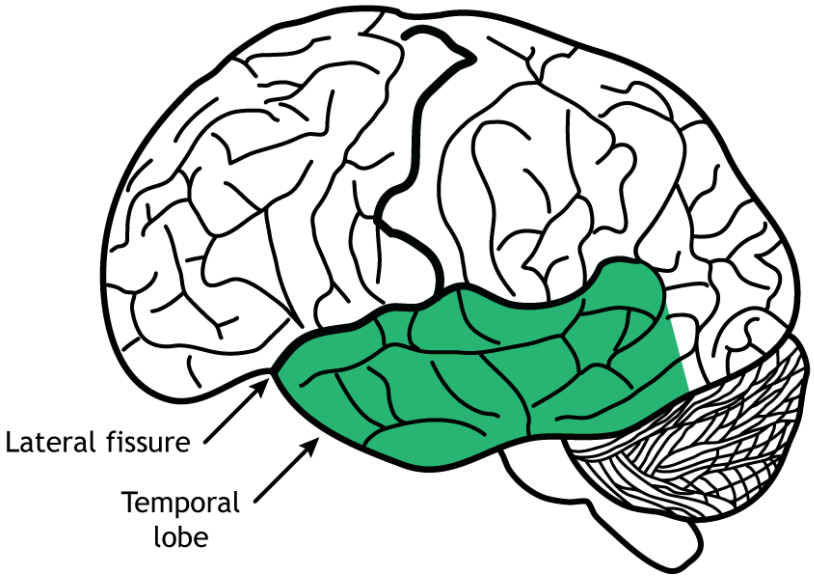

Figure 17.4. The temporal lobe is located on the side of the brain. The lateral fissure divides the temporal lobe from the frontal and parietal lobes. 'Temporal Lobe' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the temporal lobe using the BrainFacts.org 3D Brain

Occipital Lobe

The last lobes are the occipital lobes, the most caudal lobes located in the back of the brain. The occipital lobes' primary function is processing of visual information.

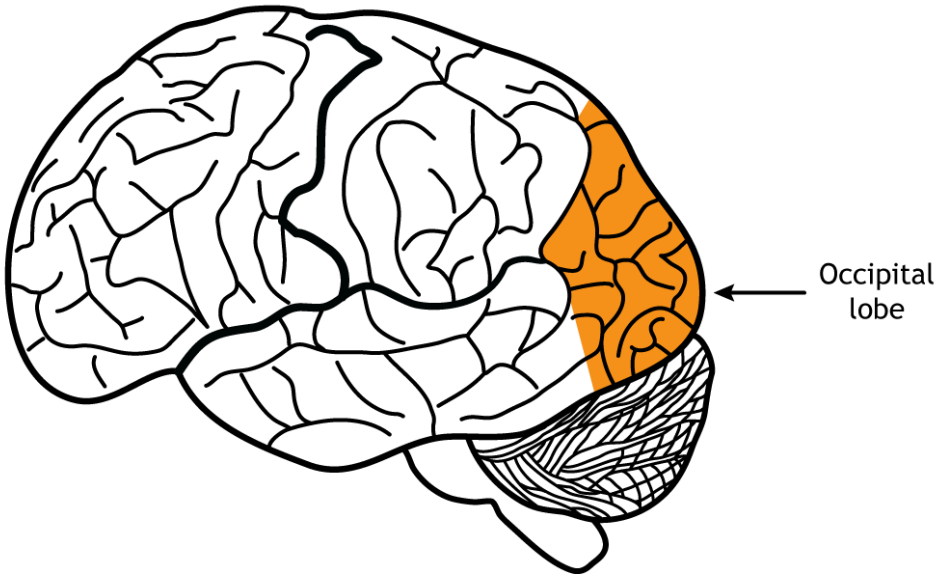

Figure 17.5. The occipital lobe is located in the back of the brain. 'Occipital Lobe' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the occipital lobe using the BrainFacts.org 3D Brain

Non-Cerebral Components

The cerebellum lies inferior to the occipital lobes. The cerebellum is also divided into two hemispheres, like the cerebral cortex. The cerebellum is best known for its role in regulation and control of movement, but it is also involved in cognitive functions like emotions.

The brainstem is located between the cerebrum and the spinal cord. It is important for regulating critical functions like heart rate, breathing, and sleep. It is also the location of most of the cranial nerves.

The spinal cord, which is part of the central nervous system but not part of the brain, is responsible for receiving sensory information from the body and sending motor information to the body. Involuntary motor reflexes are also a function of the spinal cord, indicating that the spinal cord can process information independently from the brain.

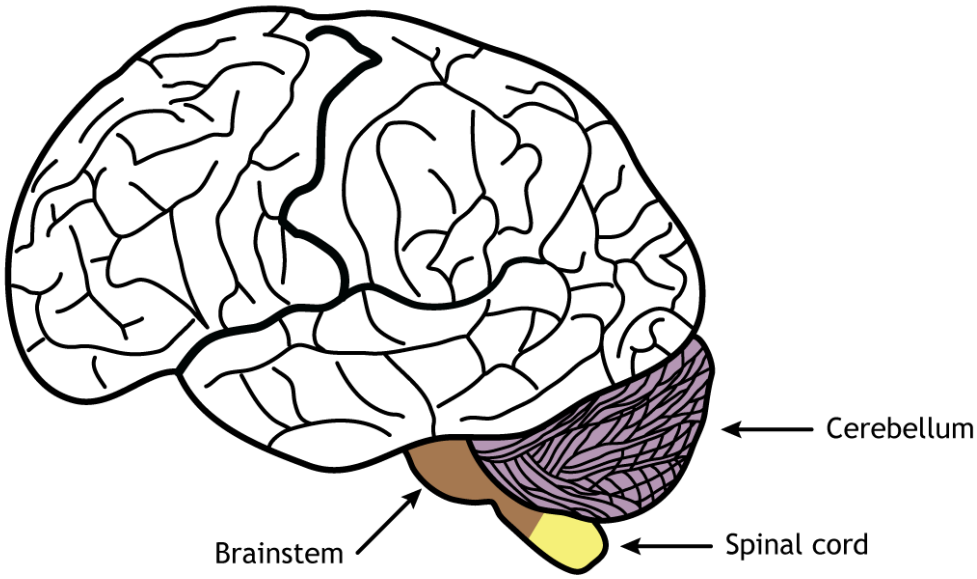

Figure 17.6. The cerebellum, brainstem, and spinal cord are located below the brain. 'Hindbrain' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the brainstem using the BrainFacts.org 3D Brain
View the cerebellum using the BrainFacts.org 3D Brain

Landmarks on the brain can be seen from different planes of view

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Dorsal View

Viewing the brain from above shows the bilateral symmetry of the left and right cerebral hemispheres, which are separated by the longitudinal fissure. The frontal, parietal, and occipital lobes can be seen. Similar to the lateral view, the central sulcus divides the frontal lobe from the parietal lobe. The precentral gyrus, which is the location of the primary motor cortex, sits rostral to the central sulcus,

whereas the postcentral gyrus, which is the location of the primary somatosensory cortex, lies caudal to the central sulcus.

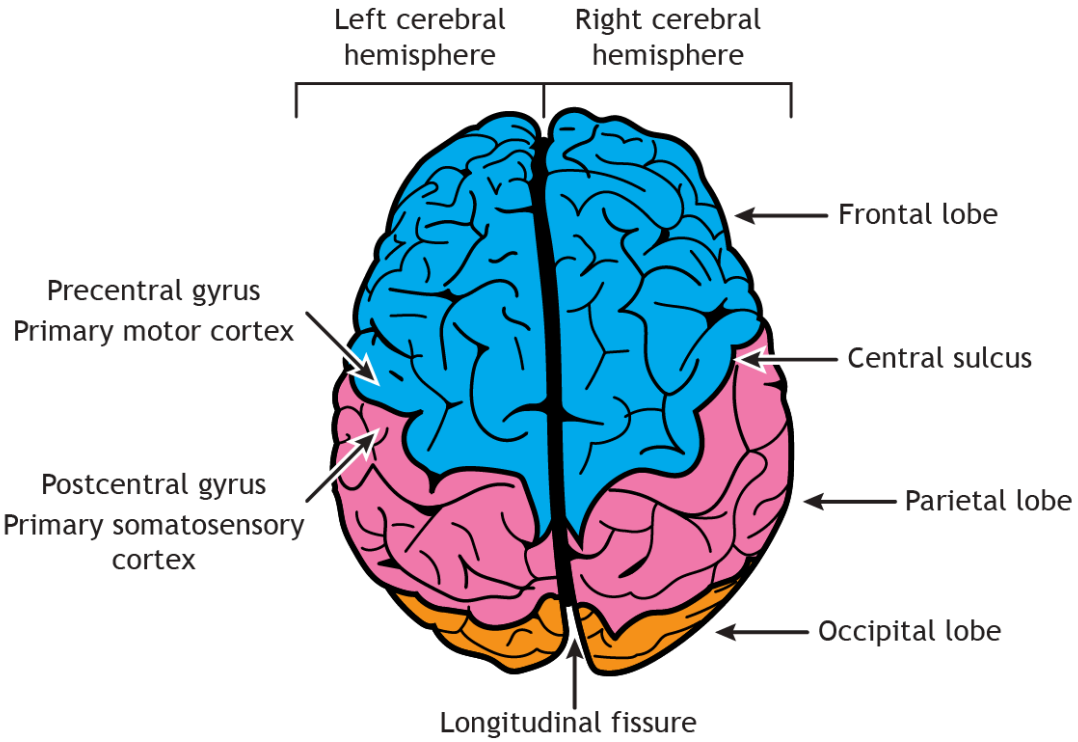

Figure 17.7. The dorsal view of the brain. The left and right cerebral hemispheres are separated by the longitudinal fissure. Three of the four lobes, the frontal, parietal, and occipital can be seen in this view. 'Dorsal Surface of Brain' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Ventral View

Underneath the brain, the frontal and temporal lobes are visible, as is the cerebellum. Like the dorsal view, the longitudinal fissure divides the cerebrum into right and left hemispheres. The pons and medulla, components of the brain stem, connect the cerebrum to the spinal cord.

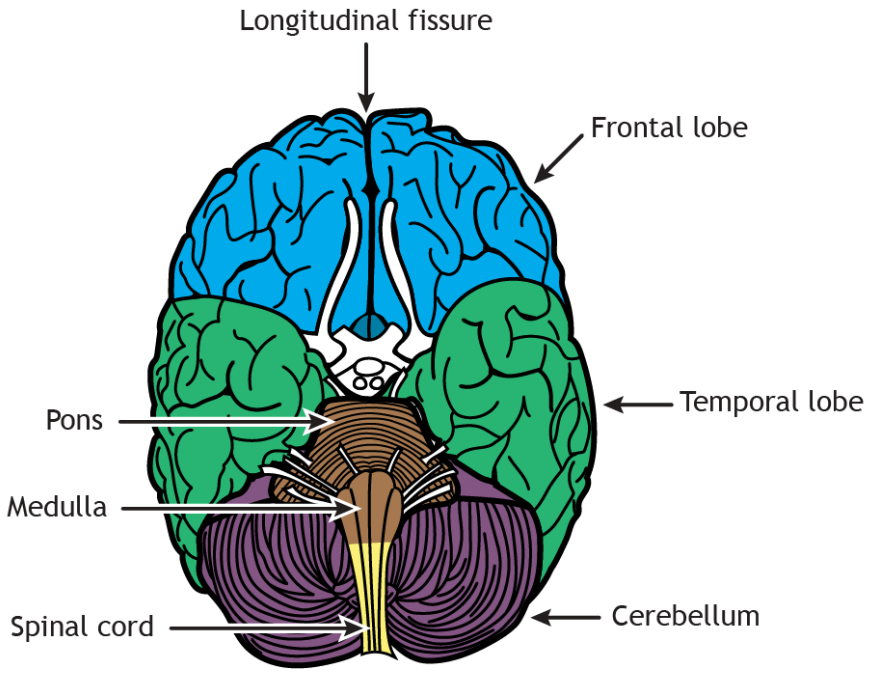

Fig 17.8. Ventral Surface of the Brain. The frontal lobe, temporal lobe, cerebellum, pons, medulla, spinal cord and longitudinal fissure can be seen when viewing the bottom of the brain. "Ventral Surface of the Brain" by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Cranial nerves are also visible on the ventral surface of the brain. The olfactory tract leads out to the olfactory bulb, which connects to the olfactory nerve. The optic tract crosses the midline at the optic chiasm, and then the optic nerve projects to the retina. Other cranial nerves enter or leave the brain at the level of the brainstem. The hypothalamus is located caudal to the pons, and the mammillary bodies project out from the hypothalamus.

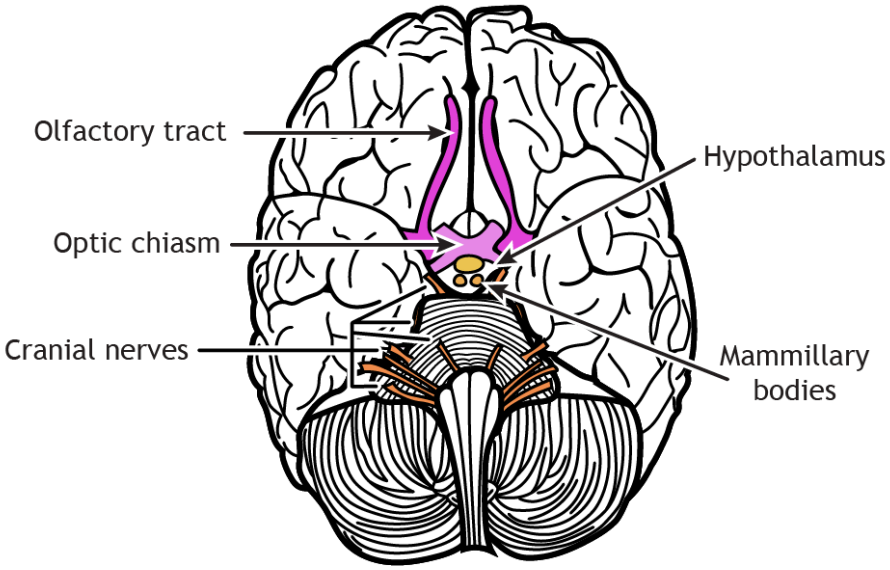

Figure 17.9. Cranial nerves, optic chiasm, and olfactory tract are visible on the bottom of the brain. In the center, the hypothalamus and mammillary bodies can also be seen. "Ventral Surface Cranial Nerves" by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Key Takeaways

- The four lobes of the cerebral cortex each have specific functions
- The cerebral cortex has gyri and sulci to increase the surface area
- The cerebral cortex, underlying structures, cerebellum, brainstem, and spinal cord form the central nervous system

Test Yourself!

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

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18.

INTERNAL BRAIN ANATOMY

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

A mid-sagittal section slices the brain through the longitudinal fissure and separates the right hemisphere from the left. It also reveals more structures. In a mid-sagittal view, all four cortical lobes are visible. The frontal lobe is separated from the parietal lobe by the central sulcus, the occipital lobe is in the posterior region of the brain, and the temporal lobe can be seen behind the brainstem. The cerebellum, pons, medulla, and spinal cord are seen caudal to the cerebrum, but in this view, the midbrain, which is made up of two regions, the tegmentum and tectum, are also visible superior to the pons. The corpus callosum is located in the center of the cerebrum and is a white matter bundle made up of axons crossing from one hemisphere to the other. Surrounding the corpus callosum is the cingulate gyrus, a region important for emotion.

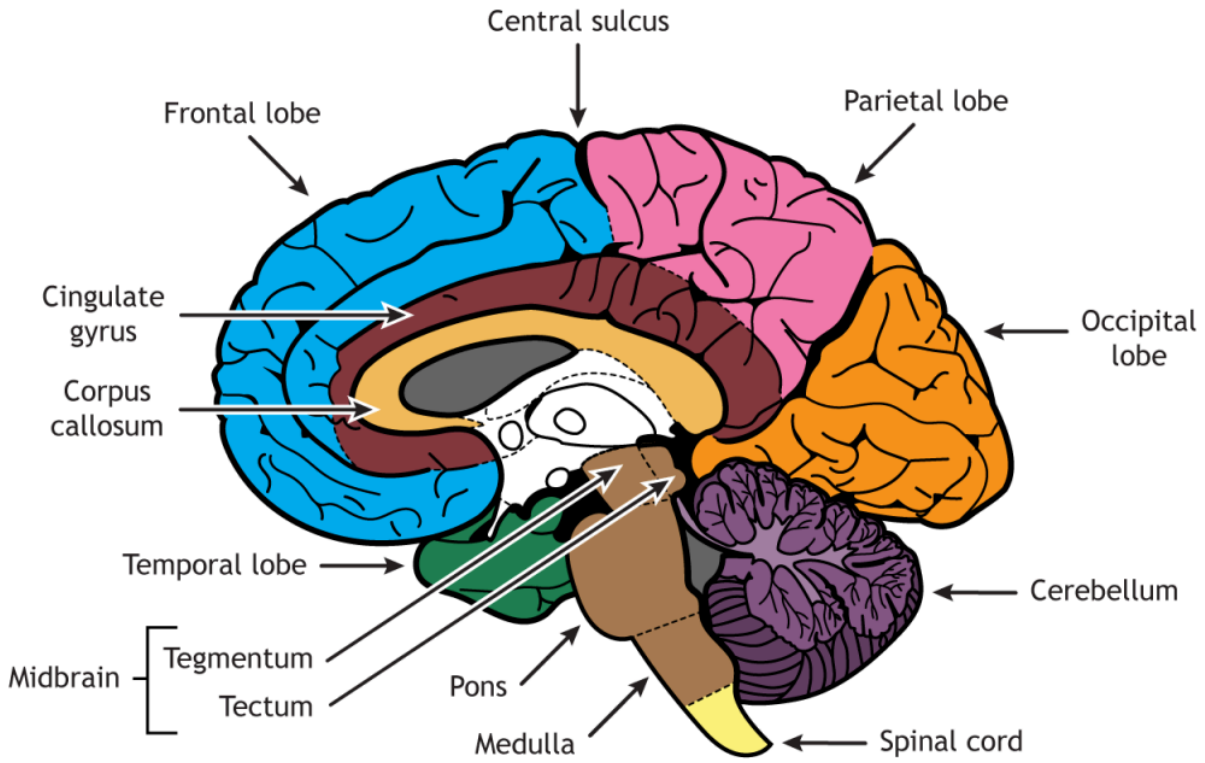

Figure 18.1. A midsagittal section of the brain. All four cerebral lobes are visible, as in the cingulate gyrus, which extends through the medial aspects of the frontal and parietal lobes. The corpus callosum sits beneath the cingulate gyrus. Below the cerebrum lies the midbrain, pons, medulla and cerebellum. 'Internal Brain Regions' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The diencephalon consists of subcortical structures and connects the forebrain to the midbrain

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The diencephalon region of the brain consists of the region around the thalamus and hypothalamus. It is located inferior to the fornix and lateral ventricle, posterior to the anterior commissure, and superior to the brainstem. The fornix is a nerve fiber bundle containing primarily output from the hippocampus. The anterior commissure sits above the hypothalamus and is white matter tract, like the corpus callosum, that allows information to cross from one hemisphere to the other. The thalamus

is best known for its role as a relay and processing location for the sensory and motor systems. The hypothalamus has a variety of functions including control of stress and the "fight or flight" response of the autonomic nervous system, reproduction, sleep, thirst, hunger, and other homeostatic functions. The mamillary bodies sit in the posterior part of the hypothalamus and are important for memory. The optic nerves from the retina cross at the optic chiasm, and then the optic tracts continue back into the diencephalon.

In the brainstem, the tectum of the midbrain consists of the superior and inferior colliculi, which are important for vision and hearing, respectively. The reticular formation is located throughout the brainstem. Networks within the reticular formation are important for regulating sleep and consciousness, pain, and motor control. The fourth ventricle lies between the brainstem and the cerebellum.

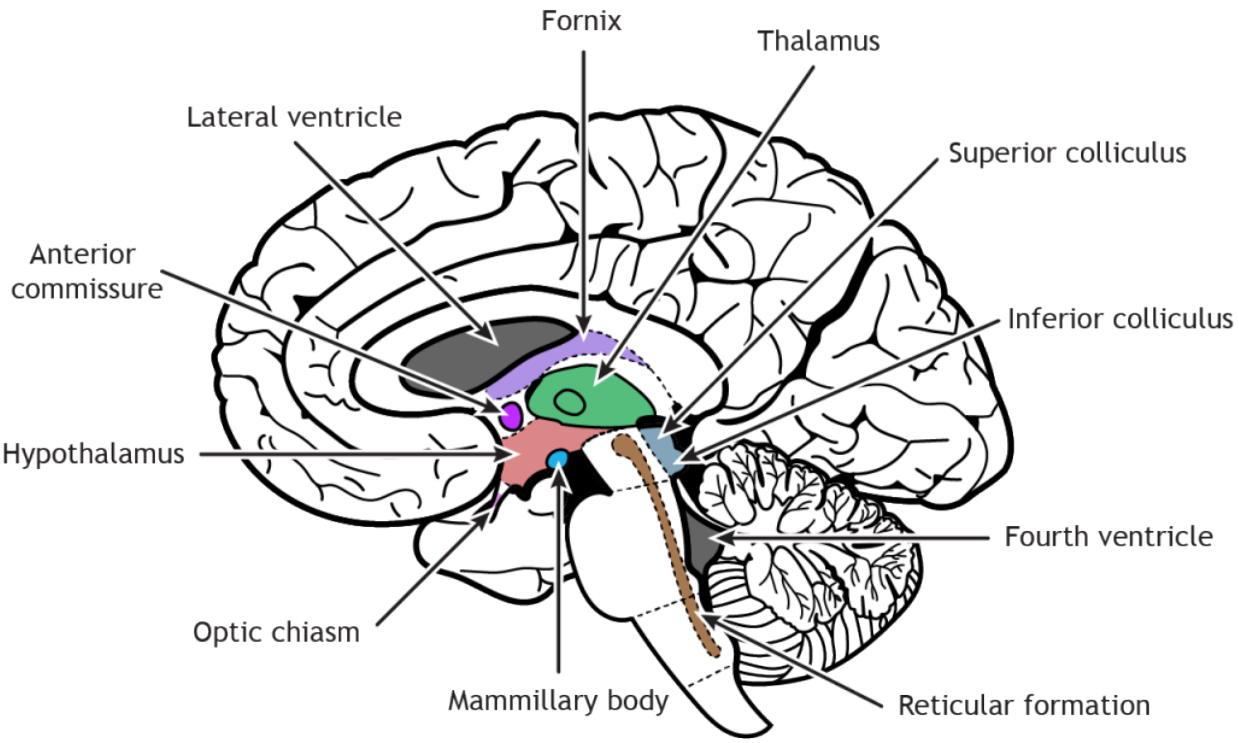

Figure 18.2. Regions of the diencephalon and brainstem in a midsagittal section. The thalamus, hypothalamus, and mammillary bodies are part of the diencephalon. The optic tracts leave the diencephalon, cross at the optic chiasm, and continue as the optic nerves out to the retina. The anterior commissure and fornix create the front and upper border of the diencephalon. The superior and inferior colliculi are part of the midbrain tectum, and the reticular formation is located throughout the brainstem. 'Midsagittal Diencephaon and Brainstem' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The basal ganglia, amygdala, and hippocampus are subcortical forebrain structures with a range of functions

Coronal sections of the brain allow deep tissue structures to be visible. A cut through the anterior portion of the temporal lobe shows the amygdala, a region important for emotion, located in the medial temporal lobe. The regions of the basal ganglia are also visible; the striatum, which consists of the caudate and the putamen, and the globus pallidus. The basal ganglia has multiple functions but is best known for its role in regulation of movement. The lateral ventricle sits medial to the basal ganglia, and above the lateral ventricle is the corpus callosum. The third ventricle is located in the middle of the brain, inferior to the lateral ventricle, and the optic chiasm lies inferior to the third ventricle. The longitudinal fissure separates the left and right cerebral hemispheres, and the lateral sulcus is the border between the frontal and temporal lobes.

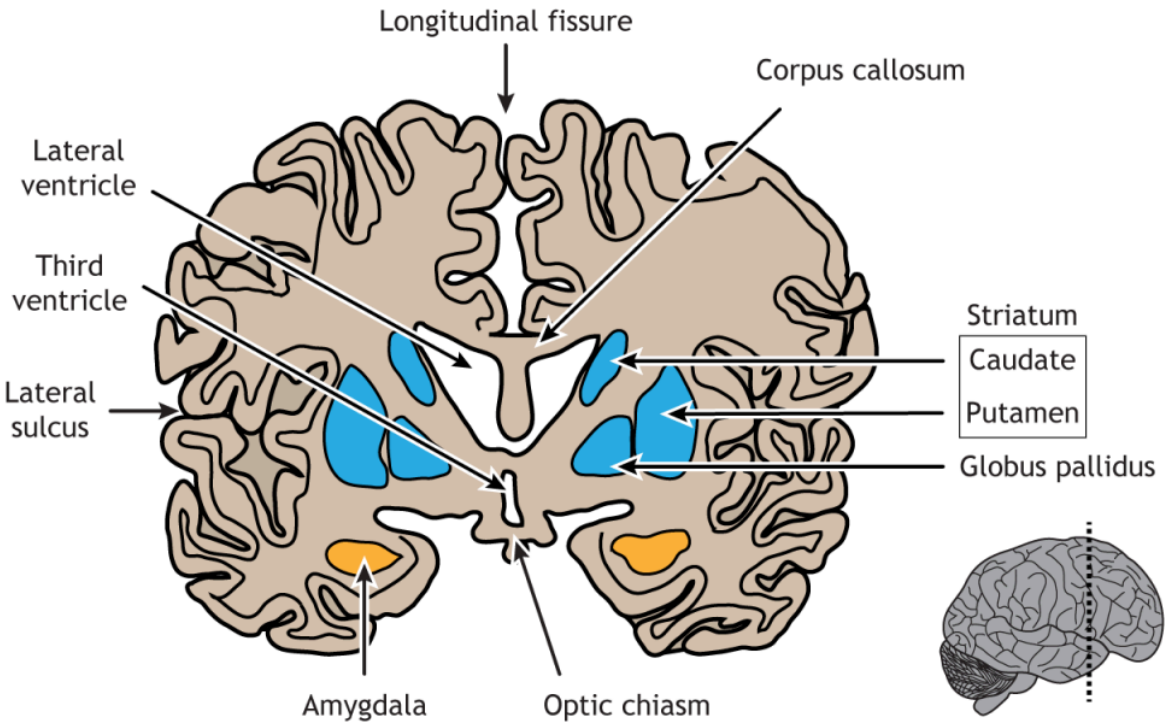

Figure 18.3. A coronal section at the location of the amygdala. The amygdala is located in the temporal lobe, and the basal ganglia is a subcortical structure located near the lateral ventricle. The corpus callosum, third ventricle, longitudinal fissure, and lateral sulcus can also be seen. 'Amygdala and Basal Ganglia' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

A coronal section taken closer to the central sulcus will make the hippocampus visible. The hippocampus is known for its role in memory and spatial awareness. At this location, the basal ganglia is more defined; the caudate and putamen are still present, but the two separate regions of the globus pallidus, the internal and external segments, can be seen, as well as the subthalamic nucleus and the substantia nigra. The thalamus is located on either side of the third ventricle. The corpus callosum is superior to the lateral ventricle. The cerebrum is divided in half by the longitudinal fissure, and the lateral sulcus separates the temporal lobe from the frontal and parietal lobes.

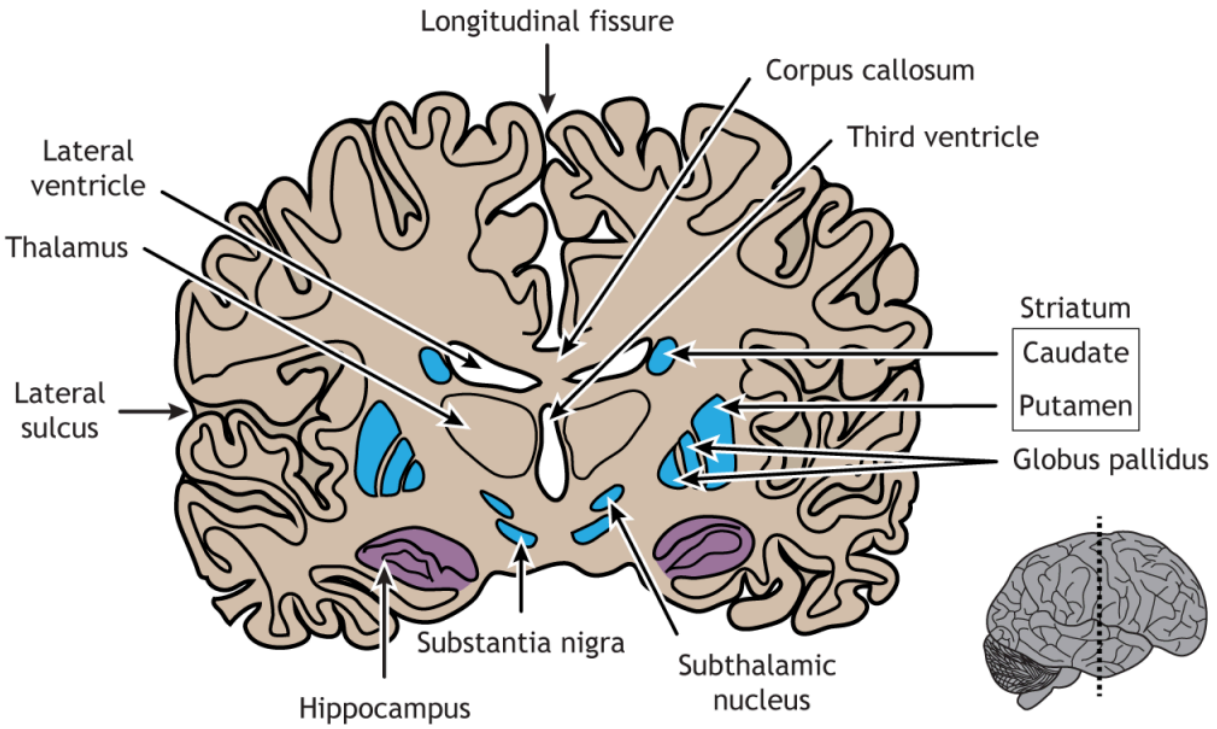

Figure 18.4. A coronal section at the location of the hippocampus. The hippocampus is located in the temporal lobe, and the basal ganglia is a subcortical structure located lateral to the thalamus and lateral ventricle. 'Hippocampus and Basal Ganglia' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Key Takeaways

- Like the external anatomy, internal structures also have specific functions
- Sectioning the brain in different ways provides views of subcortical regions

Test Yourself!

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https://openbooks.lib.msu.edu/neuroscience/?p=1622#h5p-38

Video Lecture

19.

BRAINSTEM AND SPINAL CORD

Brainstem

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

The brainstem is made up of the midbrain, pons, and medulla. It is located between the diencephalon (thalamus and hypothalamus region) and the spinal cord. All connections between the brain and the body must travel through the brainstem. The brainstem also plays an important role in the regulations of consciousness and regulates critical functions like heart rate and breathing.

The mammillary bodies are located on the ventral side of the hypothalamus. The infundibulum is the stalk between the hypothalamus and the pituitary and is located caudal to the mammillary bodies. The optic tract leaves the diencephalon and crosses the midline at the optic chiasm.

Illustration of the brainstem and diencephalon. Details in caption and text.

Figure 19.1. The brainstem and diencephalon. The pons and medulla are parts of the brainstem. The diencephalon consists of the thalamus, hypothalamus, infundibulum, mammillary body, and the optic tract and chiasm. 'Brainstem' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Cranial Nerves

A critical component of the brainstem is the presence of the twelve pairs of cranial nerves, which provide sensory and motor innervation to the head, face, and neck, as well as autonomic innervation to the organs in the abdomen. The first two cranial nerves (olfactory [I] and optic [II]) are part of the central nervous system. They carry sensory information, smell and vision, respectively. They enter the

forebrain and not the brainstem. The remaining nerves, like spinal nerves, have their axons in the peripheral nervous system. The oculomotor [III] and trochlear nerves [IV], whose functions are to move the eye, exit the brainstem from the midbrain. The trochlear nerve is the only cranial nerve to exit on the dorsal surface of the brainstem. The trigeminal nerve [V] is the largest cranial nerve and carries both sensory and motor information from the face; axons in this nerve enter and exit from the pons. The abducens nerve [VI], another eye movement nerve, exits at the junction of the pons and medulla, as do the facial [VII] and vestibulocochlear [VIII] nerves. The facial nerve contains both sensory and motor axons, whereas the vestibulocochlear nerve carries only sensory information related to hearing and balance. The glossopharyngeal [IX] and vagus [X] nerves also carry both sensory and motor information and enter/exit from the medulla. The glossopharyngeal nerve is responsible for movement of the throat muscles and taste; the vagus nerve is the primary autonomic cranial nerve and contains parasympathetic fibers that innervate the heart, lungs, and abdominal organs. Finally, the spinal accessory [XI] and hypoglossal [XII] are motor nerves with the hypoglossal exiting the brainstem from the medulla and the spinal accessory nerve exiting from the cervical spinal cord. The spinal accessory innervates muscles in the throat, shoulder, and neck, and the hypoglossal innervates muscles of the tongue.

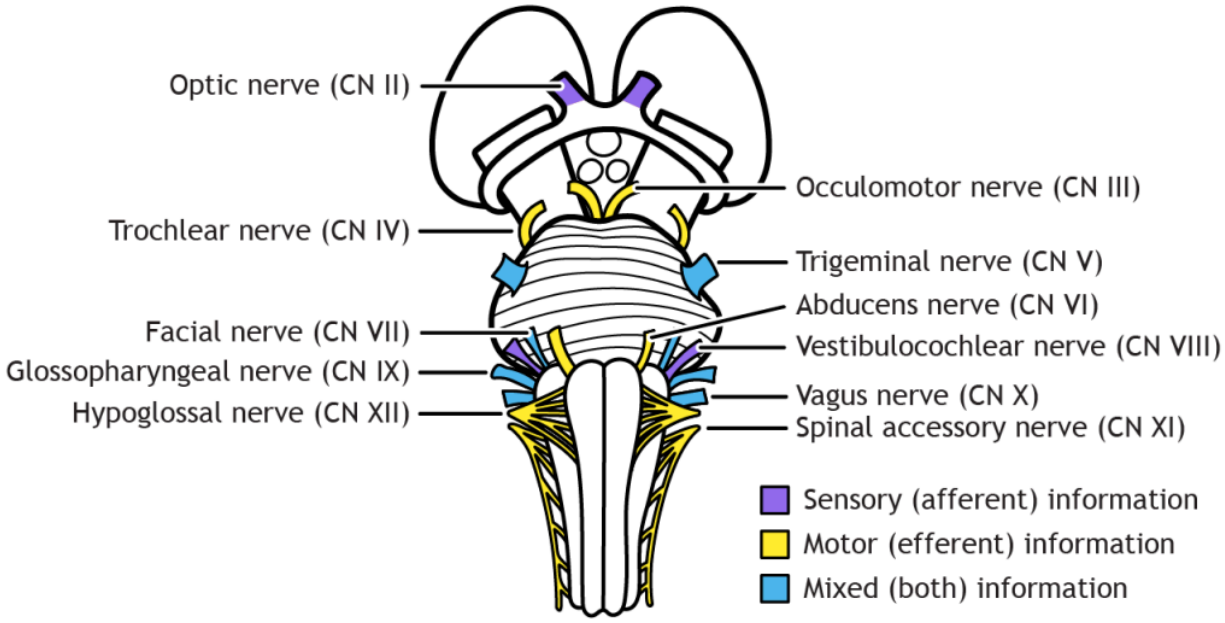


Figure 19. 2. The cranial nerves receive sensory information and send motor information to the head and neck and also carry parasympathetic fibers. The olfactory [I] (not shown), optic [II], and vestibulocochlear [VIII] nerves carry sensory information only. The oculomotor [III], trochlear [IV], abducens [VI], spinal accessory [XI], and hypoglossal [XII] carry motor output only. The trigeminal [V], facial [VII], glossopharyngeal [IX], and vagus [X] carry both sensory and motor information. Cranial nerves three through twelve exit or enter the central nervous system at the level of the brainstem. 'Cranial Nerves' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Spinal Cord

The spinal cord begins at the base of the brainstem. The vertebral column is divided into four main regions: cervical, thoracic, lumbar, and sacral. The spinal cord and spinal nerves that enter and exit the vertebral column are divided into these regions as well. The cervical division consists of seven segments (C1-C7), the thoracic consists of twelve segments (T1-T12), the lumbar consists of five segments (L1-L5), and the sacral division consists of five segments (S1-S5). The shape of the spinal cord changes over the length of the vertebral column, a result of the function of the spinal nerves. For example, motor information to the hands and arms, so the region where motor neurons are located (ventral horn) is larger than segments with minimal motor output.

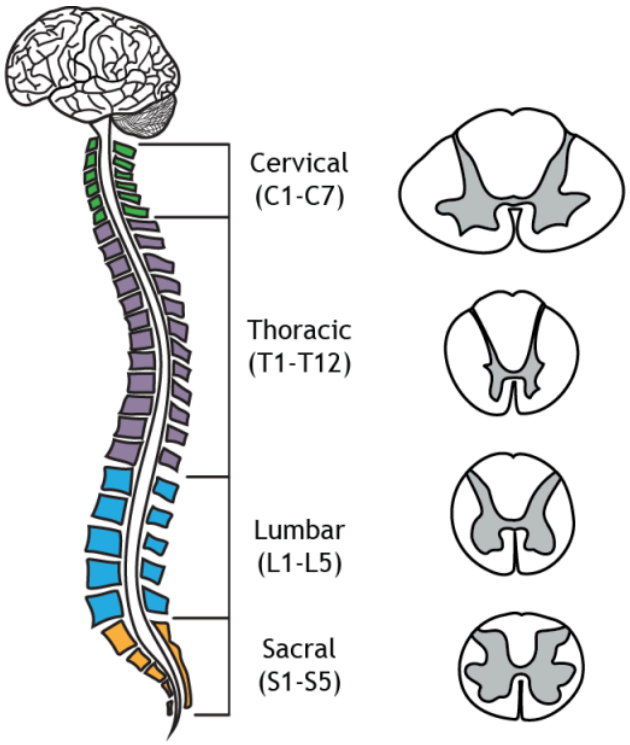


Figure 19.3. The vertebral column and representative spinal cord cross-sections. The vertebral column and corresponding spinal cord and spinal nerves are divided into four regions. The cervical division is the most rostral, starting at the base of the brainstem. The thoracic is the largest division, just caudal to the cervical. The lumbar is the next division, and the sacral is the most caudal. 'Spinal Cord' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The spinal cord is part of the central nervous system, but the fibers that leave and enter the spinal cord are located in the peripheral nervous system. These spinal nerves can then extend to or from target tissue throughout the body.

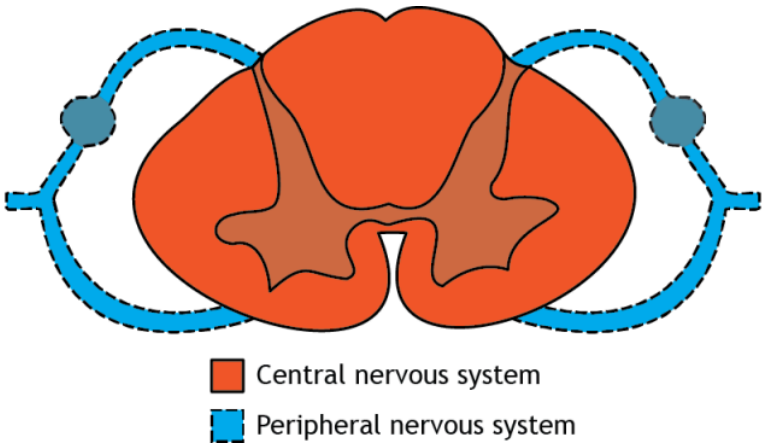


Figure 19.4. The spinal cord is part of the central nervous system, but the axons that exit and enter the spinal cord are in the peripheral nervous system. 'Spinal Cord CNS and PNS' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Like the brain, the spinal cord is also made up of regions of white matter and gray matter. White matter regions are comprised of axons. It appears white due to the myelin sheath on the axons. Gray matter regions are comprised of cell bodies and dendrites. Gray matter is the location of most synapses.

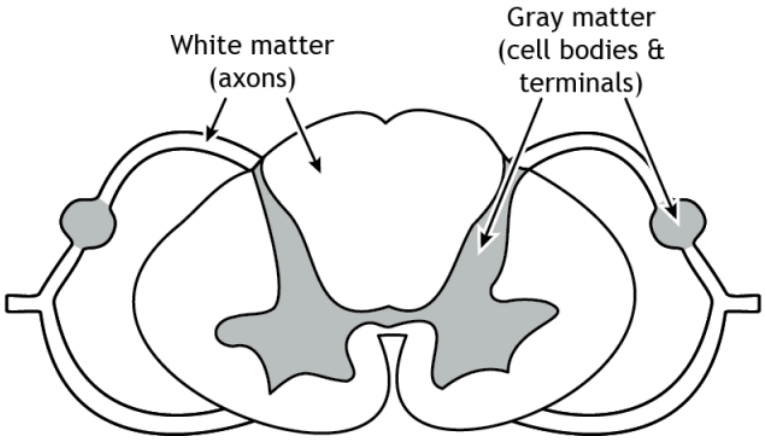


Figure 19.5. The spinal cord can be divided into white and gray matter. White matter is primarily myelinated axons. Gray matter is primarily neuronal cell bodies and dendrites. In the spinal cord, the inner part is gray matter, whereas the surround tissue is white matter. The regions that extend from the central nervous system and into the peripheral nervous system contain primarily axons traveling to or from peripheral targets and therefore are mainly white matter except for ganglia, which are clusters of cell bodies in the periphery. 'Spinal Cord White and Gray Matter' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The white matter in the spinal cord is divided into structures called columns because the axons in these regions are either ascending toward the brain or descending toward the appropriate spinal nerve. The dorsal column is on the dorsal or posterior side of the spinal cord, the ventral column is on the ventral or anterior side of the spinal cord, and the lateral column lies between them. The gray matter is likewise divided into regions called horns. The dorsal horn is the location of sensory synapses, the ventral horn is the location of motor neuron cell bodies, and the lateral horn is the location of cell bodies of the autonomic nervous system. The dorsal root and ventral root consist of the axons of afferent (dorsal) and efferent (ventral) fibers. They combine to form the spinal nerves. Sensory neuron cell bodies are located in the dorsal root ganglion, a gray matter region of the dorsal root.

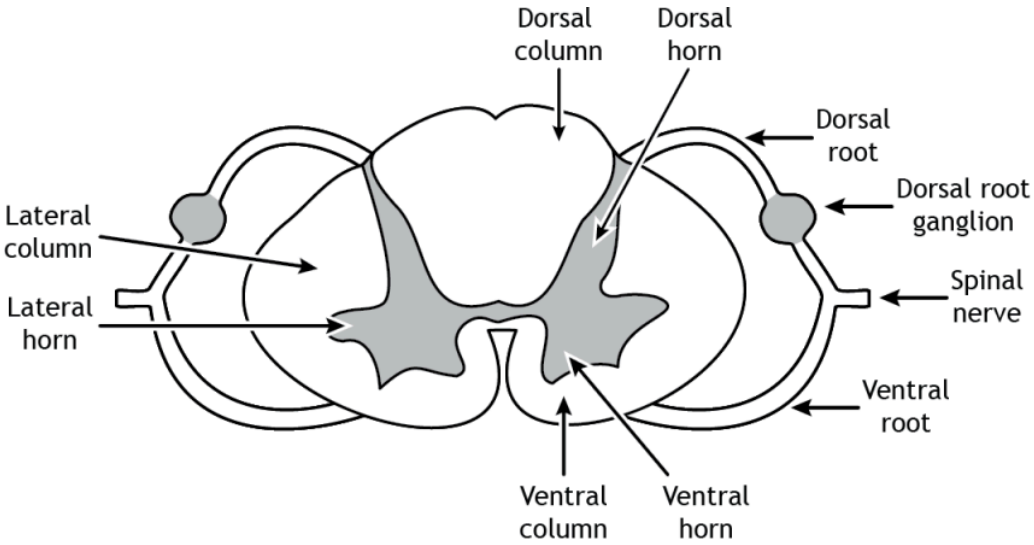


Figure 19.6. The spinal cord is comprised of white and gray matter. The dorsal column and dorsal horn are on the posterior side of the spinal cord. The ventral column and ventral horn are located on the anterior side of the spinal cord. The lateral column and lateral horn are located in the middle. The spinal nerves that extend into the periphery consist of fibers that split into the dorsal root and the ventral root to enter (dorsal) or exit (ventral) the spinal cord. The dorsal root ganglion is a gray matter region of the dorsal root. 'Spinal Cord Anatomy' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Afferent fibers coming from the periphery through the spinal nerves enter the spinal cord via the dorsal root. The cell bodies of sensory neurons are located in the dorsal root ganglion, and the axons continue into the spinal cord and typically synapse in the dorsal horn. Interneurons are very short neurons that are a communication link between cell types in the spinal cord. They can be either excitatory or inhibitory depending on their role. They can also cross the midline of the spinal cord. The cell bodies of motor neurons that innervate skeletal muscles are located in the ventral horn. The efferent axons of these neurons leave the spinal cord via the ventral root and then enter the spinal nerve on their way to their target tissue.

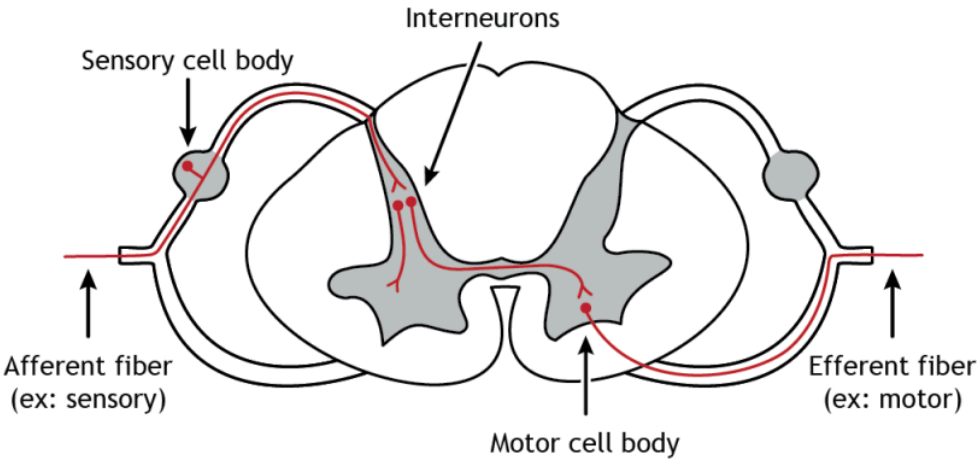


Figure 19.7. Afferent axons coming from the periphery travel through the dorsal root to enter the spinal cord. These axons can synapse on interneurons, cells with short axons which communicate with other cell types. Efferent fibers, like those of the skeletal muscle motor neurons located in the ventral horn, leave the spinal cord through the ventral root. 'Spinal Cord Fibers" 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 brainstem connects the diencephalon to the spinal cord and is responsible for critical body functions
- The cranial nerves enter and exit the central nervous system primarily through the brainstem
- The spinal cord is part of the central nervous system and spinal nerves are part of the peripheral nervous system
- Like the brain, the spinal cord is made up of both white and gray matter

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=1631#h5p-39

Video Lecture

PART IV
SENSORY SYSTEMS

20.

GENERAL PRINCIPLES OF SENSORY SYSTEMS

Each sensory system is obviously quite different in the type of stimulation that it responds to and the manner in which environmental stimuli is converted to neuronal signaling. However, there are many principles that can be generalized across sensory systems.

Sensory transduction

Our sensory systems work by converting different types of stimuli in the environment (i.e. visible light, sound waves, chemical molecules) into action potentials in the nervous system. This conversion is called sensory transduction and occurs in all sensory systems.

Sensory receptors

Sensory transduction begins at the sensory receptors. Each sensory system has specialized cells that are able to detect the environmental stimuli. Photoreceptors detect light, chemical receptors in the tongue and nose detect odors and taste, mechanoreceptors detect touch, and hair cells detect sound.

Receptor Potentials

We have learned about postsynaptic potentials in neurons, receptor potentials are similar membrane potential changes that happen in sensory receptors in response to a stimulus.

Receptive fields

Receptive fields are easiest to understand in the visual and somatosensory systems. The receptive field for a neuron is the region of the retina or skin where a stimulus (light or touch) will evoke a response in the neuron. Receptive fields in the auditory system can consist of a certain frequency of sound and/or the location of sound in space.

Receptive fields can vary in size and shape depending on the characteristics of neuron (i.e. type, location in body, location in pathway). Receptive fields become more complex as information travels to the brain.

Lateral Inhibition

Lateral inhibition is a process used by sensory systems to enhance the perception of signals, particularly at edges, points, or other changes in the stimulus. It occurs because overlapping receptive fields can inhibit each other. This inhibition enhances the perceived differences between the stimulus and the area not stimulated.

Neural Coding

There are a number of different ways in which the nervous system encodes complex information. Two that are common within the sensory systems are line coding and population coding.

Labeled Line Coding

In the labeled line coding of information, one cell encodes for one type of sensory quality. Pain is a good example of this. If a pain receptor is activated, the resulting sensation will be pain, regardless of the manner in which the receptor is stimulated. In other words, the sensory neurons are specifically tuned to one sensory stimulus. If that receptor-cell type was dysfunctional, the sensation will not be perceived. For example, there is a mutation that prevents sodium channels in pain receptors (but not other cell types) from working. When this mutation occurs, the subject cannot feel pain.

Population Coding

In populating coding, one cell can encode more than one sensory modality, and it is the combination of many cells that make up the perception. An example of this is color vision. Each color photoreceptor is most sensitive to a specific color (blue, green, or red), but a range of wavelengths can elicit changes in firing rates in the neuron. Therefore, the responses from a population of color photoreceptors must be combined to perceive the full spectrum of color.

Higher level processing of taste and olfaction also uses population coding – sometimes the sense of smell is needed in addition to the sense of taste to fully perceive a flavor. Have you ever been congested from a cold and food just doesn't taste the same? That's due to this combining of the senses for a full perception.

Pathways

In general, the route sensory information takes from the periphery to the central nervous system is similar among most of the systems. Environmental stimuli become encoded by a specialized receptor in the periphery. Information then enters the central nervous system via the spinal cord or brainstem and relays through the thalamus, a structure that sits deep in the forebrain. The only sensory system that does not relay through the thalamus is the olfactory system. The thalamus then sends projections out to the primary cortical regions for each sensory system.

Role of the Thalamus

It's common to hear that sensory information "relays" through the thalamus on the way to the cortex (for example, in the paragraph above). This language can give the impression that the thalamus is only responsible for making sure the sensory signal gets from periphery to the cortex. This greatly underestimates the thalamic role. The thalamus is known to contribute to the processing and modification of the sensory signal.

21.

VISION: THE RETINA

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

Anatomy of the Retina

The front of the eye consists of the cornea, pupil, iris, and lens. The cornea is the transparent, external part of the eye. It covers the pupil and the iris and is the first location of light refraction. The pupil is the opening in the iris that allows light to enter the eye. The iris is the colored portion of the eye that surrounds the pupil and along with local muscles can control the size of the pupil to allow for an appropriate amount of light to enter the eye. The lens is located behind the pupil and iris. The lens refracts light to focus images on the retina. Proper focusing requires the lens to stretch or relax, a process called accommodation.

The retina is the light-sensitive region in the back of the eye where the photoreceptors, the specialized cells that respond to light, are located. The retina covers the entire back portion of the eye, so it's shaped like a bowl. In the middle of the bowl is the fovea, the region of highest visual acuity, meaning the area that can form the sharpest images. The optic nerve projects to the brain from the back of the eye, carrying information from the retinal cells. Where the optic nerve leaves, there are no photoreceptors since the axons from the neurons are coming together. This region is called the optic disc and is the location of the blind spot in our visual field.

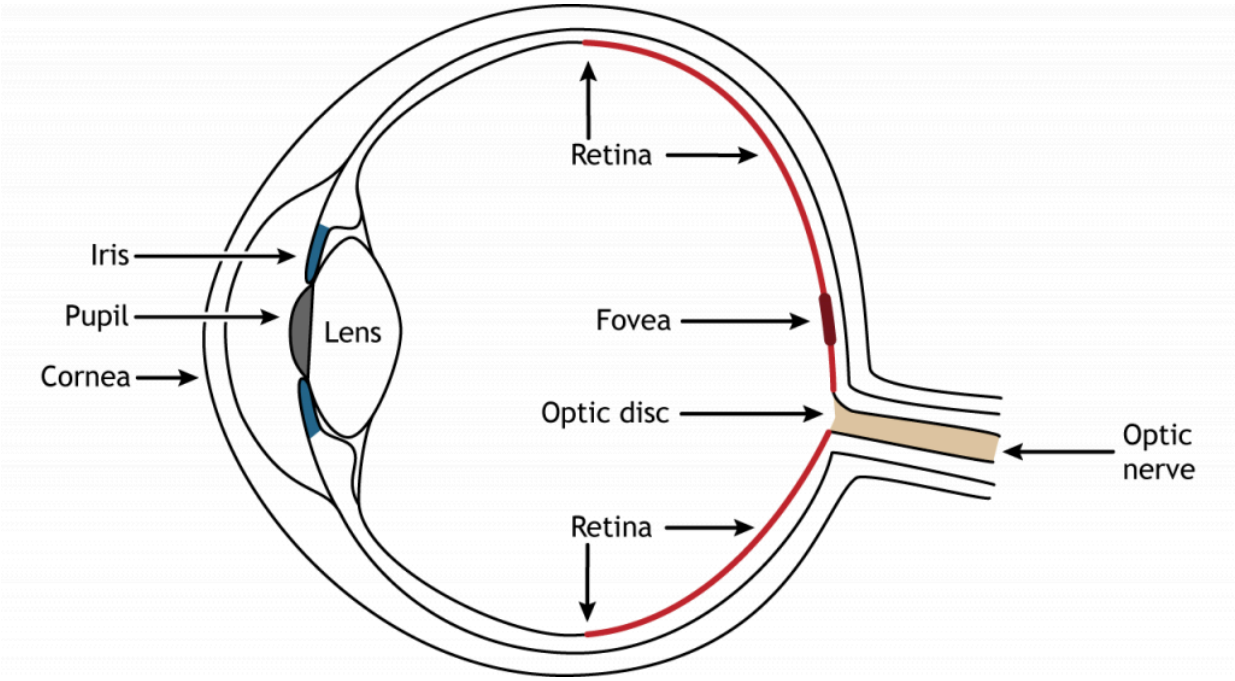


Figure 21.1. Cross section of the eye. The visible regions of the eye include the cornea, pupil (gray region), and iris (blue region). The lens sits behind the pupil and iris. The retina (red line) is located along the back of the eye. The fovea (dark red section) is a small portion of the retina where visual acuity is highest, and the optic disc is located where the optic nerve (tan region) leaves the eye. Details about the functions of each region are in the text. 'Eye Anatomy' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Retinal Cells

There are 5 primary types of cells in the retina

In addition to the photoreceptors, there are four other cell types in the retina. The photoreceptors synapse on bipolar cells, and the bipolar cells synapse on the ganglion cells. Horizontal and amacrine cells allow for communication laterally between the neurons.

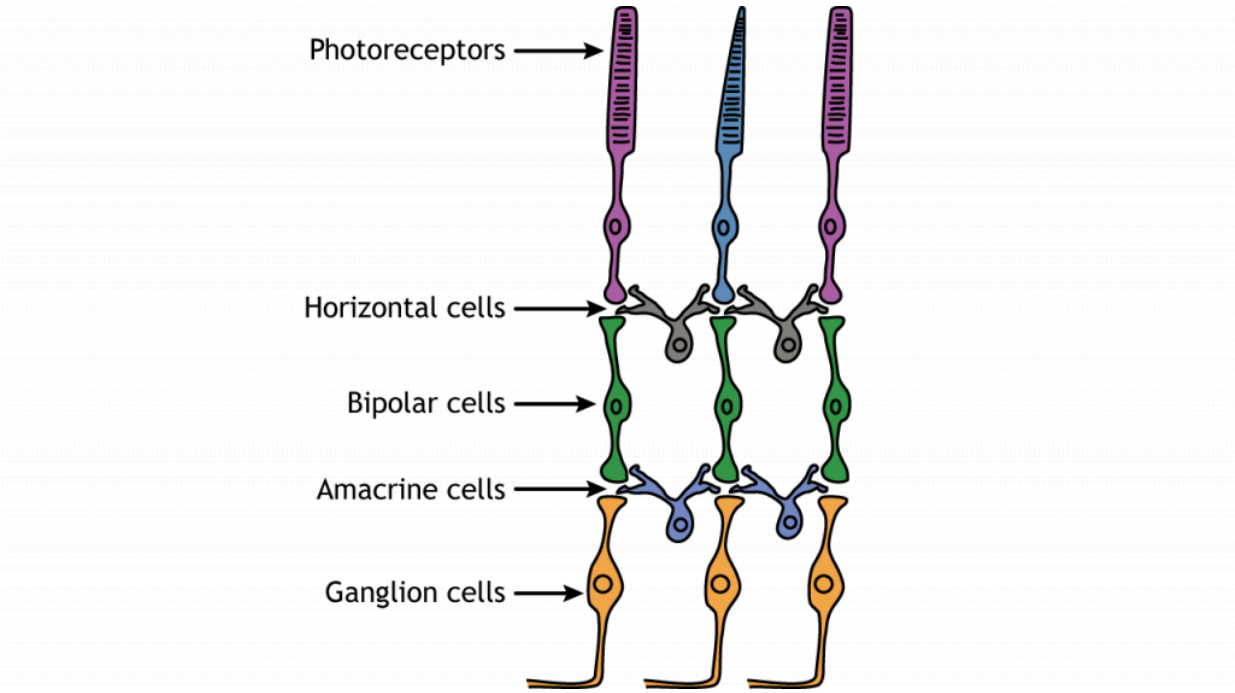


Figure 21.2. There are five cell types in the retina. The photoreceptors synapse on bipolar cells, and the bipolar cells synapse on ganglion cells. The horizonal cells allow for communication between photoreceptors by interacting with the photoreceptor-bipolar cell synapse, and the amacrine cells allow for communication between bipolar cells by interacting at the bipolar cell-ganglion cell synapse. 'Retinal Neurons' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Direction of Information

When light enters the eye and strikes the retina, it must pass through all the neuronal cell layers before reaching and activating the photoreceptors. The photoreceptors then initiate the synaptic communication back toward the ganglion cells.

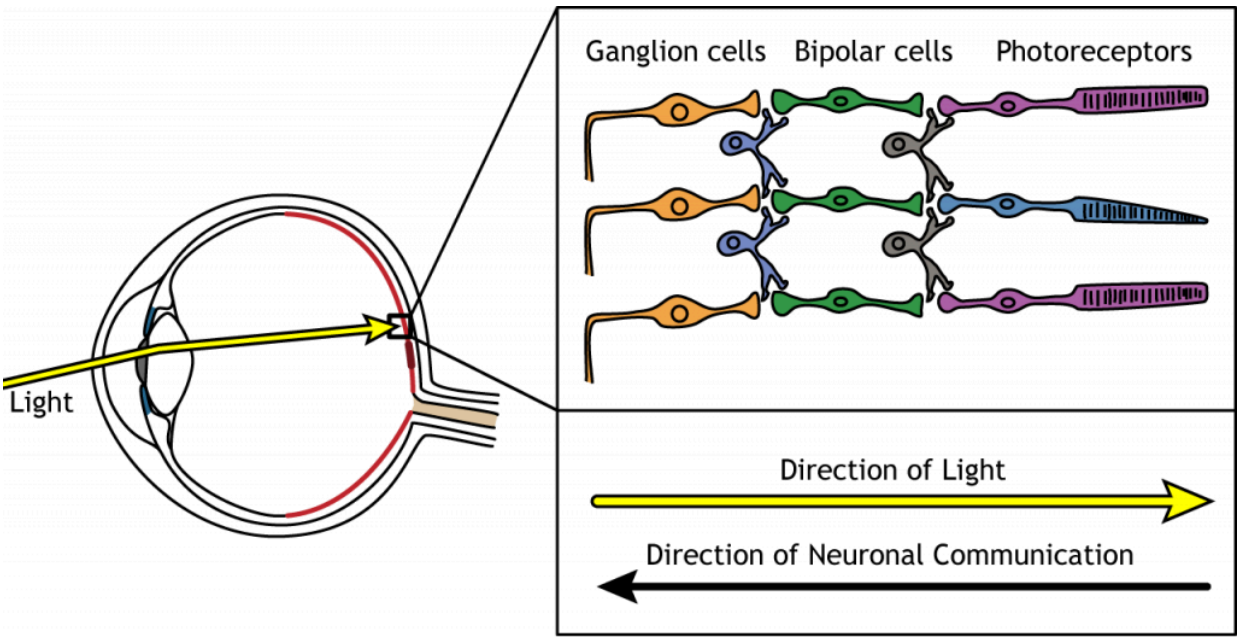


Figure 21.3. When light enters the eye, it must pass through the ganglion and bipolar cell layers before reaching the photoreceptors. The neuronal communication travels in the opposite direction from the photoreceptors toward the ganglion cells. 'Light in the Retina' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Receptors

The photoreceptors are the specialized receptors that respond to light. There are two types of photoreceptors: rods and cones. Rods are more sensitive to light, making them primarily responsible for vision in low-lighting conditions like at night. Cones are less sensitive to light and are most active in daylight conditions. The cones are also responsible for color vision.

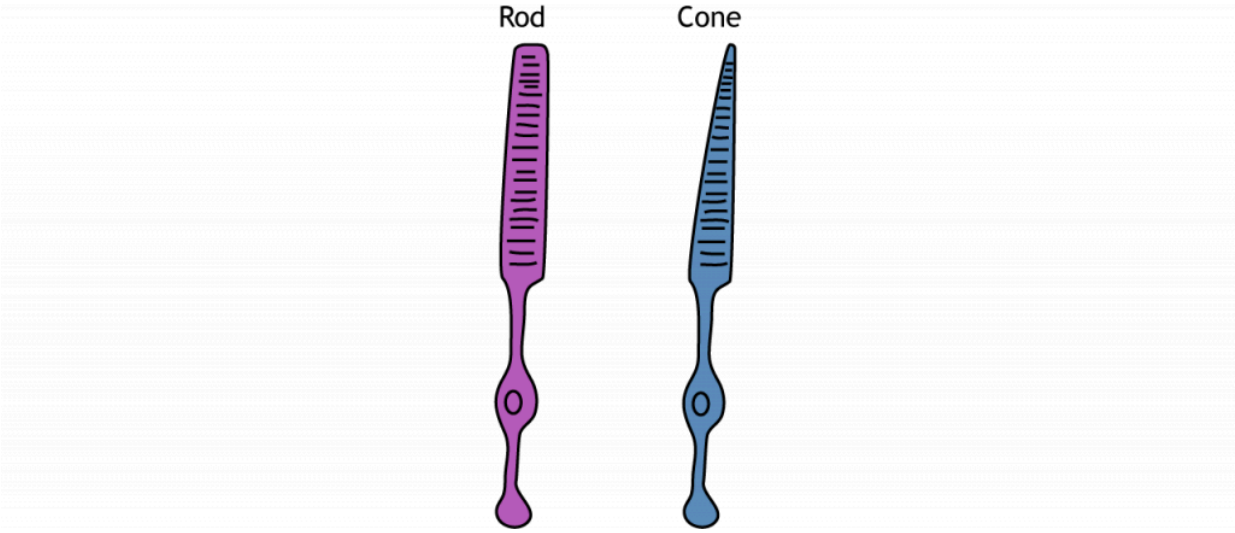


Figure 21.4. The rods and cones have different physical appearances and play separate roles in visual processing. 'Rod and Cone' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Receptor Density

In addition to having different visual functions, the rods and cones are also distributed across the retina in different densities. The cones are primarily found in the fovea, the region of the retina with the highest visual acuity. The remainder of the retina is predominantly rods. The region of the optic disc has no photoreceptors because the axons of the ganglion cells are leaving the retina and forming the optic nerve.

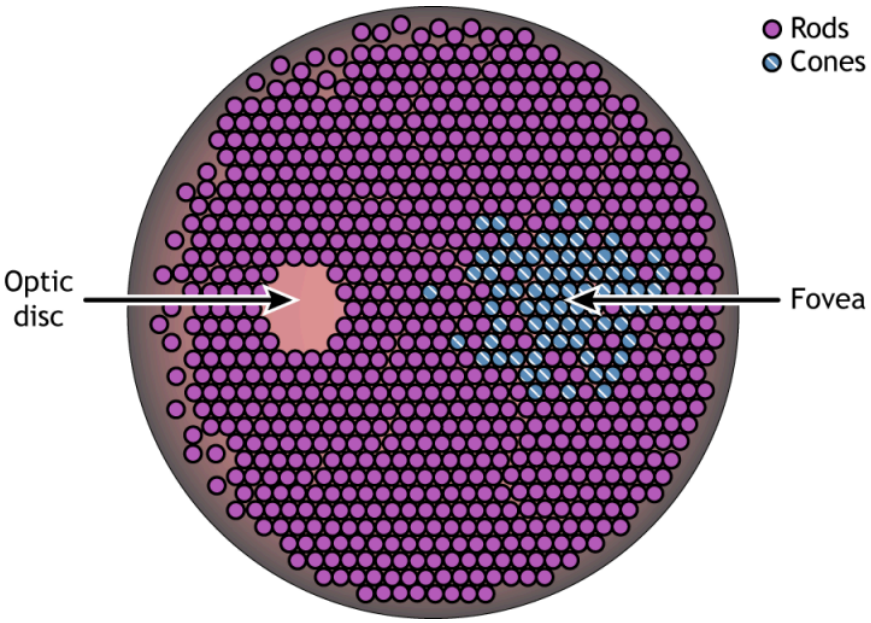


Figure 21.5. Rods and cones are distributed across the retina in different densities. Cones are located at the fovea. Rods are located everywhere else. The optic disc lacks all photoreceptors since the optic nerve fibers are exiting the eye at this location. 'Retinal Receptor Density' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Phototransduction

Photoreceptors hyperpolarize in response to light, do not fire action potentials, and release glutamate

The photoreceptors are responsible for sensory transduction in the visual system, converting light into electrical signals in the neurons. For our purposes, to examine the function of the photoreceptors, we will A) focus on black and white light (not color vision) and B) assume the cells are moving from either an area of dark to an area of light or vice versa.

Photoreceptors do not fire action potentials; they respond to light changes with graded receptor

potentials (depolarization or hyperpolarization). Despite this, the photoreceptors still release glutamate onto the bipolar cells. The amount of glutamate released changes along with the membrane potential, so a hyperpolarization will lead to less glutamate being released. Photoreceptors hyperpolarize in light and depolarize in dark. In the graphs used in this lesson, the starting membrane potential will depend on the initial lighting condition.

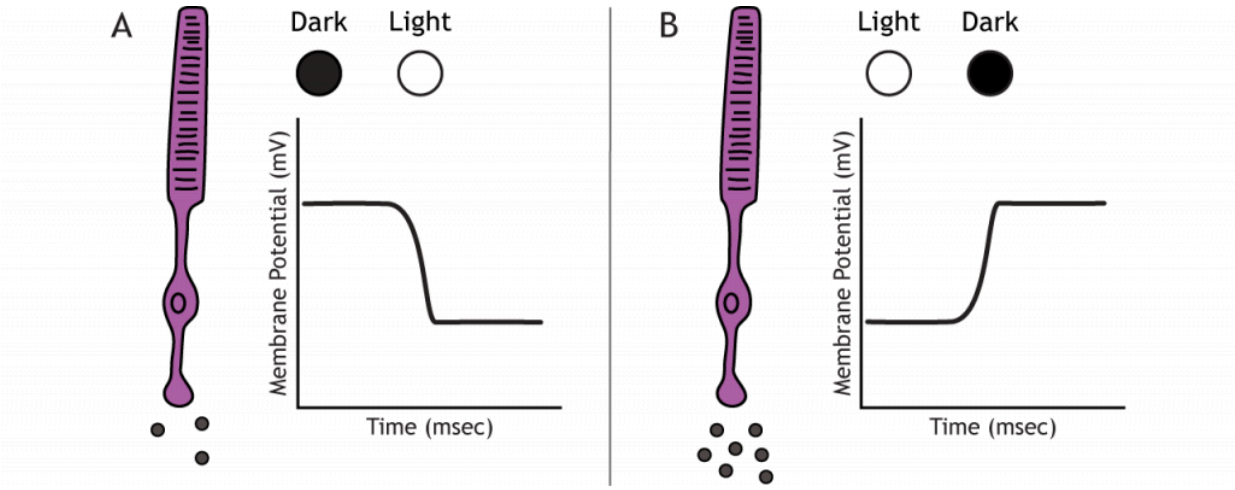


Figure 21.6. Photoreceptors respond with graded potentials when moving from light to dark or vice versa. A) When moving from dark to light, the photoreceptor will hyperpolarize, and glutamate release will decrease. B) When moving from light to dark, the photoreceptor will depolarize, and glutamate release will increase. 'Photoreceptor Receptor Potentials' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

In the dark, the photoreceptor has a membrane potential that is more depolarized than the "typical" neuron we examined in previous chapters; the photoreceptor membrane potential is approximately -40 mV. Photoreceptors have open cation channels that allow the influx of sodium and calcium in the dark. These channels are gated by the presence of cyclic GMP (cGMP), a molecule important in second-messenger cascades that is present in the photoreceptor in the dark.

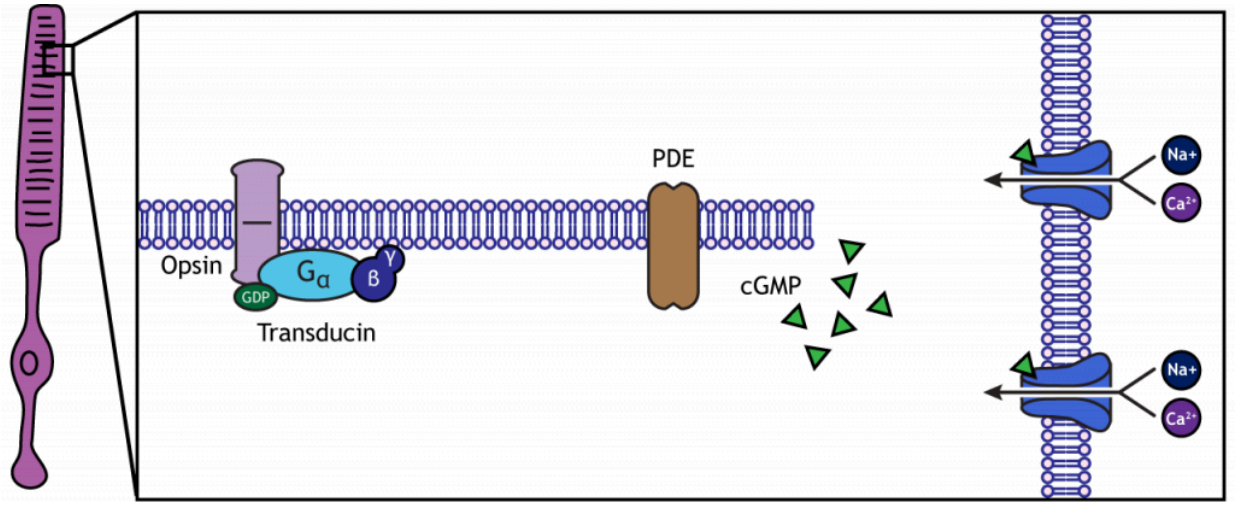


Figure 21.7. In the dark, the photoreceptor is depolarized due to an influx of sodium and calcium through open ion channels that are gated by cGMP. The photoreceptor has high levels of cGMP when it is in the dark. Additionally, the opsin proteins, the G-protein transducin, and phosphodiesterase (PDE) are all inactivated. 'Retinal Dark Current' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

When the photoreceptor moves into the light, the cell hyperpolarizes. Light enters the eye, reaches the photoreceptors, and causes a conformational change in a special protein called an opsin. This change activates a G-protein called transducin, which then activates a protein called phosphodiesterase (PDE). PDE breaks down cGMP to GMP, and the cGMP-gated ion channels that were open in the dark close. The decrease in cation flow into the cell causes the photoreceptor to hyperpolarize.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=438#video-438-1

Animation 21.1. Light reaching the photoreceptor causes a conformational change in the opsin protein, which activates the G-protein transducing. Transducin activates phosphodiesterase (PDE), which converts cGMP to GMP. Without cGMP, the cation channels close, stopping the influx of positive ions. This results in a hyperpolarization of the cell. 'Phototransduction' by Casey Henley is

 View static image of animation.

Transmission of Information within Retina

Photoreceptors synapse onto bipolar cells in the retina. There are two types of bipolar cells: OFF and ON. These cells respond in opposite ways to the glutamate released by the photoreceptors because they express different glutamate receptors. Like photoreceptors, the bipolar cells do not fire action potential and only respond with graded postsynaptic potentials.

OFF bipolar cells depolarize in the dark; ON bipolar cells depolarize in the light

---

OFF Bipolar Cells

In OFF bipolar cells, the glutamate released by the photoreceptor is excitatory. OFF bipolar cells express ionotropic glutamate receptors. In the dark, glutamate released by the photoreceptor activates the ionotropic receptors, and sodium can flow into the cell, depolarizing the membrane potential. In the light, the absence of glutamate causes the ionotropic receptors to close, preventing sodium influx, hyperpolarizing the membrane potential.

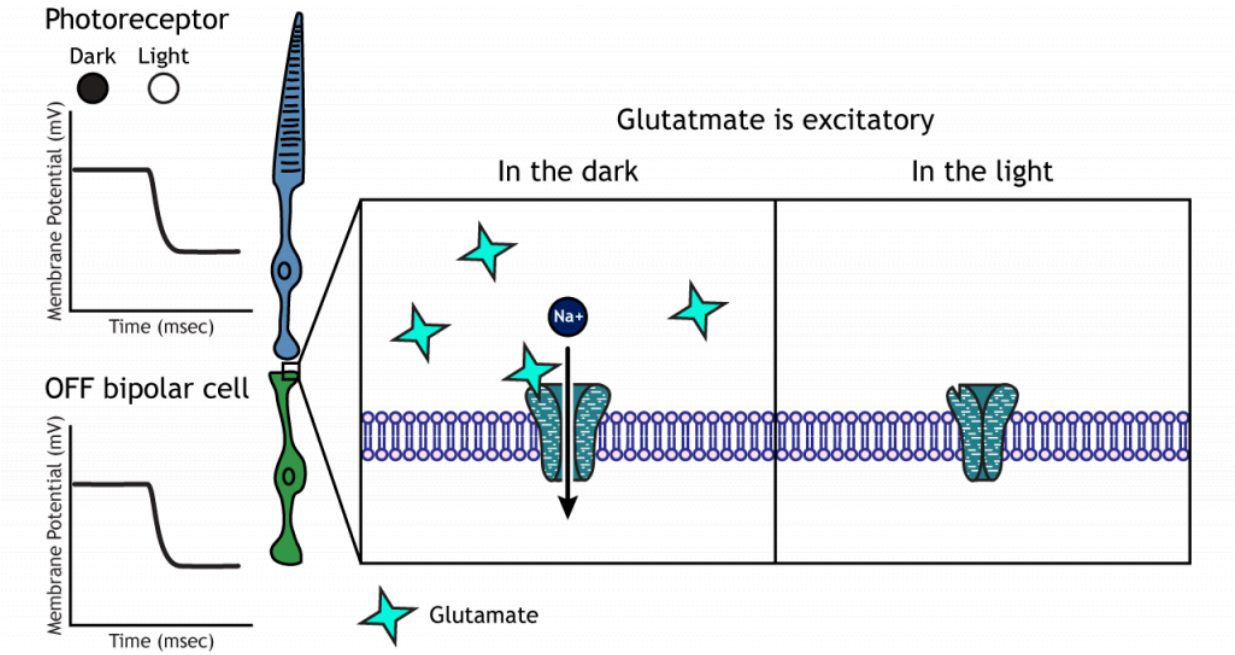


Figure 21.8. Photoreceptors hyperpolarize in light and decrease the amount of released glutamate. Glutamate is excitatory in OFF bipolar cells, opening ionotropic receptors and allowing sodium influx. In the dark, the OFF bipolar cells are depolarized, and in the light the OFF bipolar cells are hyperpolarized. 'Off Bipolar Cells' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

ON Bipolar Cells

In ON bipolar cells, the glutamate released by the photoreceptor is inhibitory. ON bipolar cells express metabotropic glutamate receptors. In the dark, glutamate released by the photoreceptor activates the metabotropic receptors, and the G-proteins close cation channels in the membrane, stopping the influx of sodium and calcium, hyperpolarizing the membrane potential. In the light, the absence of glutamate results in the ion channels being open and allowing cation influx, depolarizing the membrane potential.

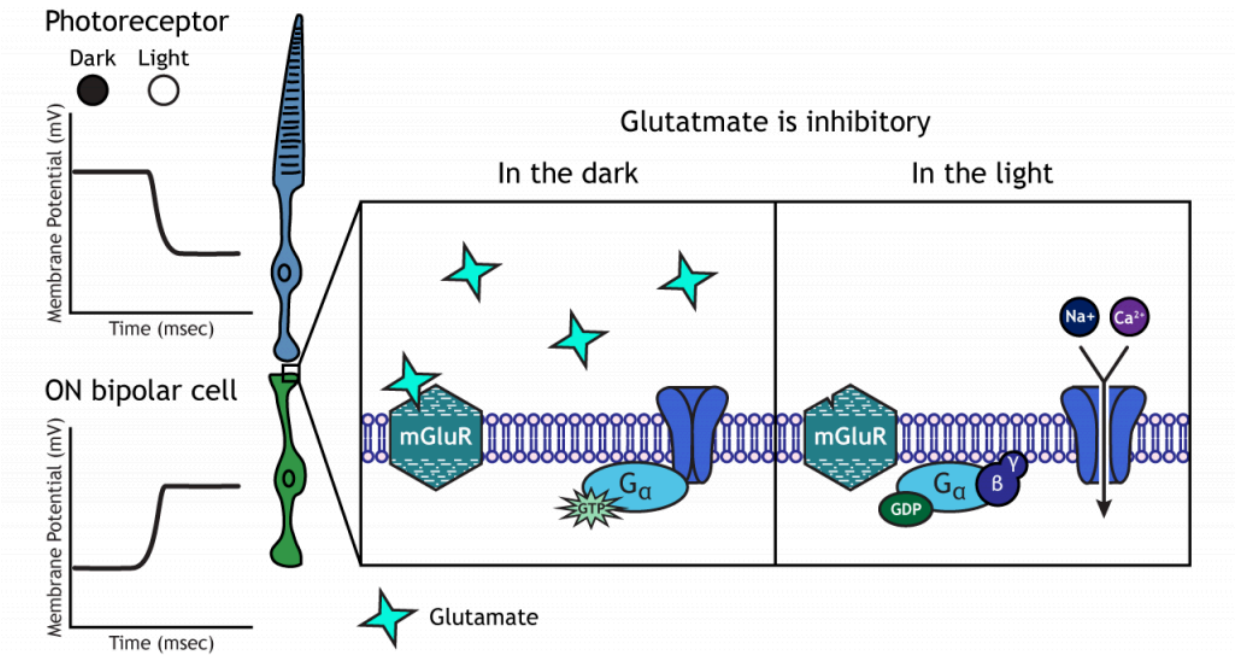


Figure 21.9. Photoreceptors hyperpolarize in light and decrease the amount of released glutamate. Glutamate is inhibitory in ON bipolar cells, activating metabotropic receptors, which closes cation channels. In the dark, the ON bipolar cells are hyperpolarized, and in the light the ON bipolar cells are depolarized. 'ON Bipolar Cells' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Ganglion Cells

OFF-center ganglion cells increase firing rate in the dark; ON-center ganglion cells increase firing rate in the light

OFF and ON bipolar cells synapse on OFF-center and ON-center ganglion cells, respectively. Ganglion cells are the only cell type to send information out of the retina, and they are also the only cell that fires action potentials. The ganglion cells fire in all lighting conditions, but it is the relative firing rate that encodes information about light. A move from dark to light will cause OFF-center ganglion cells to decrease their firing rate and ON-center ganglion cells to increase their firing rate.

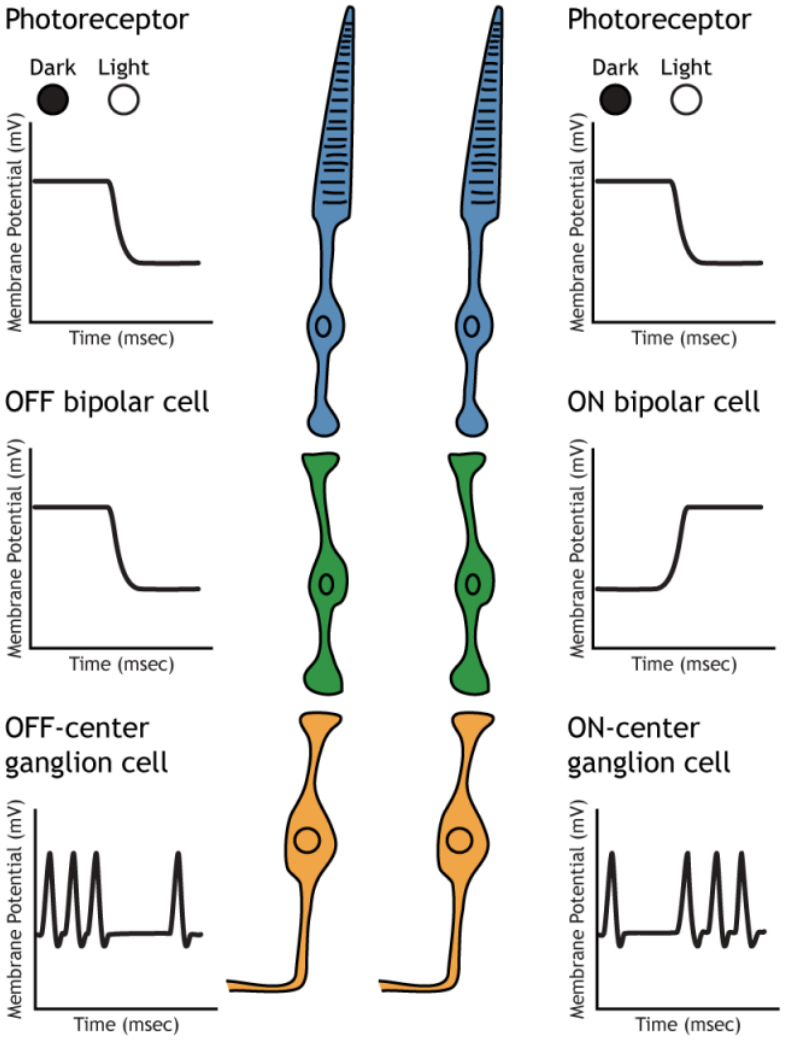


Figure 21.10. A move from dark to light will hyperpolarize all photoreceptors. OFF bipolar cells will also hyperpolarize in light, which will lead to a decreased firing rate in OFF-center ganglion cells. ON bipolar cells will depolarize in light, which will lead to an increased firing rate in ON-center ganglion cells. 'Retinal Ganglion Cells' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Receptive Fields

Each bipolar and ganglion cell responds to light stimulus in a specific area of the retina. This region of retina is the cell's receptive field. Receptive fields in the retina are circular.

Size of the receptive field can vary. The fovea has smaller receptive fields than the peripheral retina.

The size depends on the number of photoreceptors that synapse on a given bipolar cell and the number of bipolar cells that synapse on a given ganglion cell, also called the amount of convergence.

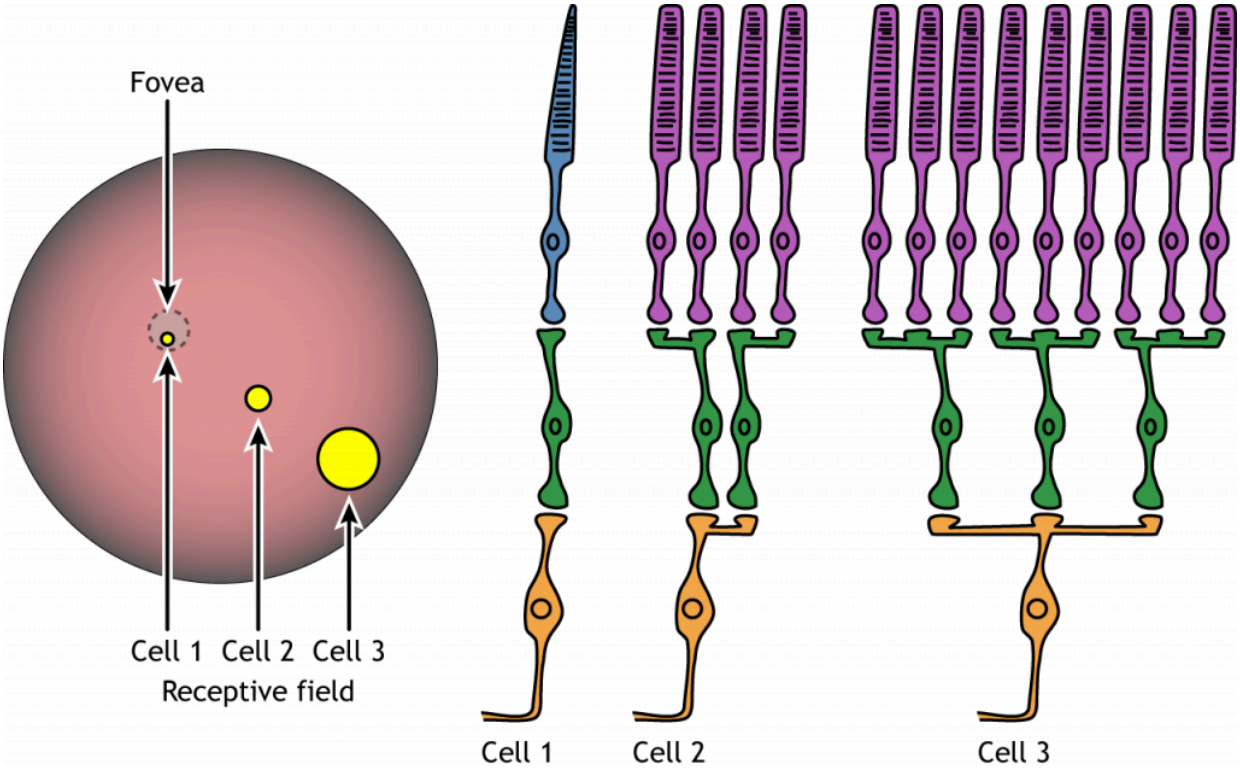


Figure 21.11. Ganglion receptive field sizes can vary depending on location of the bipolar and ganglion cells and the amount of convergence onto those cells. When the photoreceptors are in or near the fovea (Cell 1), the receptive fields are small. In the fovea, each bipolar cell receives input from only one photoreceptor and then synapses on only one ganglion cell. Toward the periphery (Cells 2 and 3), more photoreceptors synapse on each bipolar cell, and more bipolar cells synapse on each ganglion cell, making the surface area of the receptive field larger. 'Retinal Receptive Field' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Receptive Field Example

Let's use an example of an ON bipolar cell to look at the structure of receptive fields in the retina. The bipolar and ganglion cell receptive fields are divided into two regions: the center and the surround. The center of the receptive field is a result of direct innervation between the photoreceptors, bipolar cells, and ganglion cells. If a light spot covers the center of the receptive field, the ON bipolar cell would depolarize, as discussed above; the light hits the photoreceptor, it hyperpolarizes, decreasing glutamate release. Less glutamate leads to less inhibition of the ON bipolar cell, and it depolarizes.

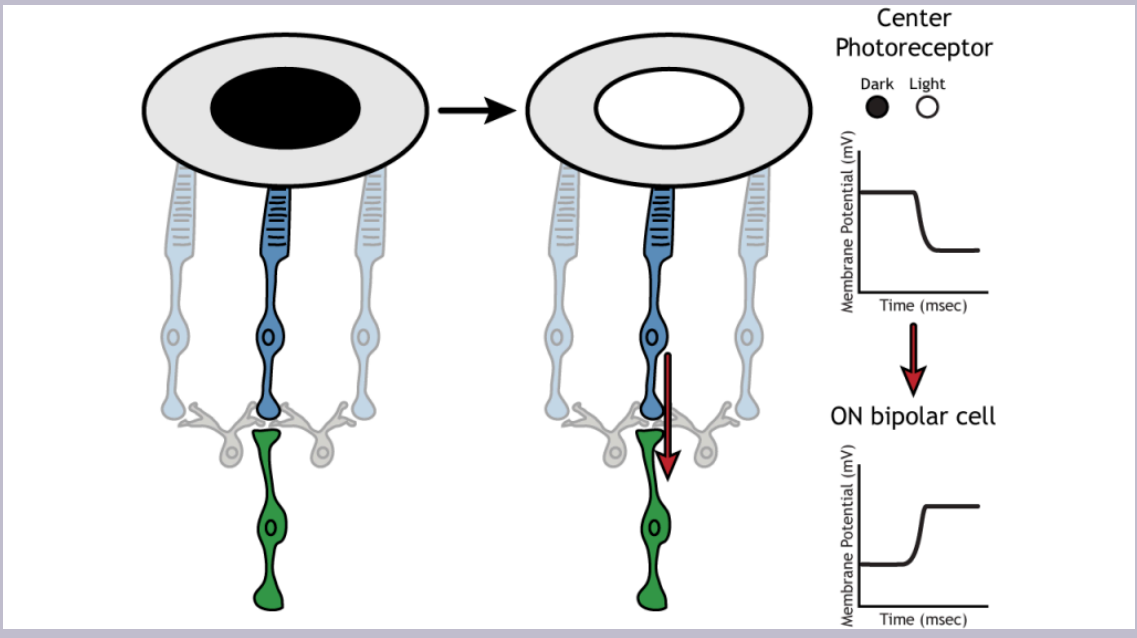


Figure 21.12. A photoreceptor in the center of an ON bipolar cell's receptive field moves from dark to light. The photoreceptor will hyperpolarize, and the ON bipolar cell will depolarize. The red arrows show the direct synaptic communication from photoreceptor to ON bipolar cell. 'Light in Center' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The surround portion of the receptive field is a result of indirect communication among the retinal neurons via horizontal and amacrine cells. The surround also has an opposing effect on the bipolar or ganglion cell compared to the effect of the center region. If a light spot covers the surround portion, the ON bipolar cell would respond by hyperpolarizing. The light would cause the photoreceptor in the surround to hyperpolarize. This would cause the

horizontal cell to also hyperpolarize. Horizontal cells have inhibitory synaptic effects, so a hyperpolarization in the horizontal cell would lead to a depolarization in the center photoreceptor. The center photoreceptor would then cause a hyperpolarization in the ON bipolar cell. These effects mimic those seen when the center is in dark. So even though the center photoreceptor is not directly experiencing a change in lighting conditions, the neurons respond as if they were moving toward dark.

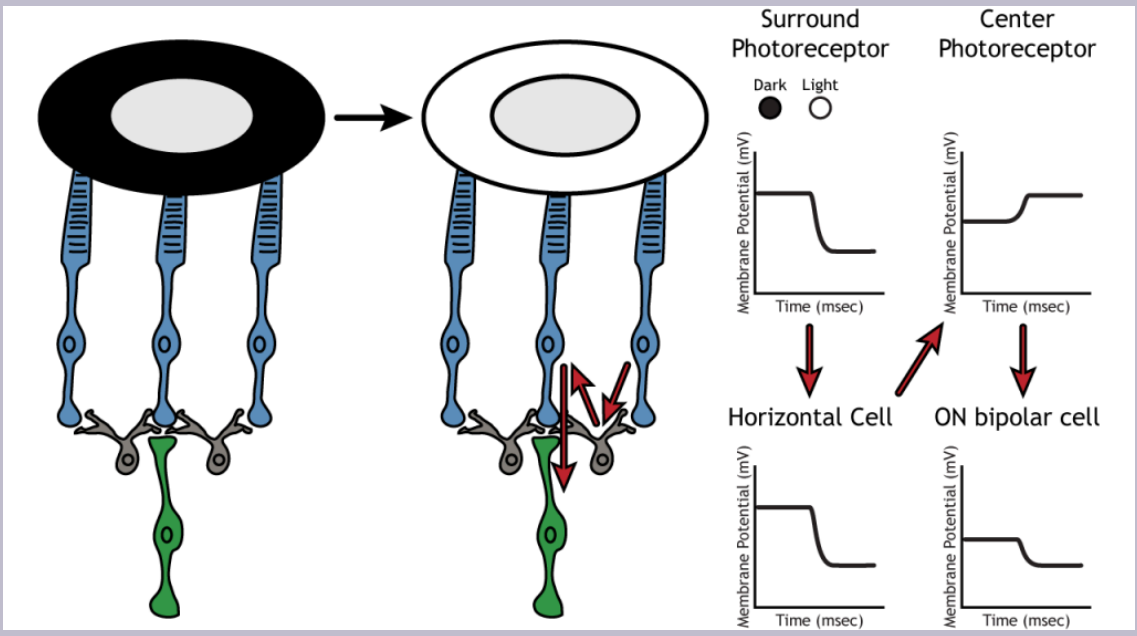


Figure 21.13. A photoreceptor in the surround of an ON bipolar cell's receptive field moves from dark to light. The photoreceptor will hyperpolarize, and the postsynaptic horizontal cell will hyperpolarize. This will cause the center photoreceptor to depolarize, and the ON bipolar cell to hyperpolarize. The red arrows show the indirect synaptic communication between the surround photoreceptor and the ON bipolar cell. The surround photoreceptor synapses on the horizontal cell, which synapses on the center photoreceptor, which synapses on the bipolar cell. 'Light in Surround' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Lateral Inhibition

Lateral inhibition is critical for the enhance perception of edges and borders

The center-surround structure of the receptive field is critical for lateral inhibition to occur. Lateral inhibition is the ability of the sensory systems to enhance the perception of edges of stimuli. It is important to note that the photoreceptors that are in the surround of one bipolar cell would also be in the center of a different bipolar cell. This leads to a direct synaptic effect on one bipolar cell while also having an indirect effect on another bipolar cell.

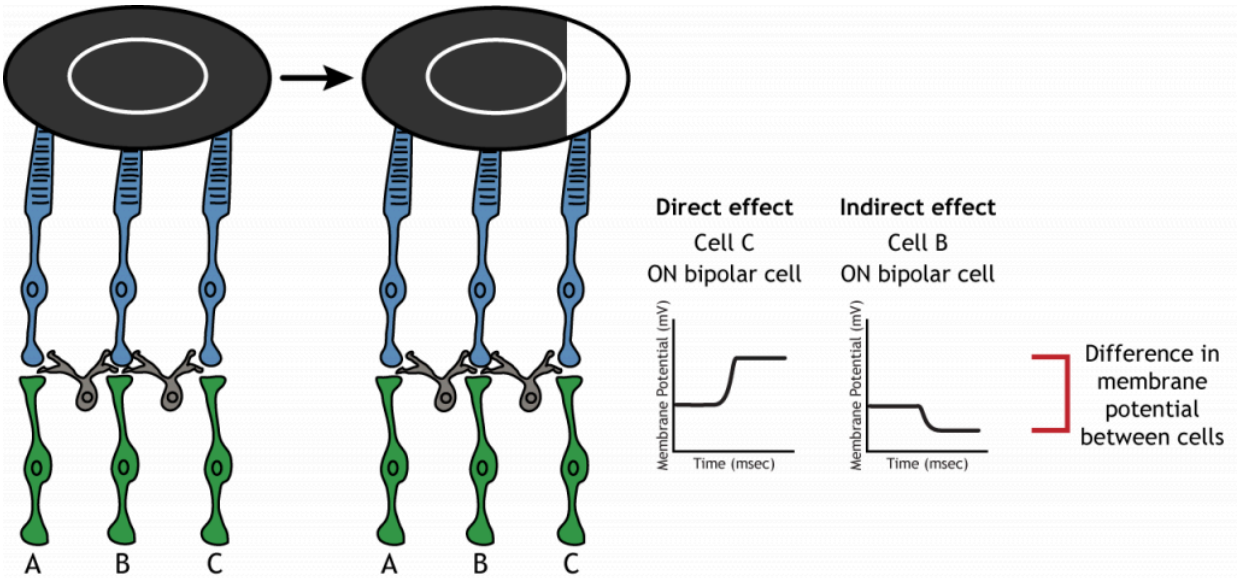


Figure 21.14. An edge of a light stimulus moves into the receptive field surround of ON bipolar cell B. This edge is also falling on the receptive field center of ON bipolar cell C. The light will cause bipolar cell C to depolarize because of the direct synapse with the photoreceptor. The light will also cause bipolar cell B to hyperpolarize because of the indirect synapses through the horizontal cell. This hyperpolarization causes a larger membrane potential difference between cells B and C that would occur if the horizontal cells were absent. The larger membrane potential difference between the cells will lead to an enhancement in the perception between the dark and light side of the edge. 'Lateral Inhibition' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Although some of the images used here will simplify the receptive field to one cell in the center and a couple in the surround, it is important to remember that photoreceptors cover the entire surface of

the retina, and the receptive field is two-dimensional. Depending on the level of convergence on the bipolar and ganglion cells, receptive fields can contain many photoreceptors.

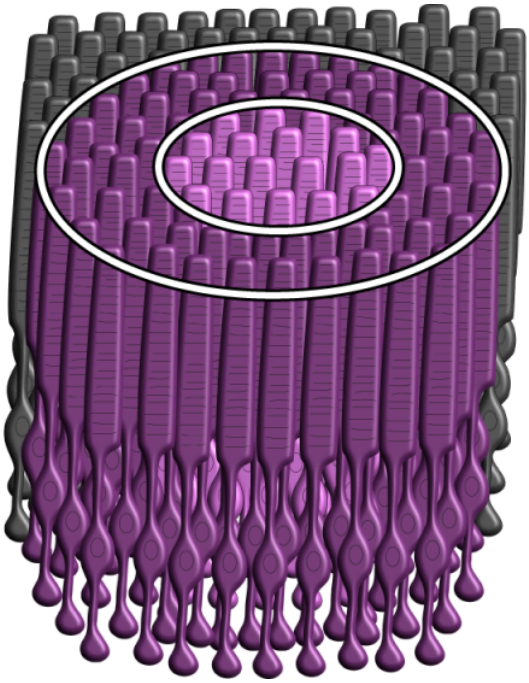


Figure 21.15. The receptive fields exist in two-dimensions along the surface of the retina. Depending on the location of the receptive field, and the amount of convergence that occurs at the bipolar or ganglion cell, the receptive field may contain many photoreceptors. 'Retinal surface' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Key Takeaways

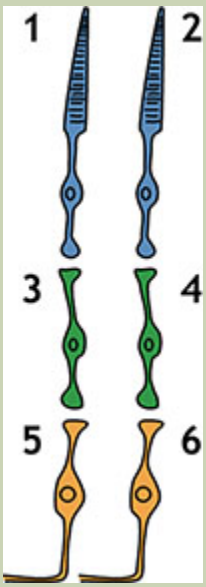
- Photoreceptors and bipolar cells do not fire action potentials
- Photoreceptors hyperpolarize in the light
- ON bipolar cells express inhibitory metabotropic glutamate receptors
- OFF bipolar cells express excitatory ionotropic glutamate receptors

- Receptive fields are circular, have a center and a surround, and vary in size
- Receptive field structure allows for lateral inhibition to occur

Test Yourself!

Try the quizzes more than once to get different questions!

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=438#h5p-18



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=438#h5p-36

- Compare and contrast rods and cones.
- Compare and contrast the fovea and the optic disc.

Video Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=438#oembed-1

22.

VISION: CENTRAL PROCESSING

Visual Fields

Before learning the pathway that visual information takes from the retina to the cortex, it is necessary to understand how the retina views the world around us. The full visual field includes everything we can see without moving our head or eyes.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

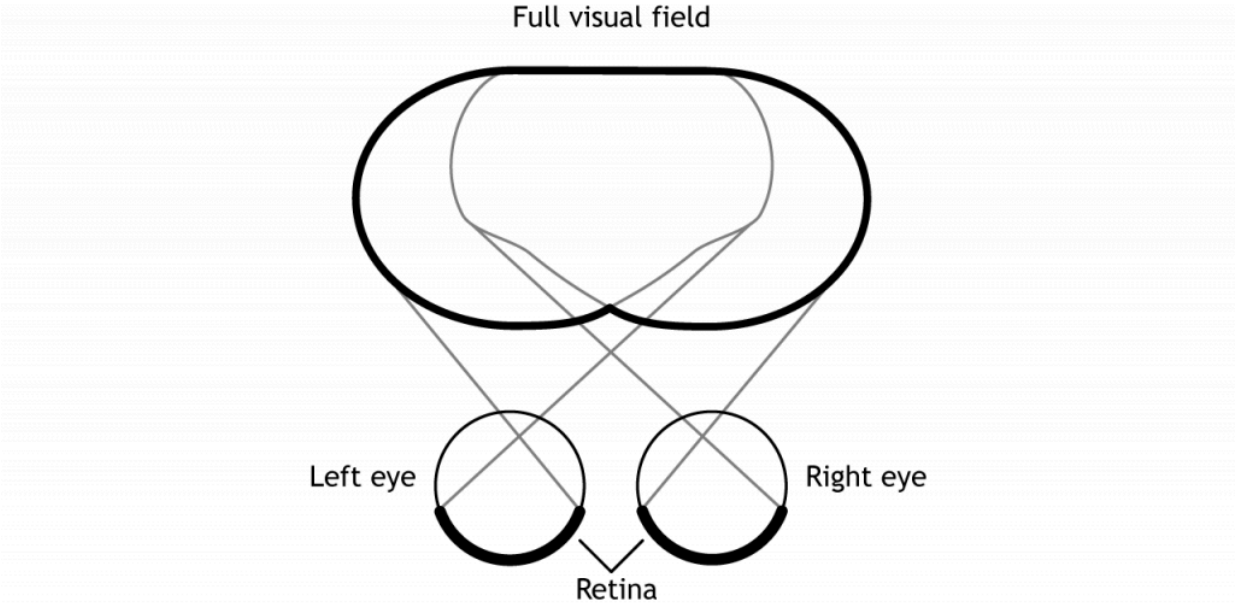


Figure 22.1. The two eyes together can view the entire visual field, which is all the visual space we can see without moving our head or eyes. 'Full Visual Field' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Visual fields can be divided in multiple ways, each dependent on different regions of the retina

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The full visual field can be divided in a few ways. Each individual eye is capable of seeing a portion of, but not the entire, visual field.

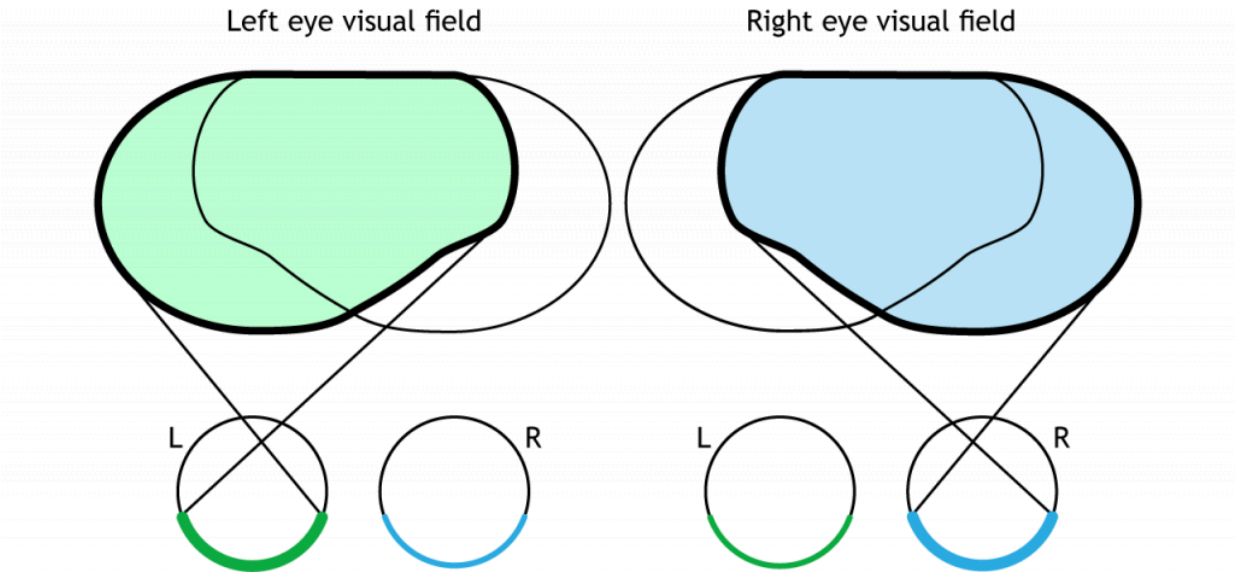

Figure 22.2. Each eye individually can view only a portion of the full visual field. 'Single Eye Fields' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The full visual field can also be divided into the right and left hemifields. The hemifields range from the most peripheral point to the center point, splitting the full visual field into two equal regions. Both eyes are involved in viewing each hemifield. The fovea separates the retina into two sections: the nasal retina and the temporal retina. The nasal retina is the medial portion that is located toward the nose. The temporal retina is the lateral portion that is located toward the temples and temporal lobe. The nasal retina from one eye along with the temporal retina from the other eye are able to view an entire hemifield.

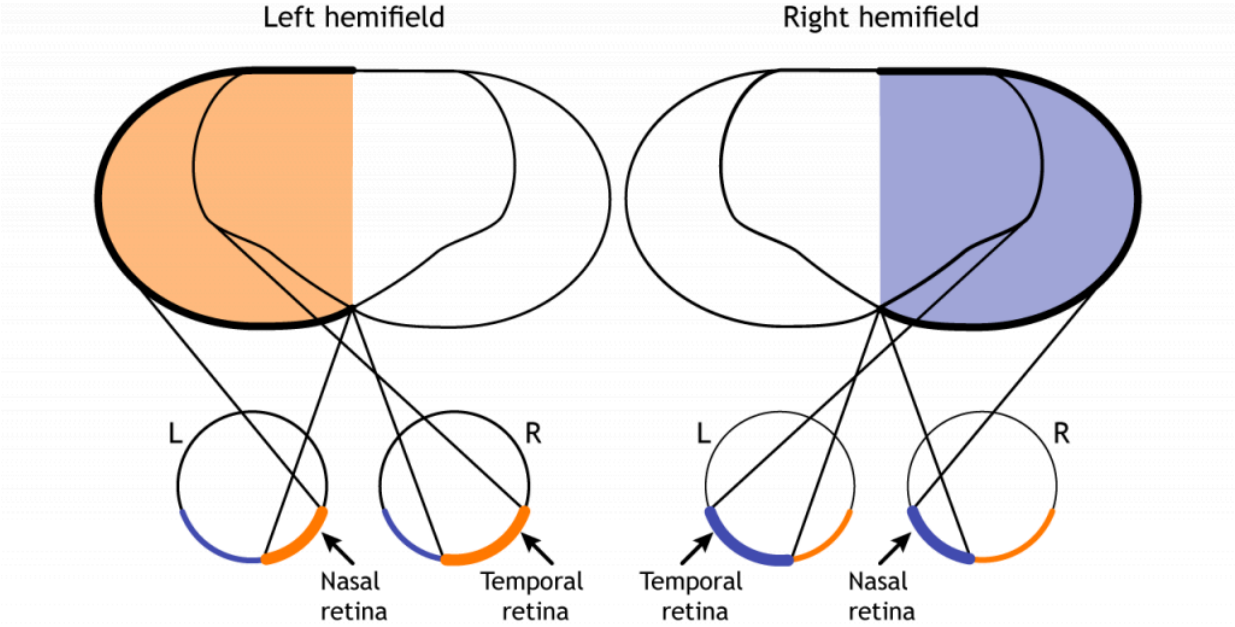

Figure 22.3. The full visual field can be divided into left and right hemifields. Both eyes contribute to viewing these regions. The nasal retina of the left eye and the temporal retina of the right eye view the left hemifield. The nasal retina of the right eye and the temporal retina of the left eye view the right hemifield. 'Visual Hemifields' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Finally, the full visual field can be separated into monocular and binocular regions. Each monocular field is visual space that can only be viewed by one eye. The binocular region is visual space that can be viewed by both eyes.

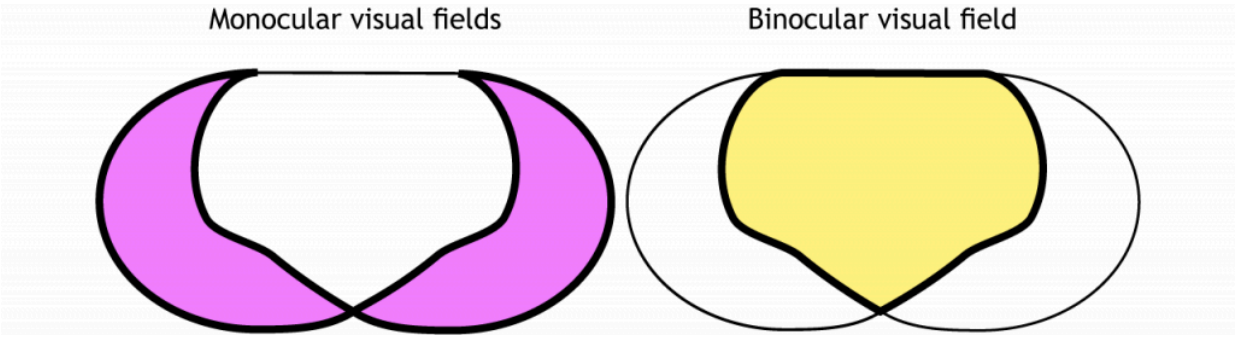

Figure 20.4. Monocular visual fields are viewed by only one eye and are located toward the periphery of the full visual field. The binocular visual field is viewed by both eyes and is located in the center of the full visual field. 'Monocular and Binocular Fields' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Pathway to Brain

The right visual field is processed by the left side of the brain; the left visual field is processed by the right side of the brain

Visual information from each eye leaves the retina via the ganglion cell axons at the optic disc, creating the optic nerve. Prior to entering the brain, axons from the nasal portion of each retina cross the midline at the optic chiasm. Since the axons from the nasal retina cross to the opposite side of the nervous system but the temporal retina axons do not, this leads to the brain processing input from the contralateral (opposite side) visual hemifield. Therefore, the right side of the brain receives visual information from the left hemifield and vice versa.

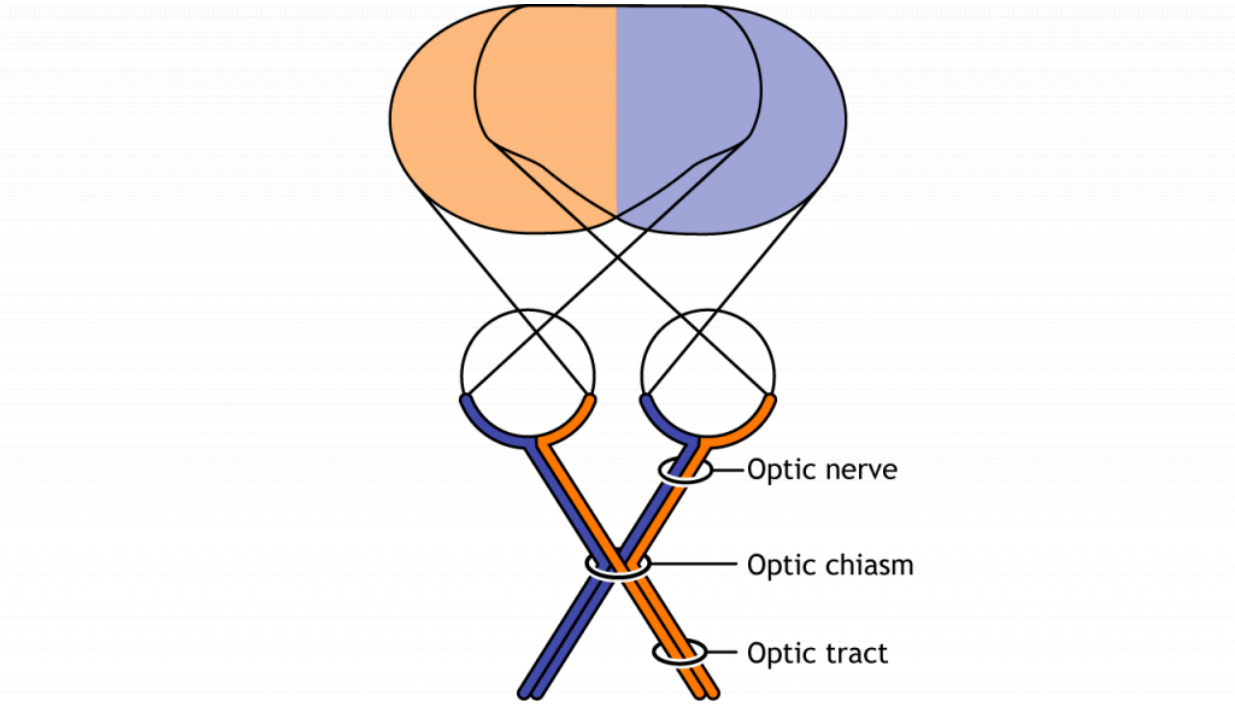

Figure 22.5. Information from each eye is carried away from the retina by the optic nerve. Information perceived by neurons in the nasal retina of each eye crosses the midline at the optic chiasm. Information from the contralateral visual hemifield then travels to the brain. 'Pathway from Retina' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the optic nerve (cranial nerve II) using the BrainFacts.org 3D Brain

The optic tract enters the brain and ascends to synapse in the lateral geniculate nucleus of the thalamus. From there, axons project to the primary visual cortex, also called the striate cortex or V1, located in the occipital lobe.

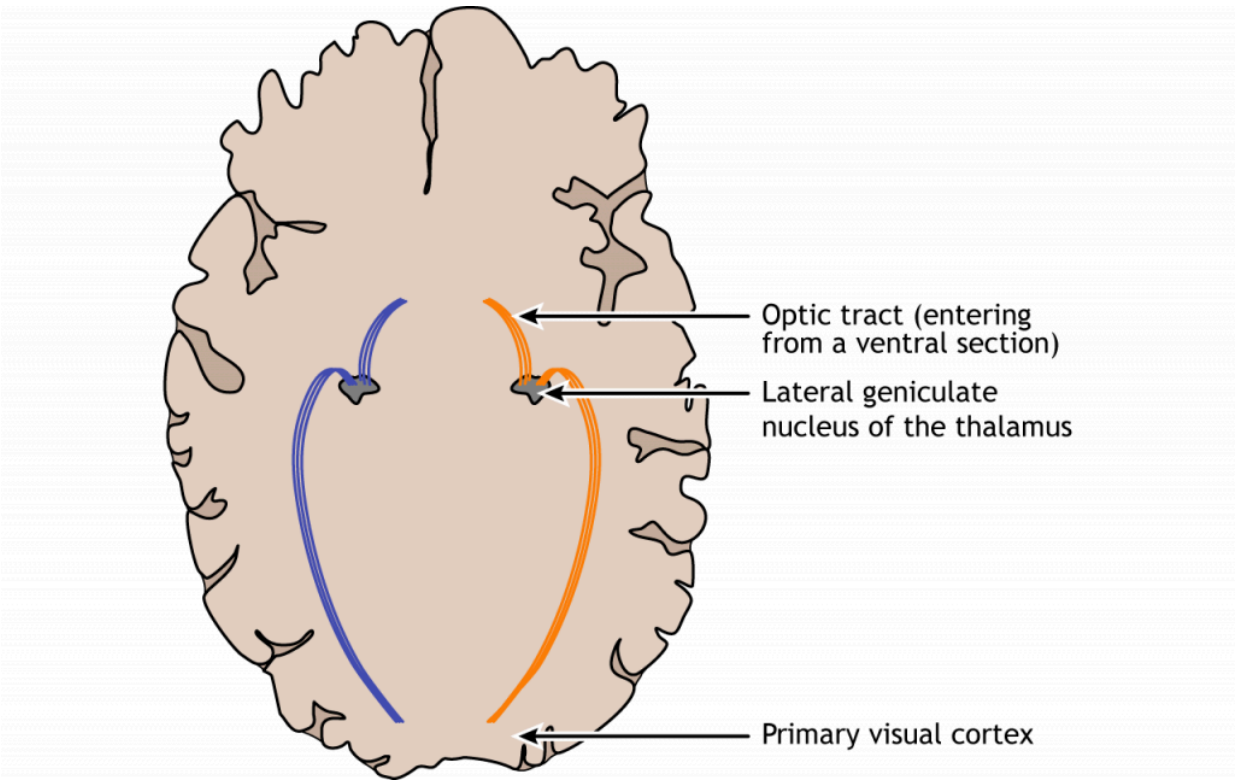

Figure 22.6. A horizontal section of the brain. The optic tract enters the brain and projects dorsally to the thalamus. Information is then sent to the primary visual cortex in the occipital lobe. 'CNS Visual Pathway' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

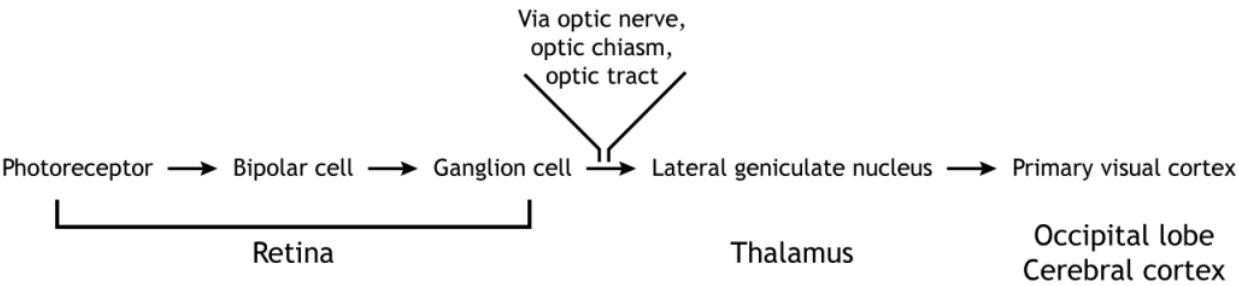

Figure 20.7. Visual information that is sent through the full visual pathway, therefore, moves from photoreceptor to bipolar cell to ganglion cell in the retina. It leaves the retina via the optic nerve, optic chiasm, and optic tract to the lateral geniculate nucleus of the thalamus and then travels to the primary visual cortex. 'Visual Pathway' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the thalamus using the BrainFacts.org 3D Brain

View the primary visual cortex using the BrainFacts.org 3D Brain

Receptive Fields

Receptive fields transition to circular to lines and then to more complex forms (like faces), orientation, and direction of movement

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As information moves from the retina to the cortex, receptive fields become larger and more complex. Receptive fields in the thalamus continue to be circular in shape like the receptive fields of the retinal neurons. However, once information reaches the primary visual cortex, these circular receptive fields combine to create receptive fields that are activated by lines.

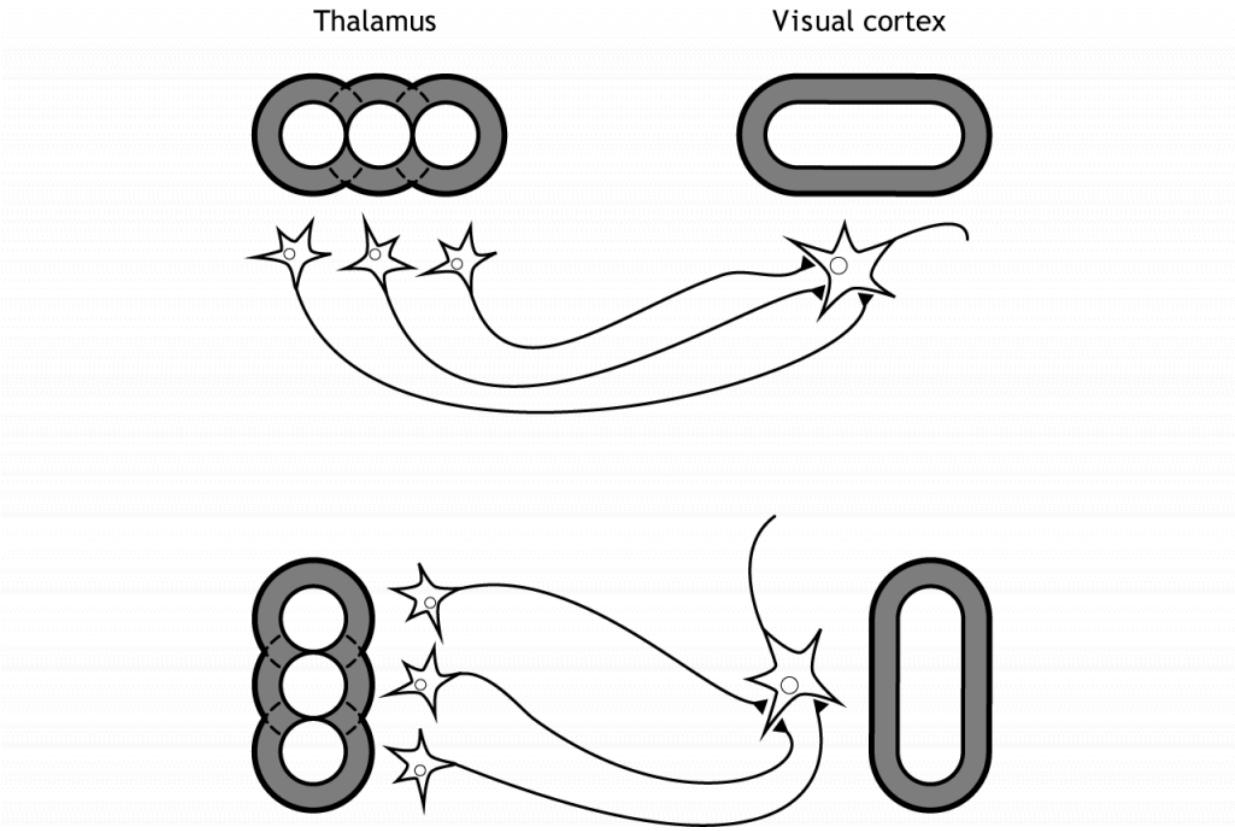

Figure 22.8. Circular receptive fields located in the thalamus combine to form straight receptive fields in the visual cortex. The orientation of the line direction in the visual cortex depends on the location of the thalamic retinal fields. 'CNS Receptive Fields' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

These receptive fields cause neurons in the primary visual cortex to respond best to a line in a specific orientation. The firing rate of the neuron will increase as the line rotates toward the "preferred" orientation. The firing rate will be highest when the line is in the exact preferred orientation. Different orientations are preferred by different neurons.

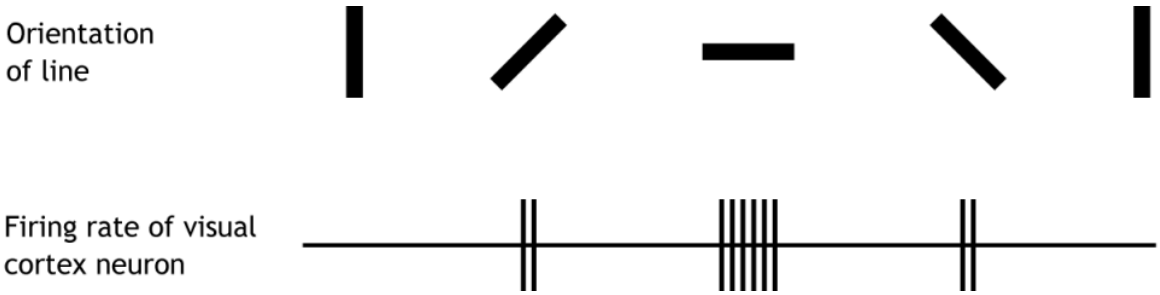

Figure 22.9. Neurons in the primary visual cortex show increased firing rates in response to a preferred line orientation. Lines rotated away from the preferred orientation will not cause activity. 'CNS Receptive Field Responses' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Higher-Level Processing of Sensory Information

Sensory system processing of input does not end upon reaching the primary sensory cortex in any sensory system. Information typically gets sent from the primary sensory cortex to other sensory association regions throughout the brain. The characteristics of sensory information becomes more complex as this higher-level processing occurs.

Post-Striatal Processing

The dorsal stream recognizes movement; the ventral stream recognizes objects

---

In the visual system, there are two broad streams of information that leave the striate cortex. Information that travels from the primary visual cortex down through the inferior temporal lobe is responsible for determining object recognition, or what an object is. Differentiating between an apple and a person occurs in this stream. Information that travels from the striate cortex up through the parietal lobe is responsible for motion or spatial components of vision.

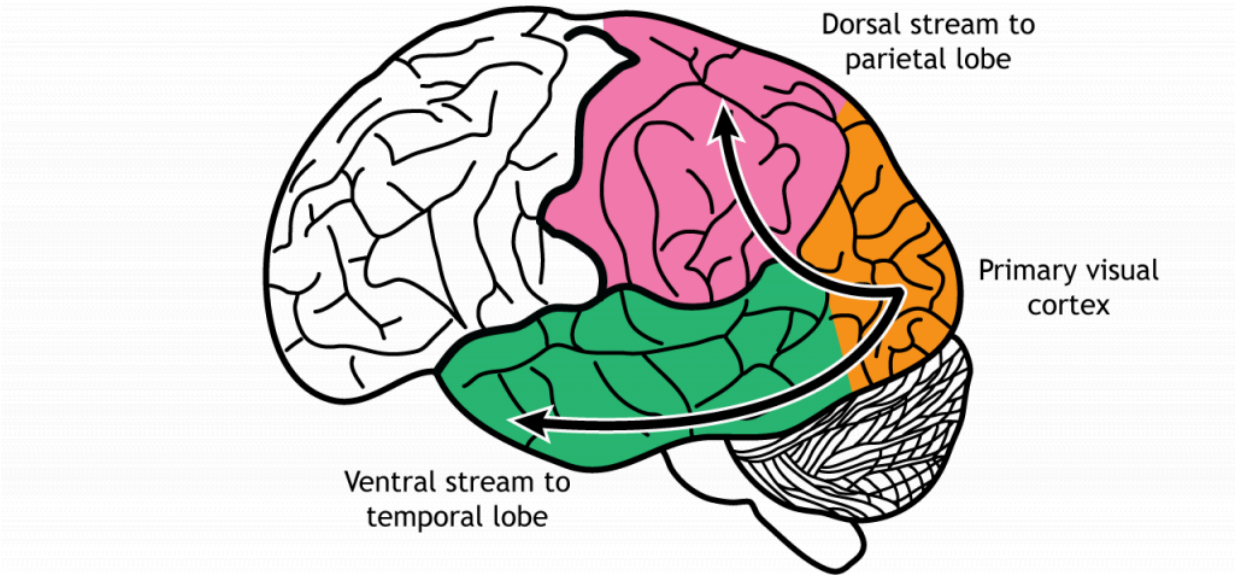

Figure 22.10. Information continues to be processed after reaching the primary visual cortex. The dorsal stream travels to the parietal cortex and is important for spatial components of vision. The ventral stream travels to the temporal lobe and is important for object recognition. 'Visual Streams' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Dorsal Stream

One of the most important regions in the dorsal pathway is region MT, also called V5. In this region, neurons are preferentially activated by a specific direction of movement by an object – for example, left to right or up to down. As an example, remember the receptive fields in the primary visual cortex were activated by lines at a specific orientation. Like that, in V5, the neurons would be activated by lines moving in a specific direction.

As information continues to be processed through the dorsal stream, the neurons become selective for more complex motions. The dorsal stream is also important for processing our actions in response to visual stimulation, for example, reaching for an object in the visual field or navigating around objects while walking.

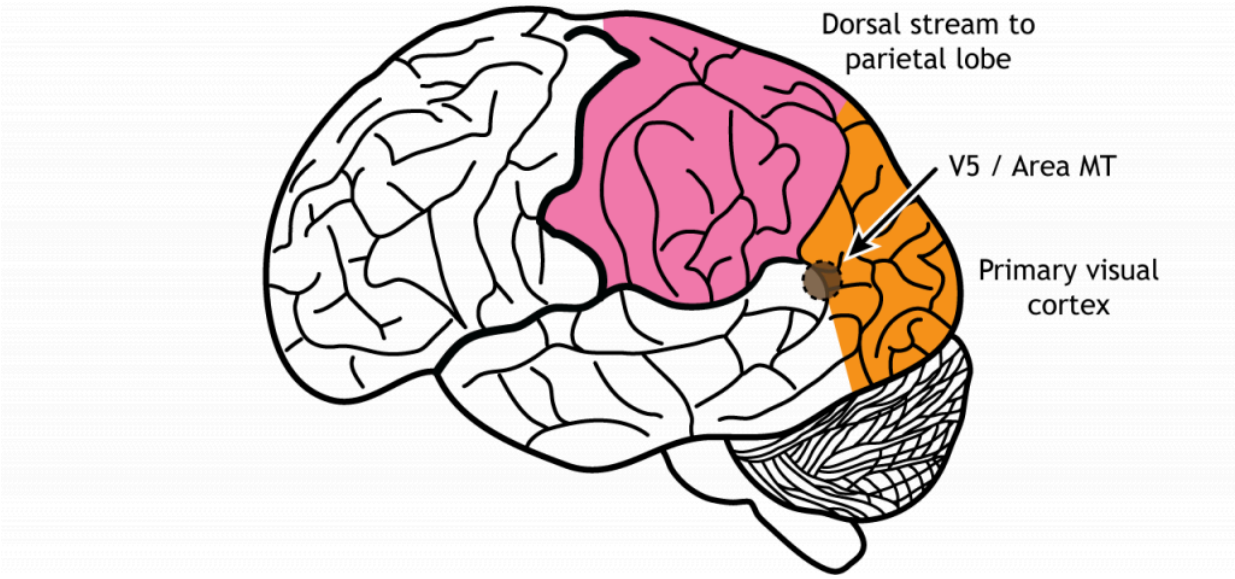

Figure 22.11. Area MT, also called V5, is an early processing region of the dorsal stream through the parietal lobe. Neurons in the region are activated by direction of an object in a specific direction. 'Area MT' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Ventral Stream

Object identification is a key function of our visual system. The ventral visual stream is responsible for this process. Like the more complex activation characteristics of region MT in the dorsal stream, neurons in Area V4 in the ventral stream show more complex receptive fields and show sensitivity to shape and color identification. As visual information continues to be processed through the inferior temporal lobe, differentiation of objects occurs. For example, in a region called the fusiform face area, located in the fusiform gyrus, which lies on the ventral aspect of the temporal lobe, neurons are activated by faces and can be specialized to one specific face.

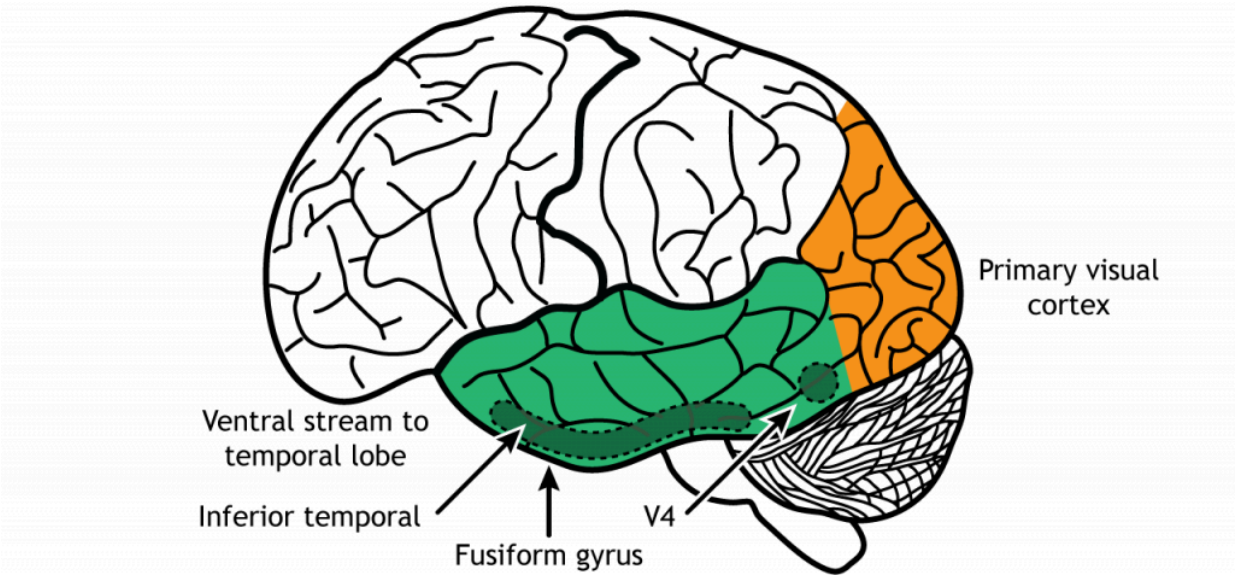

Figure 22.12. The ventral stream is first processed by area V4, which recognizes shapes and color. Information the continues through the inferior temporal lobe and sends information to regions like the fusiform gyrus, which is an area responsible for the recognition of faces. 'Ventral Stream' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The inferior temporal lobe also makes reciprocal connections with the structures in the limbic system. The limbic system plays an important role in processing emotions and memory, both of which are significant components to visual perception. The amygdala ties visual stimuli with emotions and provides value to objects. A family member will have emotional ties that a stranger will not. The hippocampus is responsible for learning and memory and helps establish memories of visual stimuli.

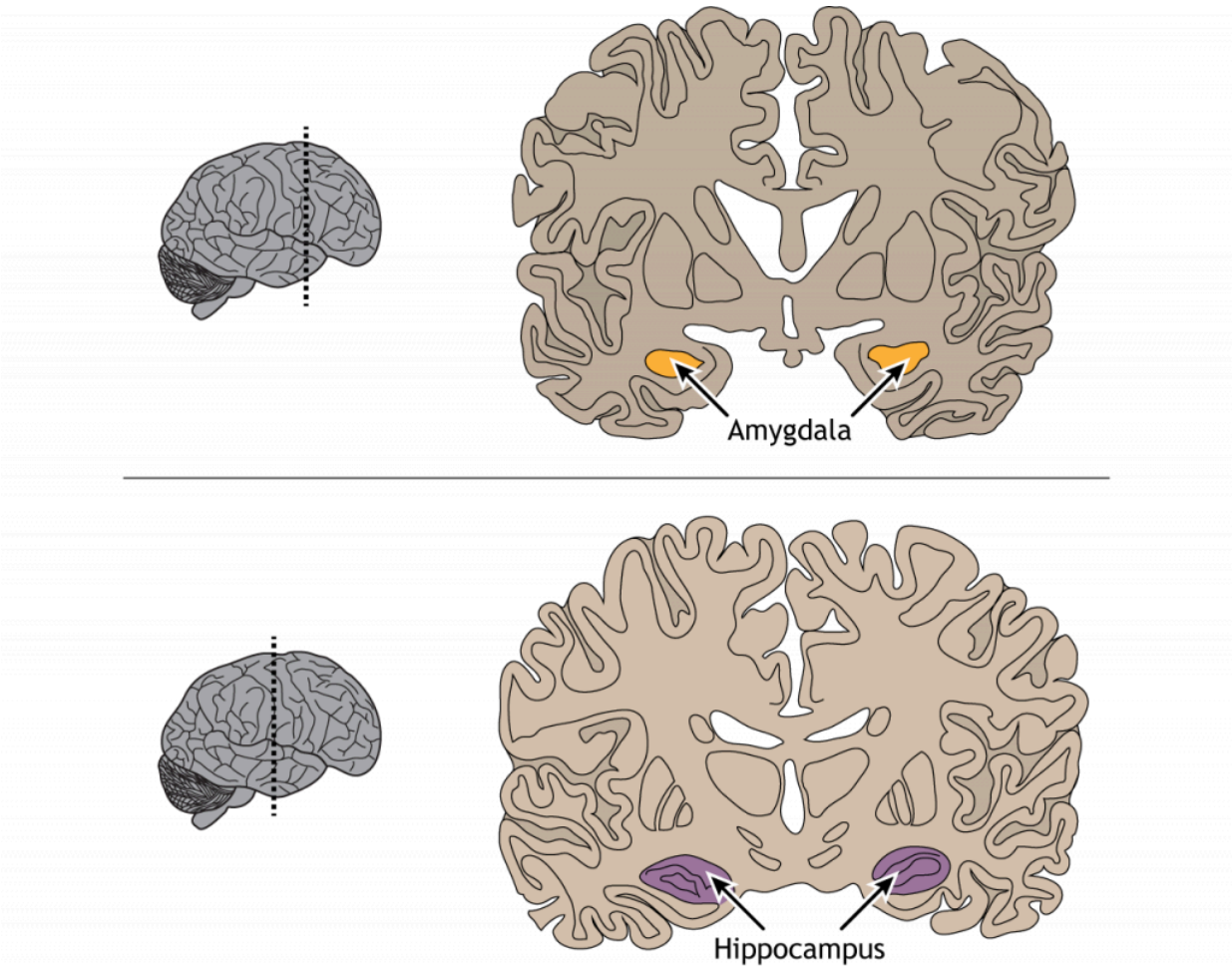

Figure 22.13. The limbic system structures, the amygdala and the hippocampus, also play important roles in visual processing. Both regions are located deep in the temporal lobe and have reciprocal connections with the ventral stream as is it moves through the temporal lobe. 'Deep Temporal Lobe' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the amygdala using the BrainFacts.org 3D Brain

View the hippocampus using the BrainFacts.org 3D Brain

Pathways through the Amygdala

The amygdala receives visual information through multiple pathways

In addition to the projections to the amygdala via the ventral stream, the amygdala also appears to rely on input from the thalamus that is independent of the ventral stream pathway. A shorter pathway travels from the retina to the amygdala via the thalamus. It is believed that this pathway allows for a rapid responses to the threats and allows visual stimuli to activate the amygdala quicker than processing through the visual cortex. In fact, studies have shown that pictures of angry or fearful faces can cause amygdala activation without conscious awareness of seeing the image, a result of images being shown for only milliseconds to the subject.

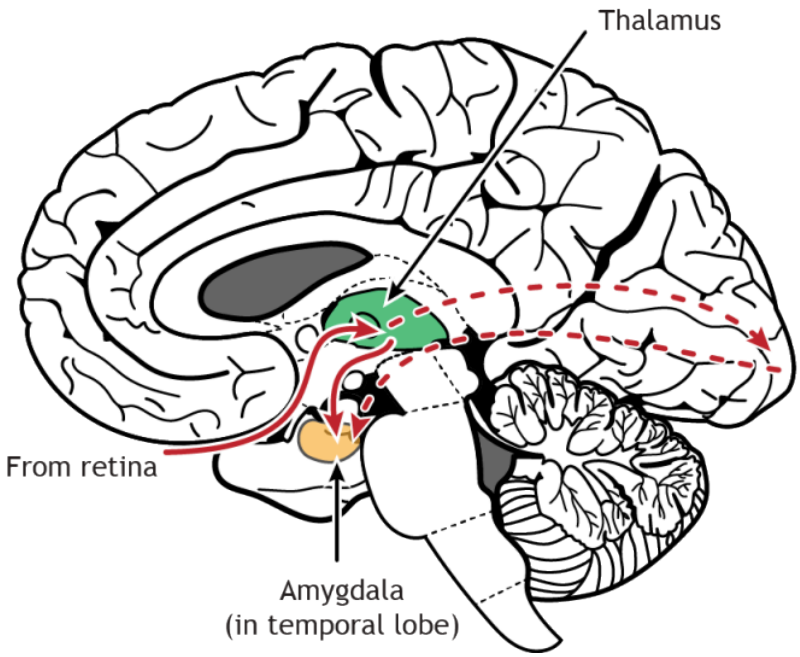

Figure 22.14. Information from the retina travels to the thalamus. From the thalamus, there is a direct pathway to the amygdala (solid red arrows) in addition to the pathway to the occipital lobe and ventral stream (dashed red arrows). 'Amygdala Visual Pathway' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Non-Thalamic Pathways

The retina sends projections to more regions than just the thalamus

Although most retinal output projects to the lateral geniculate nucleus of the thalamus and then to the primary visual cortex, there are some axons that project to other areas of the brain. A subset of specialized retinal ganglion cells project to the suprachiasmatic nucleus in the hypothalamus. This region is critical for circadian rhythms and the sleep/wake cycle. Other retinal neurons send axons to the pretectum, a midbrain region that communicates with motor nuclei and is responsible for pupillary control. Finally, other ganglion cells project to the superior colliculus, another midbrain region. This pathway is responsible for movements that will orient the head and eyes toward an object to focus the object in the center of the visual field, the region of highest visual acuity.

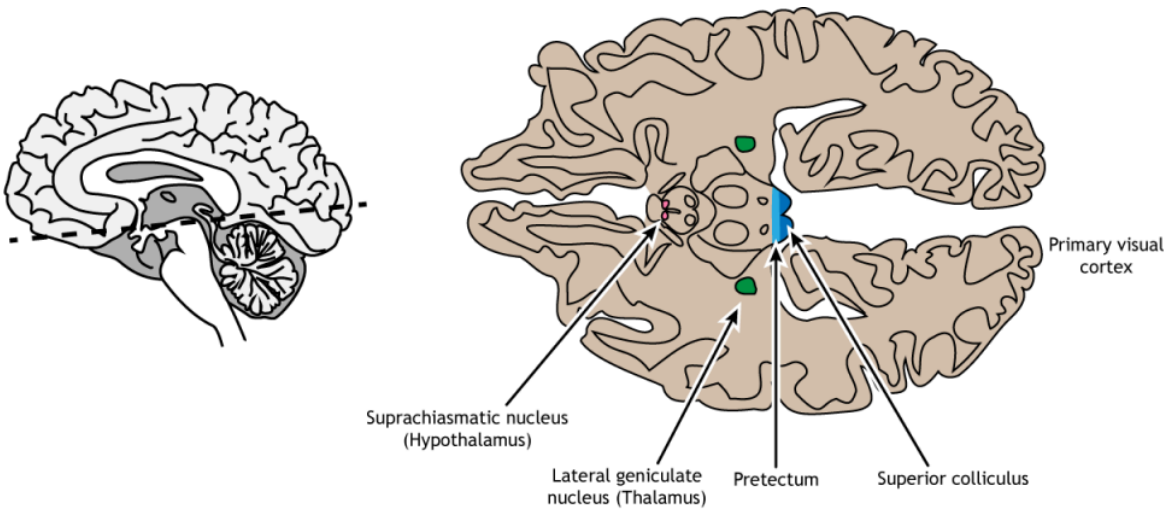

Figure 22.15. In addition to the thalamus, the retinal neurons send projections to other regions of the brain. The suprachiasmatic nucleus (pink) is located in the hypothalamus and is important for biological rhythms. The pretectum (light blue) is a midbrain structure that plays a role in muscle control of the pupil. Finally, the retina projects to the superior colliculus (blue), another midbrain region important in eye and head movements. The lateral geniculate nucleus of the thalamus (green) is also shown. 'Non-Thalamic Retinal Pathways' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the hypothalamus using the BrainFacts.org 3D Brain

View the midbrain using the BrainFacts.org 3D Brain

Key Takeaways

- The nasal and temporal retinal regions are responsible for viewing specific regions of the visual field
- Some retinal projections cross the midline at the optic chiasm, causing the left side of the brain to process the right visual hemifield and vice versa
- The retinal axons synapse in the lateral geniculate nucleus of the thalamus. Information then travels to the primary visual cortex
- Receptive fields and the preferred visual stimuli for neuron activation become more complex as information moves through the visual pathway
    - Retinal cells and thalamic neurons have circular receptive fields with inhibitory surround
    - Primary visual cortex neurons have linear receptive fields are are activated by a line in a specific orientation
    - Area MT / V5 is activated by motion in a specific direction
    - Area V4 is activated by specific shapes and colors
    - The fusiform gyrus is activated by faces
- The retina also projects to midbrain regions

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=479#h5p-19

Video Lecture

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23.

SOMATOSENSORY SYSTEMS

The somatosensory system is regulated by receptors that are spread throughout the body and measure a number of different sensory modalities in the body. These sensations can be divided into three main divisions: external stimuli, internal stimuli, and the sense of where the body is in space.

Resources

- Key Takeaways
- Test Yourself

Perception of external stimuli can include the sense of touch (via mechanoreceptors), pain (via nociceptors), and temperature (via thermal receptors). Perception of internal stimuli can include organ (visceral) sensation and pain (via multiple receptor types) and blood chemical composition (via chemoreceptors). Finally, proprioception (via proprioceptors) is the sense of where the body is in space. The ability of an individual to touch their nose easily while their eyes are closed is an example of the proprioception system.

Somatosensory Cell Bodies

All somatosensory receptor neurons have their cell bodies located in the dorsal root ganglion, a structure found just outside the dorsal aspect of the spinal cord. The receptor neurons, also called primary afferent fibers, of the somatosensory system are bipolar neurons, meaning they have one process from the cell body that splits into two branches. One travels to the location of the receptor (e.g. the skin for touch) via the spinal nerves, and one travels into the spinal cord at the dorsal horn via the dorsal root. The axon can either synapse in the spinal cord or ascend to the brain in the dorsal column.

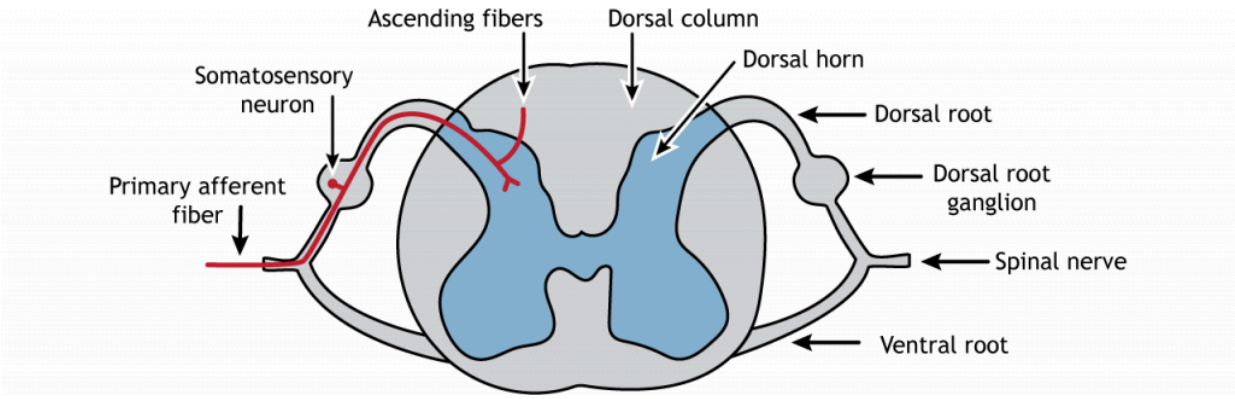

Figure 23.1. Primary afferent fibers travel from the periphery or target organs through the spinal nerve to the dorsal root ganglion where the cell body of the neuron is located. The axons then continue through the dorsal root into the dorsal horn of the spinal cord. Axons can branch and synapse in the spinal cord, or they can ascend to the brain via the dorsal column. 'Somatosensory Spinal Cord' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Primary Afferent Axons

Primary afferent axons are divided into four groups based on size and conduction speed. The groups, unfortunately, have different names depending on if the axons come from the skin (Aα, Aβ, Aδ, and C fibers; examples are touch or pain) or the muscles (Group I, II, III and IV fibers; example is proprioception). The fastest axons are the Aα or Group I type; they have the largest diameter and are heavily myelinated. The next fastest myelinated axons are the Aβ or Group II fibers, followed by the Aδ or Group III fibers. Finally, the C fibers have the smallest diameter, are unmyelinated, and are the slowest at conducting action potentials.

Afferent axon from muscle	Group 1	Group II	Group III	Group IV
Afferent axon from skin	Aα	Aβ	Aδ	C
Diameter (μm)	13-20 (Largest)	6-12	1-5	0.2-1.5 (Smallest)
Conduction speed (m/sec)	80-120 (Fastest)	35-75	5-30	0.5-2 (Slowest)

Table 21.1. Diameter and conduction speed of primary afferent axons. Group I and A alpha have the

largest diameter and fastest speed. Group II and A beta are the next largest and fastest, followed by Group III and A delta. Group IV and C fibers are the slowest and smallest of all axon types.

Different sensory information is sent via the different types of axons. Proprioceptive information from the skeletal muscles is sent to the spinal cord via Group I fibers. Touch information from the mechanoreceptors travels along Aβ fibers. Aδ fibers carry pain and temperature sensation, and C fibers convey information about pain, temperature, itch, and chemoreception.

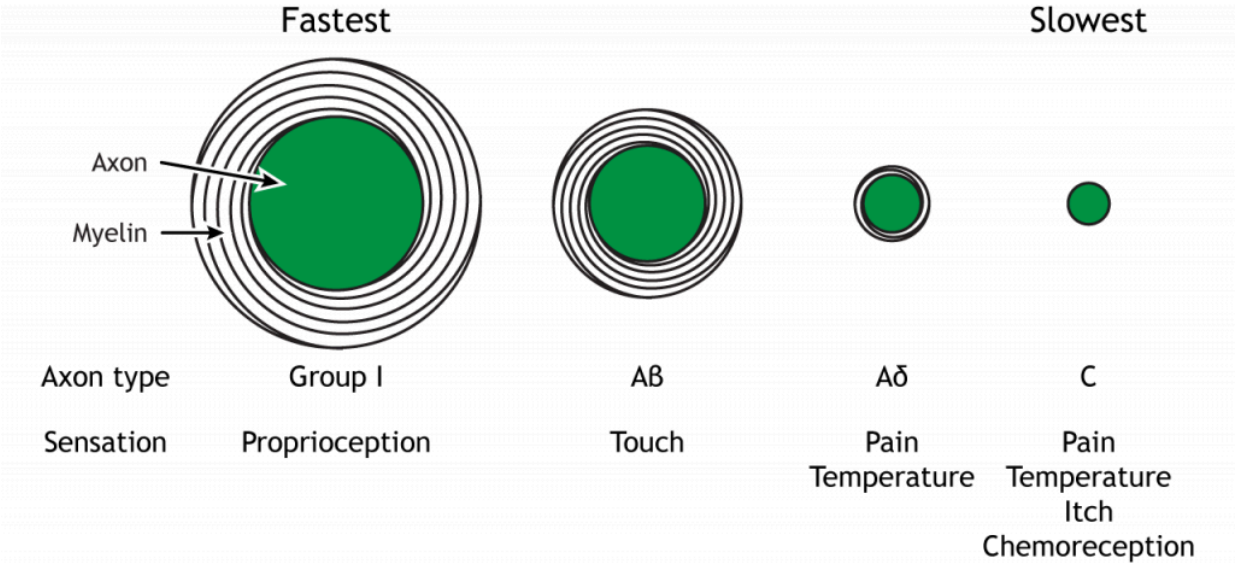

Figure 23.2. Primary afferent fibers differ in diameter and myelination, and therefore have different conduction speeds. A alpha fibers convey proprioception and are the largest and fastest of the axon types. Mechanoreception, or touch, is sent via A beta fibers, the next largest. Some aspects of pain and temperatures are sent by A delta fibers, which have small diameter and little myelination. C fibers are unmyelinated and sensory axons that detect pain, temperature, itch and chemoreception (chemical composition). These are the slowest of the somatosensory axons. 'Somatosensory Axon Types' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Dermatomes

The afferent axons from the dorsal root ganglion enter the spinal cord via the spinal nerves. Axons from nearby regions of the body enter the spinal cord together, and this forms regions of skin that are innervated by the same spinal nerve. These regions are called dermatomes. Damage to a spinal nerve will cause dysfunction along the innervated dermatome. The dermatomes and spinal nerves are divided into 4 groups. The seven cervical spinal segments are the most rostral and are located in the

neck. The twelve thoracic spinal segments are located along the chest and abdomen. The five lumbar segments are located below the thoracic segments, and the five sacral segments are the most caudal.

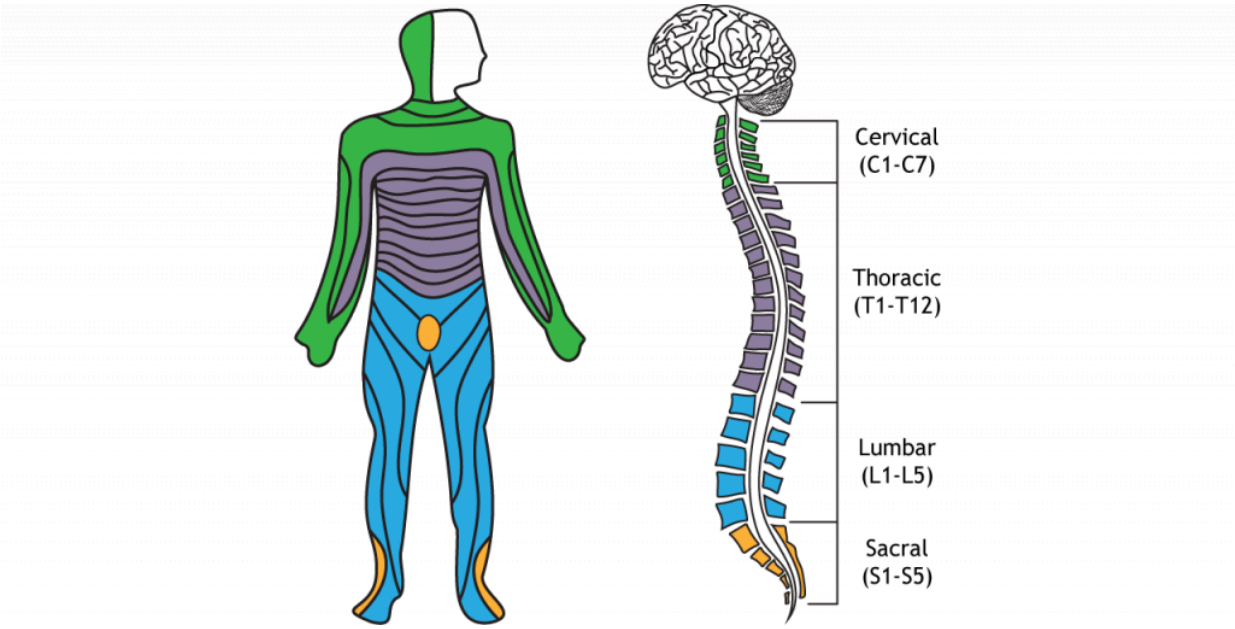

Figure 23.3. Spinal nerves exit the spinal cord and innervate a region of skin called a dermatome. There are five cervical, twelve thoracic, five lumbar, and five sacral spinal segments. 'Dermatomes' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Key Takeaways

- Somatosensory neuron cell bodies are located in the dorsal root ganglion
- Somatosensory primary afferent axons ascend to the brainstem via the dorsal column white matter tract
- Primary afferent axons vary in diameter and myelination, both of which affect action potential speed
- Different somatosensory information is carried by the different sizes afferents

- Dermatomes are the region of skin innervated by one spinal nerve

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=1211#h5p-23

24.

TOUCH: THE SKIN

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

Touch can come in many forms: pressure, vibration, stretch, motion, edges, points, etc. Receptors in the skin allow for perception of these different characteristics, and when this information is combined in the central nervous system, we are able to determine the location, strength, duration, movement, shape, and texture of the object interacting with the skin.

Receptors

We can feel different modalities of touch because of the presence of specialized sensory receptors, called mechanoreceptors, located in the skin.

The Pacinian corpuscles are located deep in the dermis of the skin and are responsible for perception of vibration.

Ruffini endings detect skin stretch and are also located within the dermis layer of the skin.

The Meissner corpuscles are stimulated by skin motion and are located in the epidermis layer.

The Merkel cells are located at the border between the dermis and epidermis and are specialized to detect edges and points.

Multiple types of mechanoreceptors allow for perception of different qualities of touch

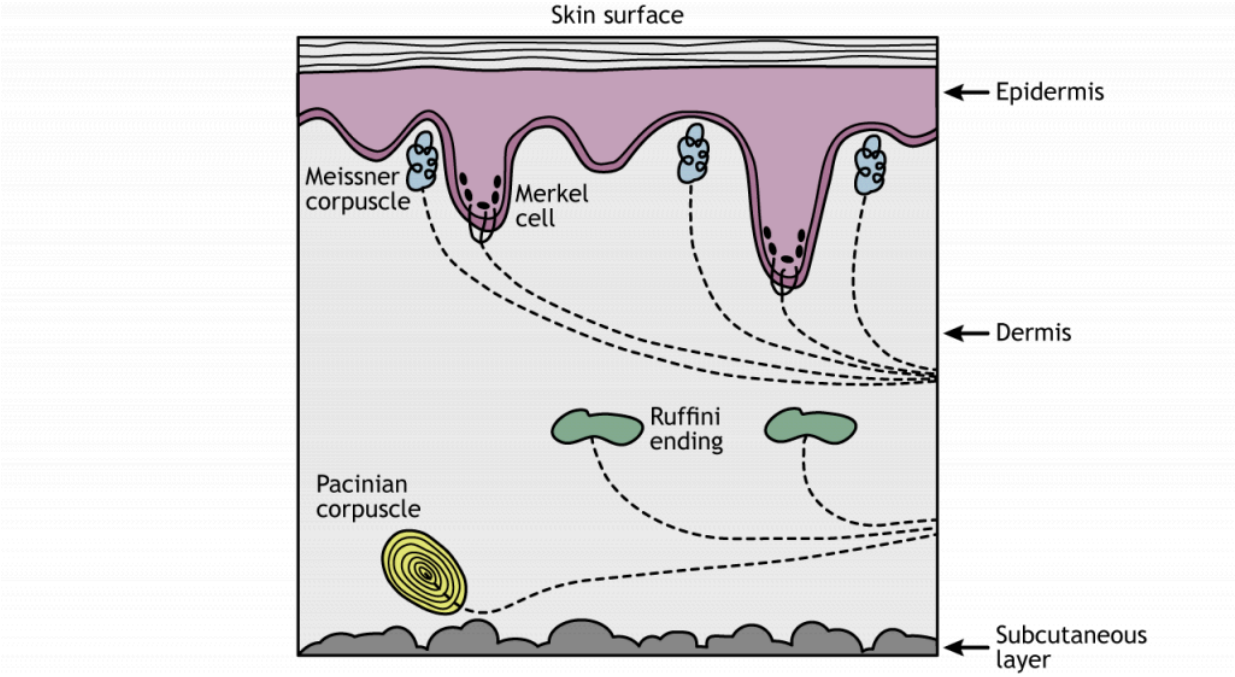

Figure 24.1. The different mechanoreceptor types are located in different regions of the skin and are responsible for perception of different characteristics of a touch timulus. Pacinian corpuscles and Ruffini endings are located deep in the dermis. Meissner corpuscles are located in the dermis near the epidermis, and Merkel cells are located in the epidermis, near the surface of the skin. 'Mechanoreceptors' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Receptive Fields

Each mechanoreceptor responds to a touch stimulus in a specific area of the skin, a region called the receptive field of the receptor. When the receptive field is touched, the mechanoreceptor will be activated.

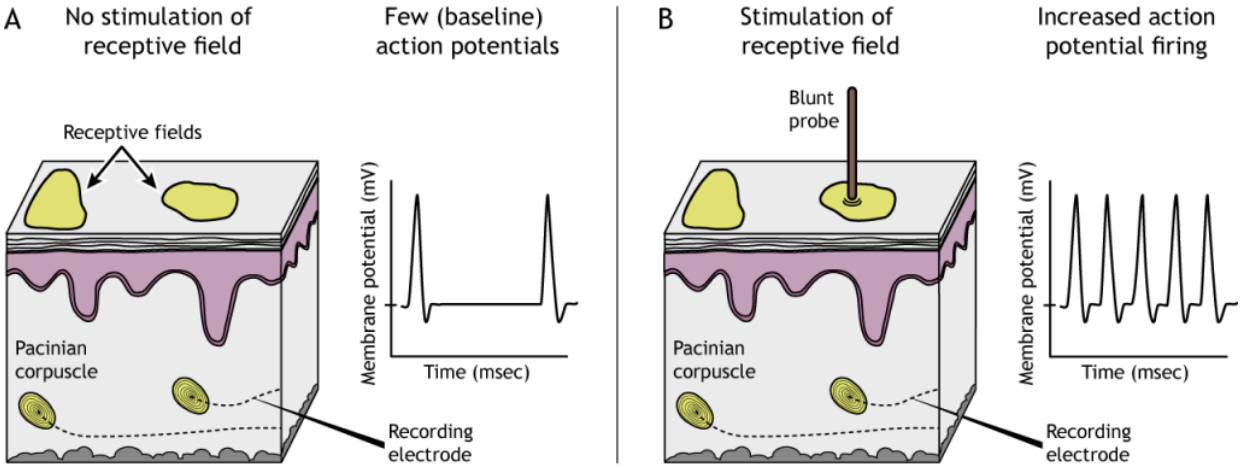

Figure 24.2. Each mechanoreceptor will be activated by a specific region of skin, the receptive field. When no stimulation of the receptive field occurs on the surface of the skin, the mechanoreceptor will show a baseline firing rate. When stimulation of the receptive field occurs, the firing rate of the mechanoreceptor will increase. 'Receptive Field Activation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Receptive field characteristics differ depending on the type of mechanoreceptor and location on the body

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Receptive Field Size

Merkel cells and Meissner corpuscles, both of which are located near the skin surface, have small receptive fields. Ruffini endings and Pacinian corpuscles, located deeper in the skin layers, have larger receptive fields than the Merkel cells and Meissner corpuscles.

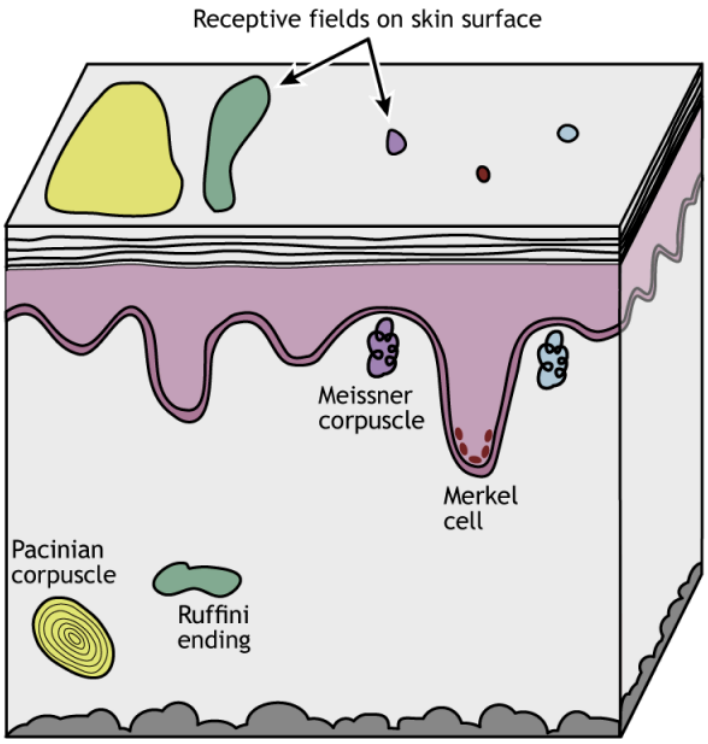

Figure 24.3. Receptive field sizes vary depending on the underlying mechanoreceptor type and location. Merkel cells and Meissner corpuscles have small receptive fields, whereas Pacinian corpuscles and Ruffini endings have large receptive fields. 'Mechanoreceptor Receptive Fields' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Receptive field sizes are different among the different mechanoreceptors, but they also vary among different body regions. Even within one receptor type (e.g. Meissner corpuscles), receptive fields in regions like the fingers or lips are smaller than in regions like the back or leg. This allows us to have finer spatial resolution with locating and identifying objects using our fingers. The smaller receptive fields in these regions are a result of a higher density of receptors in the skin.

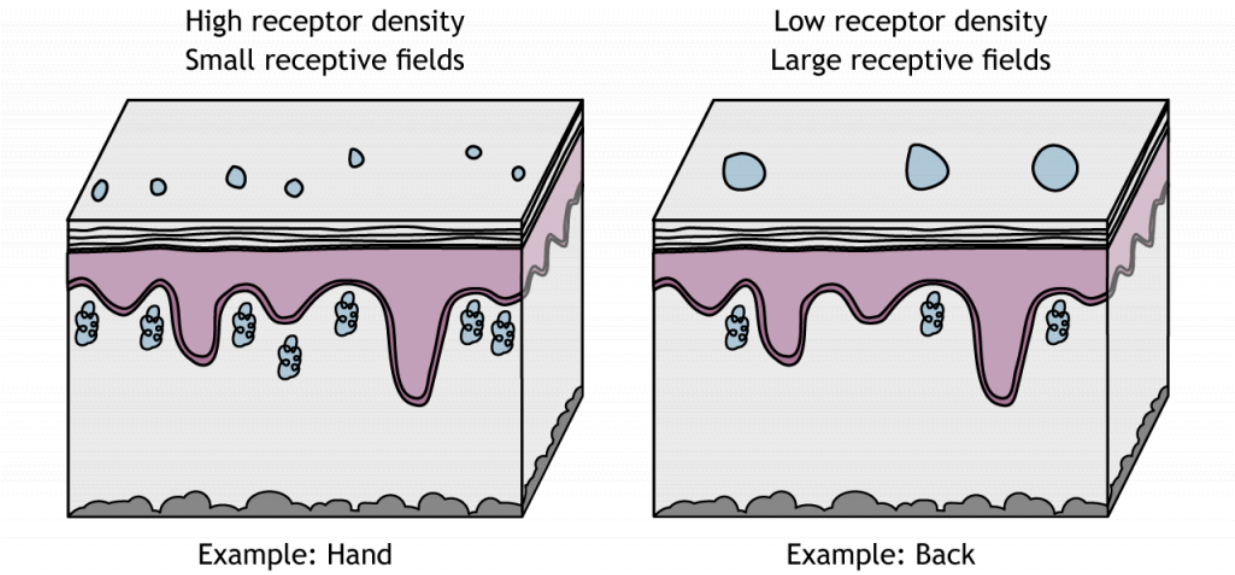

Figure 24.4. Density of mechanoreceptors can affect the size of the receptive field for each receptor. High density leads to smaller receptive fields. Density and receptive field size varies by location on the body. Regions like the hands and face have smaller receptive fields than regions like the back. 'Receptive Field Location' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Two-Point Discrimination

Receptive field sizes are important because they allow us to locate a stimulus on our bodies. Larger receptive fields are not as precise as smaller receptive fields. One measure of receptive field size is two-point discrimination (try it at home!), which determines the minimum distance needed between two stimuli to perceive two separate points on the skin and not one. The hand has a smaller threshold for discerning between two points than does the back, a result of the different sized in receptive fields.

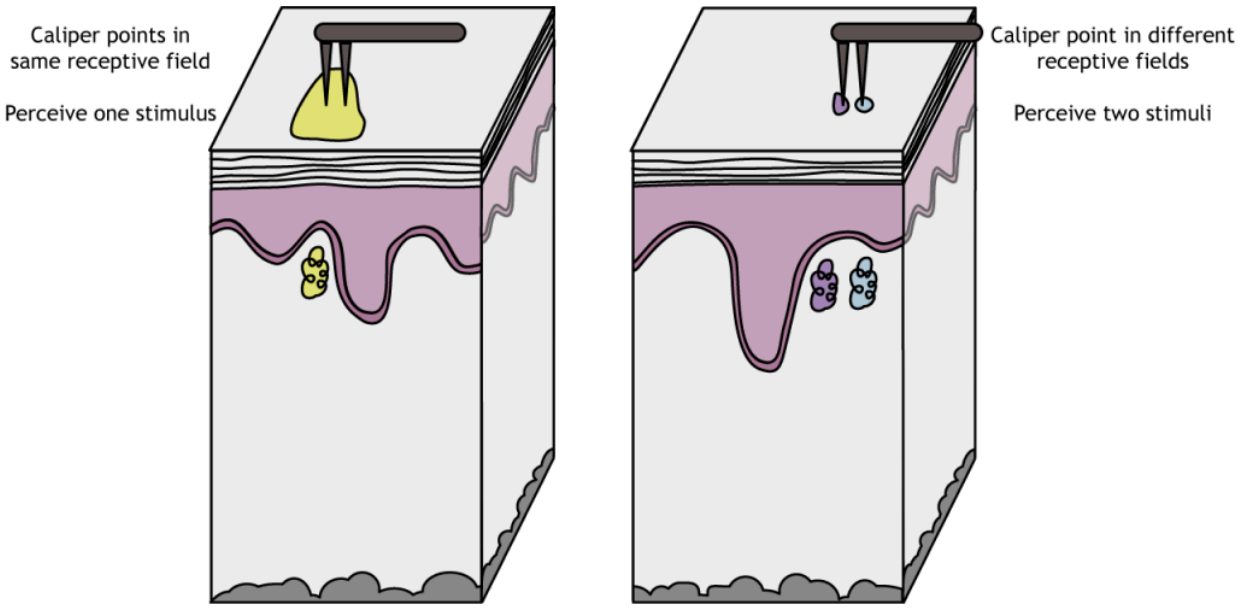

Figure 24.5. The size of the receptive fields affect the sensitivity of the skin, which can be measured by the two-point discrimination test. Tools like calipers or even a paperclip can be used to measure two-point discrimination. If the two points of the caliper feel like one point, they are both activating the same receptive field, indicating the receptive field is large. If, however, it is possible to perceive two separate points on the skin, then the calipers are activating two different receptive fields. 'Two-Point Discrimination' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Adaptation Rate

Another important characteristic of the somatic sensory receptors is that of adaptation rate. Fibers that are slowly adapting show action potential firing throughout the entire time a stimuli is present. Merkel cells and Ruffini endings are both slowly adapting fibers. Slowly adapting fibers are most useful for determining the pressure and shape of a stimulus.

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Animation 24.1. Slowly adapting mechanoreceptors continuing firing action potentials throughout the duration of a stimulus. As the stimulus moves from not present, to weak, to strong, the action potential firing of the Ruffini ending fires throughout the entire stimulus. 'Slowly Adapting Receptor' 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.

Rapidly adapting fibers fire action potentials when a stimulus changes (e.g., starts, stops, gets stronger or weaker) but not when a stimulus is constant. This firing makes rapidly adapting fibers specialized for detecting movement and vibration. Meissner and Pacinian corpuscles are rapidly adapting.

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Animation 24.2. Rapidly adapting mechanoreceptors firing action potentials when the strength of the stimulus changes. As the stimulus moves from not present, to weak, to strong, the action potential firing of the Pacinian corpuscle only fires when the stimulus changes strength. 'Rapidly Adapting Receptor' 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.

Sensory Transduction

In previous chapters we discussed ion channels that are gated by voltage changes in the neuron and channels that are gated by neurotransmitters. In the somatosensory system, we find ion channels that are gated by physical distortion or stretch of the membrane. These channels can open by stretch of the membrane itself or indirectly through movement of intra- or extracellular proteins that are linked to the channels. Sodium and calcium flow into the cell, causing both a depolarization and the initiation of second messenger cascades. If enough stimulus is applied, the depolarization reaches threshold of the axon and an action potential is sent toward the spinal cord.

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Animation 24.3. Mechanoreceptors respond to touch stimuli via stretch-gated non-selective cation channels. The channels can either open due to stretch of the membrane itself which stretches open the channel or due to proteins associated with the channels that pull the channel open. 'Stretch-Gated Ion Channels' 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

- There are multiple types of mechanoreceptors in the skin that are activated by different types of touch stimuli
- The receptive field size differs among the types of mechanoreceptors
- The adaptation rate differs among the types of mechanoreceptors
- Receptive field is a region of skin that activate a given mechanoreceptor
- Receptive field size for a specific type of mechanoreceptor can vary in size across the body
- Mechanoreceptors express stretch-gated non-selective ion channels that depolarize the cell during sensory transduction

Test Yourself!

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https://openbooks.lib.msu.edu/neuroscience/?p=493#h5p-21

- Describe the relationship between density of receptors, receptive fields, and two-point discrimination.

Video Lecture

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25.

TOUCH: CENTRAL PROCESSING

Receptive Fields and Lateral Inhibition

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

The receptive fields of the sensory neurons become more complex as information moves up the pathway. We saw in the last lesson that mechanoreceptors have receptive fields that, when touched, activate the neuron. The mechanoreceptors synapse on neurons in the dorsal column, and those neurons have more complex receptive fields. The dorsal column nuclei have receptive fields that are divided into center and surround regions. The center of the receptive field is a result of direct innervation from the mechanoreceptors. If a stimulus touches the skin in the center of a dorsal column neuron's receptive field, the neuron will increase its firing rate. The center / surround structure is like that of bipolar and ganglion cells in the vision system.

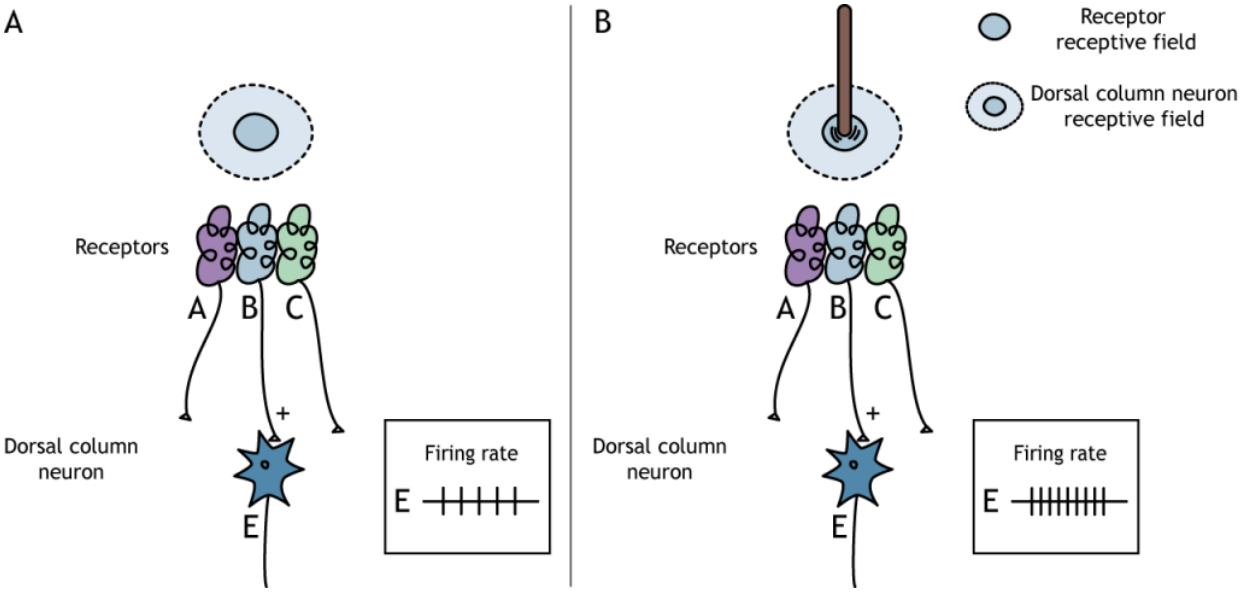

Figure 25.1. The receptive field of a dorsal column neuron has an excitatory center that is generated by the mechanoreceptors that synapse directly on the dorsal column neuron. A) When no stimulus is present, the dorsal column neuron fires at a baseline rate. B) When a stimulus touches the center of the receptive field of Cell E, the firing rate increases. 'Touch Receptive Field Center' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The surround region of the receptive field is a result of indirect communication between the receptor neurons and the dorsal column neurons via inhibitory interneurons. The surround has an inhibitory effect on the dorsal column neuron. If a stimulus touches the skin in the surround of a dorsal column neuron's receptive field, the neuron will decrease its firing rate.

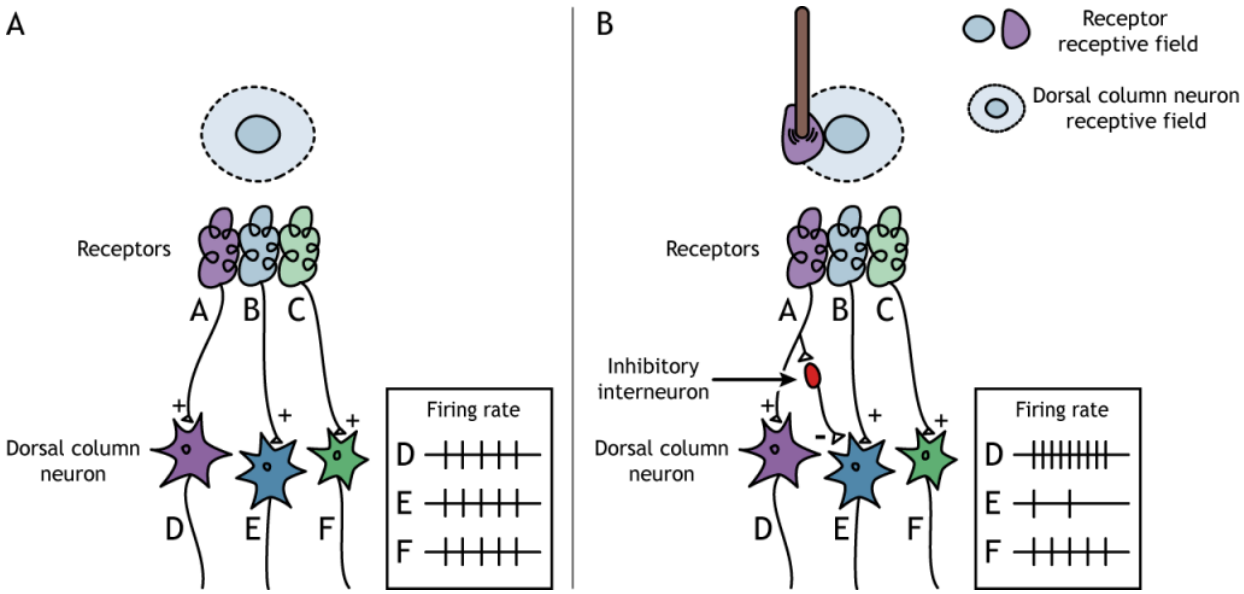

Figure 25.2. The receptive field of a dorsal column nucleus has an inhibitory surround, which is a result of the indirect connections between mechanoreceptors and the dorsal column neuron via inhibitory interneurons. A) When no stimulus is present, the dorsal column neurons fire at a baseline rate. B) When a stimulus touches the surround of the receptive field of Cell E, the firing rate decreases. Note that the stimulus is in the surround of Cell E's receptive field but is also in the center of Cell D, so the firing rate of Cell D will increase. 'Touch Receptive Field Surround' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Lateral inhibition results from overlapping receptive fields and increases perception of stimuli at edges and borders

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Lateral Inhibition

The center-surround structure of the receptive field is critical for lateral inhibition to occur. Lateral inhibition is the ability of the sensory systems to enhance the perception of edges of stimuli. At a point or an edge of a stimulus, because of the inhibitory interneurons, the perceived stimulus strength will be enhanced compared to the actual stimulus strength.

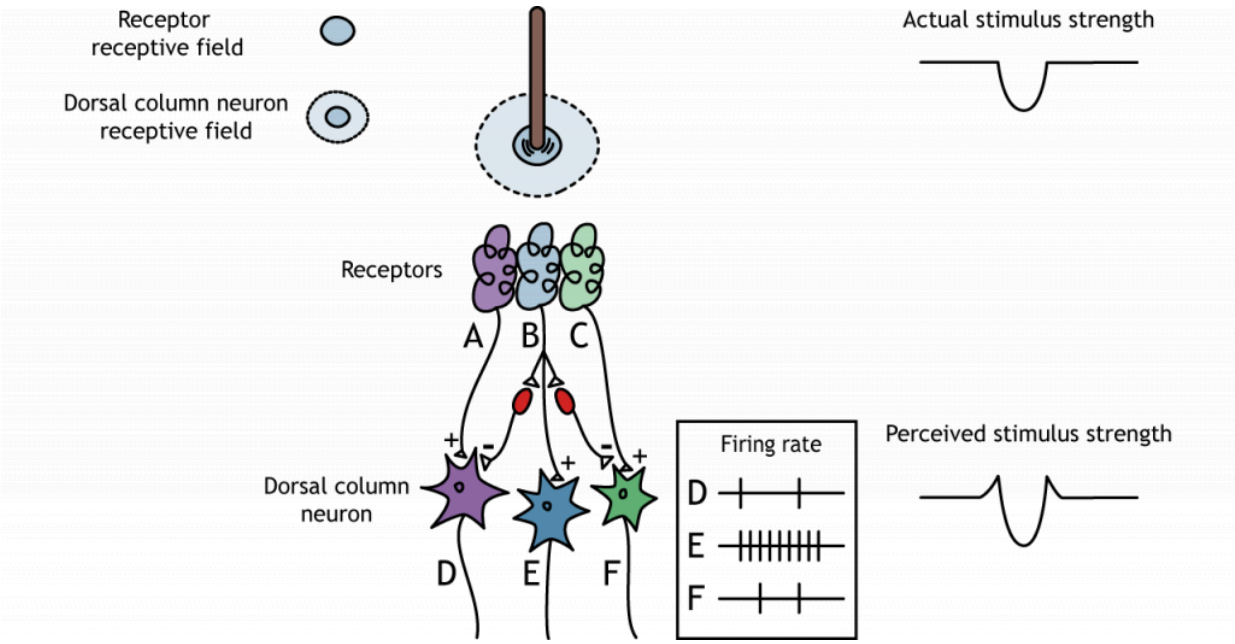

Figure 25.3. Lateral inhibition heightens the perception of edges or points on the skin. The point of a blunt probe pressing on the receptive field of Cell B will cause an increase in the firing rate of Cell E, but will also cause a decrease in the firing rate of Cells D and F. This increases the perceived difference between the point and the area next to the point that is not being stimulated. 'Touch Lateral Inhibition' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Pathway to Brain

The right side of the brain processes touch on the left side of the body; the left side of the brain processes touch on the right side of the body.

Dorsal Column-Medial Lemniscus Pathway

Primary afferent sensory fibers have their cell bodies located in the dorsal root ganglion, a structure that lies just outside of the spinal cord. The axons of these first-order neurons enter the ipsilateral

dorsal side of the spinal cord. Some axon collaterals terminate in the spinal cord and are important for reflexes. The main axon branch ascends the spinal cord toward the brain, via the dorsal column, terminating in the dorsal column nuclei located in the brainstem. The axons of sensory neurons in the lower body remain separate from the axons of sensory neurons in the upper body throughout the pathway. These two populations of neurons synapse in different regions of the brainstem. The lower body axons terminate in the gracile nucleus, whereas the upper body axons terminate in cuneate nucleus. Projections from the second-order neurons in the dorsal column nuclei cross the midline, or decussate, and ascend via a white matter tract called the medial lemniscus. The axons terminate in the ventral posterior lateral nucleus of the thalamus. The thalamic neurons then project to the primary somatosensory cortex located in the postcentral gyrus in the parietal lobe.

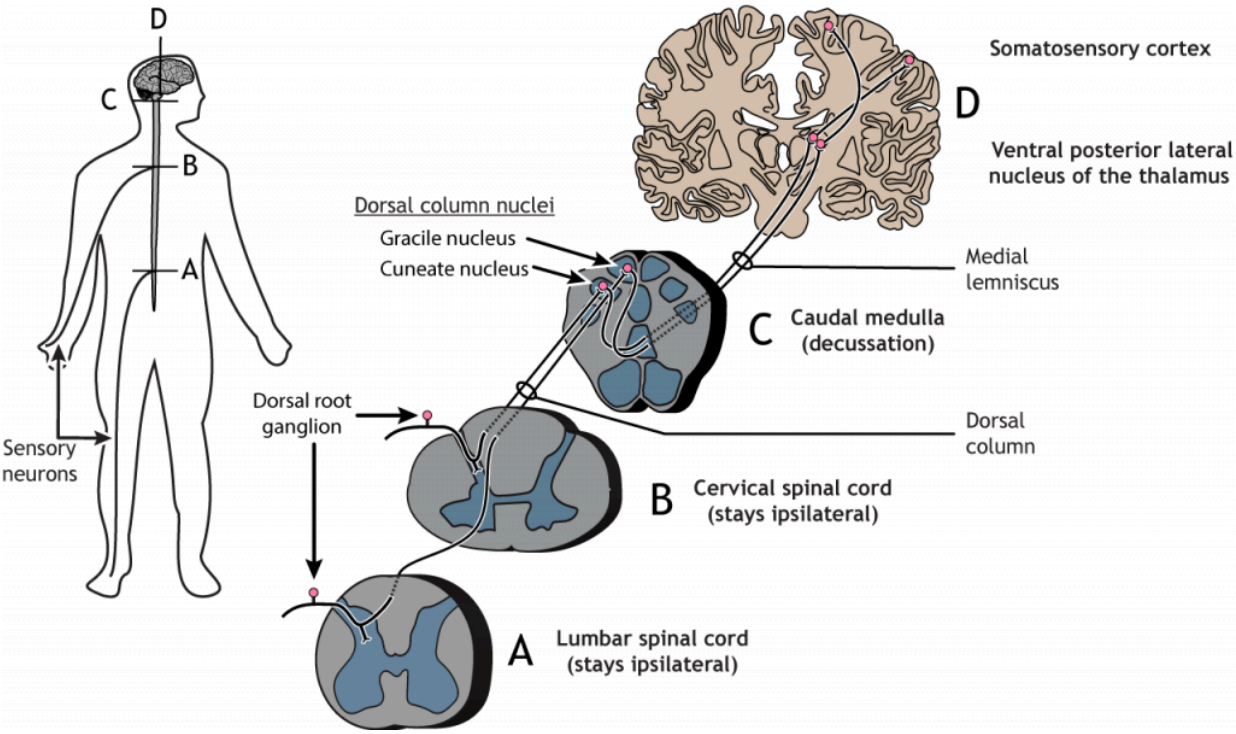

Figure 25.4 Somatosensory information from the neck and body travels through the dorsal column – medial lemniscus pathway, named for structures within the pathway. Axons enter the spinal cord and ascend through the dorsal column to the medulla where decussation, or crossing the midline, occurs. Information continues to the thalamus via the medial lemniscus, and then reaches the somatosensory cortex. Details of the pathway are found in the text. 'Touch Pathway from Body' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the thalamus using the BrainFacts.org 3D Brain

View the primary somatosensory cortex using the BrainFacts.org 3D Brain

Trigeminal Pathway

Sensory receptors in the face and head send information to the brain via cranial nerve V, the trigeminal nerve. The first-order neurons have their cell bodies in the trigeminal ganglion, located just outside of the brainstem, and they project to the ipsilateral trigeminal nucleus in the pons. The second-order neurons cross the midline and project up to the ventral posterior medial nucleus of the thalamus. These neurons then send projections to the face region of the somatosensory cortex.

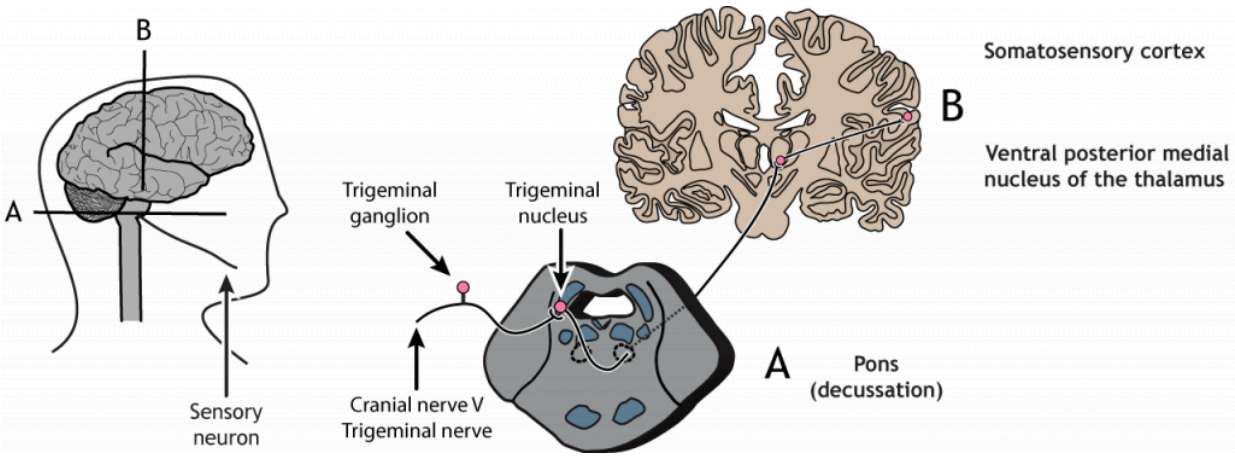

Figure 25.5. Somatosensory information from the head and face travels through the trigeminal pathway. Axons enter the brainstem at the level of the pons and decussate before traveling to the thalamus and somatosensory cortex. Details of the pathway are found in the text. 'Touch Pathway from Face' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

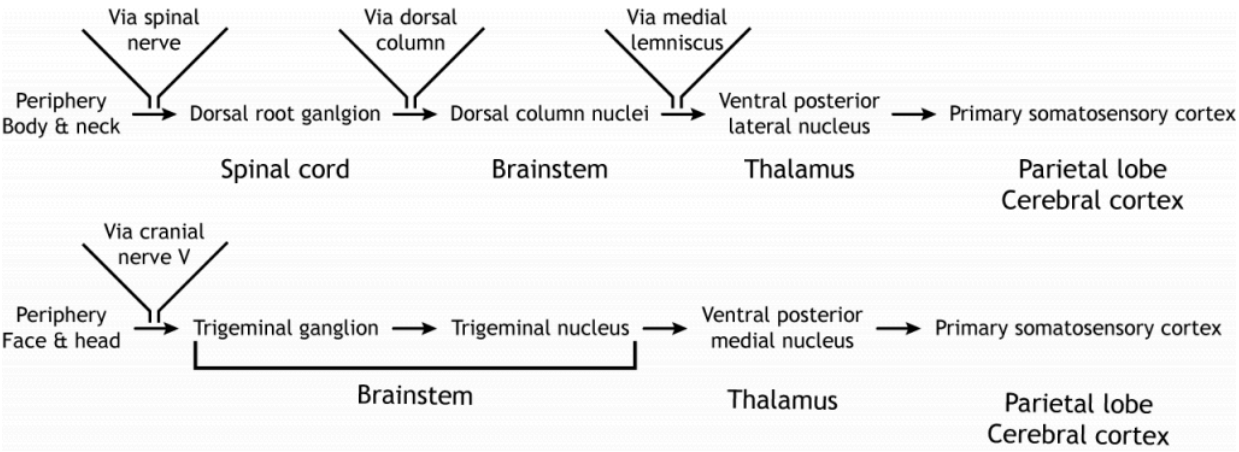

Figure 25.6. To compare the two pathways, sensory information comes in from the periphery. For the body, the peripheral axon branch travels via a spinal nerve to the cell body located in the dorsal root ganglion, which sits just outside the spinal cord. The central axon branch then enters the spinal cord and ascends via the dorsal column to the dorsal column nuclei in the brainstem. The second-order neuron crosses the midline and then projects to the ventral posterior lateral nucleus of the thalamus via the medial lemniscus tract. The thalamic third-order neuron projects to the primary somatosensory cortex in the parietal lobe. For sensory information from the face, the peripheral axon branch travels to the trigeminal ganglion via cranial nerve V. The ganglion sits outside of the brainstem, and the axons then enter the brainstem and synapse on the trigeminal nucleus. The second-order neuron travels to the ventral posterior medial nucleus of the thalamus, and the third-order neuron projects to the primary somatosensory cortex in the parietal lobe. 'Touch Pathways' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Primary Somatosensory Cortex

Anatomy

The primary somatosensory cortex is divided into four regions, each with its own input and function: areas 3a, 3b, 1, and 2. Most touch information from mechanoreceptors inputs to region 3b, whereas most proprioceptive information from the muscles inputs to region 3a. These regions then send and receive information from areas 1 and 2. As processing of somatosensory information continues, the stimuli required to activate neurons becomes more complex. For example, area 1 is involved in sensing texture, and area 2 is involved in sensing size and shape of an object. The posterior parietal cortex, an important output region of the somatosensory cortex, lies caudal to the postcentral gyrus; areas 5 and 7 are downstream structures that continue to process touch.

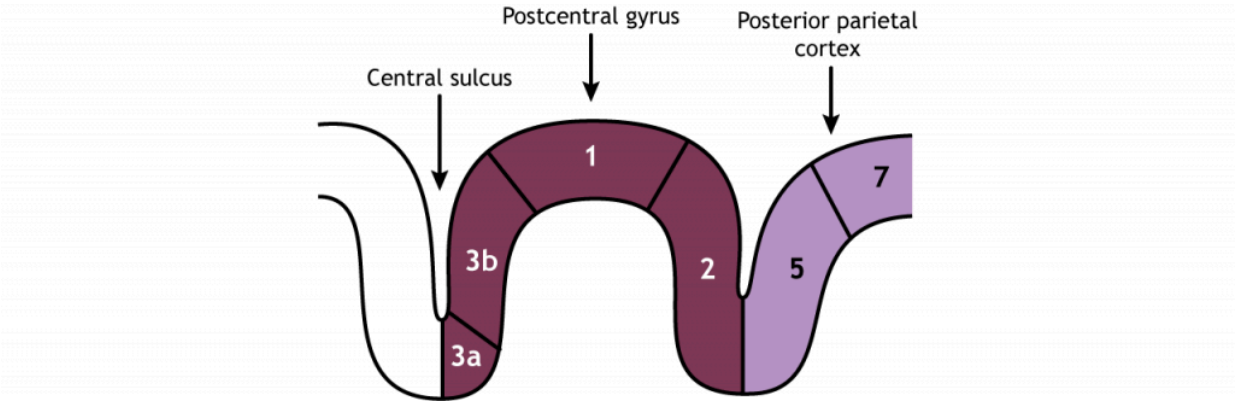

Figure 25.8. The somatosensory cortex, located in the postcentral gyrus, just posterior to the central sulcus, is divided into 4 areas: 3a, 3b, 1, and 2. The posterior parietal cortex, an output region of the somatosensory cortex, lies just posterior to the postcentral gyrus and is divided into areas 5 and 7. 'Postcentral Gyrus' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Somatotopic Map

Information from the skin is organized into a map of the body on the primary somatosensory cortex

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The receptive fields of each higher order neuron increases in size and complexity, but even cortical neurons are associated with a specific region of the body. Cortical neurons are organized by the region of the body they represent, so neurons that respond to sensation in the fingers are located close to the neurons that respond to sensation in the hand. Remember from above that axons in the dorsal column from the lower body run next to, but remain separate from, the axons from the upper body. This separation, which occurs for all body regions and at all levels of the pathway, creates a somatotopic map of the body in the primary somatosensory cortex. Each area of the somatosensory cortex (Figure 23.7) has its own, but similar, map of the body.

Regions with high receptor density in the skin, and, therefore, fine two-point discrimination, have more cortical space devoted to them. This means that the cortical representation of the body is not

true to actual physical proportions. A homunculus is a cartoon representation of what a body would look like if actual body size was proportional to the cortical representation. The hands and lips would be excessively large while the torso, arms, and legs, would be relatively small.

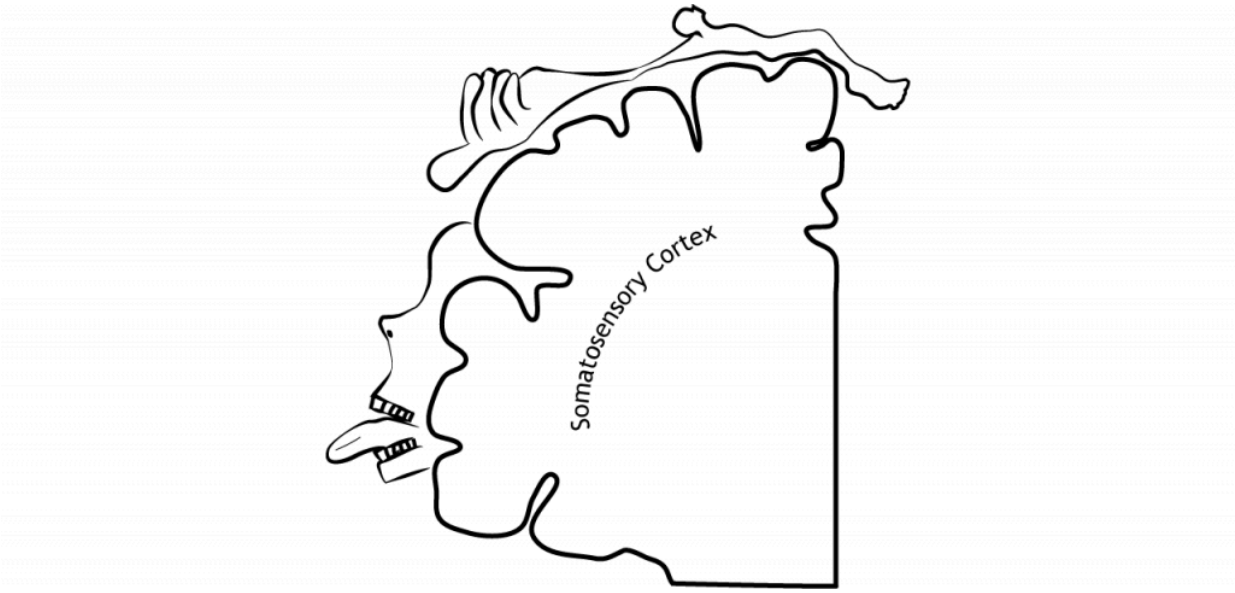

Figure 25.8. The body is mapped onto the somatosensory cortex. Regions with high touch sensitivity, and therefore high mechanoreceptor density, have more cortical space dedicated to their processing. The feet and legs are represented in the medial superior region of the cortex; the face is represented on the lateral side of the cortex; the hand and fingers fall in between. 'Somatotopic map' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Higher-Level Processing of Touch Information

The primary somatosensory cortex sends projections to other parietal lobe regions for higher-level processing of touch information.

Secondary Somatosensory Cortex

The secondary somatosensory cortex (SII) is located in the inferior parietal lobe, just above the lateral fissure. This region, like the dorsal stream of visual processing, is responsible for object recognition,

discerning texture, shape, and size. The SII also has receptive fields that represent bilateral regions of the body, so both hemispheres will be activated by touch on either side of the body. The SII sends projections to the posterior parietal cortex, the premotor cortex, the amygdala, and the hippocampus.

Posterior Parietal Cortex

The posterior parietal cortex recognizes touch characteristics like orientation and movement. It is also important for combining the touch and motor components of actions like grasping. The posterior parietal cortex outputs to the frontal motor cortex.

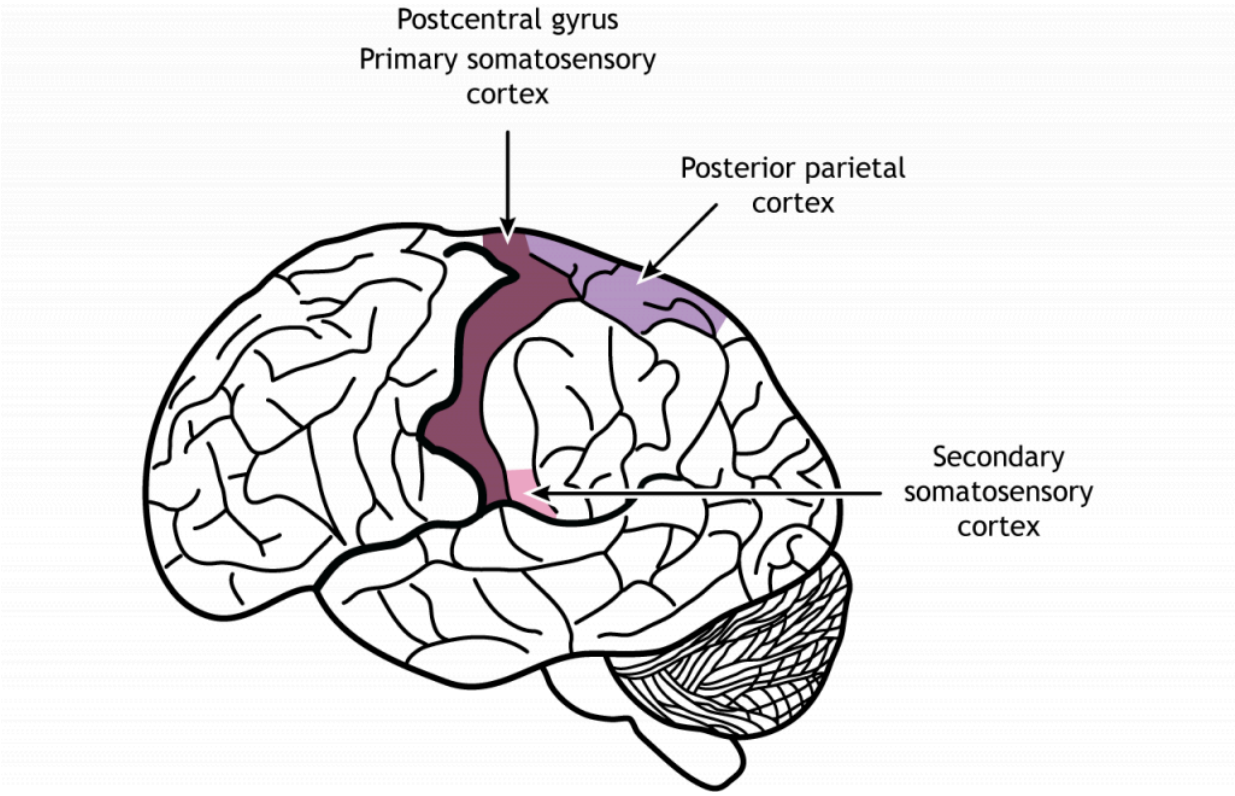

Figure 25.9. The primary somatosensory cortex is located in the postcentral gyrus. The posterior parietal cortex regions important for somatosensory lie caudal to the postcentral gyrus in the superior parietal lobe. The secondary somatosensory cortex is located dorsal to the lateral fissure, caudal to the postcentral gyrus. 'Somatosensory Streams" by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the posterior parietal cortex using the BrainFacts.org 3D Brain

Cortical Plasticity

The brain can show plasticity when sensory input changes over time

In adulthood, the brain is plastic, meaning synaptic connections can rearrange under certain conditions. Amputation or loss of a finger, for example, will lead to the associated cortical space to be functionally remapped by input from neighboring regions of the hand. The cortical neurons do not die, they begin to be activated by a different region of the body. Likewise, cortical representation can expand with use or practice. Repeated training of certain fingers can lead to an increase in cortical space mapped to those digits. Cortical plasticity is believed to underly the phenomenon of the perception of phantom limbs after amputation. In these cases, subjects that have lost a region of their body can sometimes still "feel" the missing part.

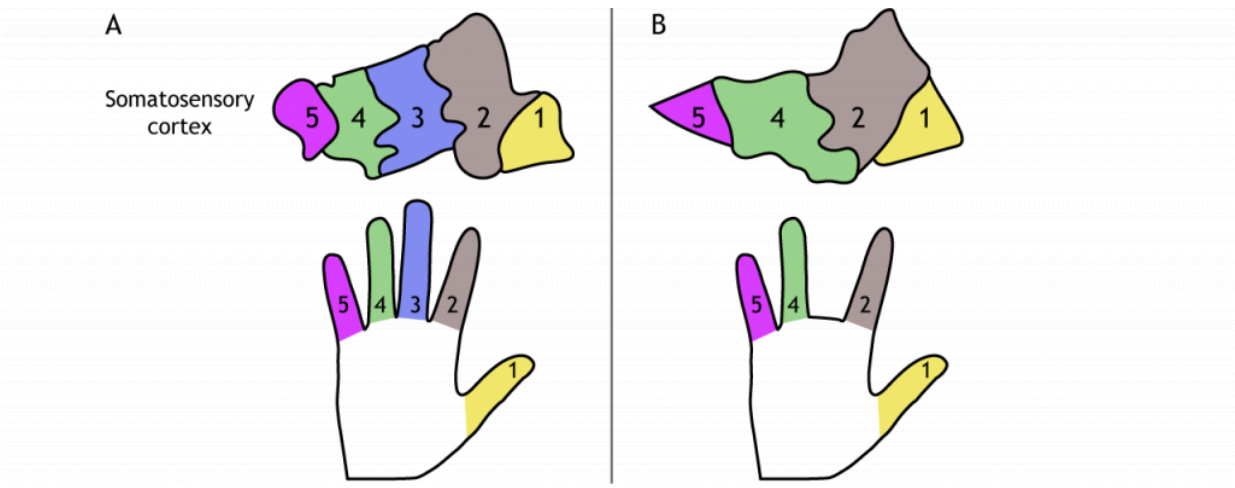

Figure 25.10. It is possible to map cortical space to regions of skin. A) The cortical space mapped to each finger for an imaginary individual is shown as an example. B) If this individual were to lose a finger, in this case digit 3 or the middle finger, and the cortical space was remapped after time had passed, the region that had once responded to touch on digit 3 would instead respond to touch on either digit 2 or 4. The brain does not let that cortical space die or go to waste; it rearranges connections to make use of all the neurons. Based on Merzenich et al., 1984. 'Cortical Plasticity' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Key Takeaways

- Receptive fields become more complex as information moves through the touch pathway
- Lateral inhibition enhances edges and borders by affecting the perceived stimulus strength
- Mechanoreceptor afferents synapse in the dorsal column nuclei in the medulla. Information then decussates and synapses in the ventral posterior nucleus of the thalamus before traveling to the primary somatosensory cortex
    - Sensory axons from the lower body synapses in the gracile nucleus in the dorsal column
    - Sensory axons from the upper body synapses in the cuneate nucleus in the dorsal column
    - Information from the neck and body synapse in the ventral posterior lateral nucleus of the thalamus
    - Information from the head and face synapse in the ventral posterior medial nucleus of the thalamus
- The primary somatosensory cortex is organized in a somatotopic map
- The cortex is plastic and connections can change with experience

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=512#h5p-22

- What is the anatomical name of the primary somatosensory cortex?
- After somatosensory information leaves the brainstem, it must relay through which structure before reaching the primary somatosensory cortex?

Video Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=512#oembed-1

26.

PAIN

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

Pain is the sensation we feel in response to activation of special branching, bare nerve endings called nociceptors. Activation of nociceptors usually occurs in response to tissue damage or the threat of damage. Depending on the type of stimulus, either lightly myelinated A delta fibers or unmyelinated C fibers transmit information to the CNS. Nociceptors are located throughout the body in skin, muscles, and viscera, but there are no nociceptors in the CNS.

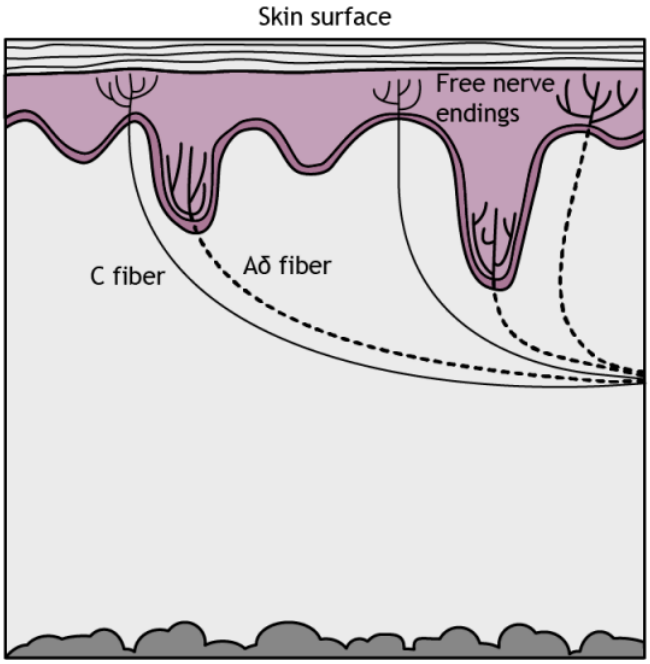

Figure 26.1. Free nerve endings in the skin and other tissues respond to tissue damage. Activation of these nociceptors lead to perceived pain sensation. Nociceptor fibers can either by unmyelinated (C fibers) or lightly myelinated (A delta fibers). 'Nociceptors' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Receptors

The type of pain perceived depends on which receptor type is activated.

There are three types of nociceptors that are each activated by different types of harmful stimuli. Type A delta I fibers have a low threshold for mechanical stimulation, such as intense pressure or an incision on the skin. Type A delta II fibers have a low threshold for thermal stimulation and activate in extremely hot or extremely cold environments. Type C fibers tend to be polymodal or activated by a range of stimuli including mechanical, chemical, and thermal.

The A delta and C fibers transmit information to the CNS at different speeds because of their different myelination levels. We can often perceive this difference in the form of "first pain" and "second pain". Think about a time where you were injured, perhaps you hit your thumb with a hammer. Immediately, you might have felt an intense, sharp pain – first pain, but then a milder, burning or aching pain that continue longer – second pain. A delta fibers are responsible for first pain transmission whereas C fibers are responsible for second pain transmission.

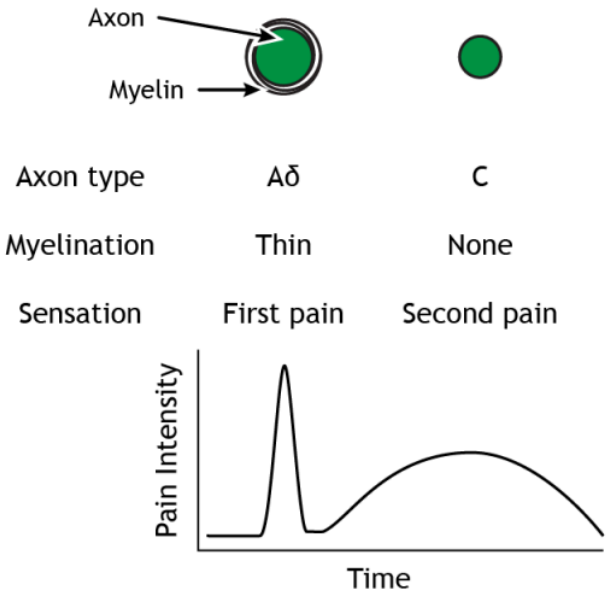

Figure 26.2. A delta pain fibers have thin myelination, whereas C fibers have none. This allows A delta fibers to transmit information to the CNS faster, resulting in the perception of the sharp, first pain after an injury. C fibers transmit information slower, causing the dull, aching, second pain perception. 'Pain fibers' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Pain Transduction

Like the other sensory systems, specialized proteins in the cell membrane of nociceptors convert noxious stimuli into electrical potentials in the neurons. A family of ion channels called transient receptor potential (TRP) channels can be expressed in the nociceptor nerve endings and have been shown to be activated by thermal and chemical components. For example, TRPV1, a non-selective cation channel found in nociceptors, can be activated by temperatures above 45 degrees C and can

also be activated by a chemical in hot peppers called capsaicin. Another family of receptors called Piezo is believed to be responsible for some mechanical pain transduction.

Once depolarization occurs in response to a painful stimulus, action potential propagation depends on the action of voltage-gated sodium and potassium channels. Lidocaine, a common local anesthetic, dulls pain by blocking these voltage-gated sodium channels, preventing signal transmission. A special type of sodium channel, Na1.7, is present only in nociceptor fibers. A mutation in this ion channel that prevents it from functioning can results in the inability to feel pain.

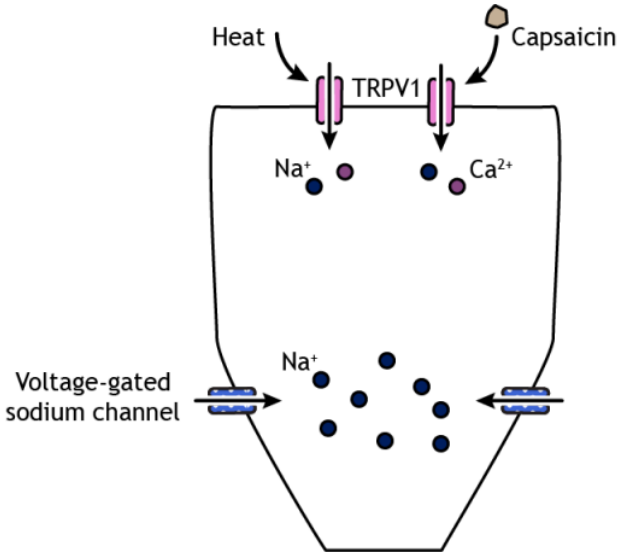

Figure 26.3. Pain transduction occurs when specialized ion channels that open in response to harmful stimuli cause depolarization and eventually activation of voltage-gated sodium channels, initiating the action potential. Different channels are responsive to different stimuli. Here, the TRPV1 channel can allow influx of sodium and calcium when opened by either heat or capsaicin, the molecule responsible for the perception of heat when eating hot peppers. 'Pain Transduction' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Pathway to Brain

Spinal Cord Branching

Primary afferent pain fibers have their cell bodies located in the dorsal root ganglion, like the fibers of the mechanoreceptors responsible for touch. The axons of these first-order neurons enter the

ipsilateral dorsal side of the spinal cord, and then they branch and travel up and down the spinal cord a couple of segments in a white matter region of the spinal cord just posterior to the dorsal horn called Lissauer's tract. All the branches terminate in the dorsal horn.

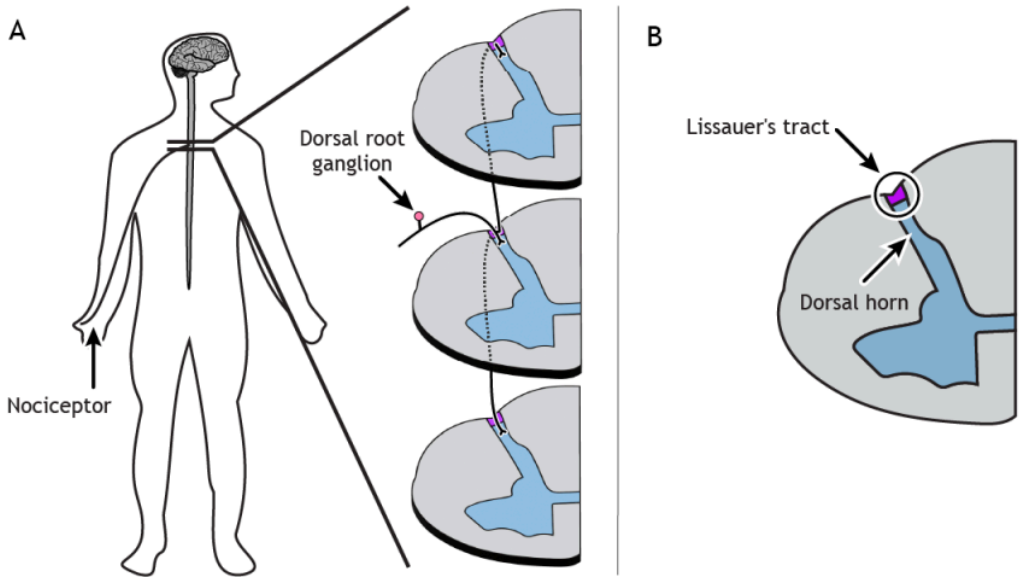

Figure 26.4. Nociceptors cell bodies are located in the dorsal root ganglia. Axons enter the spinal cord and then branch and ascend and descend a short distance. These branches travel in a region called Lissauer's tract. The neurons make synaptic connections in the dorsal horn. 'Lissauer's tract; by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Spinothalamic Pathway

The nociceptor fibers make synaptic contact with second-order neurons in the dorsal horn of the spinal cord. These neurons immediately cross the midline, or decussate, and then ascend to the brain through the anteriolateral aspect of the spinal cord and brainstem via the spinothalamic tract. The axons terminate in the ventral posterior lateral nucleus of the thalamus. The thalamic neurons then project to the primary somatosensory cortex located in the postcentral gyrus in the parietal lobe.

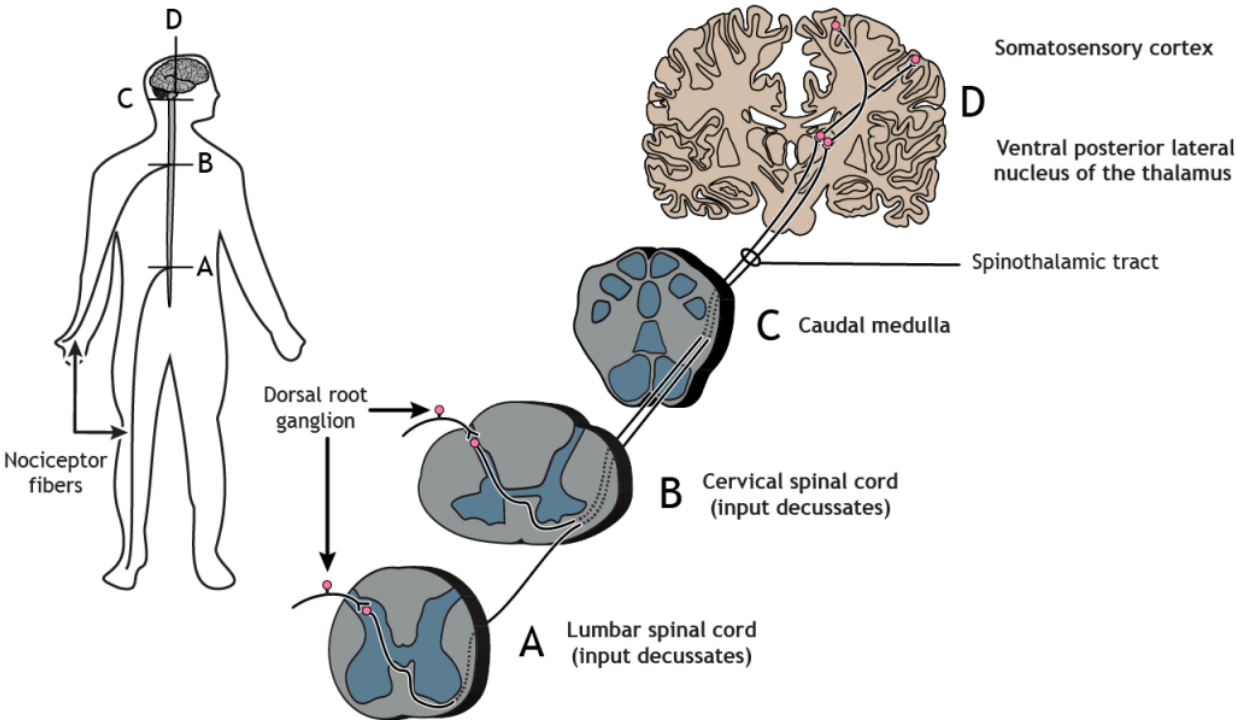

Figure 26.5. Pain and temperature information from the neck and body travels through the spinothalamic pathway, named for structures within the pathway. Axons enter the spinal cord and terminate in the dorsal horn. Second-order neurons decussate and ascend to the brain. Information continues to the thalamus, and then reaches the somatosensory cortex. Details of the pathway are found in the text. 'Pain Pathway from Body' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Trigeminothalamic Pathway

Nociceptors in the face and head send info to the brain primarily through cranial nerve V, the trigeminal nerve. The first-order neurons have their cell bodies in the trigeminal ganglion, located just outside of the brainstem. The fibers enter the brainstem and descend to the spinal trigeminal nucleus in the medulla, where they synapse on a second-order neuron. The second-order neurons cross the midline and project up to the ventral posterior medial nucleus of the thalamus. These neurons then send projections to the face region of the somatosensory cortex.

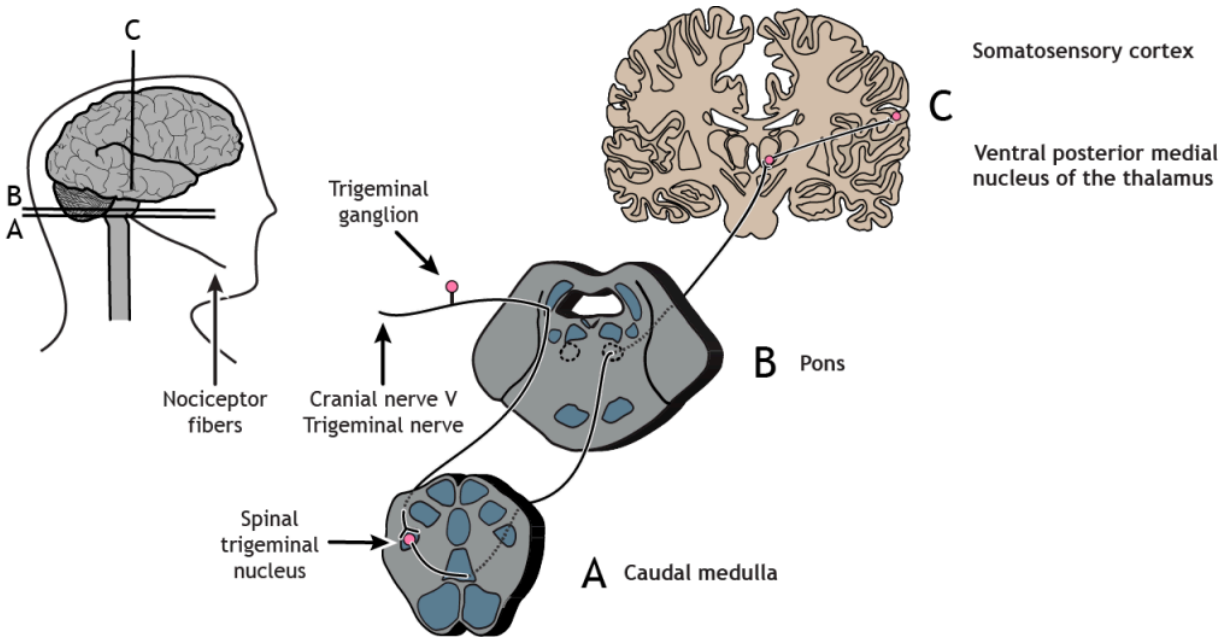

Figure 26.7. Pain and temperature information from the head and face travels through the trigeminothalamic pathway. Axons enter the brainstem at the level of the pons and descend to the medulla. They then decussate before traveling to the thalamus and somatosensory cortex. Details of the pathway are found in the text. 'Pain Pathway from Face' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Sensitization

Pain sensitization occurs after injury and causes the feeling of pain in situations that would not normally cause pain. Tissue damage causes pain signals to be sent to the CNS, as seen above, but the injured tissue also releases substances like prostaglandins, neurotransmitters, substance P, cytokines, and protons, which cause inflammation and begin the healing process. Additionally, non-neuronal cell types such as mast cells and macrophages come to the injured site, releasing more inflammatory substances. These chemicals, particularly prostaglandins, however, can act on nociceptors and cause cellular changes that allow the receptors to be more sensitive to stimuli. This results in a decreased threshold for pain sensation. There are two types of pain sensitization. Hyperalgesia is increased pain in response to a stimulus that normally causes pain but less intensely, like having a second injury at or near a previously injured site. Allodynia is pain sensation in response to a stimulus that would normally not cause pain, like a light touch on a sunburn.

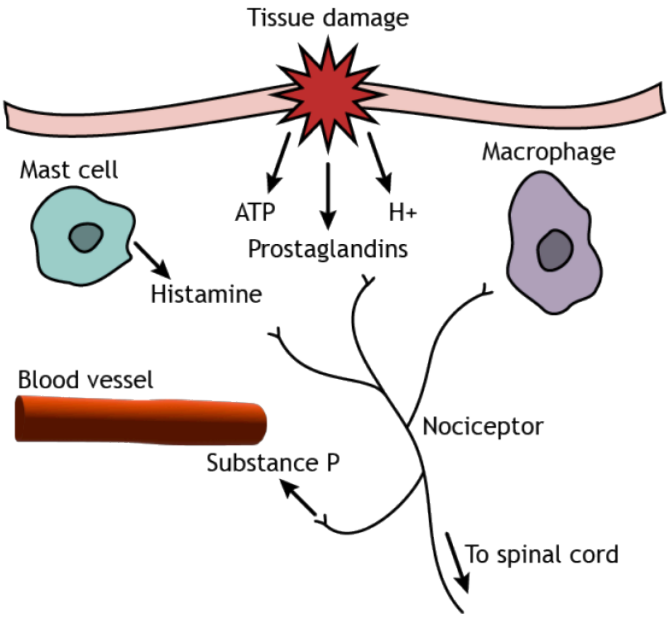

Figure 26.8. Tissue damage causes the release of chemicals including prostaglandins, neurotransmitters, and ions. Mast cells and macrophages move to the site of injury and release substances like histamine. These chemicals act upon the nociceptors and decrease stimulus threshold. Substance P, released from the nociceptor, along with the other substances causes inflammation in the area. 'Peripheral Sensitization' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Modulation of Pain

Pain signals that enter the CNS can be modified.

Peripheral

Think of a time when you cut a finger or stubbed a toe. It is common after an injury like this to put pressure at or near the injured location – squeeze the hurt finger or toe. This touch stimulation can decrease the pain sensation felt because sensory mechanoreceptors send signals through inhibitory

interneurons in the dorsal horn of the spinal cord to pain neurons that ascend to the brain. This effect is known as the gate theory of pain.

One type of therapy that is believed to activate this process is transcutaneous electrical nerve stimulation (TENS) therapy. TENS units, which use small electrical impulses at the site of the pain, are often used to minimize both long- and short-term pain in joints and muscles.

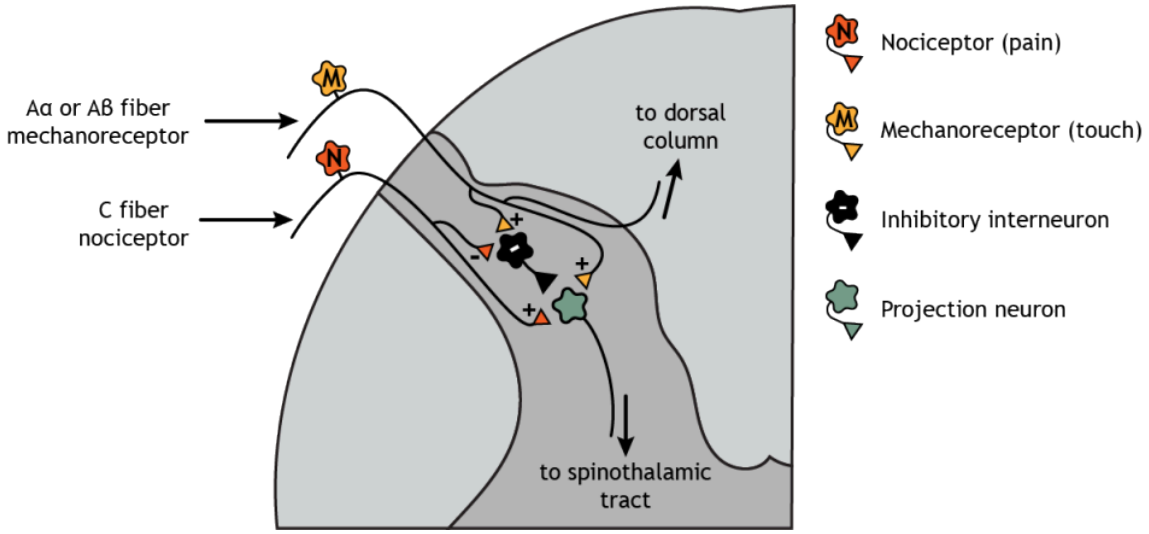

Figure 26.9. In the dorsal horn of the spinal cord, nociceptor axons enter and synapse on second-order neurons, which ascend via the spinothalamic tract, as covered earlier in this chapter. Afferent mechanoreceptor fibers also enter the dorsal horn and ascend via the dorsal column, but axon branches can also activate inhibitory interneurons, which then inhibit the second-order pain neurons, reducing the pain signal transmitted to the brain. 'Gate Theory of Pain' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Central

Descending regulation of pain also occurs. In this case, neurons from the medulla, which are innervated by the periaqueductal gray (PAG), descend and synapse in the dorsal horn of the spinal cord. The medulla neurons release either serotonin or norepinephrine onto enkephalin-releasing interneurons. These interneurons inhibit both the nociceptors and the second-order pain neurons that project to the brain. External stimulation of the PAG results in widespread analgesia.

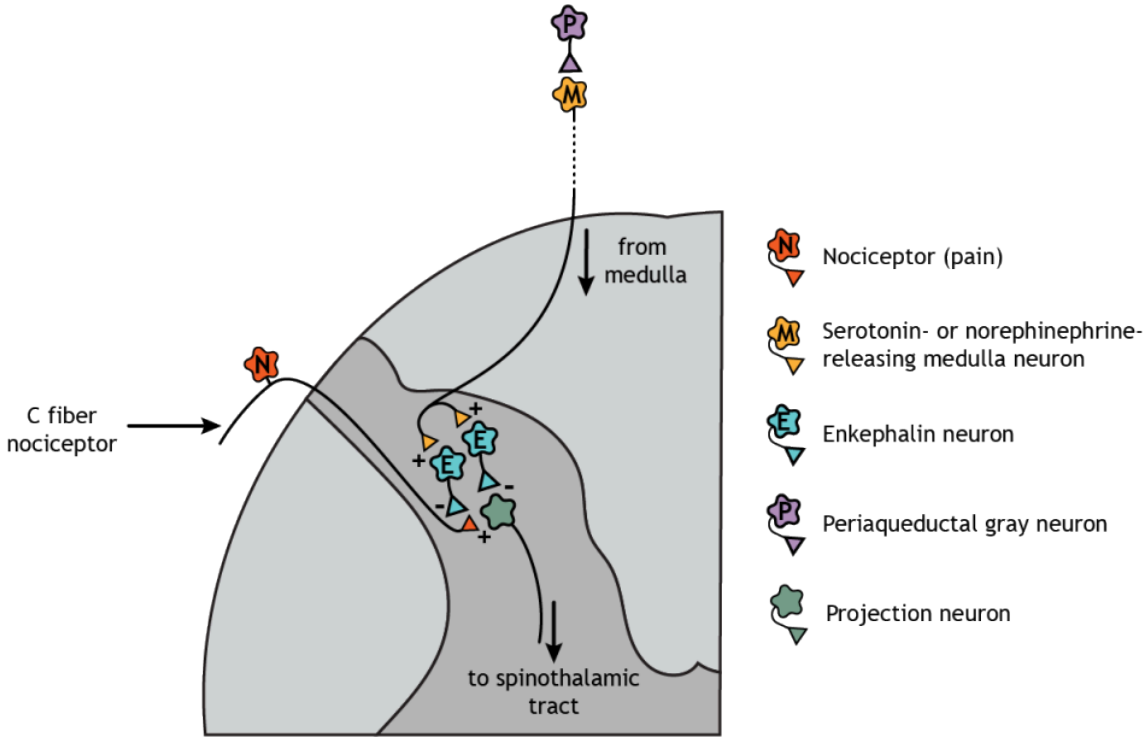

Figure 26.10. In the dorsal horn of the spinal cord, nociceptor axons enter and synapse on second-order neurons, which ascend via the spinothalamic tract, as covered earlier in this chapter. Descending medulla neurons, innervated by the periaqueductal gray, release serotonin and norepinephrine onto interneurons that release enkephalins and inhibit signal transmission in the nociceptors and projection neurons, decreasing pain sensation. 'Descending Pain Modulation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Key Takeaways

- There are multiple types of nociceptors in the skin that are activated by different types of damaging stimuli
- Nociceptors express specialized proteins that convert noxious stimuli into electrical potentials during sensory transduction

- Nociceptor afferents synapse in the dorsal horn of the spinal cord. Information immediately decussates and synapses in the ventral posterior nucleus of the thalamus
    - Information from the neck and body synapse in the ventral posterior lateral nucleus of the thalamus
    - Information from the head and face synapse in the ventral posterior medial nucleus of the thalamus
- Pain sensitization occurs after injury and causes the feeling of pain in situations that would not normally cause pain
- Pain signals can be modified via peripheral and central nervous system processes

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=1655#h5p-40

Video Lecture

27.

TASTE

Being able to sense chemicals in the environment through taste and olfaction can help an organism find food, avoid poisons, and attract mates. Humans can perceive five basic tastes: salty, sour, bitter, sweet, and umami. Bitter taste often indicates a dangerous substance like a poison, sweet taste signifies a high energy food, salty taste indicates a substance with high salt content, sour taste indicates an acidic food, and umami taste indicates a high protein food.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

Tongue anatomy

The surface of the tongue is covered in small, visible bumps called papillae. Taste buds are located within the papillae, and each taste bud is made up of taste receptor cells, along with supporting cells and basal cells, which will eventually turn into taste receptors cells. The taste cells have a lifespan of approximately two weeks, and the basal cells replace dying taste cells. The taste cells have microvilli that open into the taste pore where chemicals from the food can interact with receptors on the taste cells. Although taste cells are not technically neurons, they synapse and release neurotransmitters on afferent axons that send taste perception information to the brain.

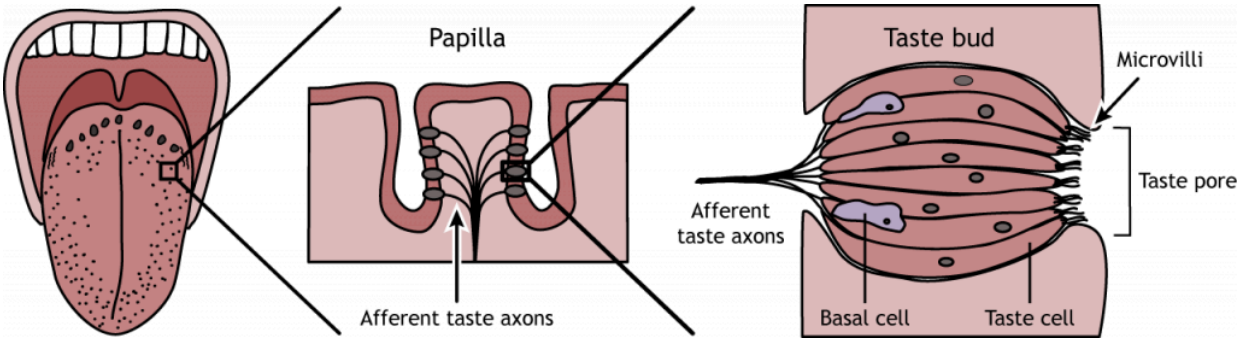

Figure 27.1. The visible bumps on the surface of the tongues are papillae that house taste buds. Taste buds are made up of taste cells and basal cells. The taste cells synapse on afferent axons that send information to the central nervous system. Tastants in food access the taste cells via the taste pore, where the food particles interact with the microvilli of the taste cells. 'Tongue Anatomy' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The entire tongue is capable of perceiving all five tastes, meaning there are taste receptors for each taste present across the entire surface. However, some regions of the tongue have a slightly lower threshold to respond to some tastes over others. The tip of the tongue is the region most sensitive to sweet, salt, and umami tastes. The sides are most sensitive to sour, and the back of the tongue to bitter tastes.

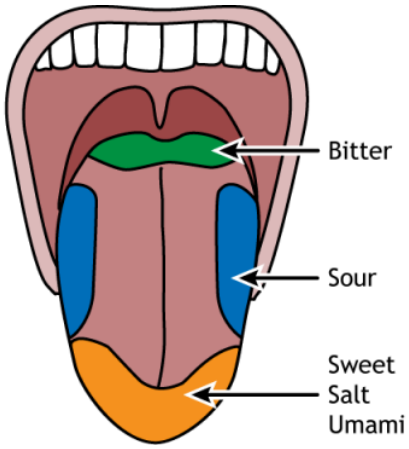

Figure 27.2. Although all tastes can be perceived across the entire tongue, sensitivity levels vary for each taste. The front of the tongue has the lowest threshold for sweet, salt, and umami tastes; the side of the tongue has the lowest threshold for sour tastes, and the back of the tongue has the lowest threshold for bitter tastes. 'Taste Map' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Taste transduction

Salt

Salt taste is mediated by the presence of epithelial sodium channels. These receptors are usually open, and when foods are ingested with high salt concentrations, sodium flows into the cell causing a depolarization. This change in membrane potential opens voltage-gated sodium and calcium channels. The increased calcium influx causes the release of serotonin-filled vesicles. The serotonin acts on the afferent taste axon causing depolarization and action potentials.

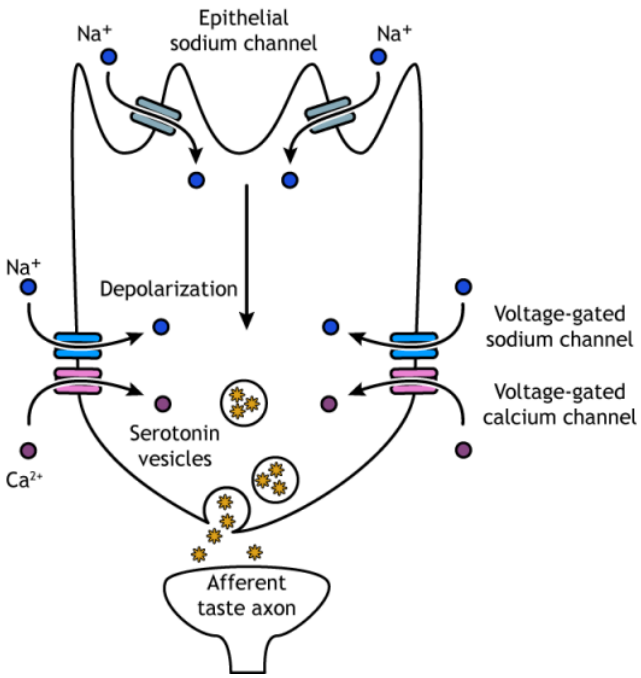

Figure 27.3. When salty foods are ingested, the sodium from the food enters the taste cell via open epithelial sodium channels. The resulting depolarization opens voltage-gated sodium and calcium channels, leading to release of serotonin onto the afferent taste axon. 'Salt Taste Transduction' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Sour

Foods taste sour because of their acidity, and when acids are present in water, they produce hydrogen

ions (protons). The exact mechanism for sour taste transduction has yet to be worked out, but it is believed that protons enter the cell through an ion channel, and then block potassium channels. The decreased efflux of potassium, along with the presence of the protons, depolarizes the cell causing voltage-gated sodium and calcium channels to open. Like salt taste transduction, the increase in intracellular calcium causes release of serotonin into the synapse.

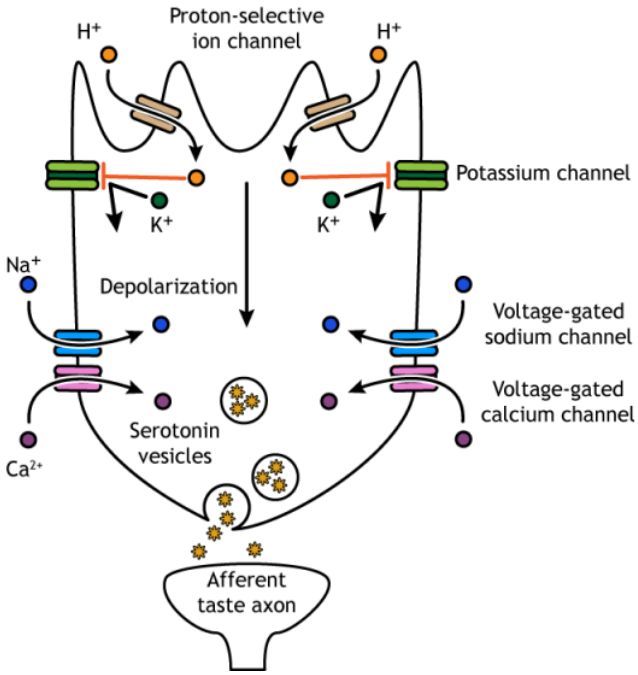

Figure 27.4. When sour foods are ingested, the protons from the acid enter the cell via open ion channels. The protons then block potassium channels. The resulting depolarization opens voltage-gated sodium and calcium channels, leading to release of serotonin onto the afferent taste axon. 'Sour Taste Transduction' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Bitter

Bitter, sweet, and umami compounds all activate taste receptor cells via G-protein coupled receptors. The bitter receptors are from the T2R family of receptor proteins; humans have over 25. Each taste cell can express most or all of the different receptor types, allowing for the detection of numerous molecules, which is important when wanting to avoid dangerous substances like poisons and toxins.

Activation of the G-protein receptor uses a second messenger system to increase intracellular

calcium, which opens ion channels, allowing the influx of sodium. These ion changes depolarize the cell and cause ATP-specific channels to open, allowing ATP to enter the synapse and act on the afferent taste axon.

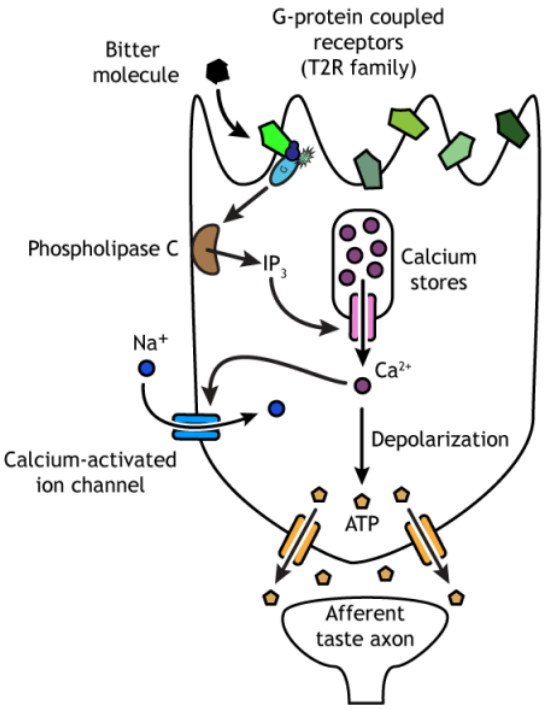

Figure 27.5. Bitter foods activate G-protein receptors, which initiate the phospholipase C second messenger system. IP3 releases calcium from intracellular stores, and the calcium opens ion channels that allow sodium influx. The resulting depolarization causes ATP release onto the afferent taste axon. 'Bitter Taste Transduction' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Sweet

Sweet and umami receptors are comprised of G-protein coupled dimers, meaning two separate proteins function together as one. The receptors are encoded by the T1R family of receptor proteins. Sweet receptors are dimers of the T1R2 and T1R3 proteins. Both proteins need to be present and functioning for activation of a sweet taste cell. Like bitter cells, activation of the G-protein receptor uses a second messenger system to release calcium from intracellular stores and increase the influx of sodium. These ion changes depolarize the cell and cause ATP-specific channels to open, allowing ATP to enter the synapse and act on the afferent taste axon.

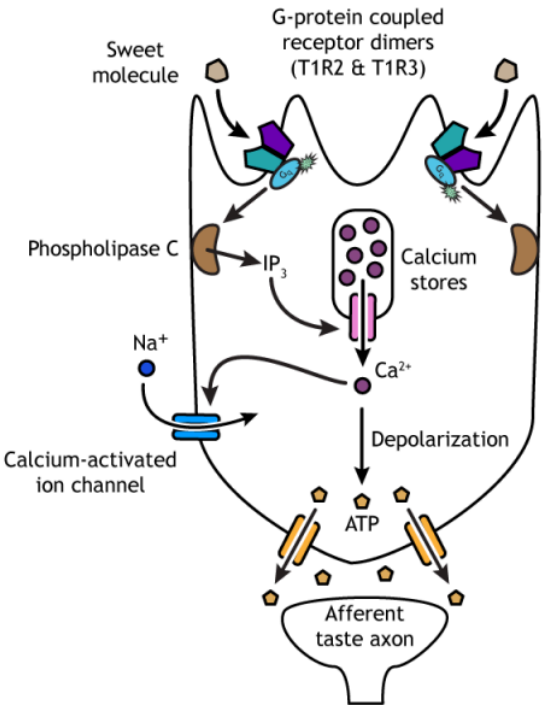

Figure 27.6. Sweet foods activate G-protein receptor dimers, which initiate the phospholipase C second messenger system. IP3 releases calcium from intracellular stores, and the calcium opens ion channels that allow sodium influx. The resulting depolarization causes ATP release onto the afferent taste axon. 'Sweet Taste Transduction' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Umami

Umami receptors are comprised of the T1R3 protein, like the sweet receptor, but it is paired with the T1R1 protein. Once the G-protein coupled receptor is activated, the transduction pathway is the same as bitter and sweet taste cells.

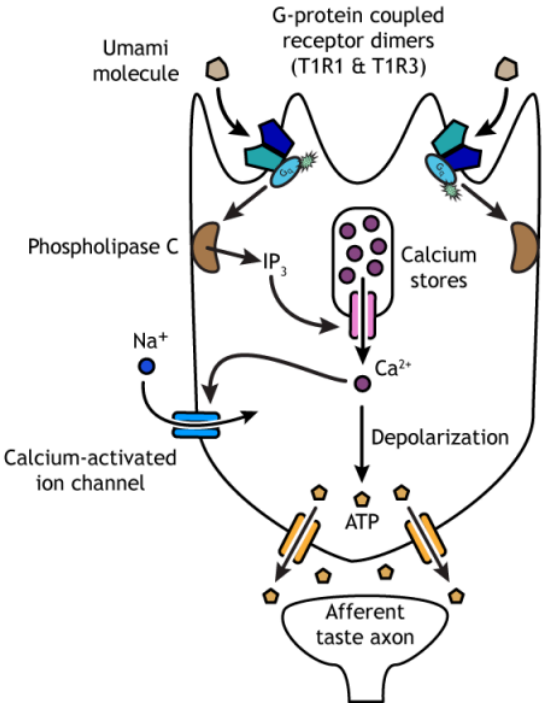

Figure 27.7. Umami compounds activate G-protein receptor dimers, which initiate the phospholipase C second messenger system. IP3 releases calcium from intracellular stores, and the calcium opens ion channels that allow sodium influx. The resulting depolarization causes ATP release onto the afferent taste axon. 'Umami Taste Transduction' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Coding Properties of Taste

Of the five tastes, only two neurotransmitters are used to communicate information to the central nervous system, so how does our brain know what tastes to perceive? The answer is how the information is encoded. Most taste cells use a labeled line coding method, which means that each cell and the related afferent taste axon only responds to one type of taste. For example, bitter cells only express bitter receptors and are only activated by bitter molecules. These bitter taste cells activate bitter sensory neurons and bitter regions of the taste cortex. A small portion of taste cells do use population coding as well, meaning more than one tastant can activate the cell, and perception is based on a combination of multiple cells each with a different response. Most information, however, is encoded via labeled line at the level of the taste cell.

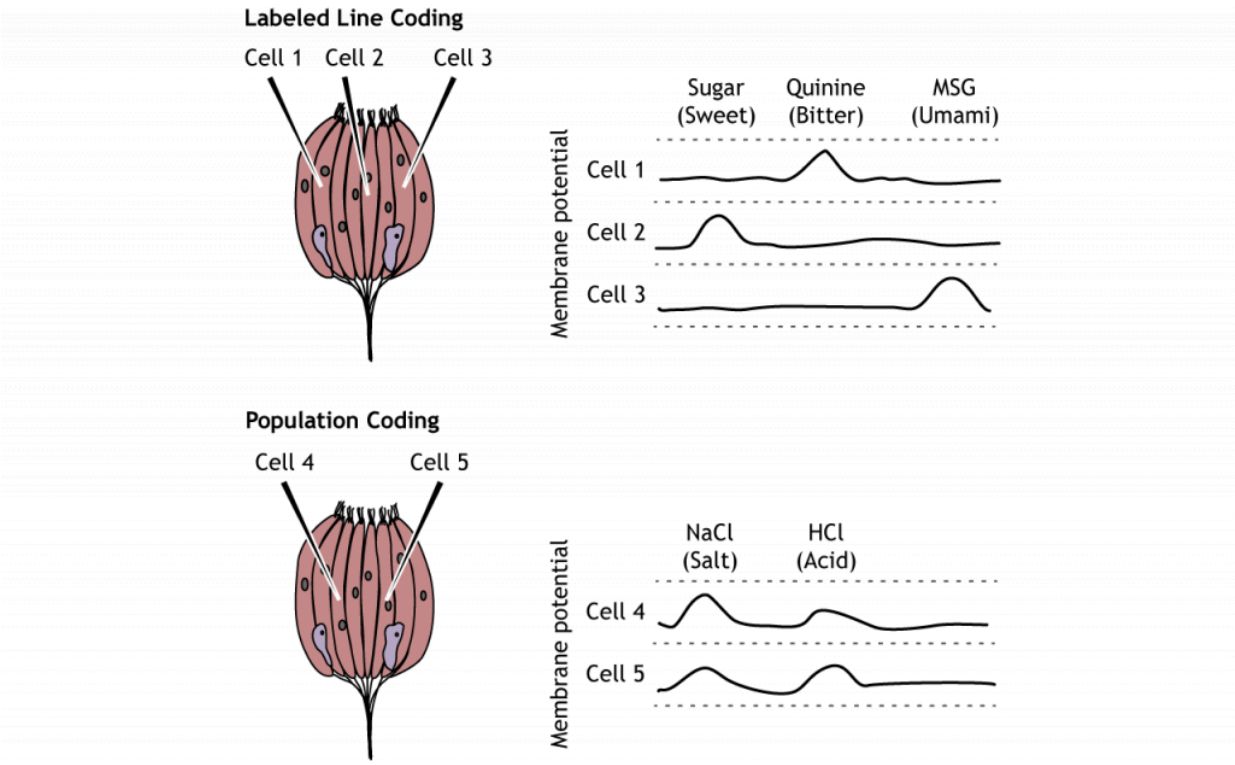

Figure 27.8. Labeled lined coding occurs when one sensation (in this case, a specific taste) leads to activation of the sensory cell. In this example, Cell 1 is activated only by quinine, a bitter compound, Cell 2 is activated only by sugar, a sweet compound, and Cell 3 is activated only by MSG, an umami compound. Most taste cells in the tongue use labeled line coding. Population coding results from broader activation, where multiple sensations can activate a sensory cell and perception is a result of information from a population of cells. In the example, Cells 4 and 5 are activated by both salt and acid compounds. 'Taste Coding' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Mouth and Throat Anatomy

Although taste receptor cells are most prevalent on the tongue, there are other regions of the mouth and throat, including the palate, pharynx, and epiglottis, that also are sensitive to food and play a role in taste perception. The olfactory system is tightly linked to our sense of taste as well, and odorant compounds from food can reach odor receptors in the nasal cavity.

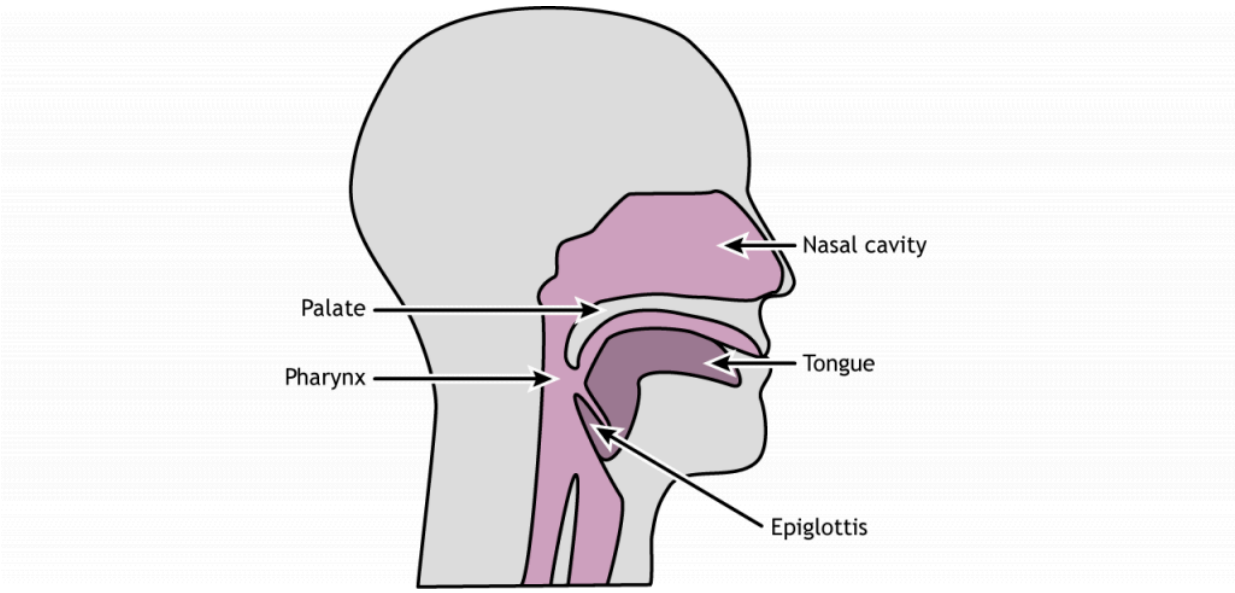

Figure 27.9. The tongue is the primary location for taste receptors cells, but receptors are also located along the palate, pharynx, and epiglottis. Additionally, airborne compounds from food can reach odor receptors in the nasal cavity. The sense of smell plays an important role in the perception of flavor. 'Throat Anatomy' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Pathway

The tongue is innervated by three cranial nerves. The front two-thirds of the tongue is innervated by cranial nerve VII. The back third is innervated by cranial nerve IX. Finally, the epiglottis and pharynx are innervated by cranial nerve X. All three cranial nerves enter the brainstem at the medulla and synapse in the nucleus of the solitary tract. From there, information is sent to the ventral posterior medial nucleus of the thalamus. Thalamic neurons send projections to the gustatory cortex. The gustatory cortex is located deep in the lateral fissure in a region called the insula. Information processing taste stays primarily on the ipsilateral side of the nervous system. Projections within the brain also exist between the taste regions and the hypothalamus and amygdala.

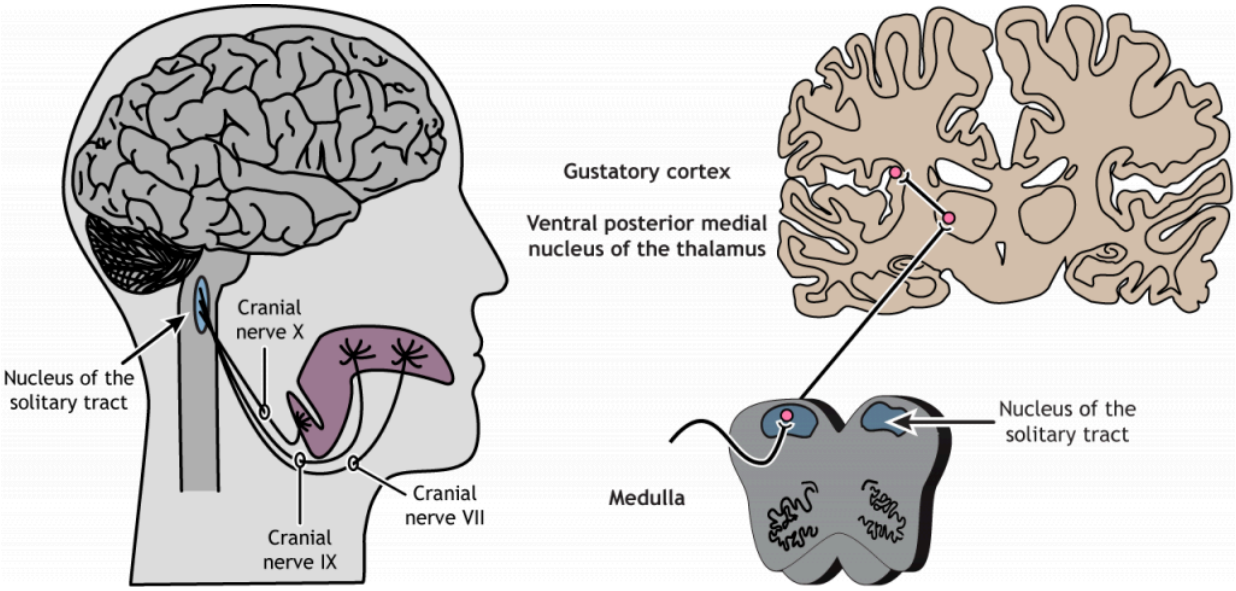

Figure 27.10. Taste information from the tongue travels through cranial nerves VII, IX, and X to the nucleus of the solitary tract in the medulla. Neurons in the brainstem project to the ventral posterior medial nucleus of the thalamus and then on to the gustatory cortex. 'Taste Pathway' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

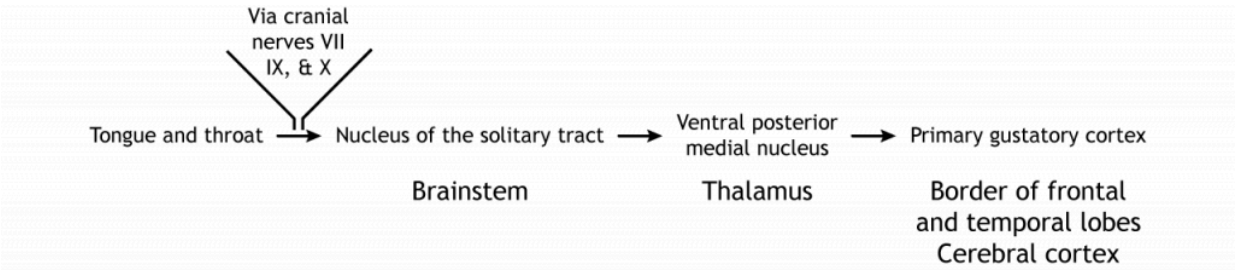

Figure 27.11 Axons from sensory afferents from the tongue and throat travel to the nucleus of the solitary tract in the brainstem via cranial nerves VII, IX, and X. The second-order brainstem neurons project to the ventral posterior medial nucleus of the thalamus. The thalamic third-order neuron projects to the primary gustatory cortex, which is located at the border of the frontal and temporal lobes. 'Taste Pathway' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the facial nerve (cranial nerve VII) using the BrainFacts.org 3D Brain

View the glossopharyngeal nerve (cranial nerve IX) using the BrainFacts.org 3D Brain

View the vagus nerve (cranial nerve X) using the BrainFacts.org 3D Brain

View the thalamus using the BrainFacts.org 3D Brain

Flavor

How do 5 basic tastes turn into the myriad complex taste sensations we experience when eating food? Olfaction plays an important role in the perception of flavor, as do vision and touch. Taste information combines with information from these other sensory systems in the orbitofrontal cortex located in the frontal lobe. This region is believed to be important for the pleasant and rewarding aspects of food. Additionally, as taste is processed in higher-order regions of the CNS, information is combined using population coding mechanisms. Test how your senses combine to create flavor at home!

View the orbitofrontal cortex using the BrainFacts.org 3D Brain

Key Takeaways

- Taste cells express specific taste receptors and are located in taste buds within the papillae
- Salt and sour taste cells rely on ion channels to depolarize the cell and release serotonin
- Bitter, sweet, and umami taste cells rely on G-protein coupled receptors and second messengers that open ATP channels
- At the level of the taste receptor cells, taste is perceived by using labeled line coding
- Multiple regions in the mouth and throat play a role in processing of taste
- Three cranial nerves innervate the tongue and throat
- The cranial nerves synapse in the nucleus of the solitary tract in the medulla. Information then travels to the ventral posterior medial nucleus of the thalamus and then to the gustatory cortex
- To perceive complex flavors, information from other sensory systems is combined with taste information in the orbitofrontal cortex

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=587#h5p-20

Video Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=587#oembed-1

PART V
MOTOR SYSTEM

28.

SPINAL CONTROL OF MOVEMENT

The motor system controls all of our skeletal muscle movement. There are multiple levels of control. Within the spinal cord, simple reflexes can function without higher input from the brain. Slightly more complex spinal control occurs when central pattern generators function during repetitive movements like walking. The motor and premotor cortices in the brain are responsible for the planning and execution of voluntary movements. And finally, the basal ganglia and cerebellum modulate the responses of the neurons in the motor cortex to help with coordination, motor learning, and balance.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

This lesson explores the lowest level of control – spinal reflexes.

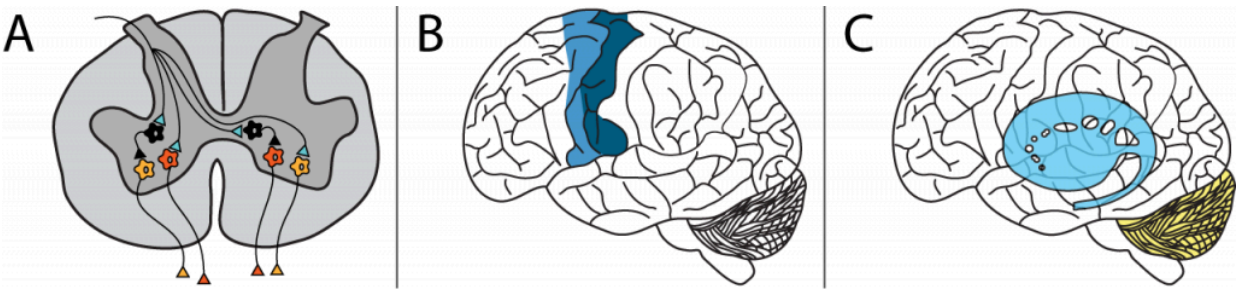

Figure 28.1. Motor output is controlled at multiple levels: A. Spinal cord and spinal neurons, B. Motor (dark blue) and premotor (light blue) cortices, C. Basal ganglia (a subcortical structure shown in light blue) and cerebellum (yellow). 'Motor Control Levels' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Alpha Motor Neurons

Muscle fibers are innervated by alpha motor neurons. The cell bodies of the alpha motor neurons are located in the central nervous system in the ventral horn of the spinal cord. Their axons leave the spinal cord via the ventral roots and travel to the muscle via efferent peripheral spinal nerves.

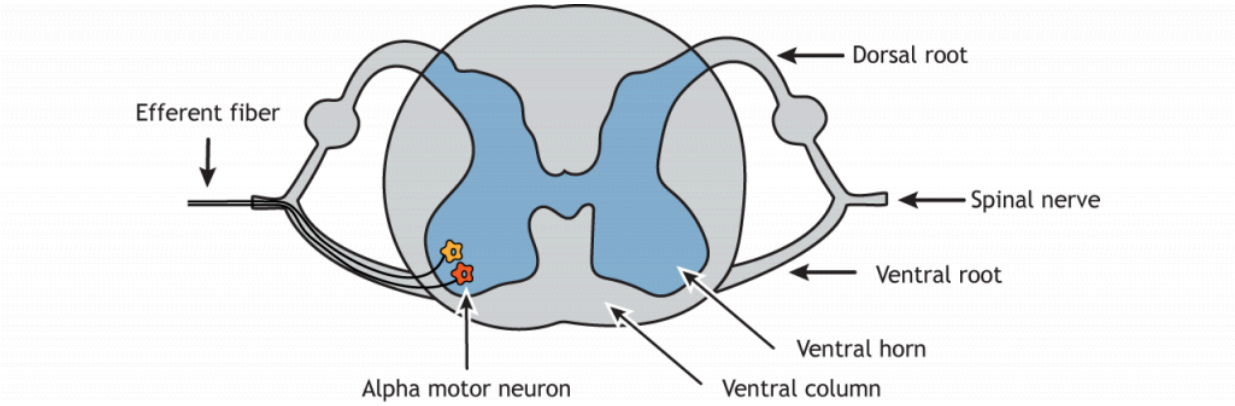

Figure 28.2. Alpha motor neurons are located in the ventral horn of spinal cord. Their axons, which are efferent fibers, travel to the muscles via spinal nerves. 'Alpha Motor Neurons' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

One alpha motor neuron can innervate multiple fibers within one muscle; the axons of a motor neuron can branch to make synaptic contacts with many fibers. A motor neuron and the fibers innervated by it are called a motor unit. The muscle fibers within one motor unit are often spread throughout the muscle to spread the contraction throughout the full muscle.

The group of motor neurons that innervate all the fibers of one muscle is called a motor pool.

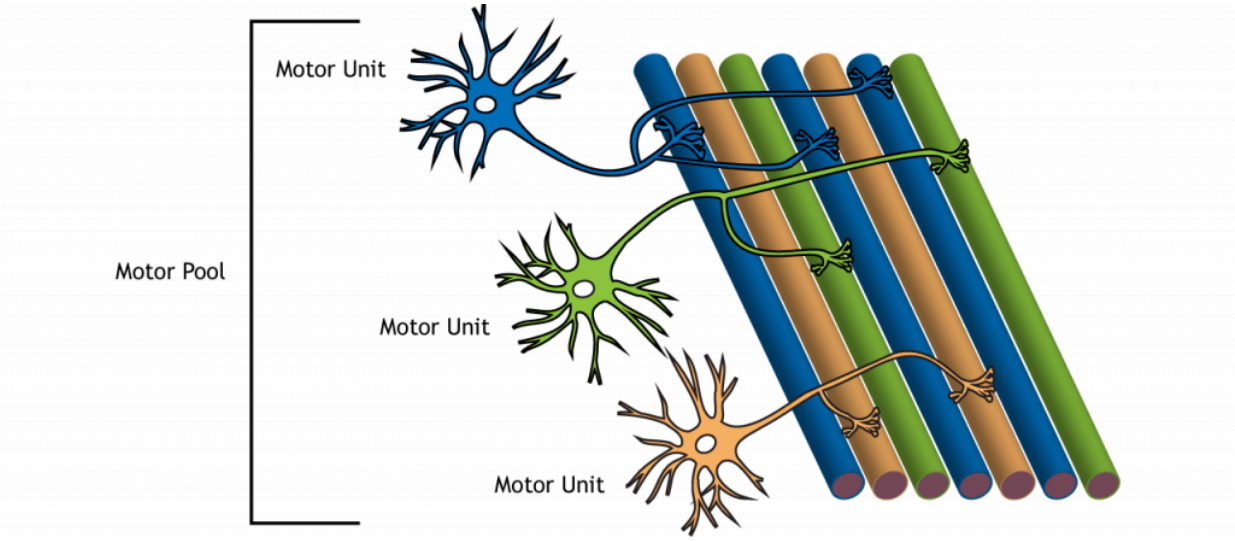

Figure 28.3. Motor neurons can innervate more than one muscle fiber within a muscle. The motor neuron and the fibers it innervates are a motor unit. Three motor units are shown in the image: one blue, one green, one orange. Those three motor units innervate all the muscles fibers in the muscle and are the motor pool for that muscle. 'Motor Unit and Pool'by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Neuromuscular Junction

The neuromuscular junction is one of the largest synapses in the body and one of the most well-studied because of its peripheral location. Acetylcholine is the neurotransmitter released at the neuromuscular junction (NMJ), and it acts upon ligand-gated, non-selective cation channels called nicotinic acetylcholine receptors that are present in postjunctional folds of the muscle fiber. Acetylcholinesterase, an enzyme that breaks down acetylcholine and terminates its action, is present in the synaptic cleft of the neuromuscular junction.

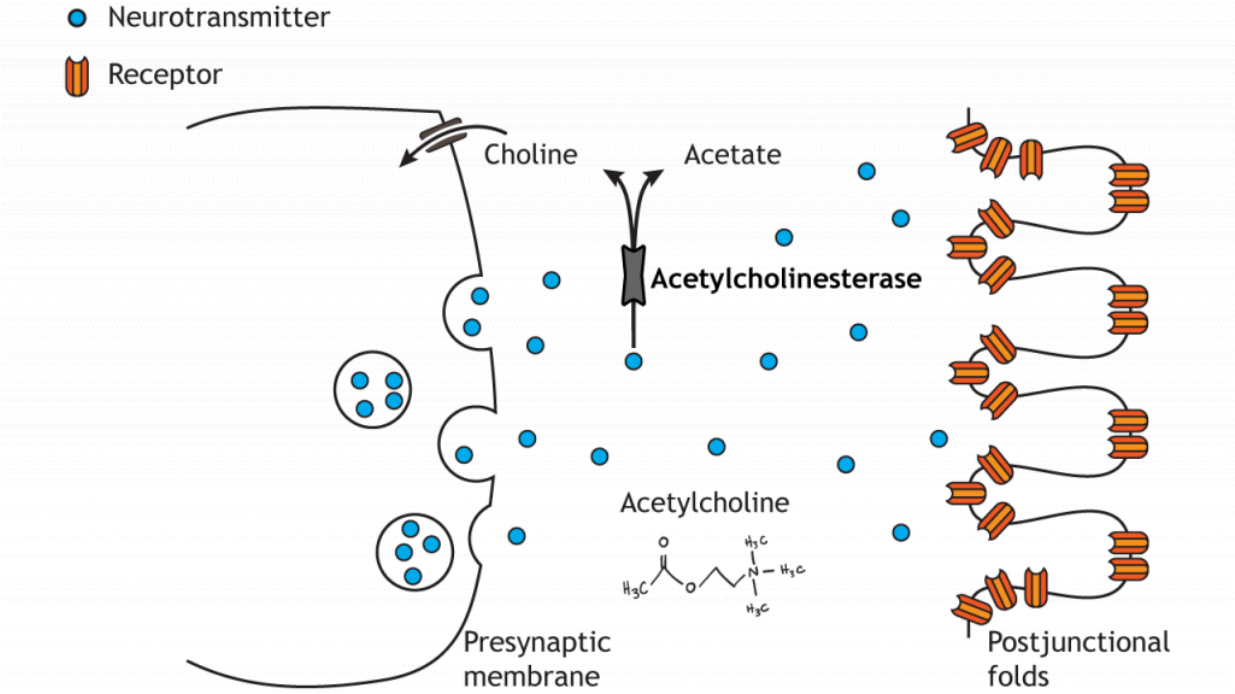

Figure 28.4. The neuromuscular junction (NMJ) is the synapse between a motor neuron and a muscle fiber. Acetylcholine is released at the NMJ and acts on nicotinic acetylcholine receptors located in the postjunctional folds of the muscle fiber. Neurotransmitter action is terminated by breakdown by acetylcholinesterase. 'Neuromuscular Junction' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Nicotinic acetylcholine receptors allow the influx of sodium ions into the muscle cell. The depolarization will cause nearby voltage-gated channels to open and fire an action potential in the muscle fiber. In a healthy system, an action potential in the motor neurons always causes an action potential in the muscle cell. The action potential leads to contraction of the muscle fiber.

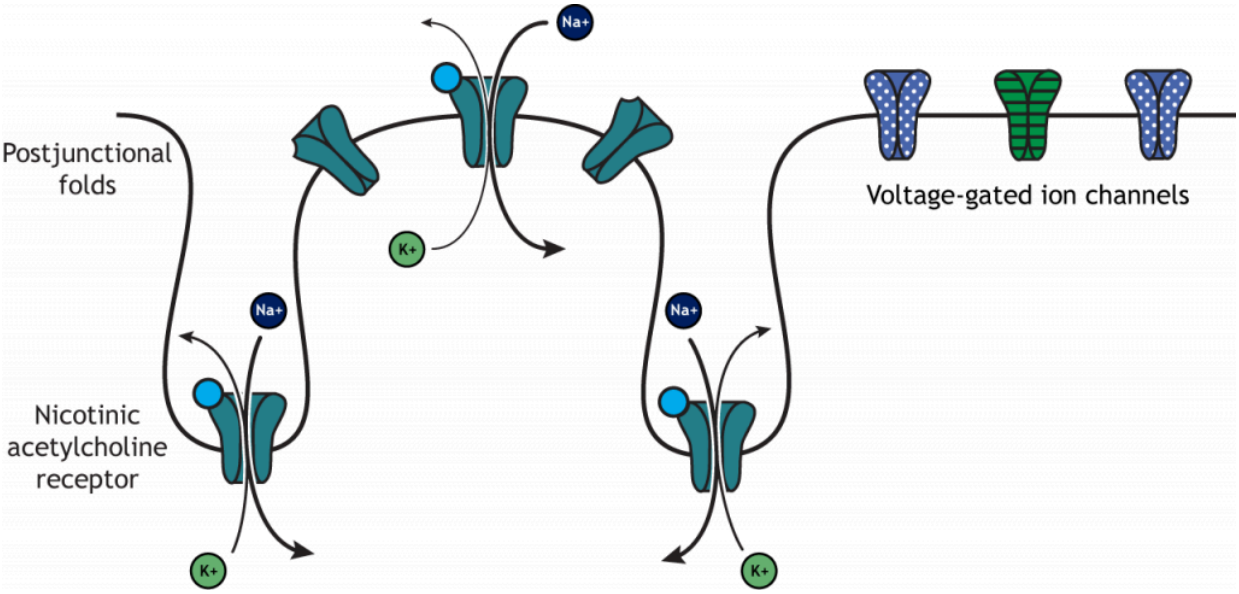

Figure 28.5. The ionotropic nicotinic acetylcholine receptors in the postjunctional folds of the muscle fiber are non-selective cation channels that allow the influx of sodium and the efflux of potassium The depolarization of the cell by the sodium influx will activate nearby voltage-gated ion channels. 'NMJ Ion Flow' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Organization

Like the sensory systems, the motor system is also organized in a topographic fashion. Within the spinal cord, alpha motor neurons that innervate muscles in the arms and legs are located in the lateral portion of the ventral horn, whereas alpha motor neurons that innervate muscles in the trunk are located in the medial portion.

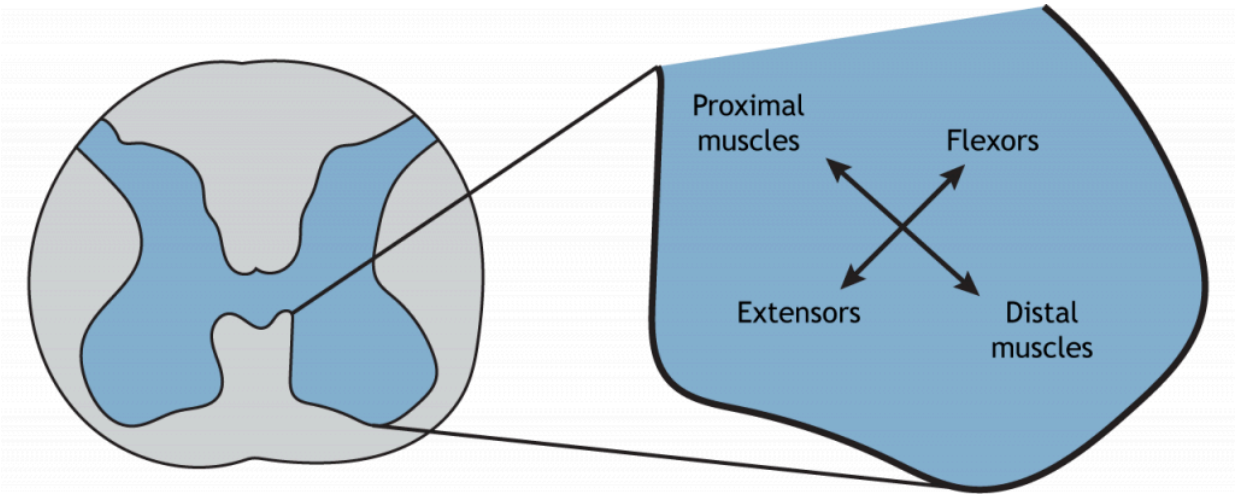

Figure 28.6. The ventral horn is organized in a topographic manner, with proximal muscles (like those in the trunk) located more medially than distal muscles (like the arms or legs). Additionally, motor neurons are organized by function with extensor motor neurons located together and flexor neurons located together. 'Spinal Cord Map' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Sensation

Proprioception is the ability to know where your body is in space and relies on the presence of sensory receptors located within the muscles. Some of these specialized structures are called muscle spindles, and they monitor muscle fiber stretch. Information is relayed to the nervous system via Group I sensory axons, which are large, myelinated fibers. Muscle spindles are important for spinal reflexes.

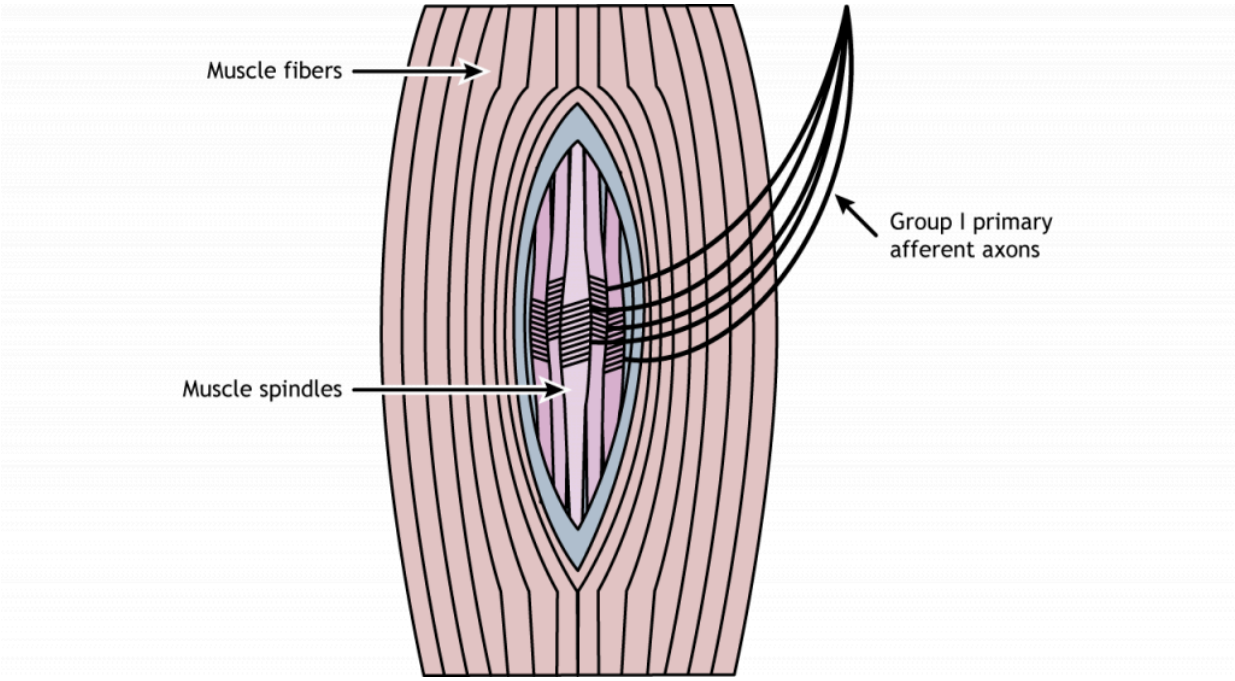

Figure 28.7. Type I primary afferent sensory axons wrap around the fibers within the muscle spindle, located deep in the muscle. When the muscle stretches, these sensory neurons are activated. 'Muscle Spindle' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Reflexes

Stretch (Myotatic) Reflex

The stretch reflex, also called the myotatic, patellar, or knee-jerk reflex, occurs in response to activation of the muscle spindle stretch receptors. The stretch reflex is a common occurrence at a doctor's visit when the doctor taps your knee with a little hammer. This usually results in the lower leg kicking up slightly. The synaptic communication for this reflex takes place completely within the spinal cord and requires no input from the brain.

The knee is tapped on the tendon that connects to the quadriceps muscle. The tendon extends enough to stretch the quadriceps muscle, activating the stretch receptors. Sensory information travels to the dorsal horn of the spinal cord where it synapses on alpha motor neurons that innervate the quadriceps. Activation of the motor neurons contracts the quadriceps, extending the lower leg. This

is called monosynaptic communication because there is only one synapse between the sensory input and the motor output.

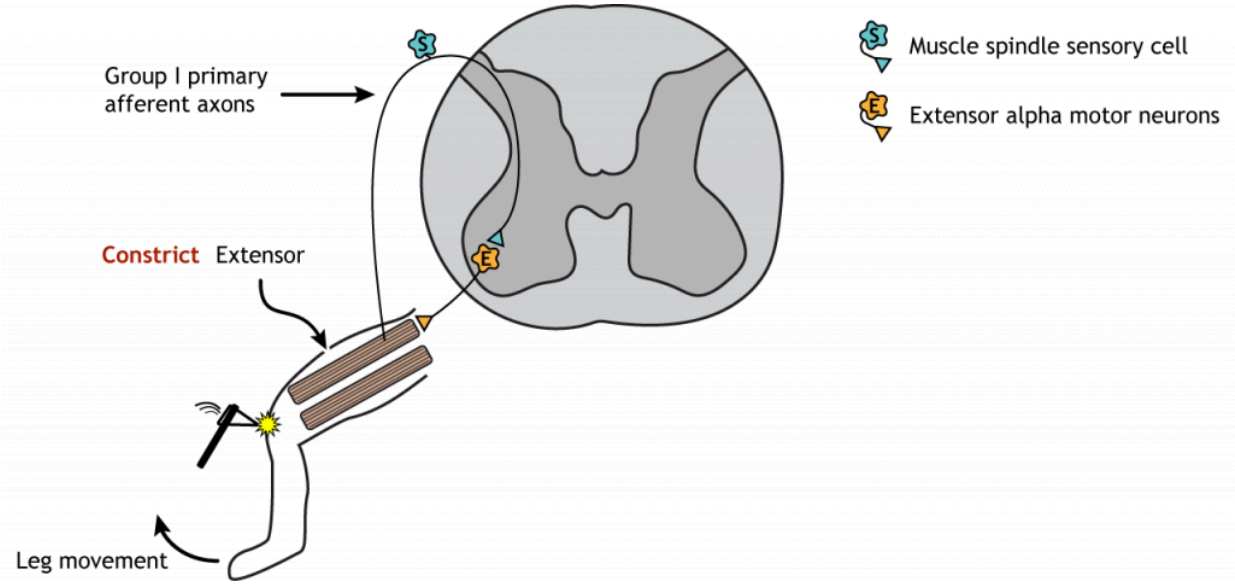

Figure 28.8. When the tendon in the knee is tapped, the extensor muscle is stretched slightly. This stretch activates the Group I sensory afferent axons (blue S neuron in dorsal root ganglion) from the muscle spindles. The sensory neurons synapse on and activate motor neurons (yellow E neuron) that constrict the extensor muscle, causing the leg to kick upward. The stretch reflex is a monosynaptic reflex. 'Stretch Reflex Extensor' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The sensory neurons also synapse on interneurons within the spinal cord that are inhibitory. These inhibitory interneurons then synapse on alpha motor neurons that innervate the hamstring, the antagonistic flexor muscle to the quadriceps. When these motor neurons are inhibited, the hamstring muscle relaxes, allowing the contraction of the quadriceps to occur with more ease.

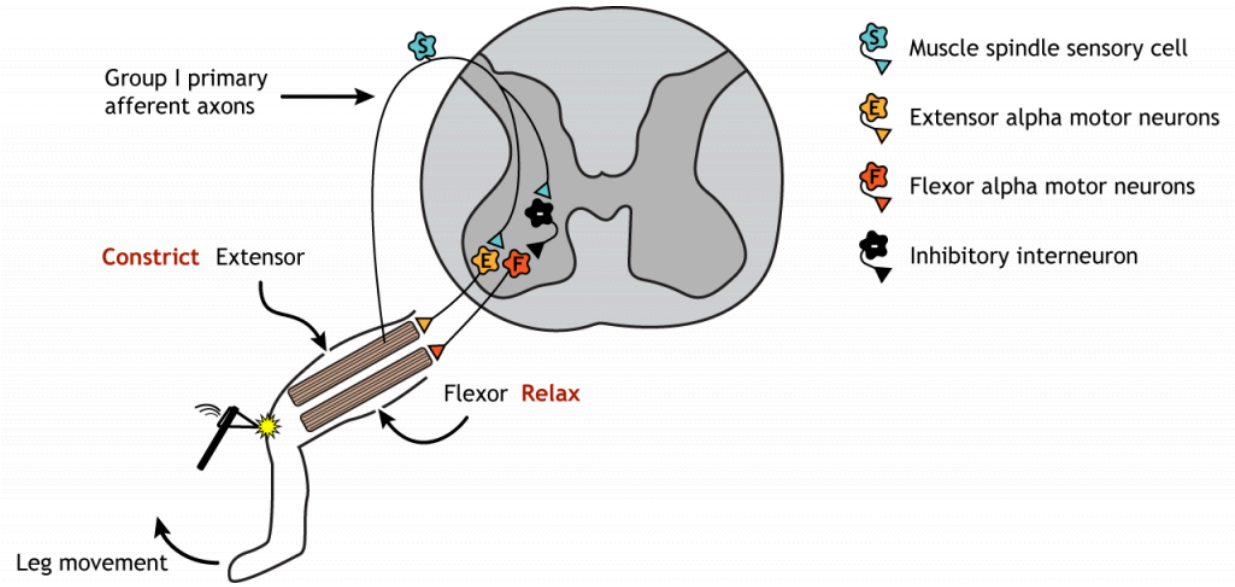

Figure 28.9. In addition to the monosynaptic extensor reflex, the sensory information from the muscle spindle sensory cell (blue S neuron) also activates inhibitory interneurons (black – neuron) in the spinal cord. These interneurons then inhibit the motor neurons (orange F neuron) that innervate the flexor muscle, causing the flexor muscle to relax. This relaxation allows the extensor muscle to kick the leg up with less opposition from the flexor muscle. 'Stretch Reflex' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Withdrawal (Flexor) Reflex

A similar process can be seen in the withdrawal reflex. In this case, instead of an extension, the muscles lead to muscle flexion in response to a stimulus. If, for example, you step on something painful, the reflex will be to lift the injured foot. The sensory information that initiates this reflex is activation of pain receptors, or nociceptors. Like with the stretch reflex, the sensory information enters the spinal cord at the dorsal horn. Unlike the stretch reflex, the withdrawal reflex is a polysynaptic reflex, meaning interneurons are present between the sensory neurons and the motor neurons. Excitatory interneurons communicate with the alpha motor neurons of the flexor muscle, whereas inhibitory interneurons communicate with the alpha motor neurons of the extensor muscle. The behavioral response is flexing of the leg upward (the opposite action of the stretch reflex).

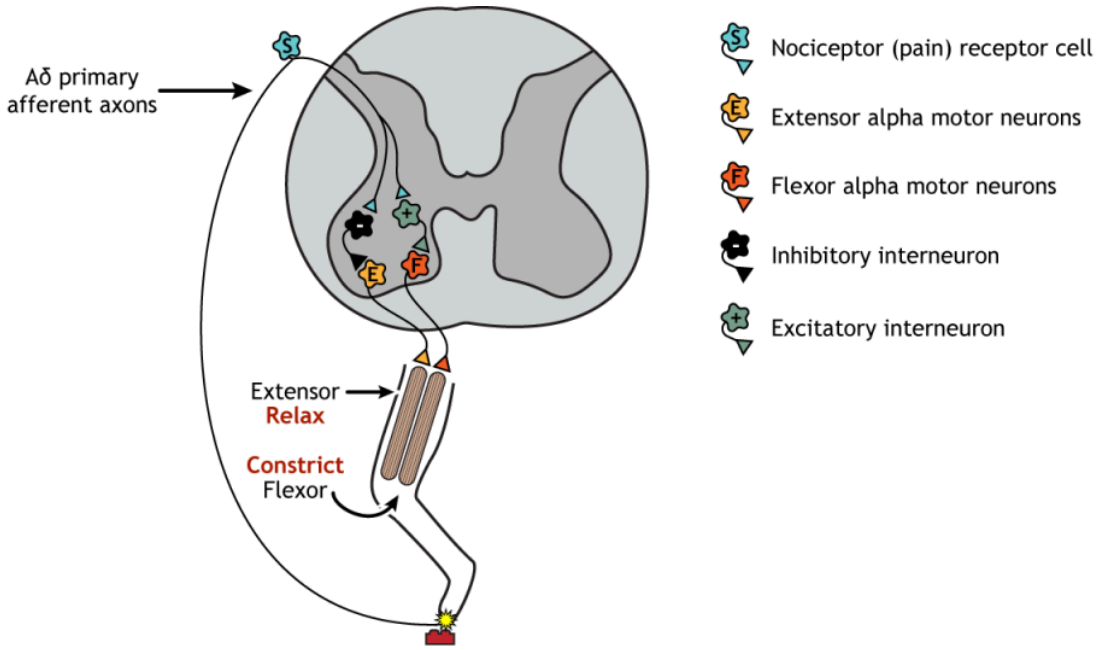

Figure 28.10. Pain information is sent from the periphery to the spinal cord via a nociceptor receptor cell (blue S neuron in dorsal root ganglion). The A delta sensory axons synapse on interneurons within the spinal cord. Excitatory interneurons (green + neuron) activate motor neurons (orange F neuron) that constrict the flexor muscle. Inhibitory interneurons (black – neuron) inhibit motor neurons (yellow E neuron) that innervate and relax the extensor muscle. The leg lifts in response. 'Withdrawal Reflex' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Crossed-Extensor Reflex

Running in parallel to the withdrawal reflex is the crossed-extensor reflex. If you step on something sharp and lift that leg, your other leg needs to be able to support your weight shift, or you would fall. This is accomplished by interneurons that cross the midline of the spinal cord and communicate with motor neurons on the contralateral side of the body. The painful sensory information that initiated the withdrawal reflex also initiates the crossed-extensor reflex. In addition to the ipsilateral interneurons active in the withdrawal reflex, the sensory axons also synapse on excitatory interneurons that cross the midline. These interneurons then synapse on excitatory interneurons that activate the alpha motor neurons of the extensor muscle and inhibitory interneurons that inhibit the alpha motor neurons of the flexor muscle (the opposite configuration to the withdrawal reflex). This leads to the leg extending, providing a stable base for the weight shift.

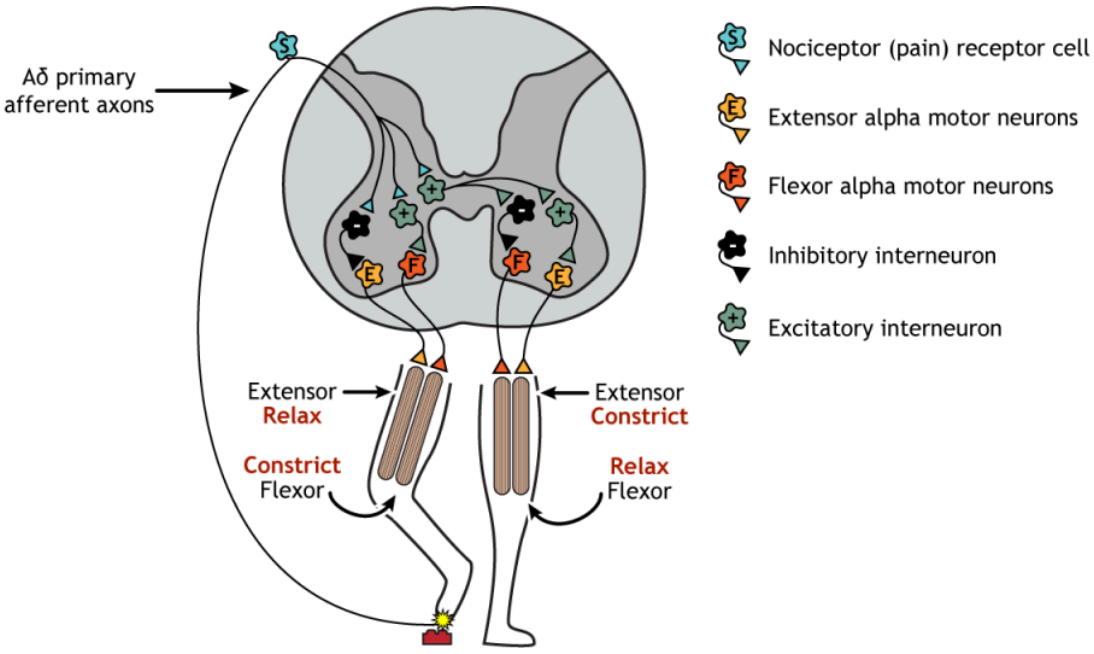

Figure 28.11. If the leg lifts due to the withdrawal reflex, the opposite leg must stabilize via contraction of extensor muscles to balance the body. This is accomplished by excitatory spinal interneurons that cross the midline and communicate the sensory information to the contralateral side of spinal cord. Inhibitory interneurons cause relaxation of the contralateral flexor muscles, and excitatory interneurons cause constriction of the contralateral extensor muscles. 'Crossed-Extensor Reflex' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Central Pattern Generators

Locomotion

Locomotion is one example of a basic, rhythmic movement that requires coordination of a number of muscle groups to work properly (other examples include swimming, flying, respiration, swallowing).

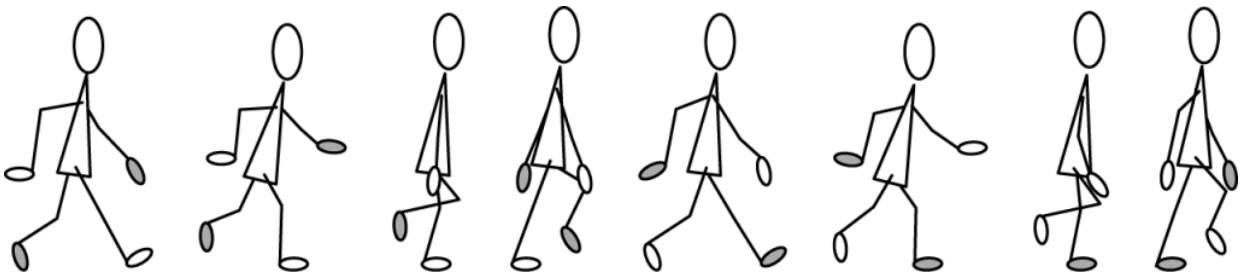

Figure 28.12. Walking cycle of a human. The arms and legs must be coordinated in opposing fashion during locomotion. The gray hand and foot are left side limbs. When one is in front of the body, the other is behind. 'Walking Cycle' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Activity of extensor and flexor muscles in both legs must be coordinated to allow smooth locomotion without falling. These rhythmical movements are controlled at the level of the spinal cord by circuits called central pattern generators. The spinal cord has circuitry that, in the case of walking, moves the legs in opposite patterns. When one leg is lifting up to move forward, the other leg is stable, touching the ground.

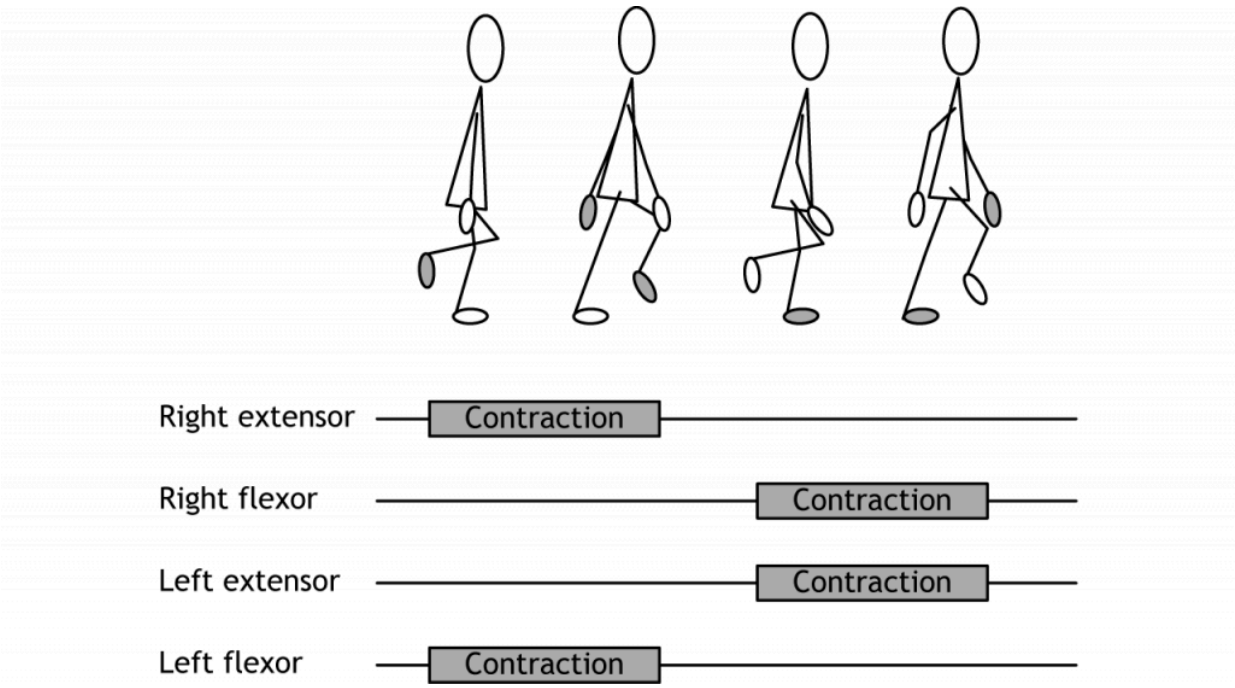

Figure 28.13. While walking, there must be coordinated, reciprocal activation of the extensor and flexor muscles of each leg; as an extensor is contracted (gray bar) the flexor must relax. Additionally, the muscle activation of one leg must be the opposite of the other leg, so the right extensor and the left flexor are activated at the same time. 'Walking Cycle Muscle Activation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Spinal Circuitry

The control of this system has multiple levels. Neurons themselves may have pacemaker properties that allow for a continuous cycle of depolarization and repolarization. These neurons are then located within multi-cell circuits involving a collection of excitatory and inhibitory interneurons that results in reciprocal inhibition of contralateral muscles. Additional networks of spinal interneurons would cause reciprocal inhibition of ipsilateral antagonistic muscles.

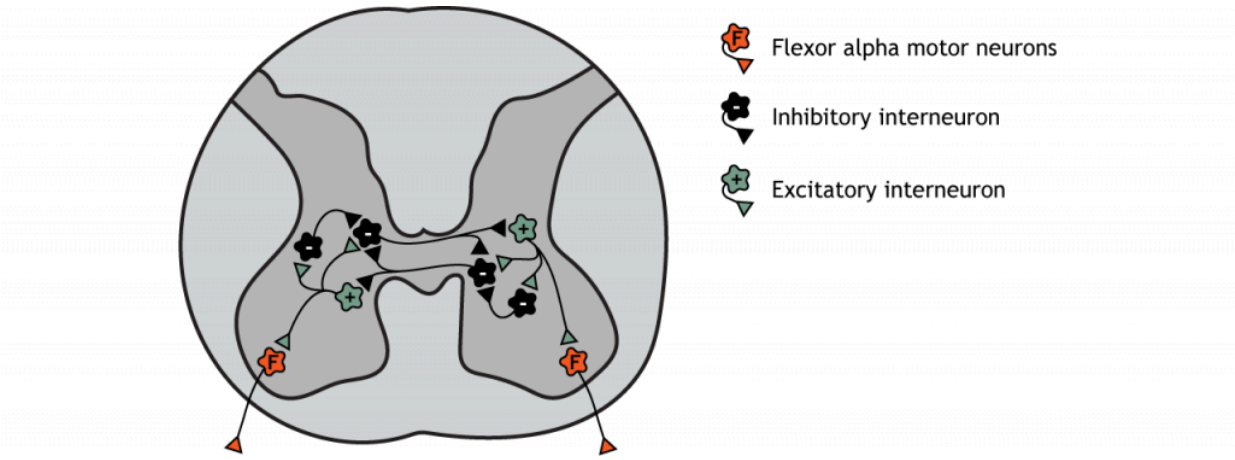

Figure 28.14. Central pattern generators are controlled by interneuron circuitry within the spinal cord. The circuit would require the motor neurons on the opposite side of the spinal cord to be activated in a reciprocal fashion. This is accomplished through a network of excitatory and inhibitory interneurons that allow for the flexor (or extensor) muscle on one side of the body to control while the contralateral muscle relaxes. 'Central Pattern Generator Circuit' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Although the spinal cord is able to control these movements on its own, there is input from both the brainstem and sensory neurons which can have an effect on modulating the pattern of neuronal activity in the spinal cord. For example, when an animal needs to slow down, speed up, or turn away from a danger, for example, those inputs can alter the spinal cord circuit.

Key Takeaways

- Motor neuron cell bodies are located in the ventral horn of the spinal cord
- Motor neuron axons are located in the peripheral nervous system and travel to muscles via spinal nerves
- Acetylcholine is released at the neuromuscular junction and acts upon ionotropic nicotinic acetylcholine receptors

- The spinal cord is topographically organized
- Control of reflexes occurs within the spinal cord and input from the brain is not needed
- Central pattern generators are circuits in the spinal cord that control repetitive, consistent movements like walking

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=535#h5p-24

1. What is the difference between a motor unit and a motor pool?

Video Lecture

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29.

PLANNING OF MOVEMENT

There are a number of steps that must take place for voluntary movement to occur. Assessment of the surrounding environment and the body's location in space, followed by determining what action is appropriate, and then initiating that action. We will first focus on the cortical regions involved in planning of voluntary movement.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

After work, you sit down on the couch to watch one episode of your favorite show. As the end credits appear, you realize it is now time to head to your study space and start working on class. To do this, you need to leave the couch, grab your computer from the table, get your coffee from the kitchen and head to a different room. All of these voluntary movements take a great deal of processing by the brain. You must assess your surrounding environment and your body's location in it, determine which actions need to be completed, and then actually initiate those actions. In this chapter we will focus on how the planning of voluntary movement occurs.

Cortical Anatomy

Much of the cortex is actually involved in the planning of voluntary movement. Sensory information, particularly the dorsal stream of the visual and somatosensory pathways, are processed in the posterior parietal lobe where Visual, tactile, and proprioceptive information are integrated.

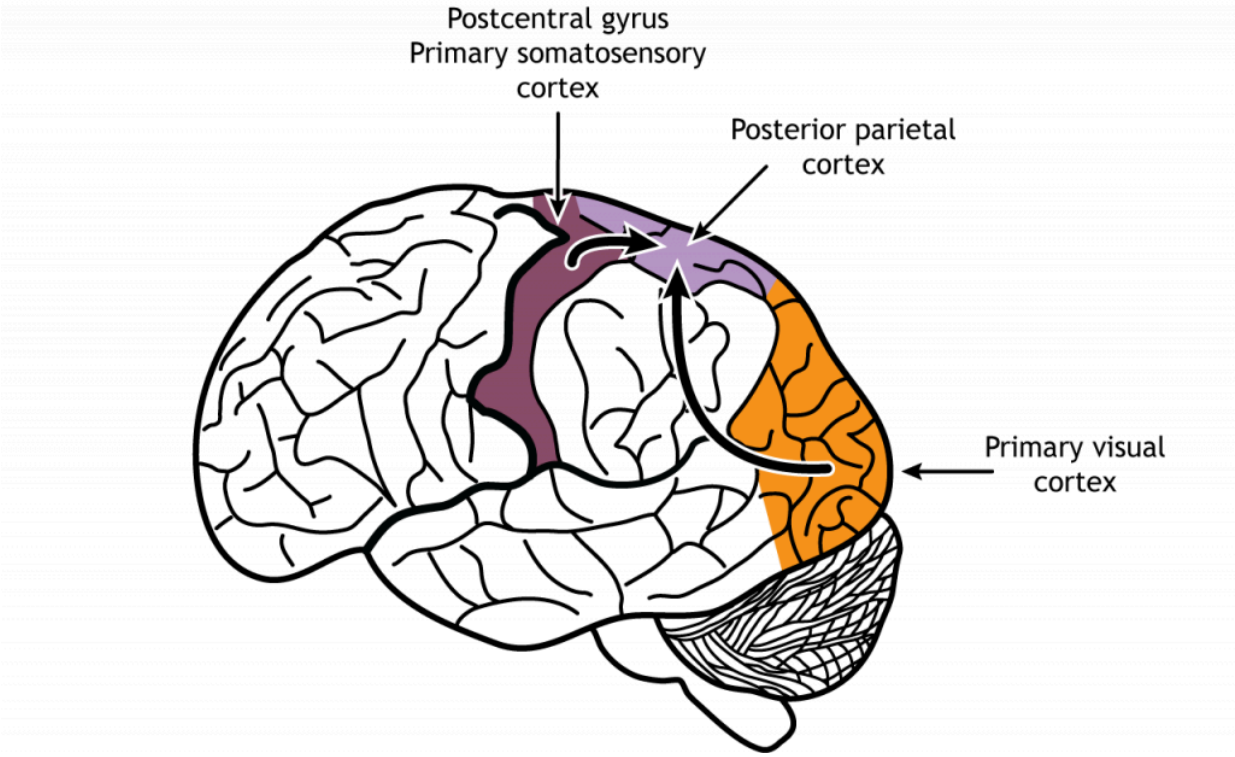

Figure 29.1. Information from multiple sensory systems are processed in the posterior parietal lobe. Projections are sent from the primary somatosensory and primary visual cortices. 'Posterior Parietal by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Connections from the posterior parietal lobe are then sent to both the premotor regions and the prefrontal cortex. The prefrontal cortex, which is located in the front of the brain in the frontal lobe, plays an important role in higher level cognitive functions like planning, critical thinking, and understanding the consequences of our behaviors. The premotor area lies just anterior to the primary motor cortex. This region helps plan and organize movement and makes decisions about which actions should be used for a situation.

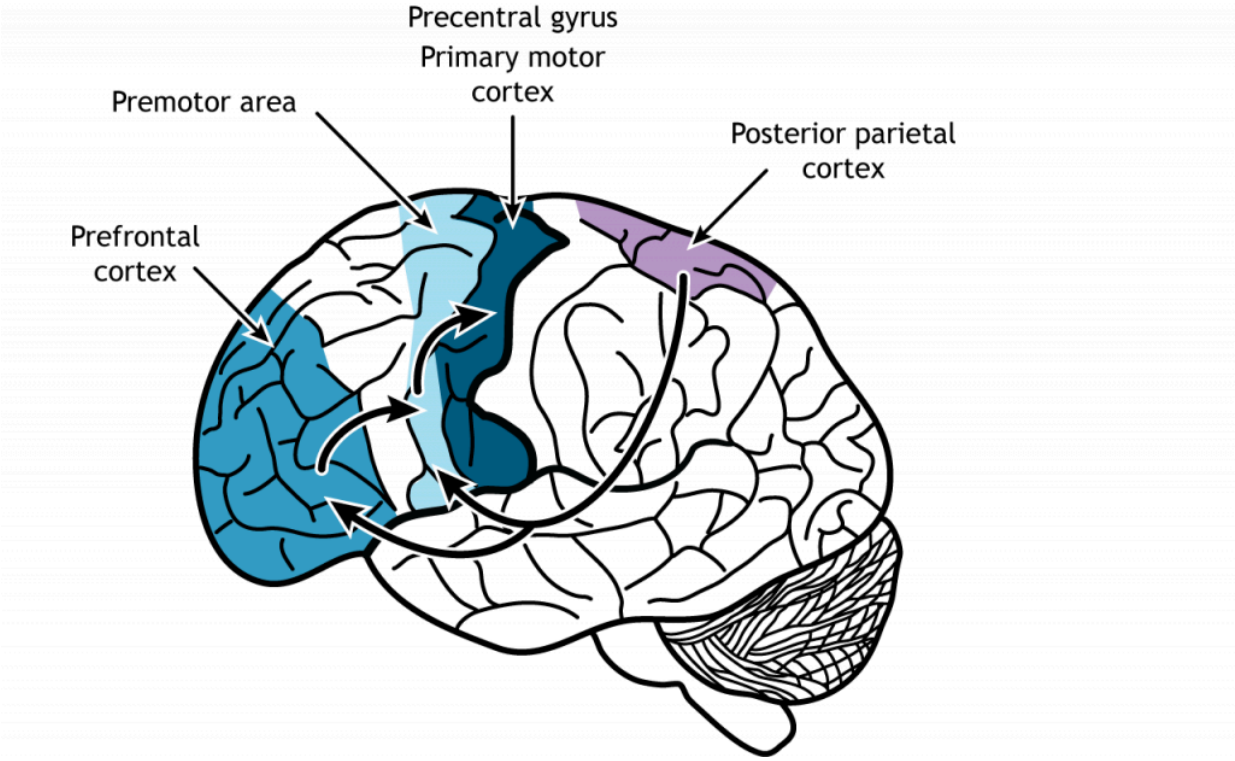

Figure 29.2. Sensory information from the posterior parietal is processed in the prefrontal cortex and premotor area, both located in the frontal cortex. These areas then send information to the primary motor cortex located in the precentral gyrus. 'Motor Regions' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the primary motor cortex using the BrainFacts.org 3D Brain

View the premotor cortex using the BrainFacts.org 3D Brain

View the prefrontal cortex using the BrainFacts.org 3D Brain

Role of Premotor Area

The premotor regions do send some axons directly to lower motor neurons in the spinal cord using the same pathways as the motor cortex (see Execution of Movement chapter). However, the premotor cortex also plays an important role in the planning of movement. Two experimental designs have demonstrated this role. Monkeys were trained on a panel that had one set of lights in a row on top and one set of buttons that could also light up in a row on the bottom. The monkeys would watch

for a top row light to turn on. This would indicate that within a few seconds, the button directly below would light up. When the button turned on, the monkeys were supposed to push the button.

Therefore, there were two light triggers in the experiment. The first required no motor movement from the monkey but did give the monkey information about where a motor movement would be needed in the near future. The second required the monkey to move to push the button. When brain activity was measured during this study, neurons in the premotor cortex became active when the first light trigger turned on, well before any movement actually took place (Weinrich and Wise, 1928).

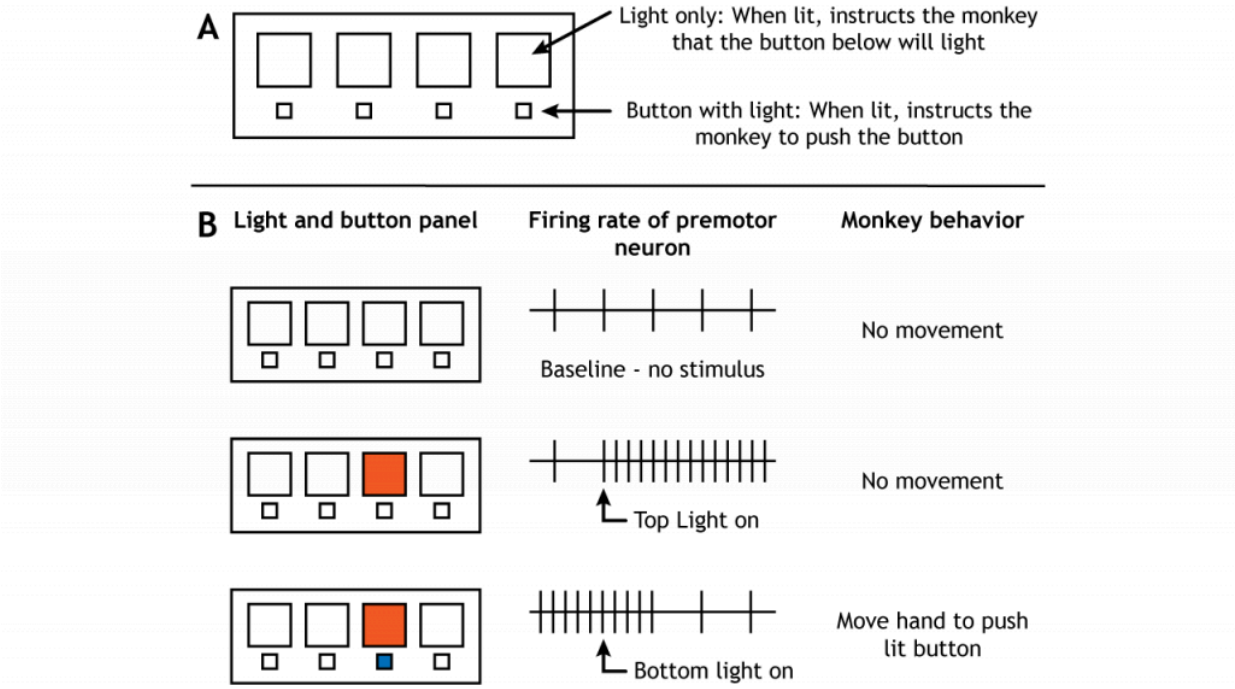

Figure 29.3. (A) Monkeys were trained to use a light panel. When lit, a light located in the top row informed the monkey that the button directly below would light up soon. Shortly after one of the top row lights turned on, the button directly below it would turn on, and the monkey would need to push that button for a reward. (B) When no lights are lit, premotor neurons fire at a baseline rate, and the monkey does not move. Neurons located in the premotor cortex increase action potential firing rate when the top row light turns on, even though the monkey makes no movement. The firing stops shortly after the monkey moves to push the bottom button after it turns on. (Based on Weinrich and Wise, 1928) 'Light Panel Experiment' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

In another experiment, people were trained to move their fingers in a specific pattern. Cerebral blood flow was then measured when they repeated the finger pattern and when they only imagined repeating

the finger pattern. When the movement was only imagined and not actually executed, the premotor regions along with parts of the prefrontal cortex were activated (Roland, et al, 1980).

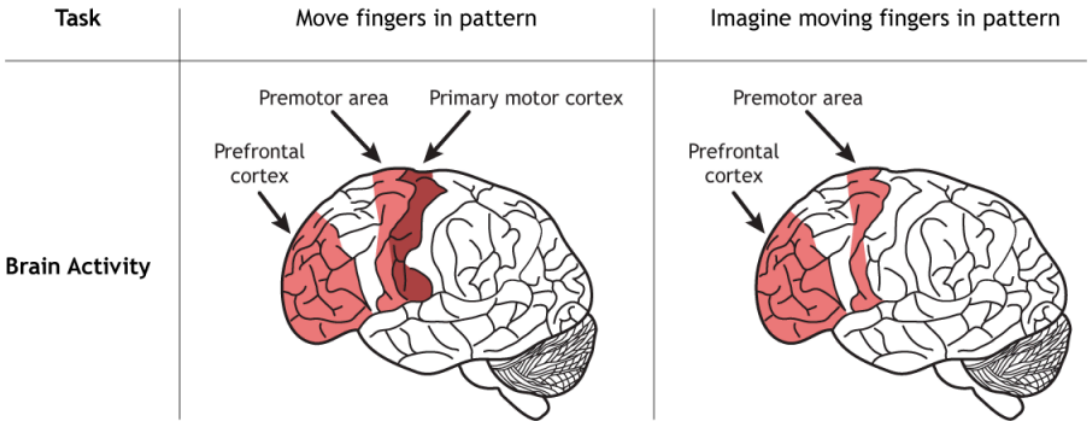

Figure 29.4. People were trained to move their fingers in a pattern. When the pattern was repeated, brain activity was seen in the primary motor cortex, along with the premotor area and prefrontal cortex. When the pattern was only imagined, and no finger movement took place, brain activity was seen in the premotor area and prefrontal cortex. (Based on Roland, et al, 1980) 'Finger Movement Experiment' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

These studies show that the premotor cortex is active prior to the execution of movement, indicating that it plays an important role in the planning of movement. The posterior parietal, prefrontal, and premotor regions, though, also communicate with a subcortical region called the basal ganglia to fully construct the movement plan. The basal ganglia are covered in the next chapter.

Key Takeaways

- Sensory information is processed in the posterior parietal before being sent to motor regions of the brain
- The prefrontal cortex and premotor cortex are critical for creating a movement plan

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=661#h5p-25

Video Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=661#oembed-1

References

Roland PE, Larsen B, Lassen NA, Skinhøj E. Supplementary motor area and other cortical areas in organization of voluntary movements in man. J Neurophysiol. 1980 Jan;43(1):118-36. doi: 10.1152/jn.1980.43.1.118. PMID: 7351547.

Weinrich M, Wise SP. The premotor cortex of the monkey. J Neurosci. 1982 Sep;2(9):1329-45. doi: 10.1523/JNEUROSCI.02-09-01329.1982. PMID: 7119878; PMCID: PMC6564318.

30.

BASAL GANGLIA

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

The basal ganglia are a group of subcortical nuclei, meaning groups of neurons that lie below the cerebral cortex. The basal ganglia is comprised of the striatum, which consists of the caudate nucleus and the putamen, the globus pallidus, the subthalamic nucleus, and the substantia nigra The basal ganglia are primarily associated with motor control, since motor disorders, such as Parkinson's or Huntington's diseases stem from dysfunction of neurons within the basal ganglia. For voluntary motor behavior, the basal ganglia are involved in the initiation or suppression of behavior and can regulate movement through modulating activity in the thalamus and cortex. In addition to motor control, the basal ganglia also communicate with non-motor regions of the cerebral cortex and play a role in other behaviors such as emotional and cognitive processing.

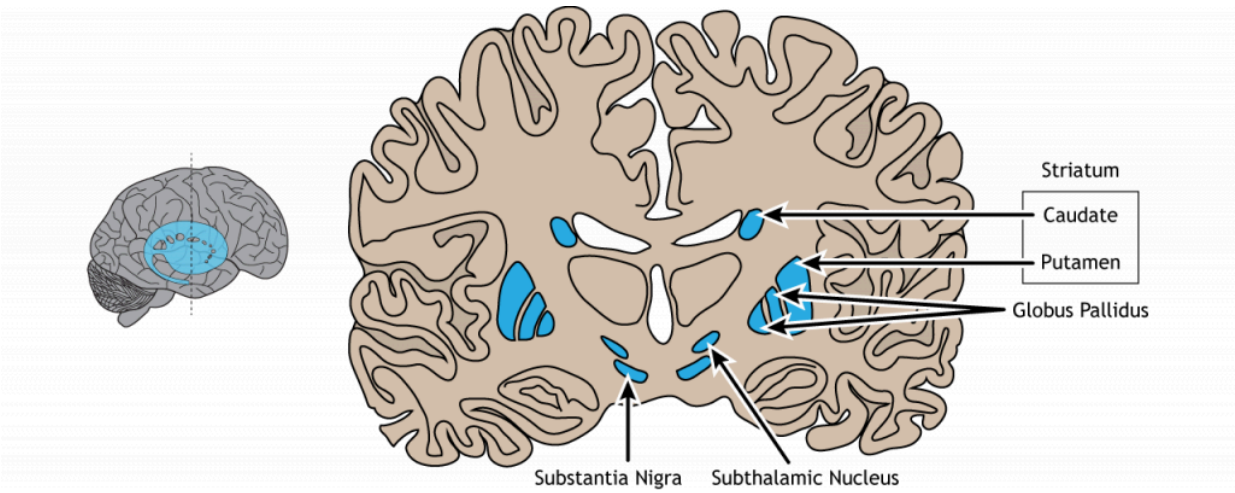

Figure 30.1. The basal ganglia are subcortical structures located at the base of the forebrain. They are comprised of the caudate and putamen, which both make up the striatum, as well as the globus pallidus, substantia nigra, and subthalamic nucleus. 'Basal Ganglia' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the basal ganglia using the BrainFacts.org 3D Brain

Basal Ganglia Input

The majority of information processed by the basal ganglia enters through the striatum. The principal source of input to the basal ganglia is from the cerebral cortex. This input is glumatergic and therefore, excitatory. The substantia nigra is also a region with critical projections to the striatum and is the main source of dopaminergic input. Dopamine plays an important role in basal ganglia function. Parkinson's disease results when dopamine neurons in the substantia nigra degenerate and no longer send appropriate inputs to the striatum. Dopamine projections can have either excitatory or inhibitory effects in the striatum, depending on the type of metabotropic dopamine receptor the striatal neuron expresses. Dopamine action at a neuron that expresses the D1 receptor is excitatory. Dopamine action at a neuron that expresses the D2 receptor is inhibitory.

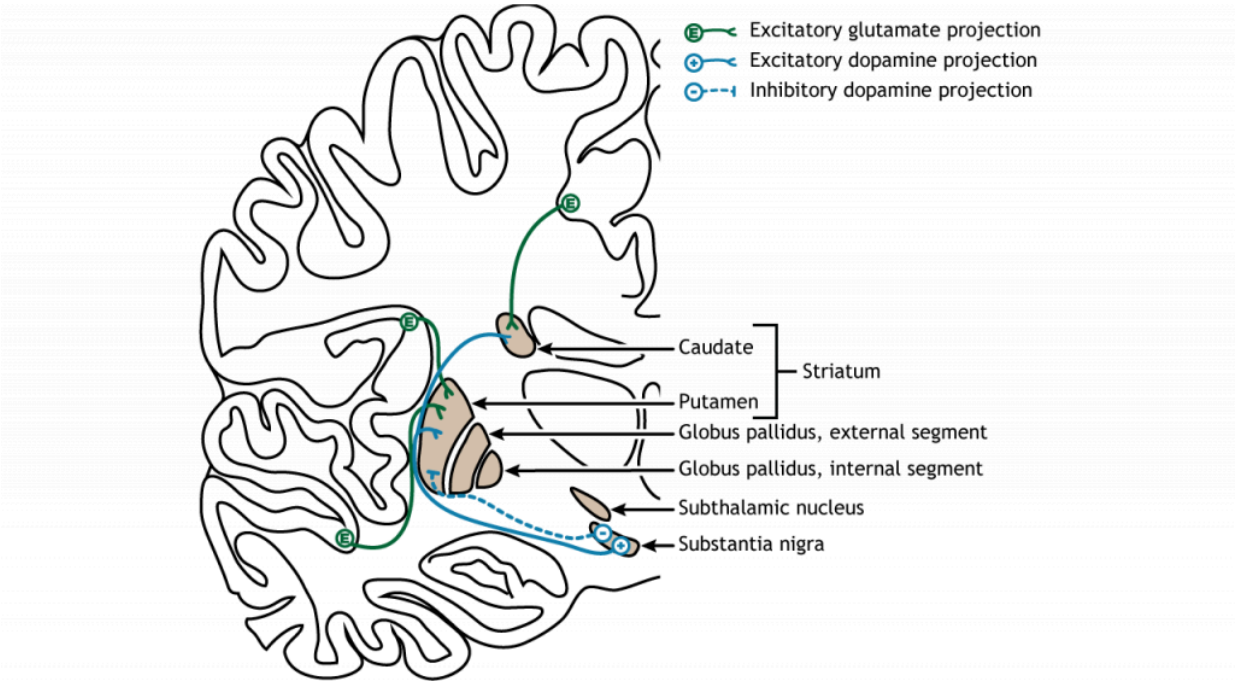

Figure 30.2. Inputs to the basal ganglia enter through the striatum (the caudate and putamen). Cortical projections (shown in green) release glutamate and are excitatory. Substantia nigra projections (shown in blue) release dopamine and can be either excitatory or inhibitory. 'Basal Ganglia Input' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

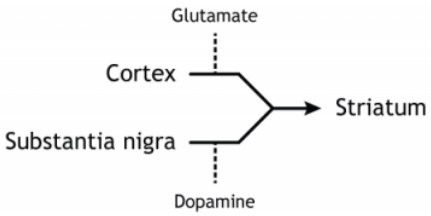

Figure 27.3. The cortex sends glutamate projections to the striatum. The substantia nigra sends dopamine projections to the striatum. 'Basal Ganglia Input – Text' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Basal Ganglia Output

The primary output region of the basal ganglia is the internal segment of the globus pallidus. This region sends inhibitory GABAergic projections to nuclei in the thalamus. This inhibitory output has a tonic, constant firing rate, which allows the basal ganglia output to both increase and decrease depending on the situation. The thalamus then projects back out to the cerebral cortex, primarily to motor areas.

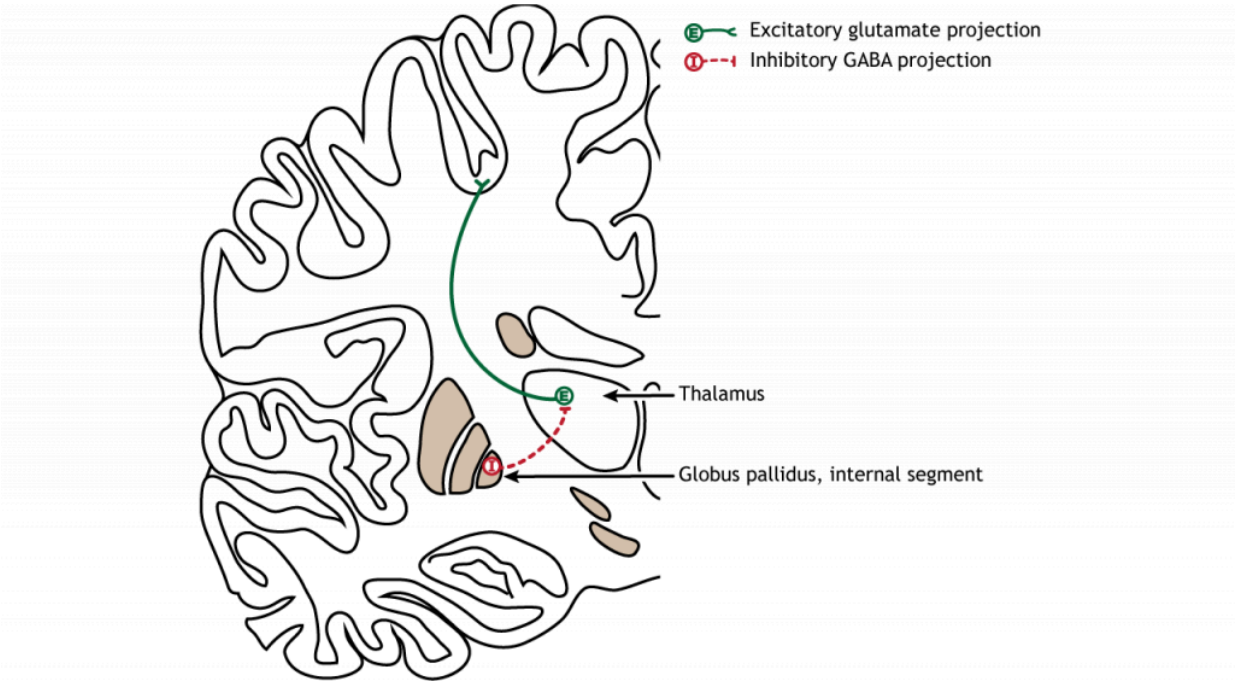

Figure 30.4. Output from the basal ganglia leaves through the internal segment of the globus pallidus. Inhibitory projections (shown in red) release GABA onto the thalamus. Excitatory thalamic projections (shown in green) communicate with the cerebral cortex. 'Basal Ganglia Output' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Figure 27.5. The internal segment of the globus pallidus sends GABA projections to the thalamus. The thalamus sends glutamate projections to the cortex. 'Basal Ganglia Output – Text' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Basal Ganglia Internal Processing

Direct Pathway

There are multiple connections within the basal ganglia structures as well. For motor control, there are two main circuits: the direct pathway and the indirect pathway. These circuits have opposing actions when activated by cortical neurons. The circuits are also modulated by dopamine release by the substantia nigra into the striatum. It is believed that the different control mechanisms allow a finely tuned balance between the direct and indirect circuits, which allows for refined control of movement.

The direct pathway begins in the striatum, which sends inhibitory projections to the internal segment of the globus pallidus (GPi). The GPi then sends inhibitory output to the thalamus.

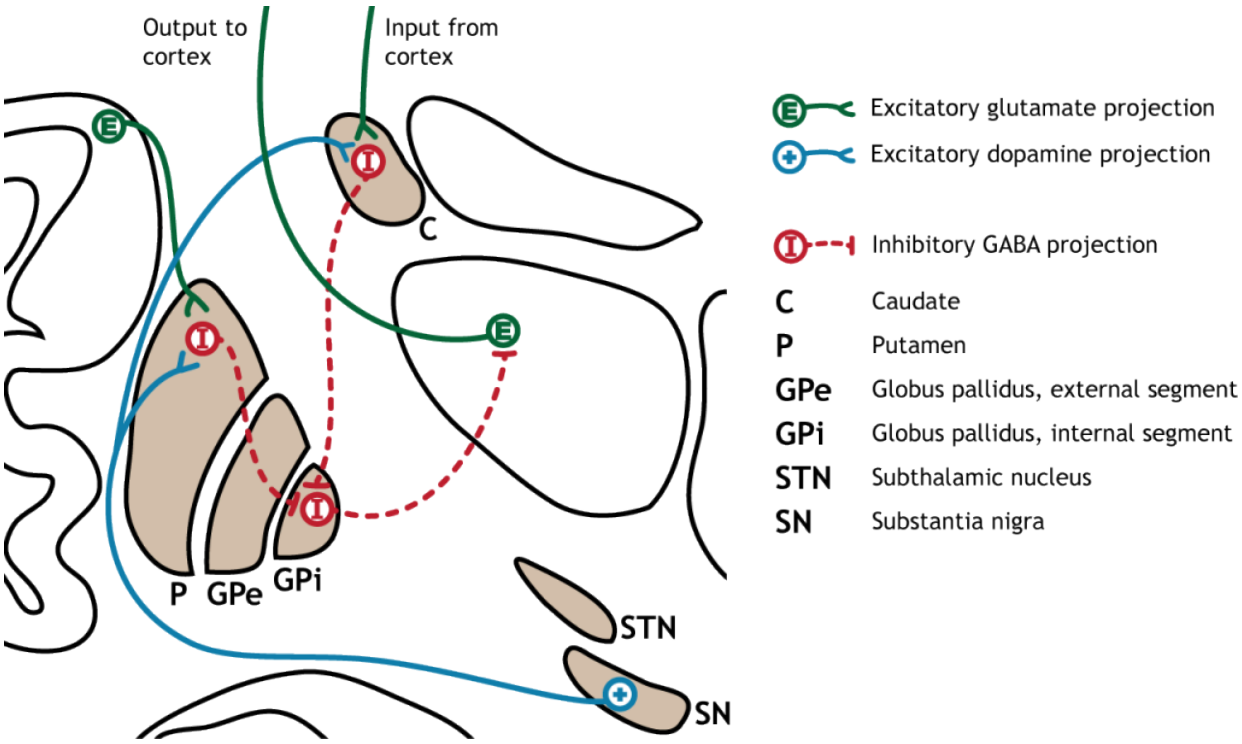

Figure 30.6. The direct pathway in the basal ganglia consists of excitatory input from the cortex via glutamate action or substantia nigra via dopamine action that synapses on inhibitory neurons in the striatum. The striatal neurons project to the internal segment of the globus pallidus (GPi). The GPi then sends inhibitory output to the thalamus. 'Basal Ganglia Direct Pathway' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

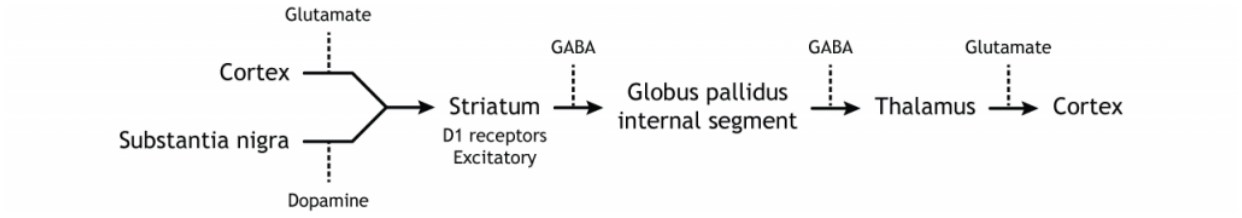

Figure 30.7. The cortex sends glutamate projections to the striatum. The substantia nigra sends dopamine projections to the striatum, which are excitatory, acting on D1 receptors in the neurons involved in the direct pathway. The striatum sends GABA projections to the internal segment of the globus pallidus (GPi). The GPi sends GABA projections to the thalamus. The thalamus sends glutamate projections to the cortex. 'Basal Ganglia Direct Pathway – Text' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Activation of the Direct Pathway

When input from either the cortex or substantia nigra increases in intensity, the direct pathway is activated. The neurons in the striatum involved in the direct pathway express the D1 metabotropic dopamine receptor, and the activation of this receptor is excitatory. Therefore, projections from both the cortex and the substantia nigra activate the neurons in the striatum. Those neurons are inhibitory and release GABA onto the internal segment of the globus pallidus (GPi). As described above, the neurons in the GPi are inhibitory, releasing GABA onto the thalamus. Activation of the striatum neurons inhibit the neurons in the GPi, releasing the inhibition on the thalamus. Inhibition of an inhibitory region is called disinhibition. Therefore, the activation of the direct pathway results in increased output from the thalamus because it is disinhibited.

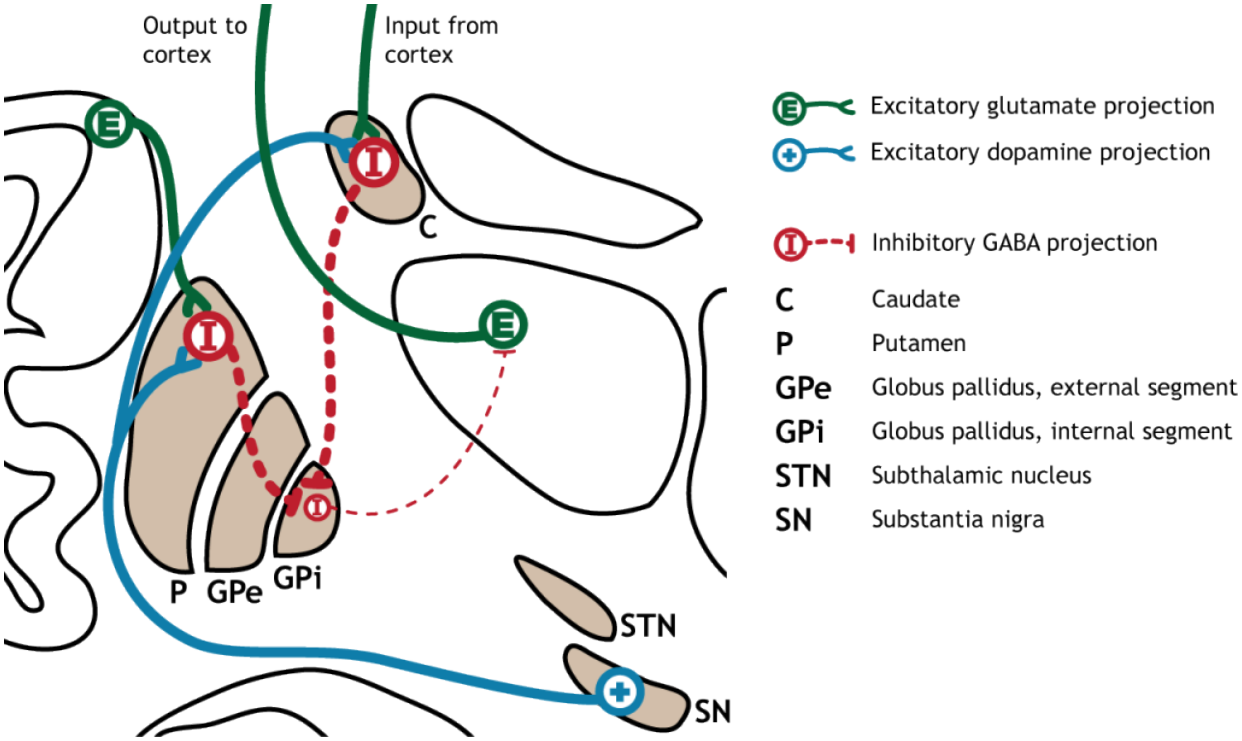

Figure 30.8. Activation of the direct pathway by either increased input from either the cortex or substantia nigra leads to increased inhibitory output from the striatum to the GPi. The inhibition on the GPi leads to less inhibitory input to the thalamus, causing increased output from the thalamus to the cortex. 'Direct Pathway Activation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

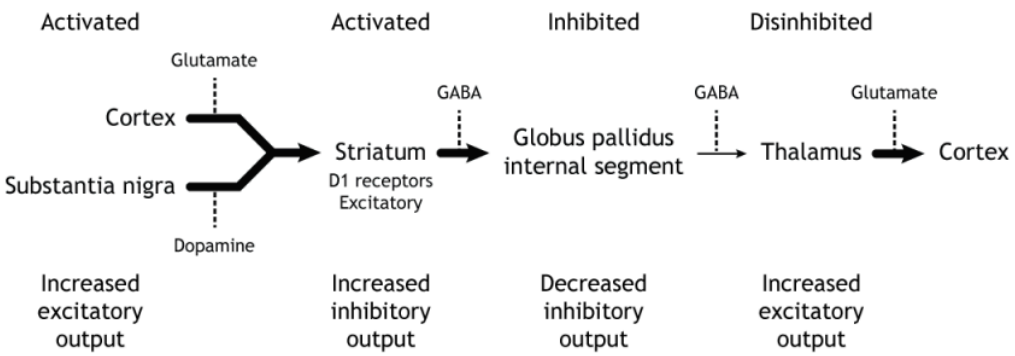

Figure 30.9. When either the cortex or the substantia nigra are activated, they send increased excitatory output to the striatum, which expresses excitatory D1 receptors in the neurons involved in the direct pathway. This input activates the striatum, which sends increased inhibitory projections to the GPi. The inhibited GPi sends decreased inhibitory projections to the thalamus, disinhibiting the thalamus. The thalamus then sends increased excitatory output to the cortex. 'Direct Pathway Activation – Text' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Indirect pathway

The indirect pathway is a little more complex. Like the direct pathway, input into the basal ganglia arises from the cortex and substantia nigra, but there are more internal connections within the basal ganglia that what occurs in the direct pathway. Inhibitory neurons in the striatum involved in the indirect pathway project to the external segment of the globus pallidus (GPe). GABA-ergic neurons in the GPe project to the subthalamic nucleus, which then sends excitatory output to the GPi, which outputs to the thalamus.

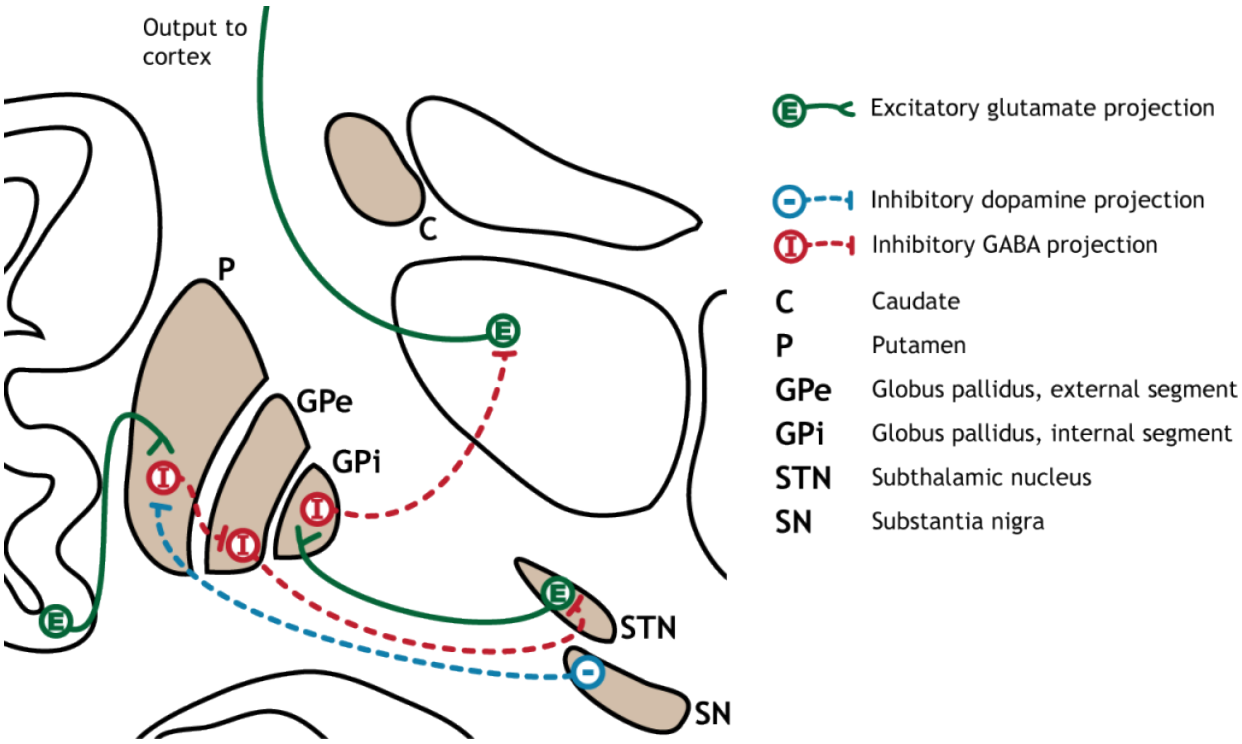

Figure 30.10. The indirect pathway in the basal ganglia consists of excitatory input from the cortex via glutamate action or inhibitory input from the substantia nigra via dopamine action that synapses on inhibitory neurons in the striatum. The striatal neurons project to the external segment of the globus pallidus (GPe). The GPe the sends inhibitory output to the subthalamic nucleus, which had excitatory projections to the GPi. The GPi then sends inhibitory output to the thalamus. 'Basal Ganglia Indirect Pathway' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

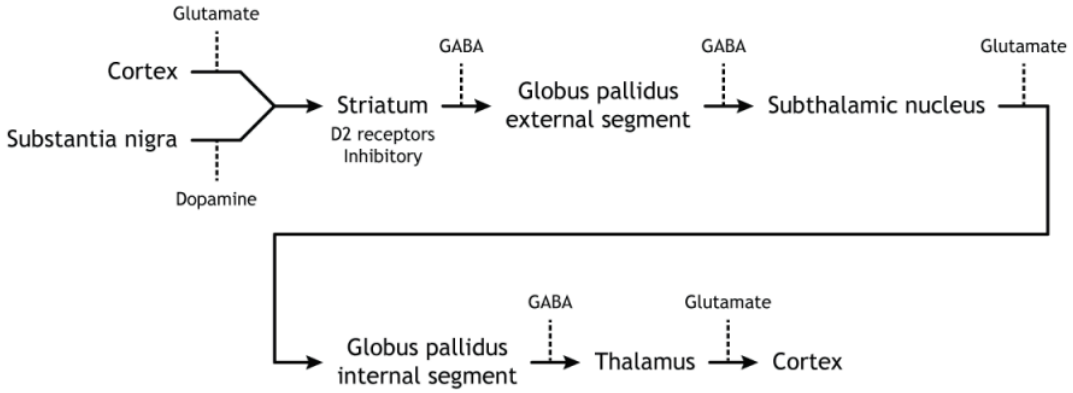

Figure 30.11. The cortex sends glutamate projections to the striatum. The substantia nigra sends dopamine projections to the striatum, which are inhibitory, acting on D2 receptors in the neurons involved in the indirect pathway. The striatum sends GABA projections to the external segment of the globus pallidus (GPe). The GPe sends GABA projections to the subthalamic nucleus. The subthalamic nucleus sends glutamate projections to the GPi. The GPi send GABA projections to the thalamus. The thalamus sends glutamate projections to the cortex. 'Basal Ganglia Indirect Pathway – Text' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Activation of the Indirect Pathway

The indirect pathway is activated by excitatory cortical input, activating the inhibitory striatal neurons. This leads to inhibition of the GPe neurons, resulting in disinhibition of the excitatory neurons in the subthalamic nucleus. The excitatory output from the subthalamic nucleus to the GPi increases inhibition of the thalamus, leading to decreased thalamic output to the cortex.

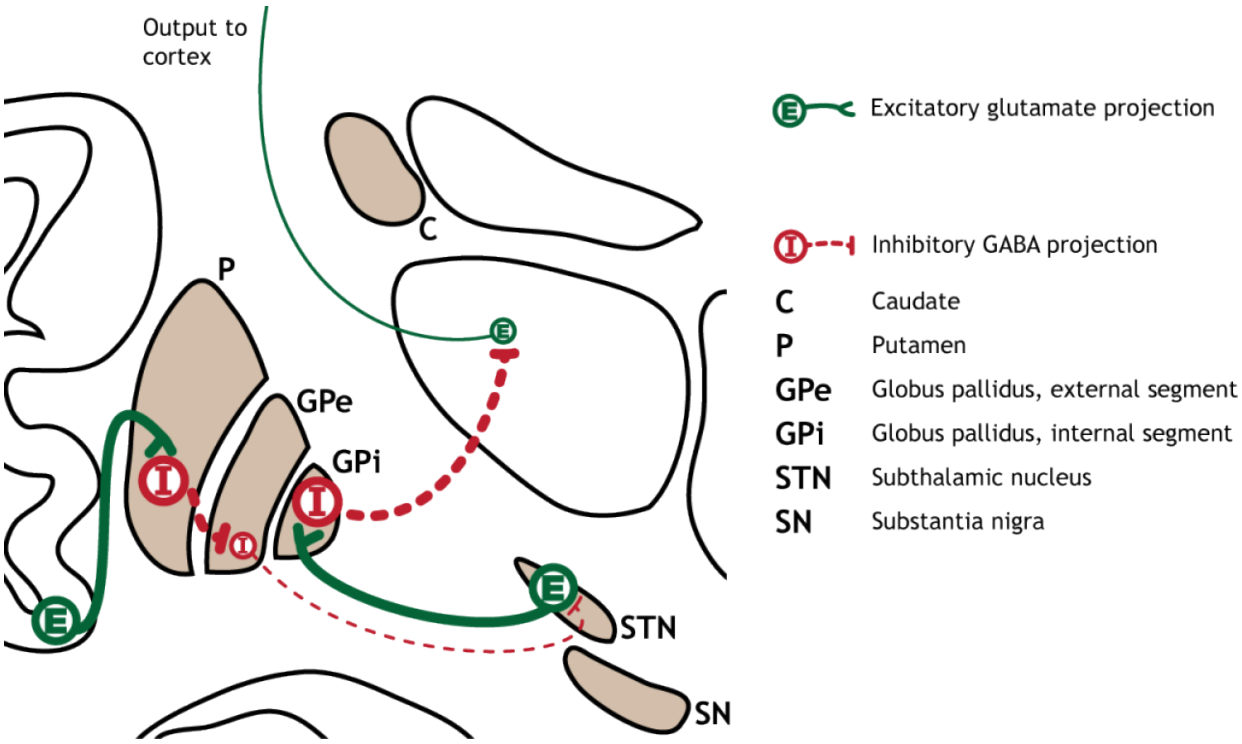

Figure 30.12. Activation of the indirect pathway by excitatory cortical input to the striatum leads to increased inhibitory output to the GPe. The inhibited GPe sends decreased inhibitory output to the subthalamic nucleus, causing increased excitatory output from the subthalamic nucleus to the GPi. Activation of the GPi inhibits the thalamus, resulting in decreased output from the thalamus to the cortex. 'Indirect Pathway Activation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

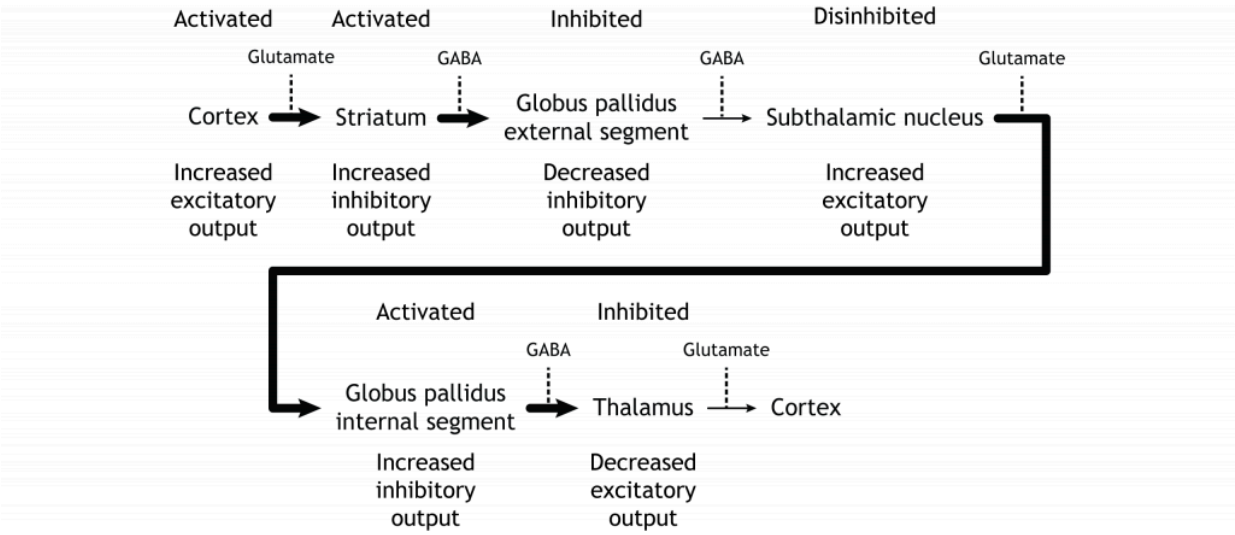

Figure 30.13. When the cortex is activated, it sends increased excitatory output to the striatum. This input activates the striatum, which sends increased inhibitory projections to the GPe. The inhibited GPe sends decreased inhibitory projections to the subthalamic nucleus, disinhibiting the region. The subthalamic nucleus then sends increased excitatory output to the GPi. The activated GPi sends increased inhibitory projections to the thalamus, which sends decreased excitatory output to the cortex. 'Indirect Pathway Activation – Text' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Inhibition of the Indirect Pathway

The indirect pathway can be inhibited by dopamine release from the substantia nigra. The neurons in the striatum involved in the indirect pathway express the D2 metabotropic dopamine receptor. The activation of this receptor is inhibitory. If the indirect pathway is inhibited by dopamine projections from the substantia nigra, the inhibitory striatal neurons are inhibited. This leads to disinhibiton of the GPe neurons, resulting in inhibition of the excitatory neurons in the subthalamic nucleus. This decreased excitatory output to the GPi decreases inhibition of the thalamus, leading to increased thalamic output to the cortex.

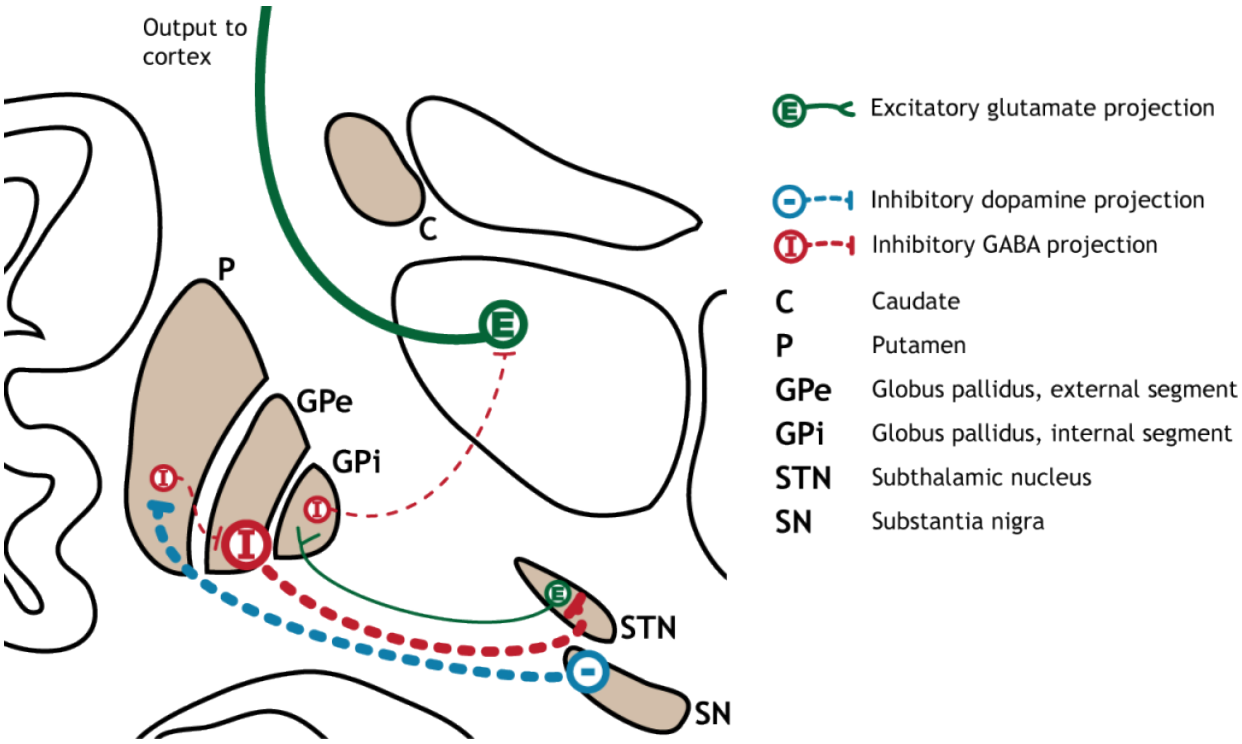

Figure 30.14. Inhibition of the indirect pathway by inhibitory input from the substantia nigra to the striatum leads to decreased inhibitory output to the GPe. The disinhibited GPe sends increased inhibitory output to the subthalamic nucleus, causing decreased excitatory output from the subthalamic nucleus to the GPi. A decrease in activation of the GPi releases the inhibition on the thalamus, resulting in increased output from the thalamus to the cortex. 'Indirect Pathway Inhibition' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

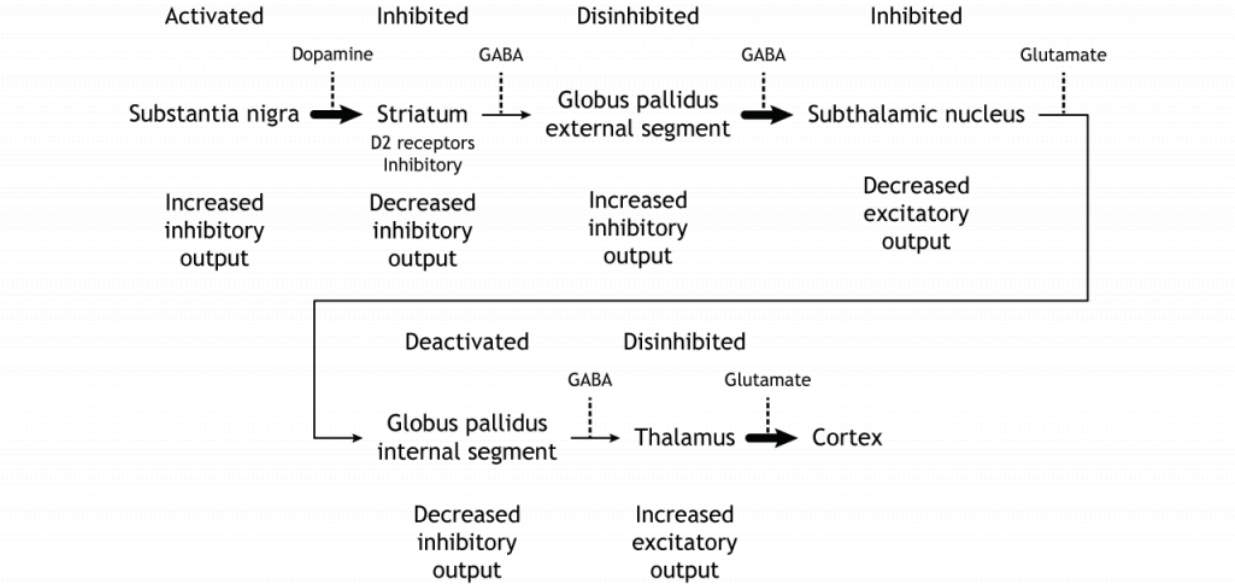

Figure 30.15. When the substantia nigra is activated, it sends increased inhibitory output to the striatum, which expresses inhibitory De receptors in the neurons involved in the indirect pathway. This input inhibits the striatum, which sends decreased inhibitory projections to the GPe. The disinhibited GPe sends increased inhibitory projections to the subthalamic nucleus, inhibiting the region. The subthalamic nucleus then sends decreased excitatory output to the GPi. The deactivated GPi sends decreased inhibitory projections to the thalamus, which sends increased excitatory output to the cortex. 'Indirect Pathway inhibition – Text' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Summary of Internal Processing

To put it all together, there is input to the striatum from two different locations: cortex (glutamate) and substantia nigra (dopamine).

- Cortical activation of the direct pathway leads to increased thalamic output
- Cortical activation of the indirect pathway leads to decreased thalamic output
- Substantia nigra activation (via D1) of the direct pathway leads to increased thalamic output
- Substantia nigra inhibition (via D2) of the indirect pathway leads to increased thalamic output

It is the combination of these pathway that allows for precise control of motor movement.

Loops through the Basal Ganglia

There are multiple circuits that pass through the basal ganglia:

- The motor circuit, which plays a role in voluntary movement
- The oculomotor circuit, which plays a role in eye movement
- The associative circuit, which plays a role in executive functions like behavioral inhibition (preventing impulsive behaviors) planning and problem solving, and mediating socially appropriate behaviors
- The limbic or emotional circuit, which plays a role in the processing of emotion and reward.

Although the circuits each use different circuits within the basal ganglia, the general loop is the same: cortical input to the striatum leads to internal processing within the basal ganglia structures. Basal ganglia output projects from the pallidum to the thalamus, which then projects back to the cortex. It is important to recognize that the basal ganglia plays an important role in a number of functions. For example, medications that are used to treat Parkinson's can sometimes lead to the presentation of impulse control disorders, a result of dopaminergic changes in the limbic loop through the basal ganglia.

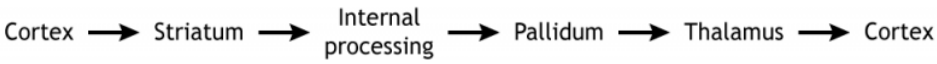

Figure 30.16. Loops through the basal ganglia have different functions but follow the same general circuit. The cortex inputs to the striatum. Internal processing through basal ganglia circuits occurs, and then the output from the pallidum projects to the thalamus, which sends output to the cortex. 'Basal Ganglia Loops' 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 subcortical basal ganglia nuclei receive information from the cortex and send output to the thalamus
- Motor control through the basal ganglia occurs through both the direct and indirect pathways
- Disinhibition is when an inhibitory region is itself inhibited
- The basal ganglia are best known for their role in motor control but are also critical for emotion and behavioral inhibition

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=673#h5p-27

Video Lecture

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31.

EXECUTION OF MOVEMENT

Motor cortex

Once the plan for movement has been created, the primary motor cortex is responsible for the execution of that action. The primary motor cortex lies just anterior to the primary somatosensory cortex in the precentral gyrus located in the frontal lobe.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

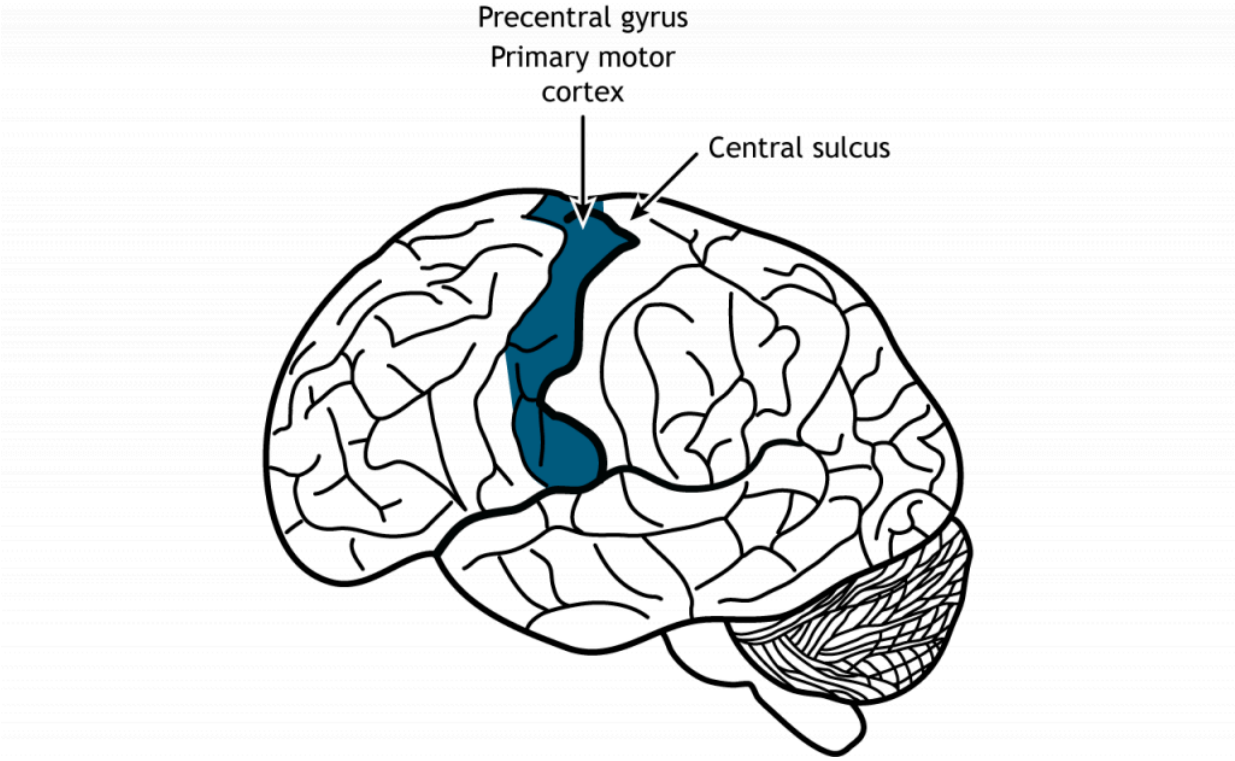

Figure 31.1. The primary motor cortex is located in the frontal lobe in the precentral gyrus, just anterior to the central sulcus. 'Primary Motor Cortex' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Like the somatosensory cortex, the motor cortex is organized by a somatotopic map. However, the motor cortex does not map onto the body in such an exact way as does the somatosensory system. It is believed that upper motor neurons in the motor cortex control multiple lower motor neurons in the spinal cord that innervate multiple muscles. This results in activation of an upper motor neuron causing excitation or inhibition in different neurons at once, indicating that the primary motor cortex is responsible for movements and not simply activation of one muscle. Stimulation of motor neurons in monkeys can lead to complex motions like bringing the hand to the mouth or moving into a defensive position (Graziano et al, 2005).

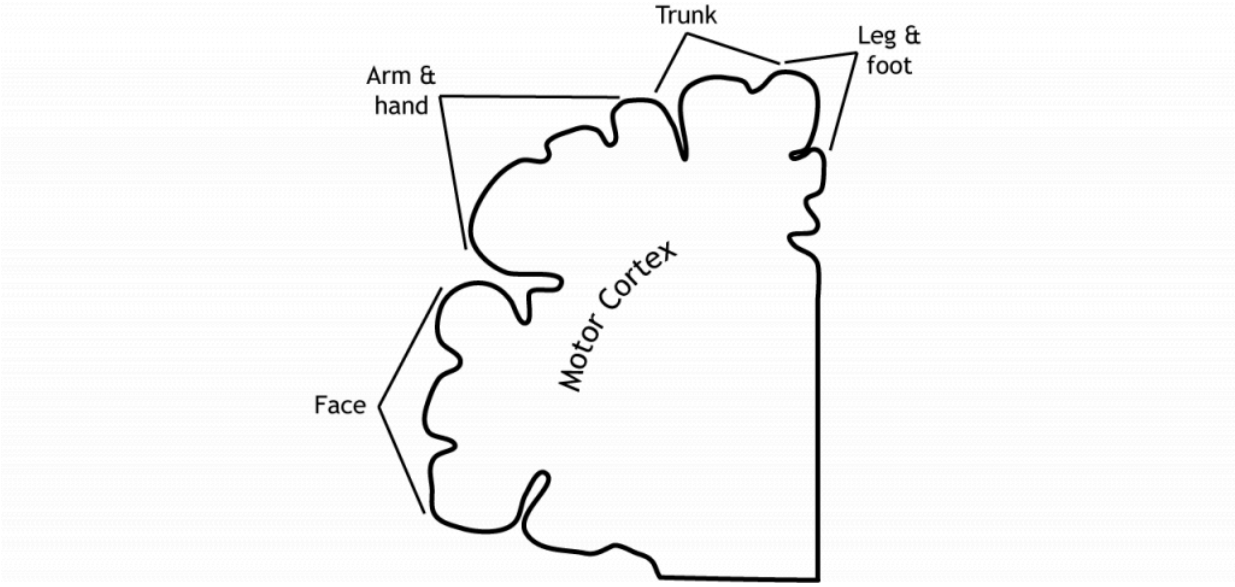

Figure 31.2. The map of the body that exists on the motor cortex is less specific than the somatosensory map because cortical neurons control multiple muscles at the same time. Instead, regions of the cortex are associated with larger body regions, such as the face, arm and hand, trunk, or leg and foot. 'Motor Cortex Map' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Population coding

The motor cortex controls movement by using population coding mechanisms. Upper motor neurons are broadly tuned to a certain movement in a certain direction, meaning firing rate is highest when moving in one direction, but firing also occurs when moving in nearby directions. For example, when a monkey is trained to move its hand toward the left, neurons "tuned" toward left movement will be active immediately before and during the movement. Neurons tuned to other directions will also be active but at lower rates (Georgopoulos, et al, 1982). This means that the firing rate of one specific neuron does not give enough information to know direction of movement. It is the combined firing rates of an entire population of neurons that indicates direction.

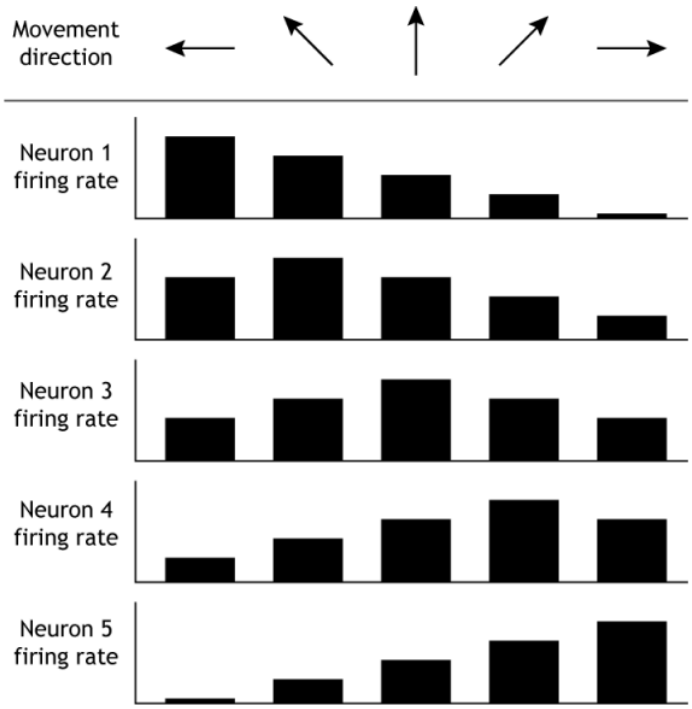

Figure 31.3. Motor movement is coded via population coding in the primary motor cortex. Information from one neuron is not enough to determine the direction of movement; a population of neurons must be used. Some neurons will be "tuned" to fire most rapidly in response to a specific direct. For example, Neuron 1 in the figure shows the highest firing rate when movement of the hand is to the left and a low firing rate when the hand is moving to the right, whereas Neuron 3 fires the most when the movement is forward. The combination of the firing patterns of many neurons provides a precise direction for the movement. 'Population Coding' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Descending Spinal Tracts

There are multiple descending tracts within the spinal cord that send information from the brain to the motor neurons in the ventral horn. The lateral tracts are responsible for carrying information about voluntary movement of the arms and legs. The ventromedial pathways are responsible for carrying information about posture and balance.

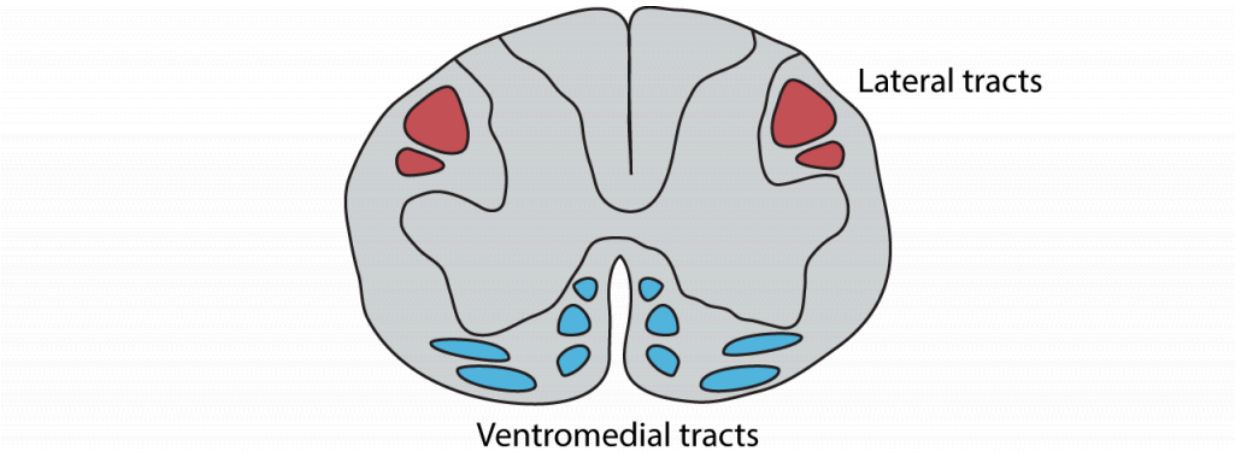

Figure 31.4. The descending motor tracts travel from the brain through the white matter in the spinal cord. The lateral tracts descend in the dorsolateral white matter, and the ventromedial tracts descend in the ventromedial white matter. 'Descending Spinal Tracts' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Lateral Tracts

Coticospinal Tract

The largest of the lateral pathways is the corticospinal tract. This pathway sends information directly from the motor and premotor cortices down to the motor neurons in the spinal cord. Cortical axons travel through the brainstem and then cross the midline at the base of the medulla; like the somatosensory system, the right side of the cortex processes information for the left side of the body and vice versa. In the spinal cord, the axons travel through the lateral column and synapse in the ventral horn on motor neurons that typically innervate distal muscles.

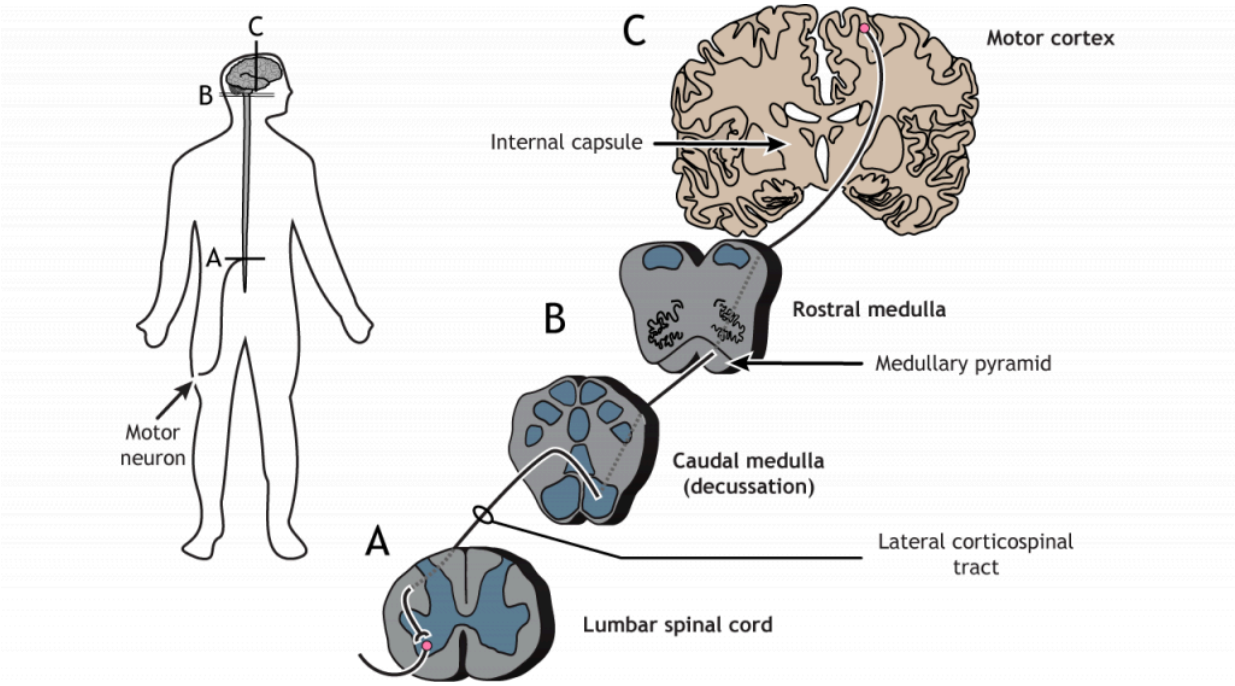

Figure 31.5. Motor information to the arms and legs travels from the primary motor cortex to the medulla via the internal capsule, a white matter structure in the brain. The corticospinal tract passes through the medullary pyramids and then decussates in the caudal medulla. The axons continue traveling through the lateral corticospinal tract and synapse on an alpha motor neurons in the ventral horn of the spinal cord. 'Corticospinal Tract' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Corticobulbar Tract

The corticobulbar tract is another lateral tract and sends motor information to cranial nerves for motor control of the face. This path travels ipsilateral from the cortex into the brainstem where it branches off at the appropriate cranial nerve level in either the pons or the medulla and then innervates cranial nerve neurons bilaterally.

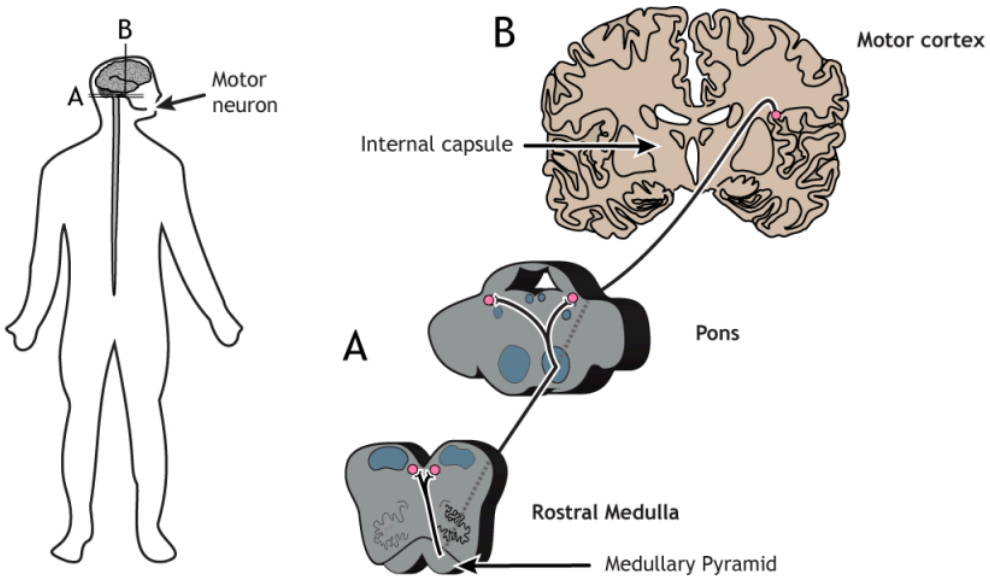

Figure 31.6. Motor information to the face travels from the primary motor cortex through the internal capsule to the pons and medulla where it branches to synapse on cranial nerve nuclei on both sides of the brainstem. 'Corticobulbar Tract' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Ventromedial Tracts

There are four ventromedial pathways that travel in the spinal cord as well. These tracts begin in the brainstem and descend through the ventromedial columns. They receive input from motor areas of the cortex as well as integrating information from multiple sensory regions.

- The vestibulospinal tract is important for head balance as we move. This tract begins in the vestibular nucleus.
- The tectospinal tract is responsible for moving the head in response to visual stimuli. This tract begins in the superior colliculus.
- The two reticulospinal tracts play a role in managing anti-gravity reflexes needed for posture and standing. These tracts begin in the reticular formation.

Key Takeaways

- The motor cortex is located in the frontal lobe
- The motor map is not as detailed as the somatosensory homunculus
- The motor cortex uses population coding to encode direction of movement
- The lateral tracts carry information about voluntary movement of the arms and legs
- The ventromedial pathways carry information about posture and balance

Test Yourself!

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References

Georgopoulos AP, Kalaska JF, Caminiti R, Massey JT. J Neurosci. 1982 Nov;2(11):1527-37.

Graziano et al, 2005 J Neurophysiol 94: 4209-4223.

PART VI
BEHAVIOR

32.

NEURAL CONTROL OF STRESS

It is likely every reader of this chapter has experienced some form of stress, perhaps due to a big exam, a looming deadline, or an unplanned interaction with a spider. The physical reactions to stress, like increased heart rate and breathing, are a result of brain activation.

Resources

- Key Takeaways
- Test Yourself
- Video Lecture

Types of stress

Stress is often split into two categories: physical and psychological. Physical stress can be caused by trauma, illness, or injury. Blood loss, dehydration or allergic reactions are examples of physical stressors. Psychological stress has an emotional and mental component. Fear, anxiety, and grief are examples of psychological stress. The neural circuits involved in responding to the different stressors are overlapping but separate.

Stress response systems

The body has two main systems for responding to stress: the autonomic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis. The autonomic nervous system response occurs very quickly because it is synaptic in nature and is responsible for the "fight or flight" response, which stimulates heart rate and breathing and inhibits digestion. The HPA axis is a hormonal response, so it is a slower response relative to the autonomic system. Its downstream effects also promote energy use.

Neural Control

Hypothalamus

The hypothalamus plays a critical role in stress, activating both the autonomic and hormonal responses. The hypothalamus is a region right above the brainstem on either side of the 3rd ventricle. The hypothalamus manages hormone release in the body and maintains homeostasis; this small structure is critical for numerous functions including hunger and thirst, temperature control, regulation of blood composition, sleep, reproduction, and stress.

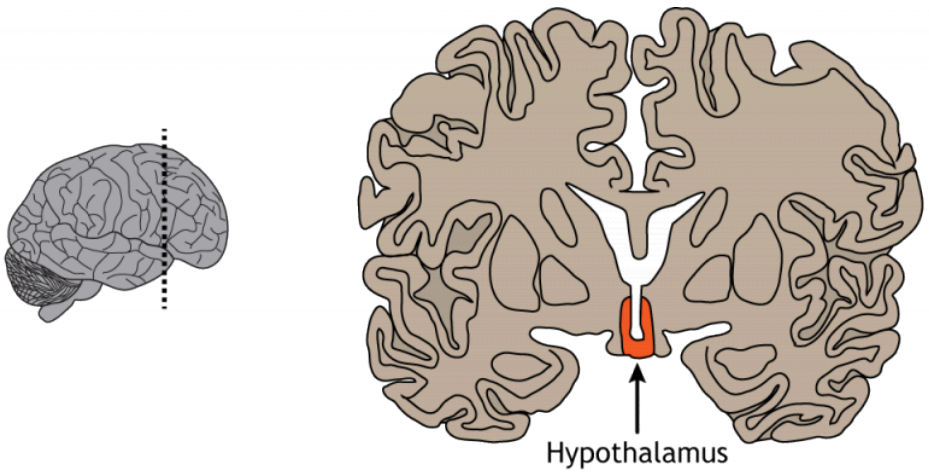

Figure 32.1. The hypothalamus, shown in orange in this coronal view, is located adjacent to the third ventricle. 'Hypothalamus Coronal View' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the hypothalamus using the BrainFacts.org 3D Brain

Although the hypothalamus directly controls the body's response to stress, it is influenced by activity in other regions of the brain. When information from the environment is processed, activity is seen in the prefrontal cortex, hippocampus, and amygdala. These regions have direct and indirect connections to the hypothalamus. The prefrontal cortex plays an executive decision-making role, the hippocampus places events in context with previous memories, and the amygdala assesses a wide range of stimuli for their potential ability to cause harm and places an emotional value on them.

Amygdala

The amygdala is located medially in the temporal lobe. The amygdala, which means "almond" in Latin, is responsible for the processing of emotions and consolidating emotional memories. It is especially active during fear learning and evaluates the salience, or importance, of a situation. For instance, when we look at frightened faces, our amygdala is more activated than when we see neutral faces. Conditions such as anxiety, depression, and post-traumatic stress disorder are all linked to amygdala dysfunction.

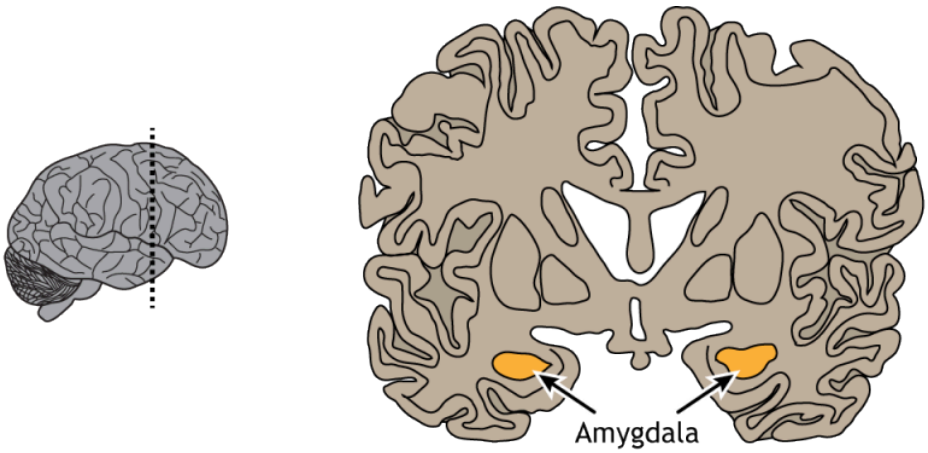

Figure 32.2. The amygdala, shown in yellow in a coronal view, is located in the deep in the anterior portion of the temporal lobe. 'Amygdala' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the amygdala using the BrainFacts.org 3D Brain

Hippocampus

Just posterior to the amygdala lies the hippocampus. The hippocampus, which means "seahorse" due to the similarity between its shape and the animal, is important in the long-term consolidation of memories, spatial navigation, and associating contextual cues with events and memories.

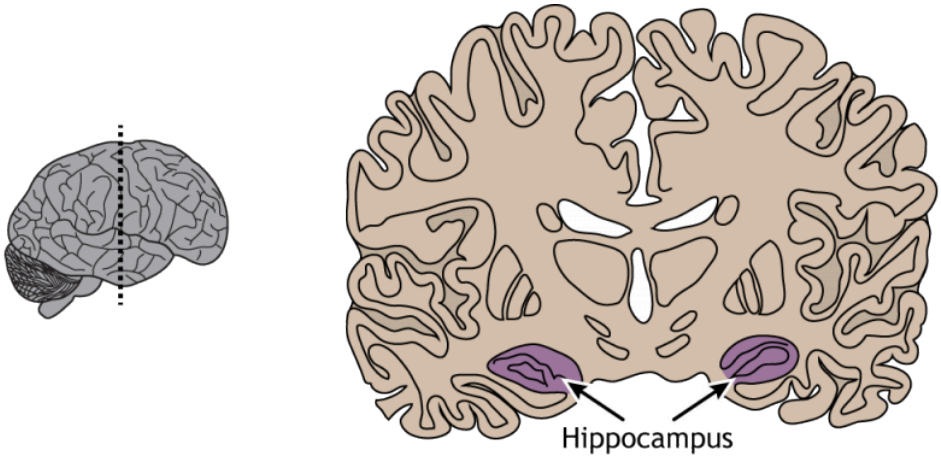

Figure 32.3. The hippocampus, shown in purple in a coronal view, is located in the deep in the temporal lobe. Hippocampus by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the hippocampus using the BrainFacts.org 3D Brain

Prefrontal Cortex

Finally, the prefrontal cortex, which is located in the front of the brain in the frontal lobe, contributes to higher level cognitive functions like planning, critical thinking, understanding the consequences of our behaviors, and is also associated with the inhibition of impulsive behaviors. The prefrontal cortex is one of the last brain regions to fully develop and may not be fully developed until an individual reaches their mid-twenties. Experts think this might explain why teens are more likely than adults to participate in risky behaviors.

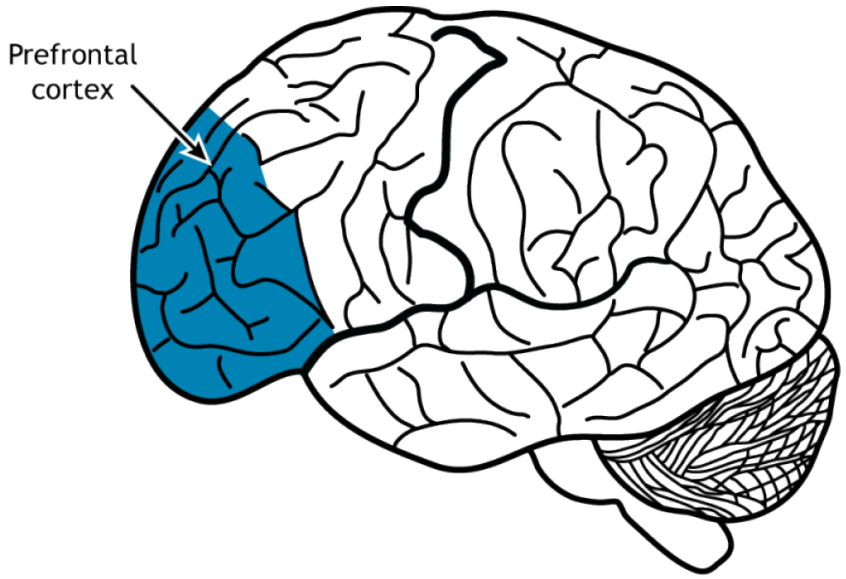

Figure 32.4. The prefrontal cortex, shown in blue in an external view of the brain, is located in the anterior portion of the frontal lobe. 'Prefrontal Cortex' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the prefrontal cortex using the BrainFacts.org 3D Brain

Key Takeaways

- There are two systems that manage physical responses to stress: the autonomic nervous system and the HPA axis
- The hypothalamus is located on either side of the 3rd ventricle, inferior to the thalamus and directly controls both the autonomic nervous system and the HPA axis
- The amygdala, hippocampus, and prefrontal cortex all influence the activity of the hypothalamus

Test Yourself!

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Video Lecture

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33.

HPA AXIS

When presented with a stressor, our brain activates the hypothalamic-pituitary-adrenal (HPA) axis, which initiates a hormonal response.

Resources

- Key Takeaways
- Video Lecture

Hypothalamus

The hypothalamus, which sits below the thalamus, integrates information from many regions of the central nervous system and plays a critical role in maintaining homeostasis in the body. The hypothalamus regulates temperature, hunger, thirst, blood volume and pressure, sleep and wakefulness, reproductive functions, and stress and fear responses.

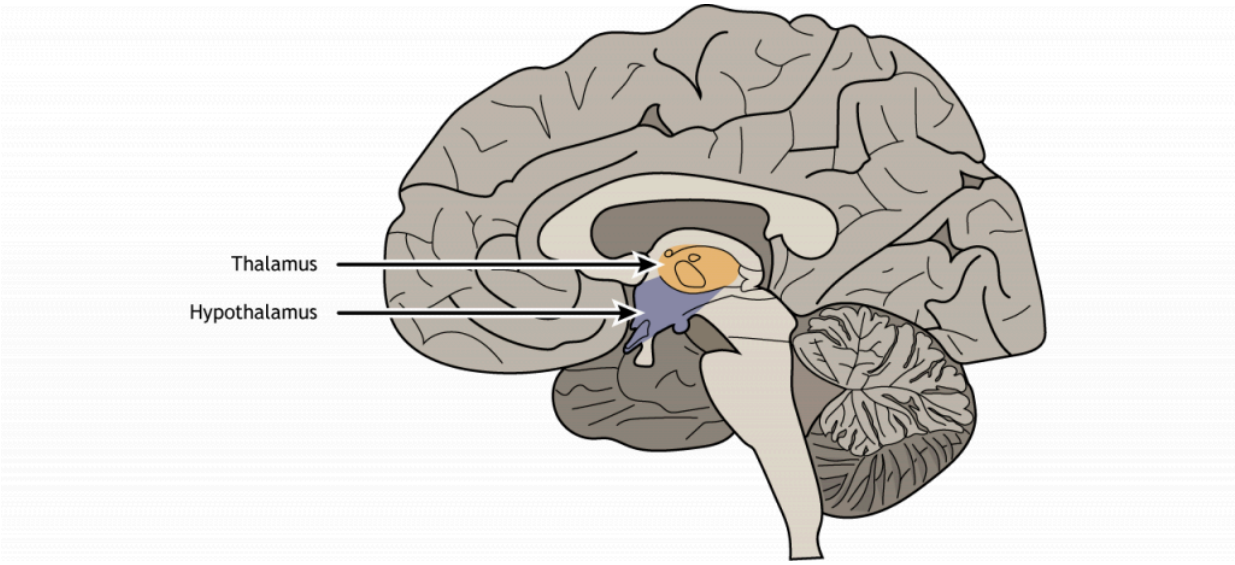

Figure 33.1. The hypothalamus, shown in blue in a mid-sagittal section, sits below the thalamus, shown in orange. 'Hypothalamus Sagittal' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the hypothalamus using the BrainFacts.org 3D Brain

Pituitary

The hypothalamic regulation of the body's response to stress is managed via hormone release by the pituitary gland. The pituitary gland is located inferior to the hypothalamus. The pituitary is divided into two lobes, the anterior and the posterior pituitary. These regions are responsible for the release of different hormones and are controlled by the hypothalamus in different ways.

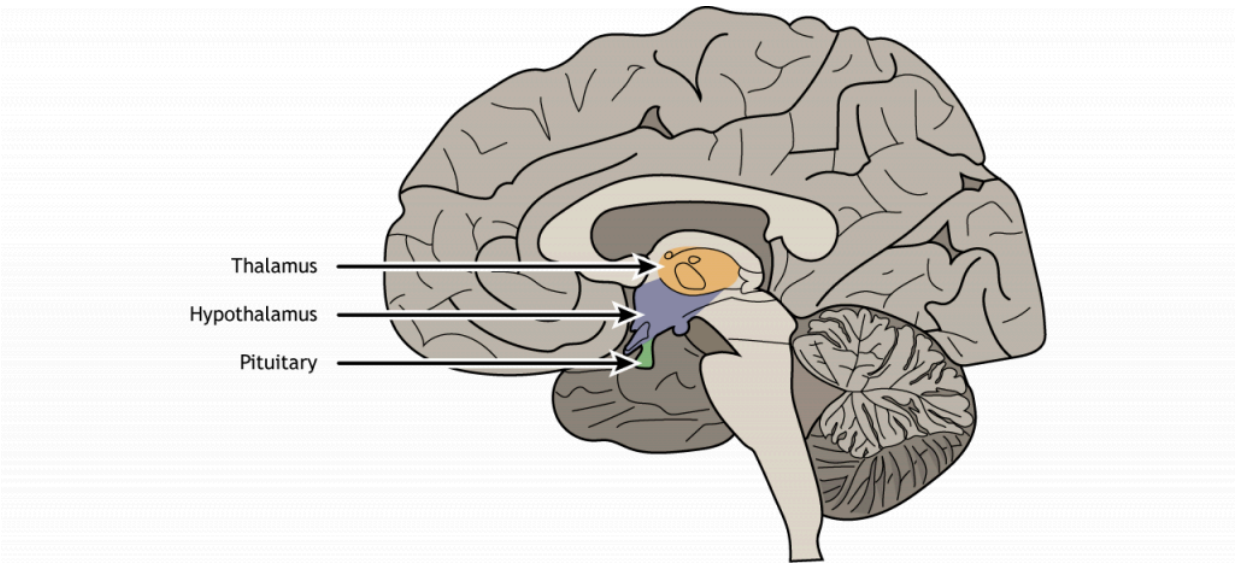

Figure 33.2. The pituitary, shown in green in a mid-sagittal section, lies just below the hypothalamus, shown in blue. 'Hypothalamus and Pituitary' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the pituitary using the BrainFacts.org 3D Brain

Hormone Release

The stress response relies on anterior pituitary function. The hypothalamus contains two types of neurons that secrete hormones into the pituitary: parvocellular neurosecretory cells and magnocellular neurosecretory cells. Parvocellular cells are smaller than the magnocellular neurons (parvus means "small" in Latin). In the HPA axis, the parvocellular neurosecretory cells release a hormone called corticotropin-releasing hormone (CRH) into a specialized capillary system that lies between the hypothalamus and the pituitary called the hypophyseal portal circulation. When CRH reaches the anterior pituitary, it causes the endocrine cells of the pituitary to release adrenocorticotropic hormone (ACTH) into the general circulation.

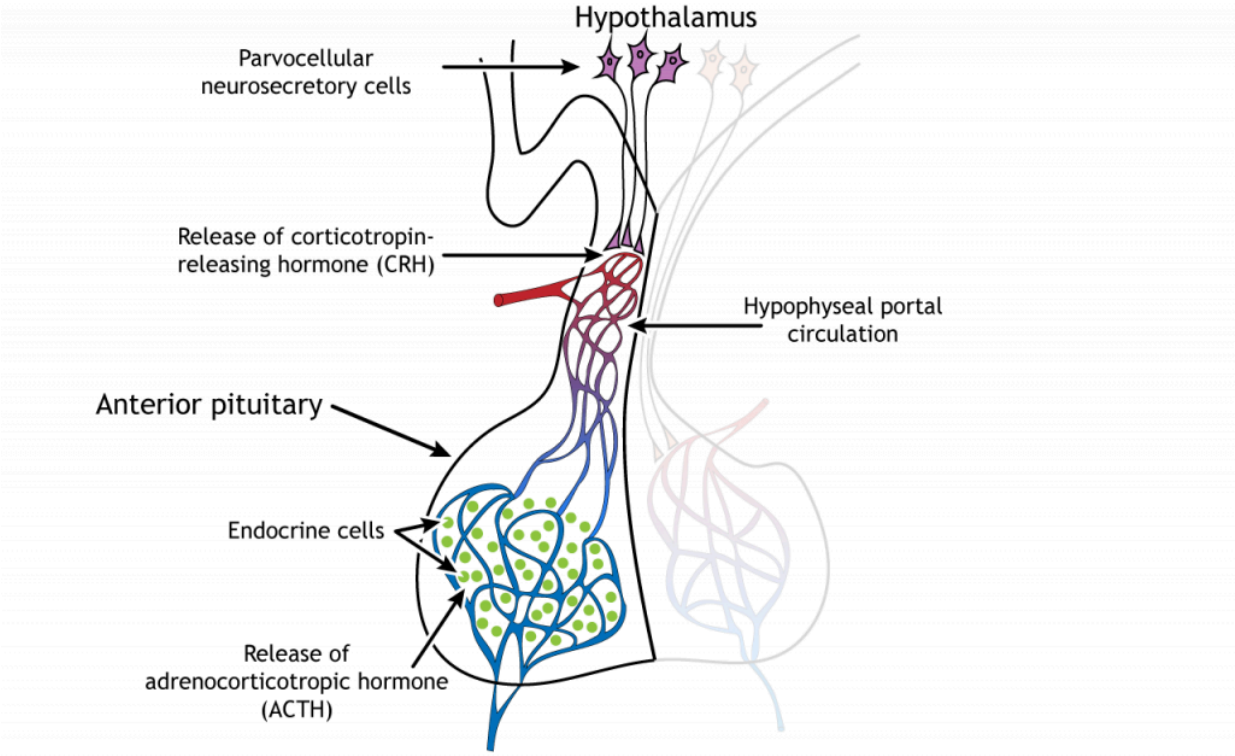

Figure 33.3. In response to stress, the hypothalamic parvocellular neurosecretory neurons release corticotropin-releasing hormone (CRH) into the hypophyseal portal circulation, causing the hormone-releasing endocrine cells in the anterior pituitary to release adrenocorticotropic hormone (ACTH). 'CRH and ACTH Release' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The ACTH travels through the circulatory system and can act on the adrenal cortex, a gland located on top of the kidney. The adrenal cortex releases cortisol, a glucocorticoid hormone, into the blood stream. Cortisol travels throughout the body and has many effects that prepare the body for either fleeing or fighting the stressor. Promotion of energy use (for a quick escape or for defense) occurs through the release of glucose, the sugar the body uses for energy.

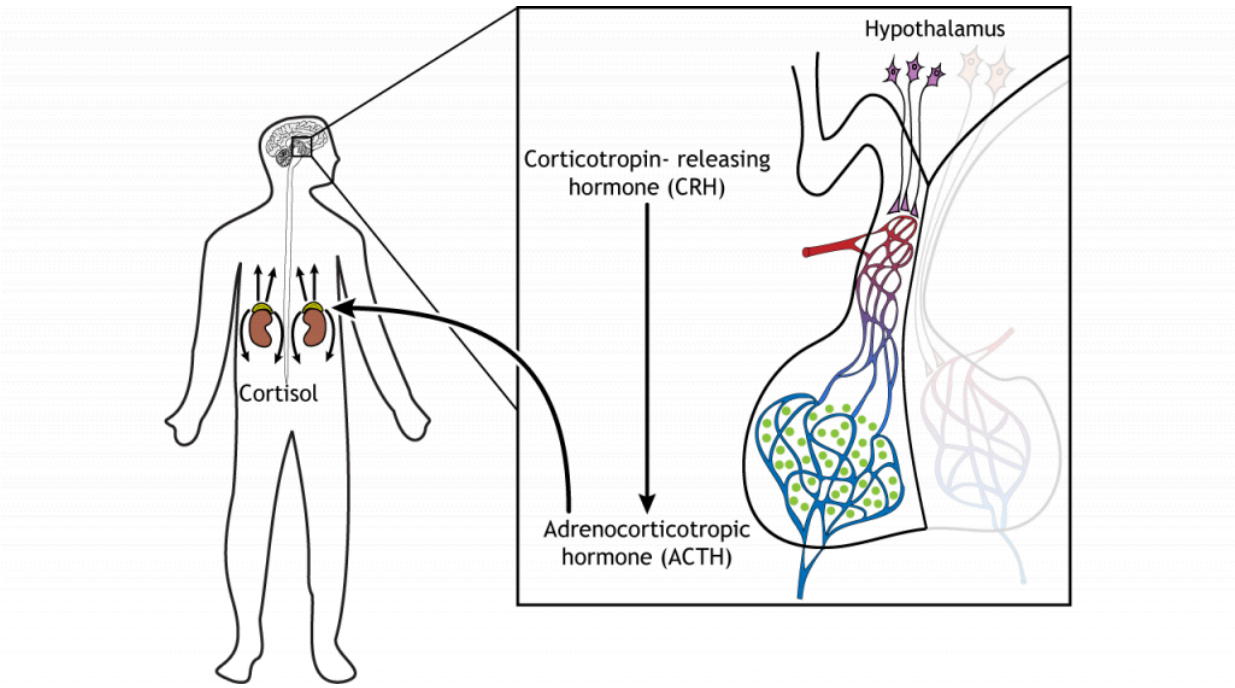

Figure 33.4. The adrenal glands, which sit on top of the kidney, release cortisol into the bloodstream in response to release of ACTH by the anterior pituitary. 'HPA Axis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Hormone Action

Cortisol is a steroid hormone; steroid hormones are synthesized from cholesterol and are able to cross the phospholipid bilayer because they are lipid soluble. Glucocorticoid receptors are located in the cytoplasm of many cell types across the body. The receptors dimerize after cortisol binds, and the dimer moves to the nucleus where it can alter DNA transcription.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=698#video-698-1

Animation 33.1. Cortisol can cross the phospholipid bilayer and bind to glucocorticoid receptors. The receptors dimerize, move to the nucleus, and interact with DNA, altering transcription of certain genes. 'Cortisol Action' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Negative Feedback

Once the stress response has been initiated, and cortisol enters the circulation, cortisol itself is able to act on the hypothalamus and pituitary and inhibit production of CRH and ACTH. This is called a negative feedback loop; the active hormone (cortisol) can shut off its own production. Negative feedback is possible because neurons in the hypothalamus and pituitary express glucocorticoid receptors that are activated by cortisol.

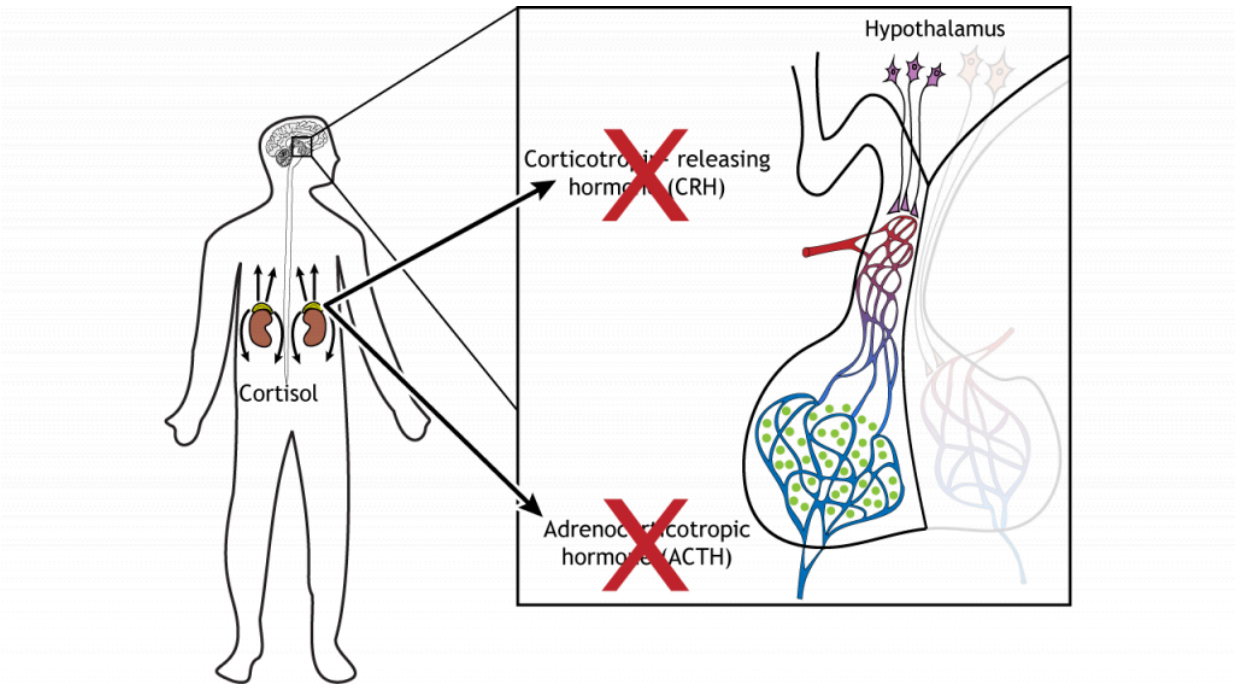

Figure 33.5. Cortisol released by the adrenal cortex inhibits the synthesis and release of CRH and ACTH from the hypothalamus and pituitary, respectively. via a negative feedback loop. 'Cortisol Feedback' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Chronic Stress

While this cortisol response to stress is particularly important in certain situations, like moments of danger, chronic stress is an unhealthy scenario which can put people at risk for heart disease and other illnesses. Chronic stress can cause structural and functional changes, like cell death or alterations in the dendritic arbor, within the cortical regions that play a role in control of the HPA axis due to long-lasting exposure to cortisol.

Key Takeaways

- The hypothalamus directly controls the stress response by controlling hormone release from the anterior pituitary
- The hypothalamus releases corticotropin-releasing hormone (CRH)
- The anterior pituitary releases adrenocorticotropic hormone (ACTH)
- The adrenal cortex releases cortisol
- Cortisol binds to receptors and alters DNA transcription
- Cortisol can shut off its own production via a negative feedback loop

Video Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=698#oembed-1

34.

HPG AXIS

Resources

- Key Takeaways
- Video Lecture

Control of gonadal hormone release relies on activation of the hypothalamic-pituitary-gonadal (HPG) axis. Gonadal hormones are important for development of the body and brain, changes during puberty, and the activation of some behavior in adulthood like reproductive behavior and aggression.

Hypothalamus

As a refresher, the hypothalamus, which is located inferior to the thalamus, integrates information from many regions of the central nervous system and maintains homeostasis in the body. They hypothalamic regulation of gonadal hormones and sex behavior is managed via hormone release by the pituitary gland.

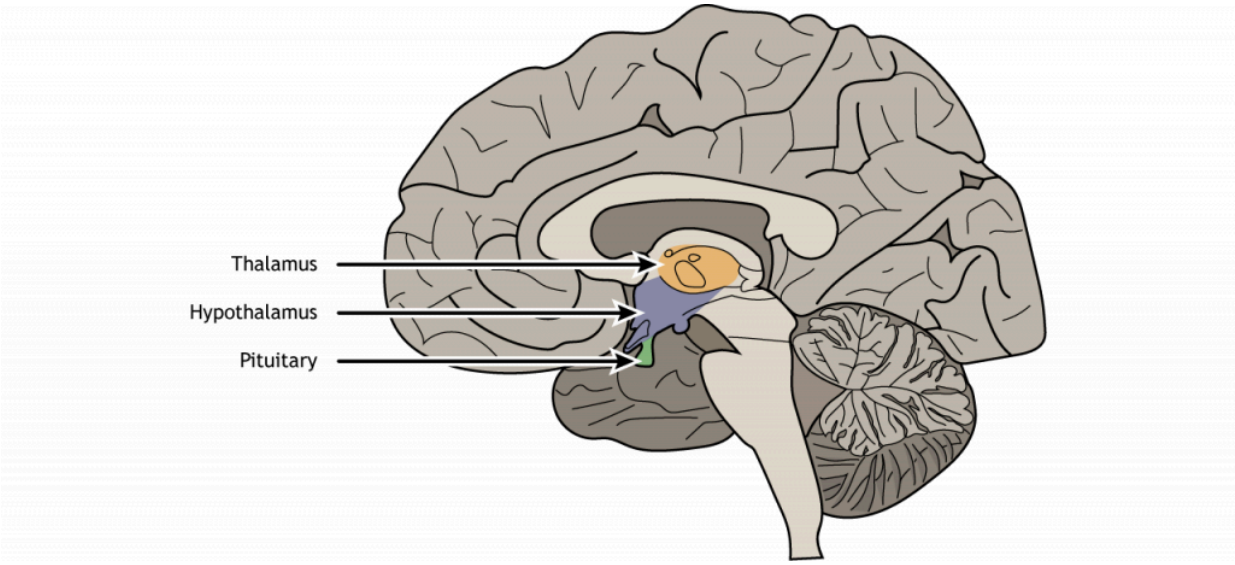

Figure 34.1. The pituitary, shown in green in a mid-sagittal section, lies inferior to the hypothalamus, shown in blue. 'Hypothalamus and Pituitary' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the hypothalamus using the BrainFacts.org 3D Brain

View the pituitary using the BrainFacts.org 3D Brain

Hormone Release

Gonadal hormone release relies on anterior pituitary function. In the hypothalamus, the parvocellular neurosecretory cells release a hormone called gonadotropin-releasing hormone (GnRH) into the hypophyseal portal circulation. When GnRH reaches the anterior pituitary, it causes the endocrine cells of the pituitary to release luteinizing hormone (LH) and follicle-stimulating hormone (FSH) into the general circulation.

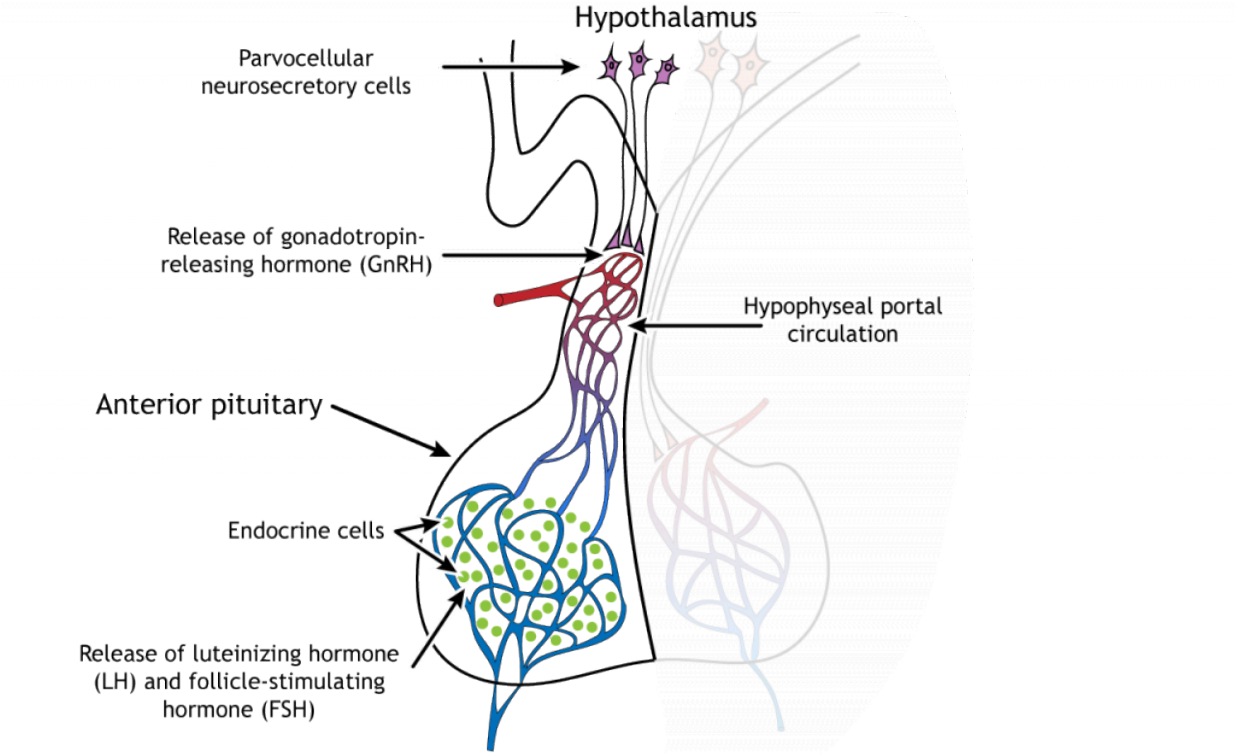

Figure 34.2. In the HPG axis, the hypothalamic parvocellular neurosecretory neurons release gonadotropin-releasing hormone (GnRH) into the hypophyseal portal circulation, causing the hormone-releasing endocrine cells in the anterior pituitary to release luteinizing hormone (LH) and follicle-stimulating hormone (FSH). 'LH and FSH Release' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The LH and FSH travel through the circulatory system and can act on the gonads, either the testes in males or ovaries in females. In response to the pituitary hormones, the testes release testosterone, an androgen, and the ovaries release estradiol, an estrogen, into the blood stream. After puberty, the LH and FSH are also critical for the maturation of sperm and egg cells.

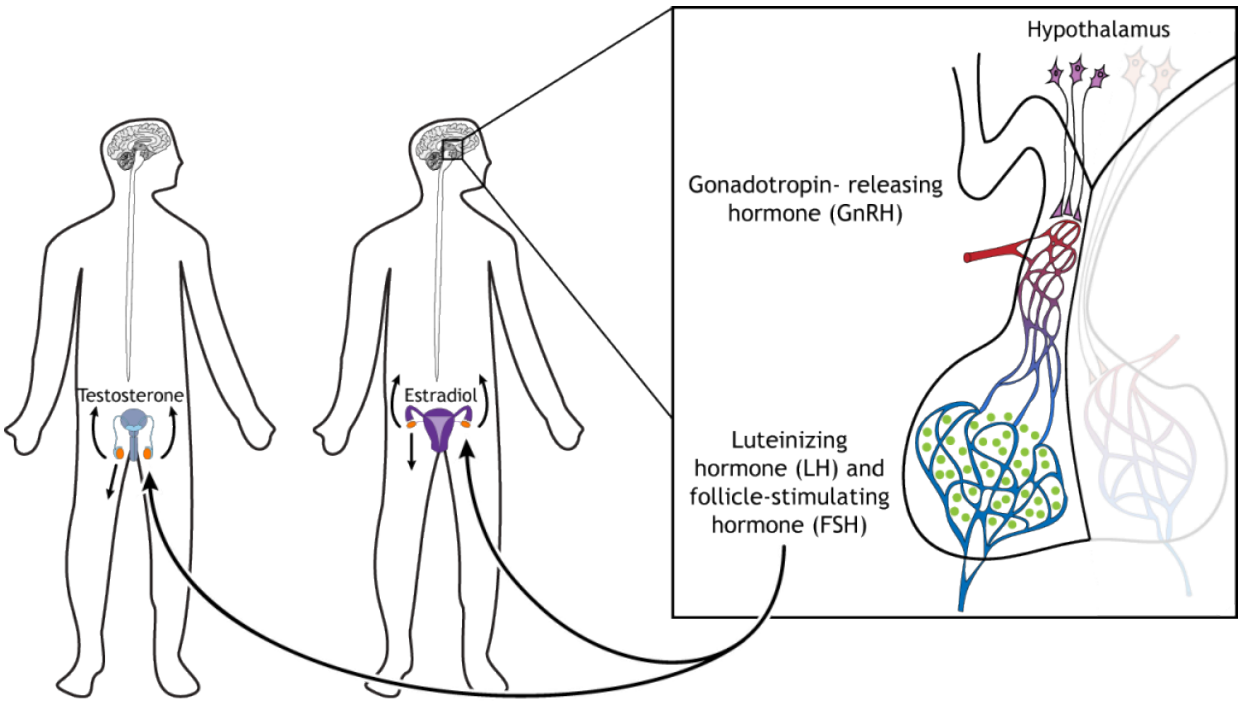

Figure 34.3. The gonads release either testosterone (testes) or estradiol (ovaries) into the bloodstream in response to release of LH and FSH by the anterior pituitary. 'HPg Axis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Hormone Action

Once the gonadal hormones enter the circulation, they are able to act on cells that express either androgen receptors or estrogen receptors. Like cortisol, testosterone and estradiol are steroid hormones and can cross the phospholipid bilayer. Inside the cell, the hormones bind to receptors which then dimerize and move to the nucleus The receptors can bind to DNA at special promotor regions and act as transcription factors, turning on specific genes.

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=1401#video-1401-1

Animation 34.1. Steroid hormones can cross the phospholipid bilayer and bind to hormone receptors. The receptors dimerize, move to the nucleus, and interact with DNA, altering transcription of certain genes. 'Estradiol Action' 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 hypothalamus directly controls release of gonadal hormones by controlling hormone release from the anterior pituitary
- The hypothalamus releases gonadotropin-releasing hormone (GnRH)
- The anterior pituitary releases luteinizing hormone (LH) and follicle-stimulating hormone (FSH)
- The ovaries release estradiol
- The testes release testosterone
- Gonadal hormones bind to receptors and alter DNA transcription

Video Version of Lecture

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=1401#oembed-1

35.

SEXUAL DIFFERENTIATION

Sexual differentiation is the process by which a person develops into either a male or a female. For the purpose of this chapter, the content will be based on a male / female binary to introduce the basic concepts of reproductive development. However, it is important to recognize that in real life, chromosomal sex, physical sex, and gender exist on a continuum and cannot always be simplified into a two-structure system.

Resources

- Key Takeaways
- Video Version

During development, the body and the brain undergo either A) feminization and de-masculinization or B) masculinization and de-feminization. In most cases, the differentiated brain will lead to behaviors that correspond appropriately to the differentiated gonads.

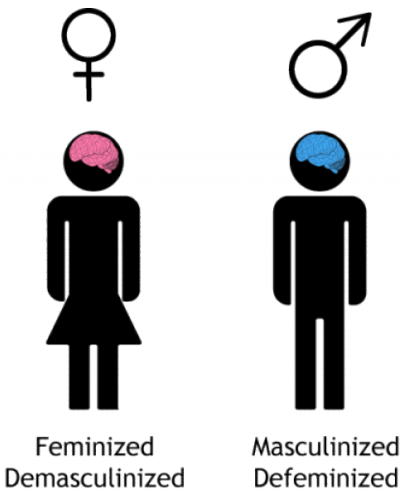

Figure 35.1. In most cases, human females have feminized and desmasculinized brains and bodies whereas human males have masculinized and defeminized brains and bodes. 'Gender Icons' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Chromosomal Sex

In humans, DNA is organized into 46 chromosomes. One set of 23 chromosomes comes from the mother and the other set comes from the father. Twenty-two pairs are called autosomal chromosomes. These chromosome are similar in length and have the same genes present at the same location regardless of if they are received from the mother or father. However, for all genes, the allele, or version, present for each gene may be different from each parent. The last pair of chromosomes is responsible for determining if an individual becomes a male or female; these are called the sex chromosomes. In humans the sex chromosomes are named either X or Y.

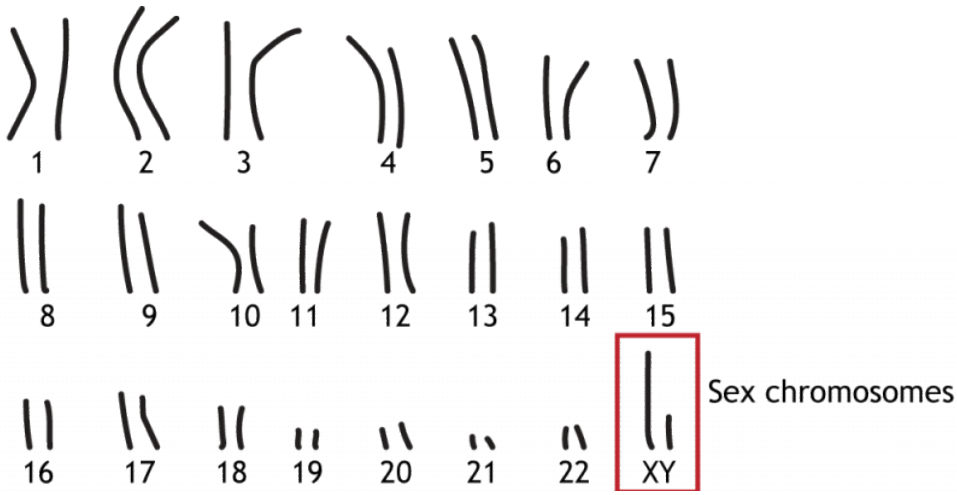

Figure 35.2. Humans have 23 pairs of chromosomes, making 46 total. 22 pairs are called autosomal and have similar structure from each parent. The final pair are the sex chromosomes and determine if the individual is a male or female. Sex chromosomes are named either X or Y. 'Chromosomes' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Fertilization occurs when a sperm cell from the father fuses with an egg cell from the mother. All egg cells contain one X sex chromosome. Sperm cells contain either one X or one Y chromosome, which means chromosomal sex in humans is determined by the sperm. If a sperm carrying an X chromosome fertilizes an egg, the resulting fetus will be XX and a female, whereas if a sperm carrying a Y chromosome fertilizes an egg, the resulting fetus will be XY and a male.

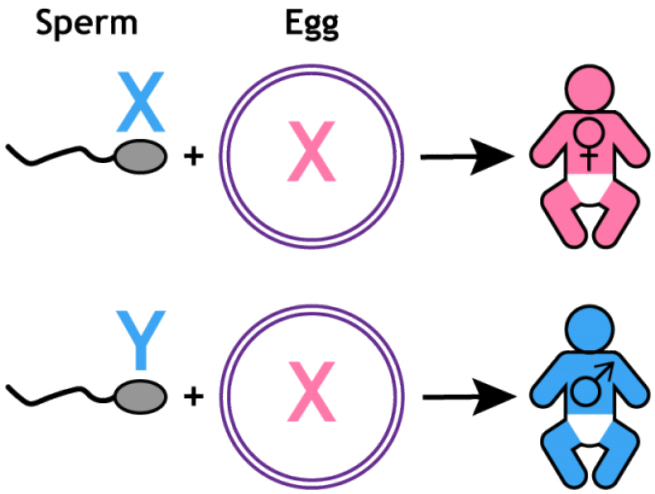

Figure 35.3. The combination of an X-containing sperm cell and an X-containing egg cell will result in a XX individual who will develop as a female. The combination of a Y-containing sperm cell and an X-containing egg cell will result in a XY individual who will develop as a male. 'Fertilization' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Gonadal Differentiation

On the Y chromosome is a gene called the sex-determining region (SRY) of the Y chromosome. The SRY gene is required for masculinization of the embryonic gonads. The SRY gene encodes for a protein called the testis-determining factor (TDF), which causes the embryonic gonads to differentiate into the testes. The testes then begin secreting both testosterone and a hormone called the Müllerian inhibiting substance (MIS). Testosterone causes Wolffian ducts to develop into the vas deferens, seminal vesicles, and epididymis. MIS causes the Müllerian ducts to degenerate. The presence of testosterone also results in the development of the prostate gland and penis.

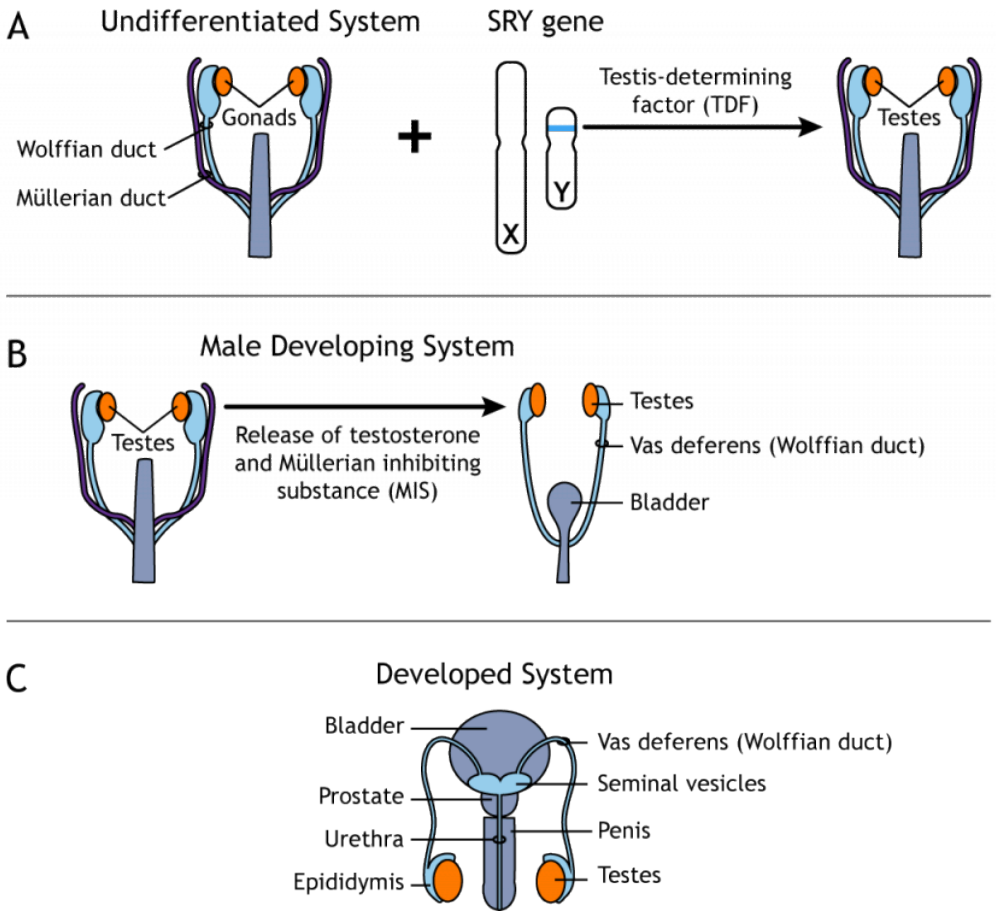

Figure 35.4. A. The undifferentiated gonadal system is the same for both sexes. In males, the SRY gene, located on the Y chromosome, is activated during development, producing testis-determining factor, which results in the gonads becoming testes. B. The testes begin releasing testosterone and Müllerian inhibiting substance, which cause the Wolffian ducts to become the vas deferens, seminal vesicles, and epididymis and cause the Müllerian ducts to degenerate. C. The presence of testosterone also causes the development of the penis and prostate gland in the fully developed system. 'Male Gonad Differentiation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

In females, when the SRY gene and secreted hormones are absent, the gonads differentiate into the ovaries, the Müllerian ducts develop into the fallopian tubes, uterus, and vagina, and the Wolffian ducts degenerate.

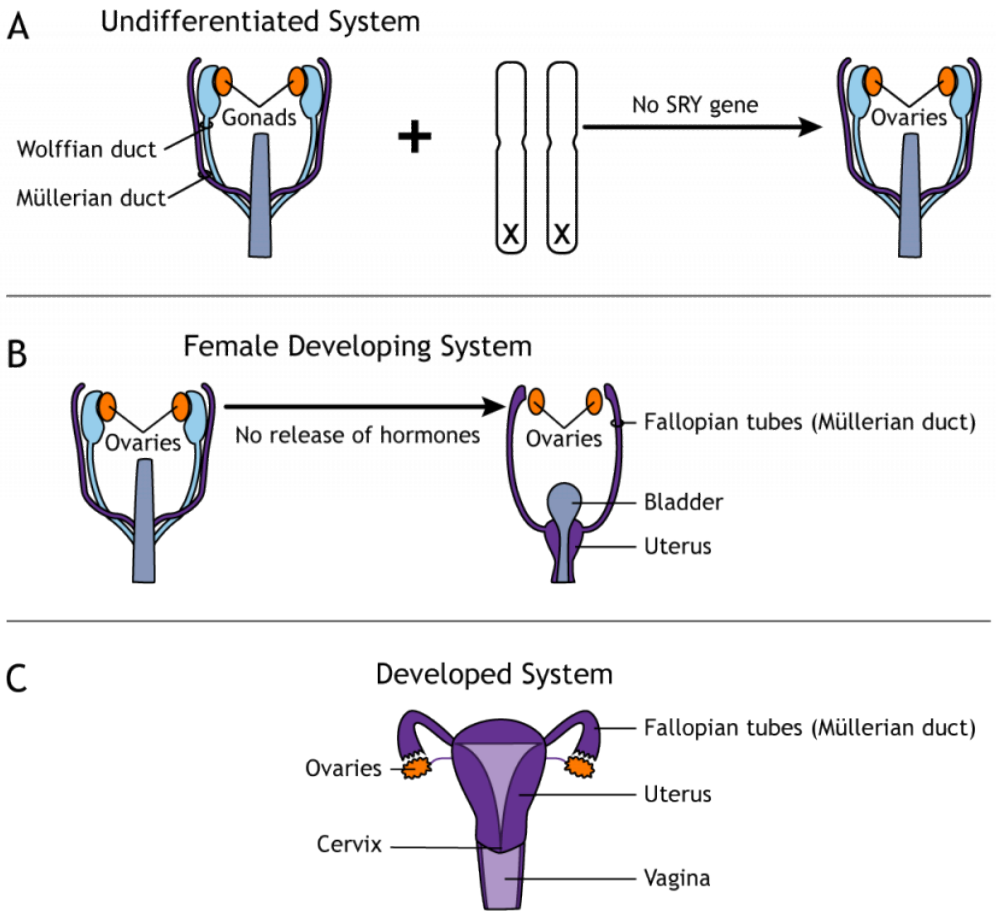

Figure 35.5. A. The undifferentiated gonadal system is the same for both sexes. In the absence of the SRY gene during the 6th to 12th week of gestation, the gonads become the ovaries. B. The ovaries do not produce any hormones during development which causes the Müllerian ducts to become the fallopian tubes, uterus, and vagina, and the Wolffian ducts degenerate. C. In the fully developed system, the cervix is the lower part of the uterus, which separates the uterus from the vagina. 'Female Gonad Differentiation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Hormones During Development

In addition to differentiating the reproductive duct system, the presence or absence of gonadal hormones during development also differentiates the rest of the body, including the brain. Testosterone causes the brain, body, and behavior of the individual to be masculinized and defeminized. The quiescent ovaries do not release hormones which causes the brain, body, and behavior of the individual to be feminized and demasculinized.

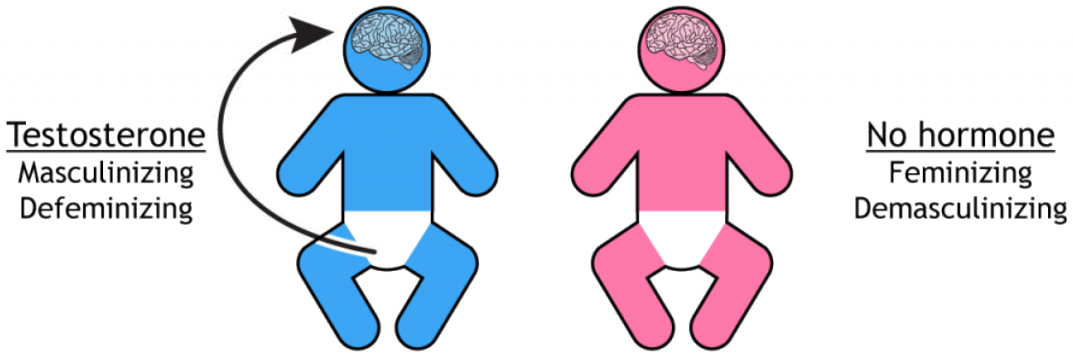

Figure 35.6. Testosterone presence during development masculinizes and defeminizes the brain, body, and behavior. No hormone exposure during development feminizes and demasculinizes the brain, body, and behavior. 'Developmental Hormones' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Critical Period

These hormonal effects of secreted testosterone on the brain must take place during a specific time in development, called a critical period. This early role of testosterone is called an organizational effect and results in a permanent change in the nervous system and therefore behavior. Organizational effects of hormones lead to major, generally irreversible, aspects of cell and tissue differentiation. Organizational effects take place during critical periods like prenatal development and puberty.

In adulthood, the same hormones trigger physiological or behavioral responses like inducing reproductive behavior or ovulation, but these influences, called activational effects, are reversible and short-lived. Removal of the activating hormone will cause the behavior to stop, but replacement later will cause the response to begin again because the brain has previously been organized to produce those behaviors when hormones are present.

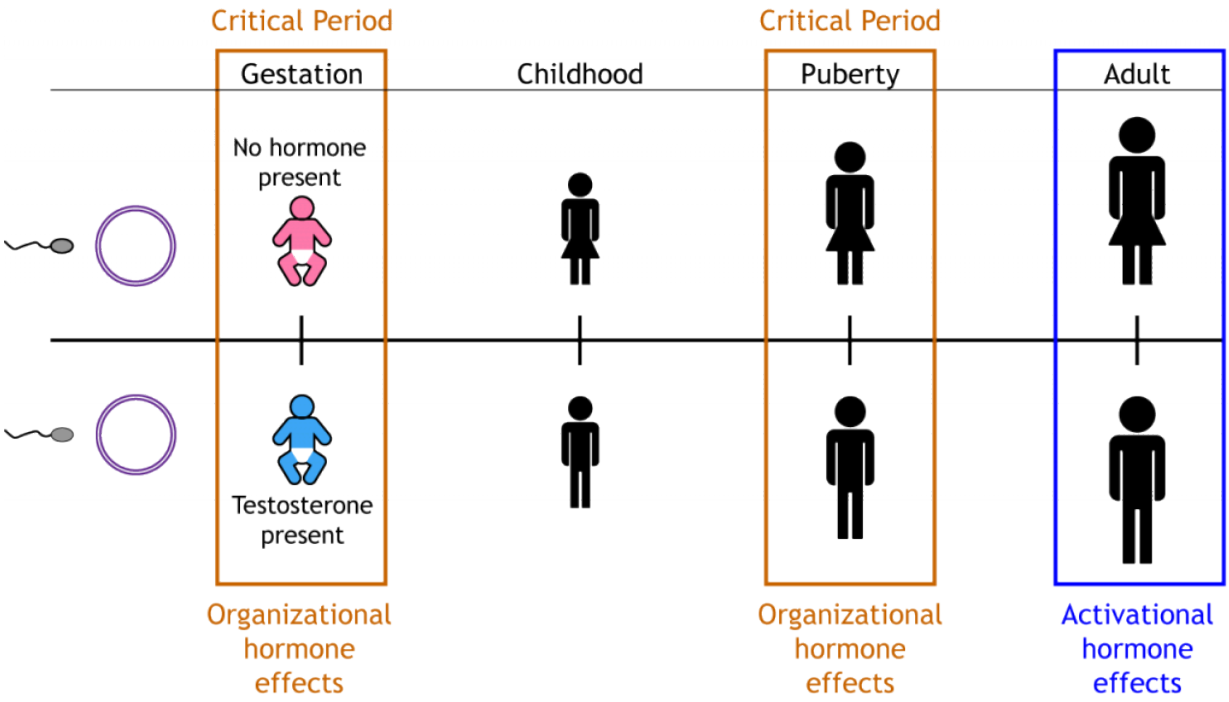

Figure 35.7. Hormones can have long-lasting, organizational effects when present during critical periods such as during the prenatal period or puberty. During these critical periods, hormones will alter the structure of the nervous system, setting up cells and circuits needed to display sex-typical behaviors later in life. Those sex-typical behaviors are then activated in adulthood by the presence of gonadal hormones. 'Organizational versus Activational' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The role of activational hormones can be demonstrated by adult castration in male rats. Healthy males with intact testes will show sexual behavior when placed with a female rat. Castration, the removal of the testes, will cause males to stop showing sexual behavior because the activating hormone, testosterone, is no longer present. However, if the castrated males receive testosterone replacement, they will resume showing sexual behavior. The sexual behavior brain circuit was organized during development by exposure to gonadal hormones, and in adulthood that circuit can be activated by testosterone. The adult behavior can only be seen when the activating hormone is present.

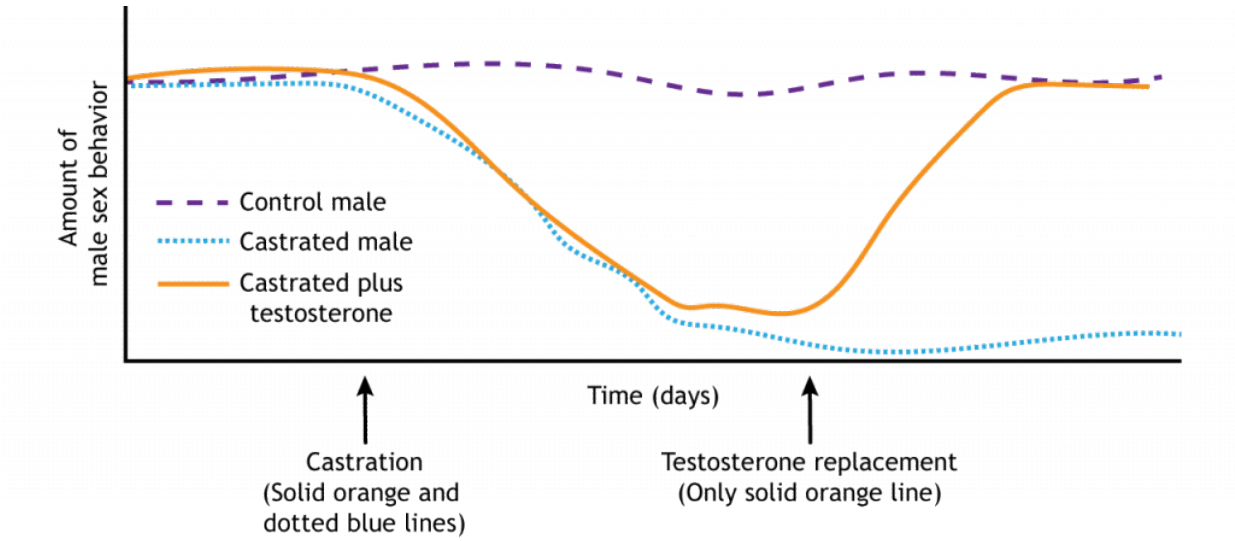

Figure 35.8. Removing testosterone by castrating an adult male rat will decrease the amount of sexual behavior displayed because the hormone can no longer activate sexual behaviors (solid orange and dotted blue lines). However, if the castrated animal is treated with testosterone, sexual behavior returns (solid orange line). 'Castration Effects' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Key Takeaways

- During development, the body and the brain undergo either A) feminization and de-masculinization or B) masculinization and de-feminization
- The sex chromosomes, X and Y, make up one pair of the 23 total pairs of chromosomes in humans
- Females are genetically XX and males are genetically XY
- The SRY gene on the Y chromosome is responsible for the development of the male reproductive system
- In the absence of hormones, the female reproductive system develops
- Organizational, long-lasting hormone effects take place during critical periods in

development
- Activational, short-lasting hormone effects “activate” the circuits organized by hormones in development

Video Version of Lesson

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=720#oembed-1

36.

MASCULINIZING EFFECTS OF ESTROGEN

Resources

- Key Takeaways
- Video Version

Steroid hormones like testosterone and estradiol are able to pass through the phospholipid membrane of a neuron. Some neurons express receptors for these hormones. Androgen receptors bind androgens like testosterone while estrogen receptors bind estrogens like estradiol. When a hormone binds to a receptor in the neuron, the hormone-receptor complex dimerizes and moves into the nucleus where it can bind to specific sites on the DNA and act as a transcription factor to turn on or off certain genes.

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Animation 361. Steroid hormones, like testosterone and estradiol, can cross the cell membrane without assistance. In the cell, the hormones can bind to hormone receptors, which dimerize, move to the nucleus, and act as transcription factors on the DNA. 'Testosterone Action' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Testosterone Pathways in the Cell

When the testes secrete testosterone during the prenatal critical period, the effect is to masculinize and defeminize the brain, body, and behavior, and this is accomplished through the transcription of a specific set of genes. However, many of those genes are not transcribed by the action of androgen receptors interacting with the DNA. When testosterone enters the cell, it does not always bind to androgen receptors. Some neurons also express proteins that can break testosterone down into its metabolites. 5-alpha reductase converts testosterone into dihydrotestosterone, or DHT, another androgen that is able to bind the androgen receptor. The enzyme aromatase converts testosterone into estradiol, an estrogen that can bind to the estrogen receptor.

Estrogen Effects

In some mammals, like rodents, this conversion of testosterone to estradiol is the main process by which neurons and the brain are masculinized. The estrogen receptors cause the transcription of masculinizing genes. Therefore, somewhat surprisingly, even though estrogen is typically thought of as a female hormone, its actions during development are responsible for much of the masculinization that occurs in the brain in some animals. It should be noted, though, that estrogen does not appear to have these same masculinizing effects during human development.

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Animation 36.2. After testosterone enters the cell, if it does not bind to an androgen receptor, it can be metabolized by enzymes in the cell. 5-alpha reductase converts testosterone into dihydrotestosterone. DHT, like testosterone, can bind to an activate androgen receptors. The enzyme aromatase converts testosterone into estradiol. Estradiol is an estrogen and can bind to and activate estrogen receptors. During developmental critical periods, the aromatization of testosterone to estradiol leads to the transcription of masculinizing genes in some animals like rodents. 'Aromatization' by Casey Henley is

Key Takeaways

- Steroid hormones can cross the phospholipid bilayer
- Hormone receptors dimerize, move to the nucleus, and act as transcription factors
- In the cell, testosterone can
    - Bind to androgen receptors
    - Be converted to dihydrotestosterone by 5-alpha reductase
    - Be converted to estradiol by aromatase
- In some animals, estradiol action is responsible for the transcription of masculinizing and de-feminizing genes

Video Version of Lesson

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=722#oembed-1

37.

MOTIVATION AND REWARD

Motivated behaviors are voluntary behaviors that individuals find rewarding or pleasurable. Certain behaviors or stimuli, like food or sex, are naturally rewarding because they are necessary for the survival of a species; they are adaptive, and the nervous system has evolved to make these behaviors pleasurable. Rewarding stimuli increases brain activation in brain regions that comprise the reward circuit.

Resources

- Key Takeaways
- Video Version

Reward Circuit

The reward circuit depends on the action of dopamine. Dopamine is synthesized and released by neurons located in the ventral tegmental area (VTA), a midbrain region adjacent to the substantia nigra (remember the substantia nigra from the basal ganglia chapter).

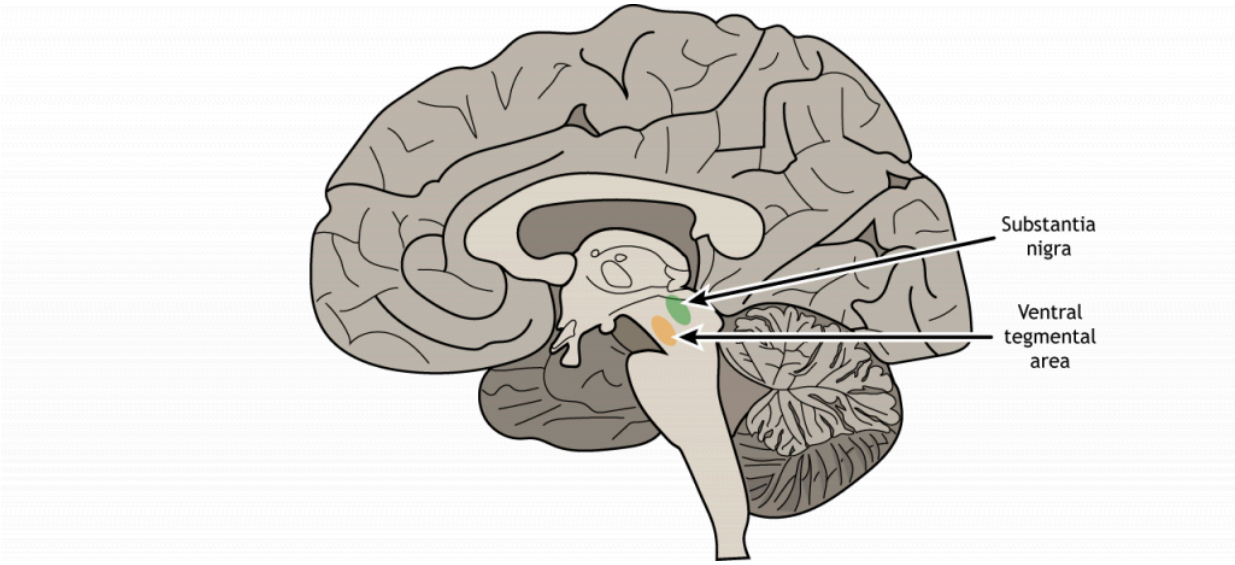


Figure 37.1. The ventral tegmental area (orange region) is located in the midbrain region near the substantia nigra (green region). Both regions release dopamine onto downstream targets. 'Ventral Tegmental Area' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

There are two primary pathways from the VTA that are important for reward. The mesolimbic pathway connects the VTA to the nucleus accumbens, a region located in the ventral striatum (again, remember the basal ganglia chapter). The mesocortical pathway connects the VTA with the prefrontal cortex.

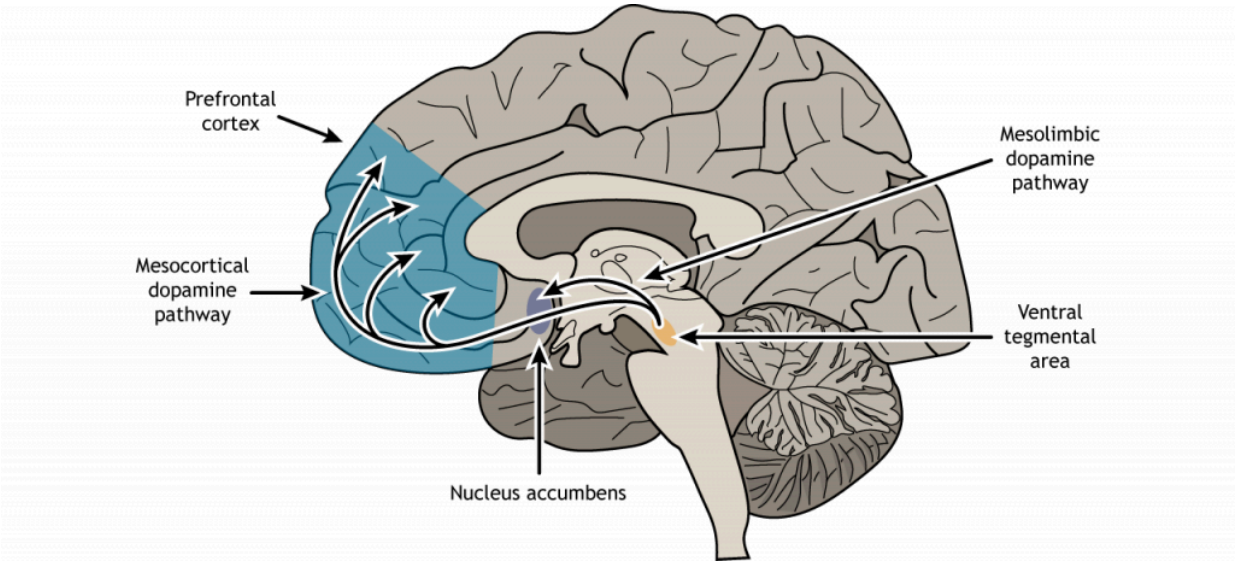


Figure 37.2. The ventral tegmental area (orange region) releases dopamine into the nucleus accumbens (purple region) via the mesolimbic pathway and releases dopamine into the prefrontal cortex (blue region via the mesocortical pathway. 'Mesolimbic and Mesocortical Pathways' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

View the amygdala using the BrainFacts.org 3D Brain

View the amygdala using the BrainFacts.org 3D Brain

Early experimental studies showed that rodents with an electrode placed along these dopaminergic pathways will complete tasks, like a bar press, to self-stimulate the regions. Often the animals would forgo other behaviors, like eating, to continue pressing the bar. Treatment with drugs that block the receptors for dopamine reduce the self-stimulating behavior, indicating that dopamine is the critical neurotransmitter involved in making the stimulation of these brain regions rewarding.

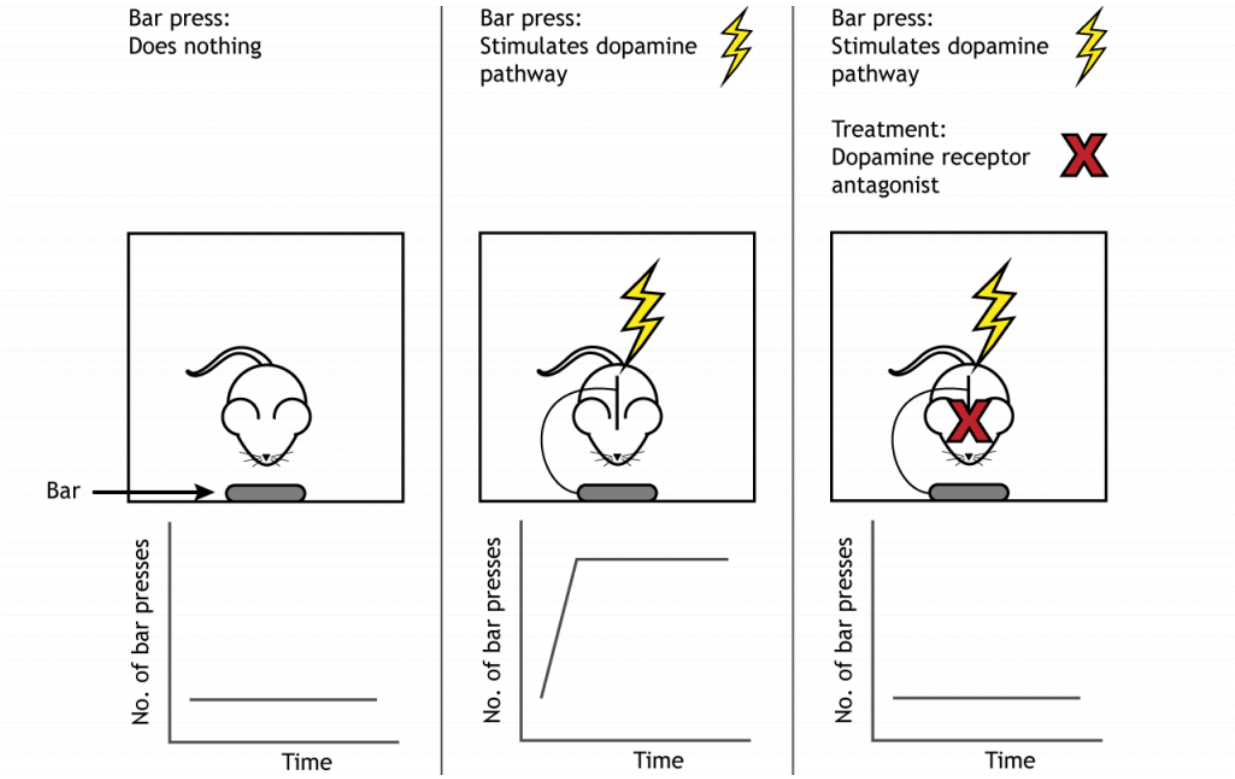


Figure 37.3. When an activity like bar pressing is paired with stimulation of the reward system circuitry, rats will show a marked increased in the behavior (center panel) compared to controls (left panel). If a dopamine receptor antagonist is given in addition to the bar press stimulation, the behavior decreases, presumably because dopamine cannot have its reward effect (right panel). 'Dopamine Pathway Stimulation' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

However, continued research suggests the connection between dopamine release and reward may not be as simple as the self-stimulation studies imply. It appears that it is not the reward itself that increases dopamine, but the predicted expectation of the reward . Dopamine signaling increases during anticipation of a predicted reward. If the level of reward is more than predicted, reward learning occurs, and dopamine signaling and motivation to repeat that behavior increases. If the level of reward is less than predicted, then dopamine signaling decreases as does motivation to repeat the behavior.

Rewarding stimuli

Natural rewards that increase survival and fitness of a species activate the reward circuit. These behaviors and stimuli include certain food (like those containing high sugar or fat levels), social bonding, parental bonding, and sex. Most drugs of abuse also activate the reward circuit and dopamine signaling, which plays a critical role in the formation of addiction. For example, cocaine blocks dopamine reuptake into presynaptic VTA terminals; heroin and nicotine increase dopamine release from the VTA. These alterations increase dopamine effect on neurons in the nucleus accumbens.

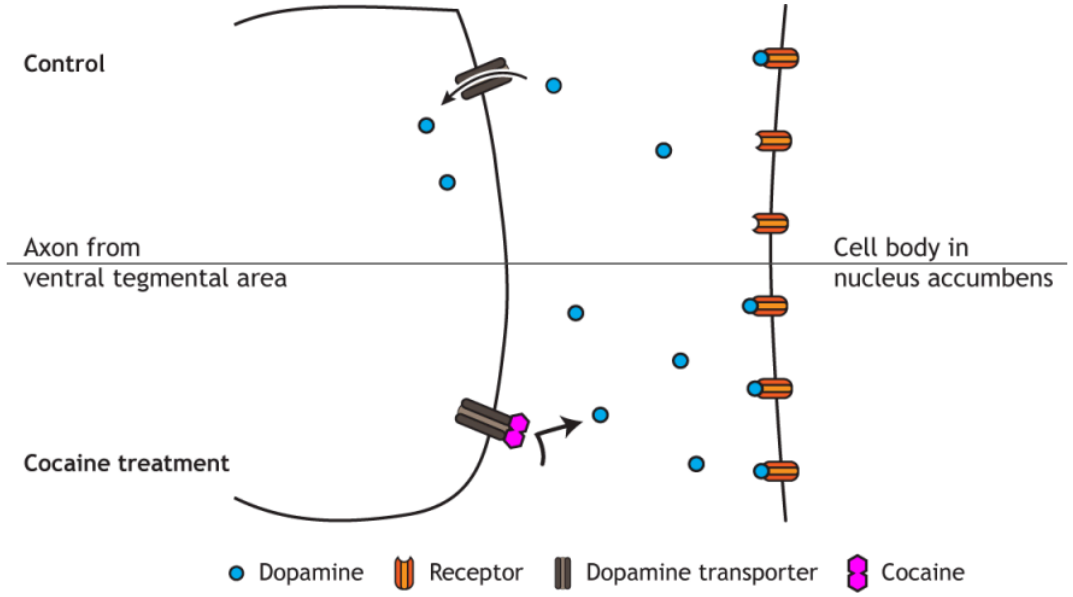


Figure 37.4. Control (top) panel: Dopamine effects are typically terminated by reuptake into the presynaptic terminal via the dopamine transporter (DAT). Cocaine treatment (bottom) panel: Cocaine blocks DAT, preventing reuptake of dopamine. The increased action of dopamine on the nucleus accumbens leads to increased activation of the reward circuit, a mechanism underlying addiction to the drug. 'Cocaine Effects' 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 reward circuit involves dopamine release from the ventral tegmental area into the nucleus accumbens and prefrontal cortex.
- Self-stimulation experiments demonstrate the role of dopamine and the reward circuit
- Dopamine signaling likely predicts reward value and can be altered if predicted outcomes differ from actual outcomes
- Drugs of abuse act upon the reward circuit

Video Version of Lesson

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://openbooks.lib.msu.edu/neuroscience/?p=1427#oembed-1

38.

SOCIAL BONDING

Long-term attachment, which includes pair bonding with a sexual partner and parental bonding with offspring, are naturally rewarding behaviors in some species of mammals.

Hormone control

The hypothalamus is a critical region for the formation of social bonds. Magnocellular neurosecretory cells, the larger type of neurosecretory cell compared to parvocellular neurons, send axons from the hypothalamus down to pituitary stalk where they terminate on capillaries of the general circulation located within the posterior pituitary. Therefore, unlike the control of stress and gonadal hormones, where the hypothalamic neurons release hormones onto anterior pituitary endocrine cells, release of hormones from the posterior pituitary comes directly from hypothalamic neurons.

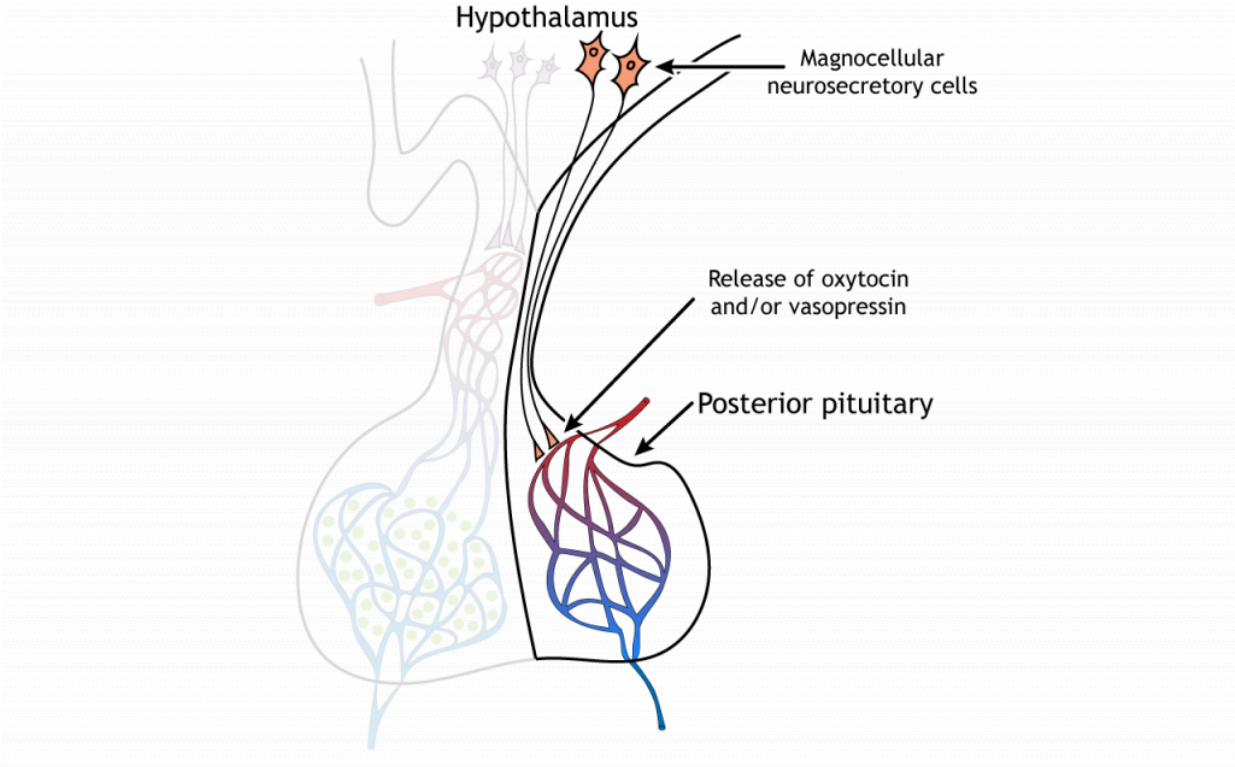


Figure 38.1. The hypothalamic magnocellular neurosecretory neurons release oxytocin and/or vasopressin into the general circulation via capillaries located in the posterior pituitary. 'Oxytocin and Vasopressin Release' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

The magnocellular neurons synthesize and release oxytocin and vasopressin, two neuropeptides, into the blood. Oxytocin, often referred to as the love hormone, promotes social bonding. It is released during reproduction and alsocauses uterine contractions during labor and the milk letdown reflex after birth. Vasopressin, also called antidiuretic hormone, plays a role in regulating salt concentration in the blood by acting on the kidneys to promote water retention and decrease urine production. Vasopressin has also been shown to be involved in bonding, parenting, territoriality, and mate guarding in some animals.

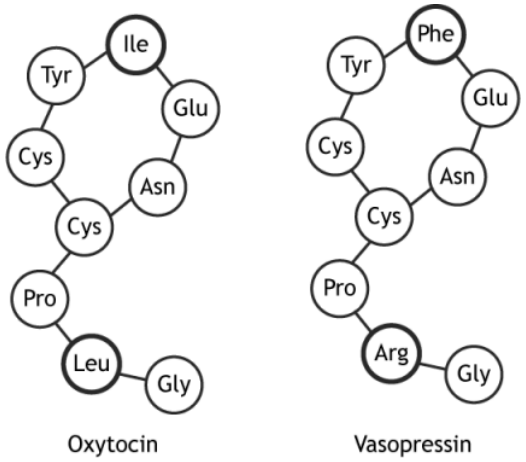


Figure 38.2. Amino acid sequences of oxytocin and vasopressin. The amino acids that are different between the two neuropeptides are bolded. 'Oxytocin and Vasopressin' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Animal Model

Much of the research on social attachment has been done using voles as the animal model. Voles are useful because there are closely related species that display considerably different reproductive behavior. The prairie vole is a monogamous rodent, with males and females displaying strong pair bonds and both sexes showing parental behavior. The montane vole, on the other hand, is a non-social species. Pair bonds are not formed, and only the female cares for the young. Differences in brain and behavior can be studied between these species.

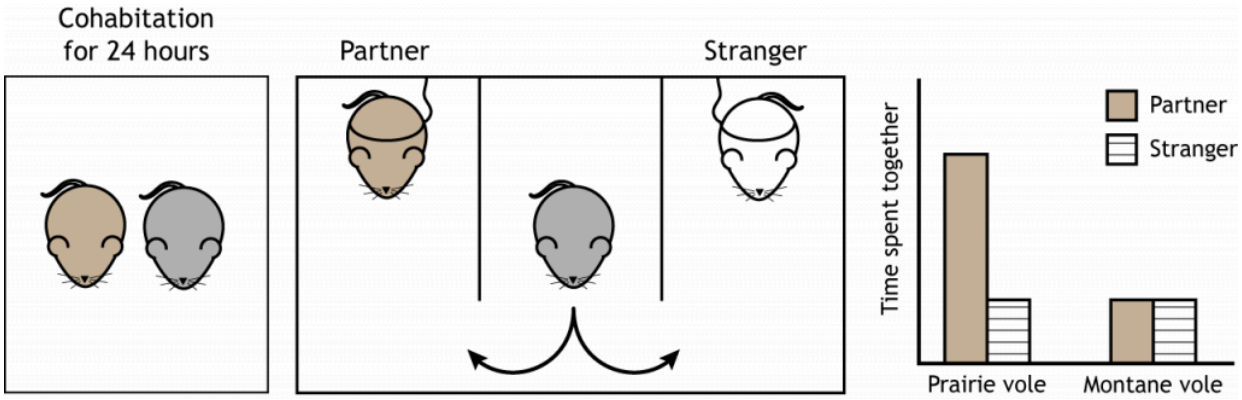


Figure 38.3. Partner preference tests can be conducted to examine social bonds in voles. First, voles are allowed to cohabitate and mate for 24 hours. Then, one of the pair is placed into a preference testing chamber and is allowed to spend time with either the partner animal or a novel stranger. In social voles like the prairie vole, mating will induce a strong preference for the partner animal over a stranger. This effect is not seen in non-monogamous voles like the montane vole. 'Vole Preference' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

In social voles, oxytocin and vasopressin are released by the hypothalamus in response to mating and act on regions of the reward and limbic systems. Female prairie voles express higher levels of oxytocin receptors in the nucleus accumbens compared to montane voles, whereas male prairie voles express higher levels of vasopressin receptors in the ventral pallidum compared to montane voles. The nucleus accumbens (also called ventral striatum) and ventral pallidum are both located in the basal ganglia and are involved in the limbic loop, which is responsible for processing of emotions, rewards, and motivation.

Human bonding

Oxytocin, vasopressin, and the reward system also appear to be important for bonding in humans. When presented with pictures of either their own children or partners, subjects in an fMRI show increased activation in regions like the ventral tegmental area and striatum compared to when viewing pictures of friends. These regions are also known to express oxytocin and vasopressin receptors, and the hormones are released during times of bond formation, like breastfeeding and intercourse.

39.

STUDYING FEAR

Scientists have long realized there are at least two distinct types of fear:

- Innate fear in which subjects avoid certain stimuli such as snakes or spiders even though they may never have seen them before
- Learned fear in which a stimulus or situation causes arousal or anxiety because it has been associated with a painful or negative experience in the past

There are two important protocols used to examine learned fear: fear conditioning and conditioned defeat.

Fear Conditioning

One of the best studied laboratory models of fear comes from the work of John LeDoux who studied the brain circuit that mediates learned or conditioned fear in laboratory rats. In these studies, LeDoux used a classical conditioning procedure to induce what he called "conditioned fear". In classical conditioning (think Pavlov's dogs), a neutral stimulus that normally would not cause any physiological response (called a conditioned stimulus, e.g., a ringing bell) is paired with a meaningful stimulus (called an unconditioned stimulus, e.g., the presence of food) that elicits a behavioral response (unconditioned response, e.g., drooling). Eventually, the behavior (drooling) occurs in response to the conditioned stimulus (bell) alone.

Instead of pairing the conditioned stimulus with a positive unconditioned stimulus like food, LeDoux paired the conditioned stimulus with an electrical shock. After pairing the shock to the stimulus multiple times, the animals responded to the conditioned stimulus alone (no shock) in the same way they did to the electrical shock alone. This is referred to as the conditioned emotional response.

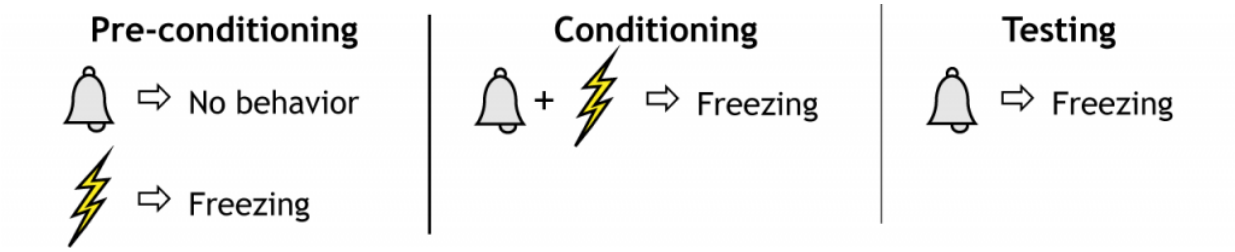


Figure 39.1 Fear conditioning. Left panel: Prior to conditioning, the conditioned stimulus (an auditory tone) has no effect on behavior. The unconditioned stimulus (shock) leads to startle-like behaviors that researchers refer to as "freezing". Middle panel: During fear conditioning, the tone is paired with the shock and freezing behavior is seen. Right panel: After successful fear conditioning, the tone alone can elicit freezing behavior. 'Fear Conditioning' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Conditioned Defeat

In this model the experimental subject (the animal whose behavior is being examined) is placed in the home cage of a larger, resident animal. This typically results in aggressive behaviors displayed by the resident animal toward the experimental subject. The resident animal will usually win the encounter because it is larger and in its own territory. The experimental animals will show submissive and defensive posturing and does not attack or threaten its opponent.

Experiencing this defeat has major long-lasting effects on the experimental subject. Following defeat, the animal rarely shows aggression even to non-aggressive hamsters placed in the subject's home cage (an intruder would typically cause aggression). Because this paradigm has parallels with the earlier fear conditioning studies that paired an acoustical tone with electrical shock to the feet, it is often referred to as "conditioned defeat;" the experimental subject has been conditioned to respond to all other hamsters with submissive defensive postures.

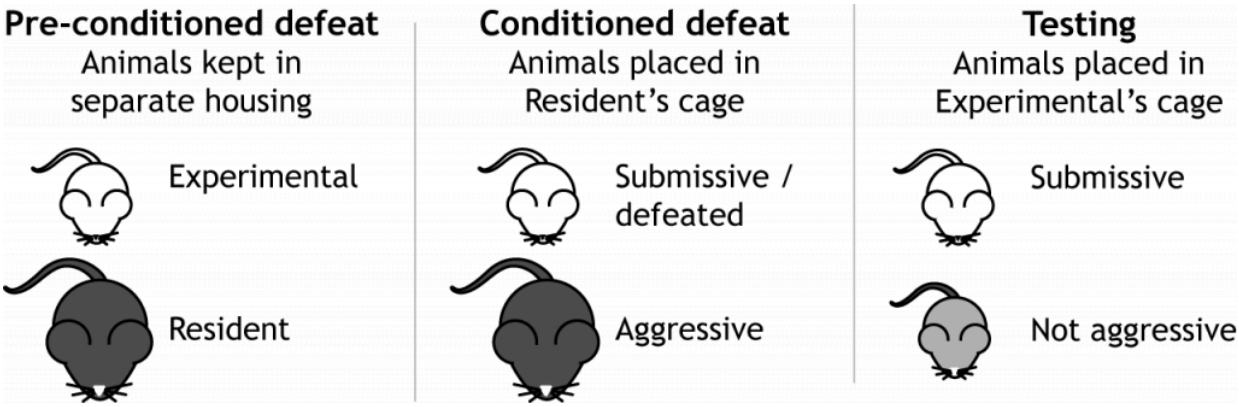


Figure 39.2. Conditioned defeat. Left panel: Prior to defeat, the experimental subject and resident animal are kept separate, and behavior is normal. Middle panel: During the conditioned defeat trial, the experimental animal is placed into the home cage of the larger, resident animal. The resident will defend its territory, acting aggressively toward the smaller, experimental animal. The experimental animal will show submissive and defensive behaviors. Right panel: After defeat, the experimental animal will show submissive behaviors even toward non-aggressive animals placed into the experimental animal's home cage. 'Conditioned Defeat' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Key Takeaways

- Learned fear can be studied using either fear conditioning or conditioned defeat tests
- Fear conditioning pairs a neutral stimulus, like a light or a tone, to a harmful stimulus, like a shock
- Conditioned defeat submits an experimental animal to aggressive behaviors from another animal, after which the experimental animal will continuously show submissive behaviors to others

40.

POST-TRAUMATIC STRESS DISORDER

What is Post-Traumatic Stress Disorder (PTSD)?

PTSD is an anxiety-like disorder that develops after experiencing or witnessing some form of trauma. It is the only psychiatric disorder with a definitive known cause – traumatic stress. PTSD causes an altered, exaggerate stress response. Those individuals diagnosed with PTSD may feel stressed or frightened even when they are in a safe environment, and they may have triggers that activate their stress response.

Who can get PTSD?

Anyone can be diagnosed with PTSD at any point in their lives. Some of the most common events that lead to a PTSD diagnosis include combat experience, physical, emotional, or sexual assault or abuse, accidents, and natural disasters. Women are twice as likely as men to be diagnosed with PTSD. Genetic influence appears to account for approximately 30-40% of risk.

Symptoms of PTSD

The symptoms of PTSD are usually divided into three categories:

- Re-experiencing
- Avoidance
- Hyper-arousal

Re-experiencing symptoms arise when stimuli cause PTSD patients to relive their traumatic experience in flashbacks, frightening thoughts, or nightmares.

Avoidance symptoms arise when PTSD patients feel lack or emotion, lose interest in activities they once enjoyed, or withdraw from family and friends. These symptoms may be a result of trying to avoid reminders or triggers of the traumatic event.

Hyper-arousal symptoms appear as increased anxiety or feeling tense in safe environments. PTSD patients can be easily frightened, may have trouble sleeping, and may have frequent angry outbursts.

Nervous System Dysfunction

PTSD patients show differences in structure and function of certain brain regions compared to healthy controls. Not surprisingly, areas critical for the stress response are often altered. The hippocampus is involved in the recognition of environmental cues. The amygdala has a crucial role in the detection of threat, fear learning, fear expression and heightening memory for emotional events. The prefrontal cortex is involved in executive functions and decision making. In PTSD, these three regions are altered structurally and functionally. The hippocampus and prefrontal cortex show reduced activity and volume, and the amygdala has increased activity. These changes lead to the hippocampus and prefrontal cortex being less effective at inhibiting the stress response while the amygdala becomes more effective at activating it, resulting in increased stress sensitivity and a generalization of the fear response to non-threatening stimuli.

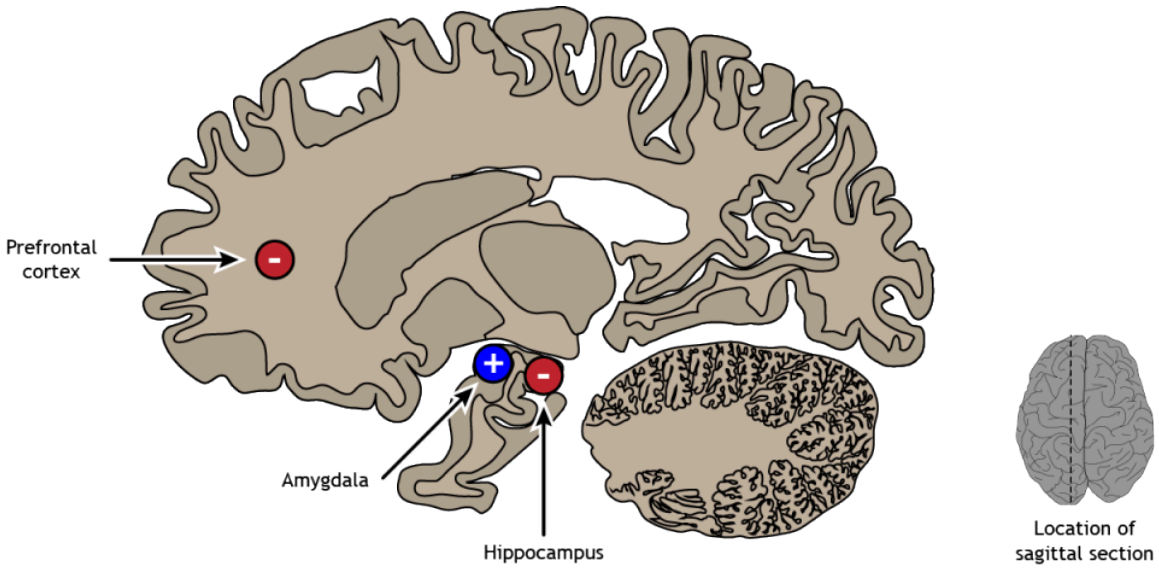


Figure 40.1. PTSD patients show an underactive prefrontal cortex and hippocampus and an overactive amygdala. The sagittal section is taken slightly lateral to the midline of the brain. 'PTSD Sagittal' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

IMAGES OF ANIMATIONS

Chapter 1

Animation 1

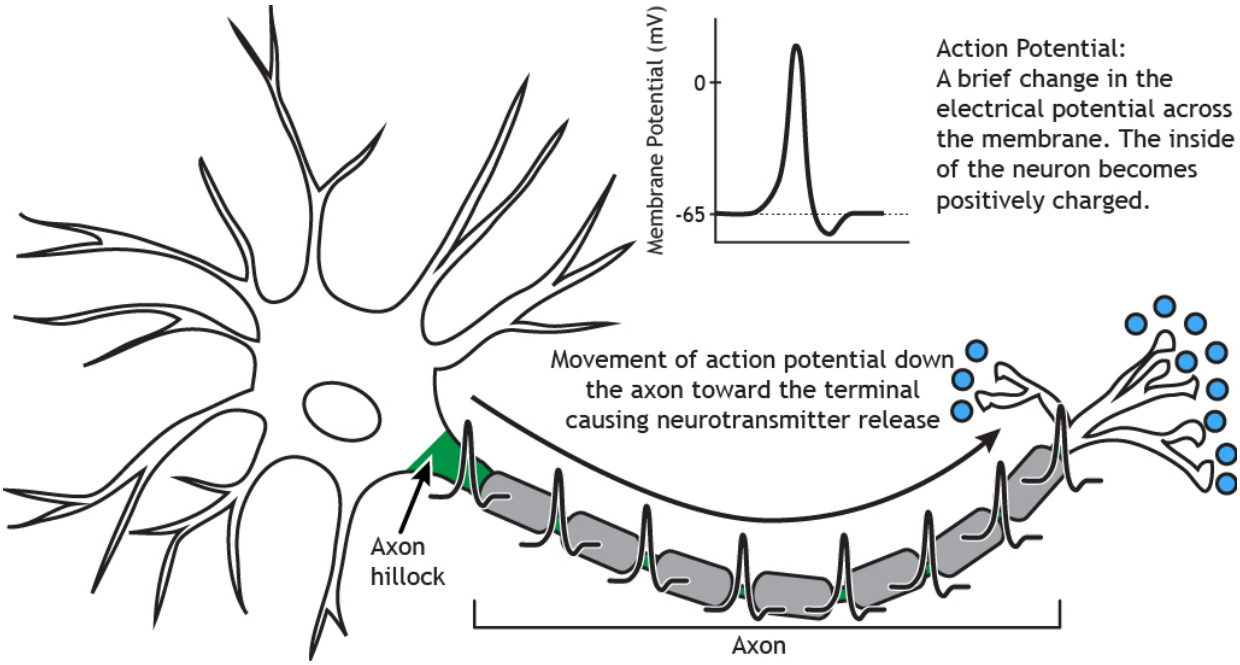


Figure 1.11. The action potential is a brief but significant change in electrical potential across the membrane. The membrane potential will move from a negative, resting membrane potential, shown here as -65 mV, and will rapidly become positive and then rapidly return to rest during an action potential. 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.

Chapter 2

Animation 1

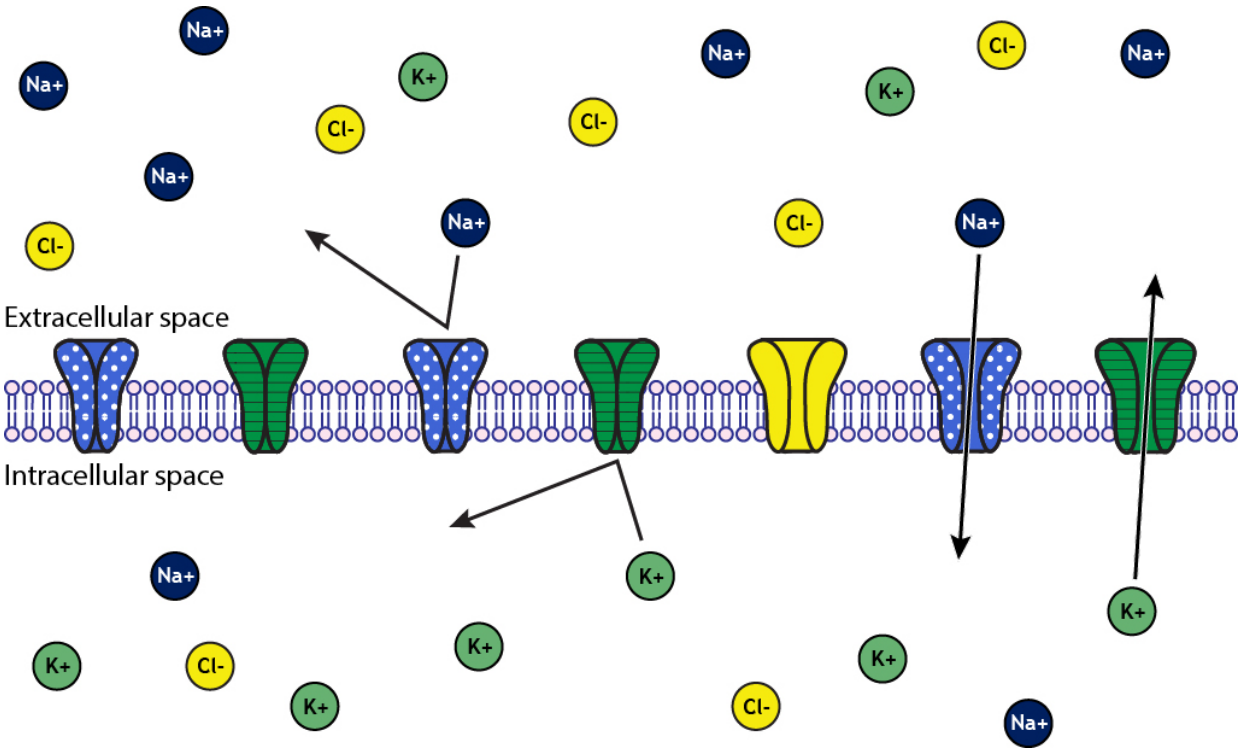


Figure 2.3. When ion channels in the membrane are closed, ions cannot move into or out of the neuron. Ions can only cross the cell membrane when the appropriate channel is open. For example, only sodium can pass through open sodium channels. The dotted, blue channels represent sodium channels; the striped, 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.

Animation 2

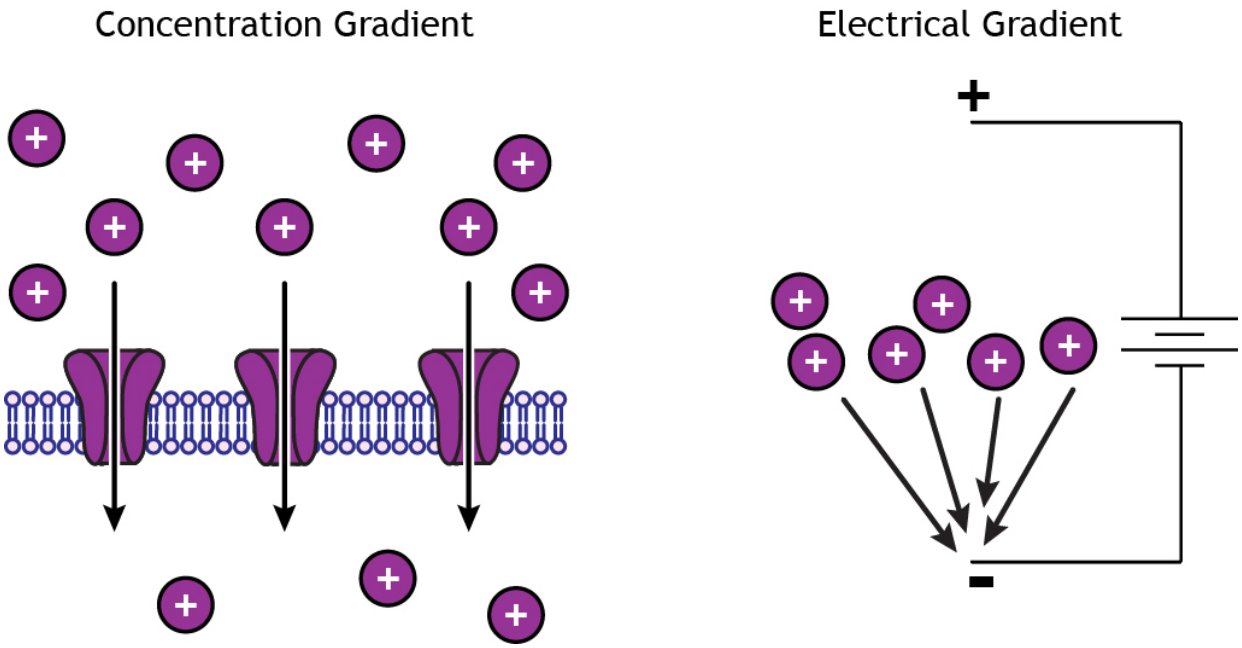


Figure 2.4. Concentration and electrical gradients drive ion movement. Ions diffuse down concentration gradients from regions of high concentration to regions of low concentration. Ions also move toward regions of opposite electrical charge. 'Gradients' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial (CC-BY-NC) 4.0 International License.

Animation 3

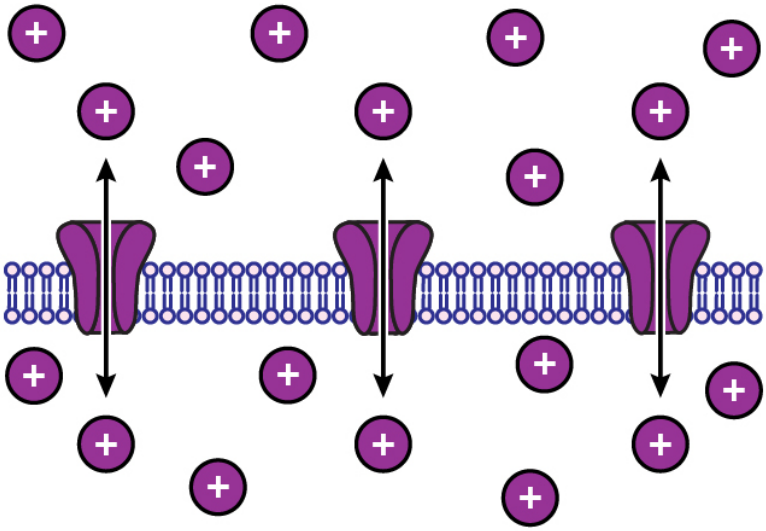


Figure 2.5. When an ion is at equilibrium, which occurs when the concentration and electrical gradients acting on the ion balance, there is no net movement of the ion. The ions continue to move across the membrane through open channels, but the ion flow into and out of the cell is equal . In this animation, 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.

Chapter 3

Animation 1

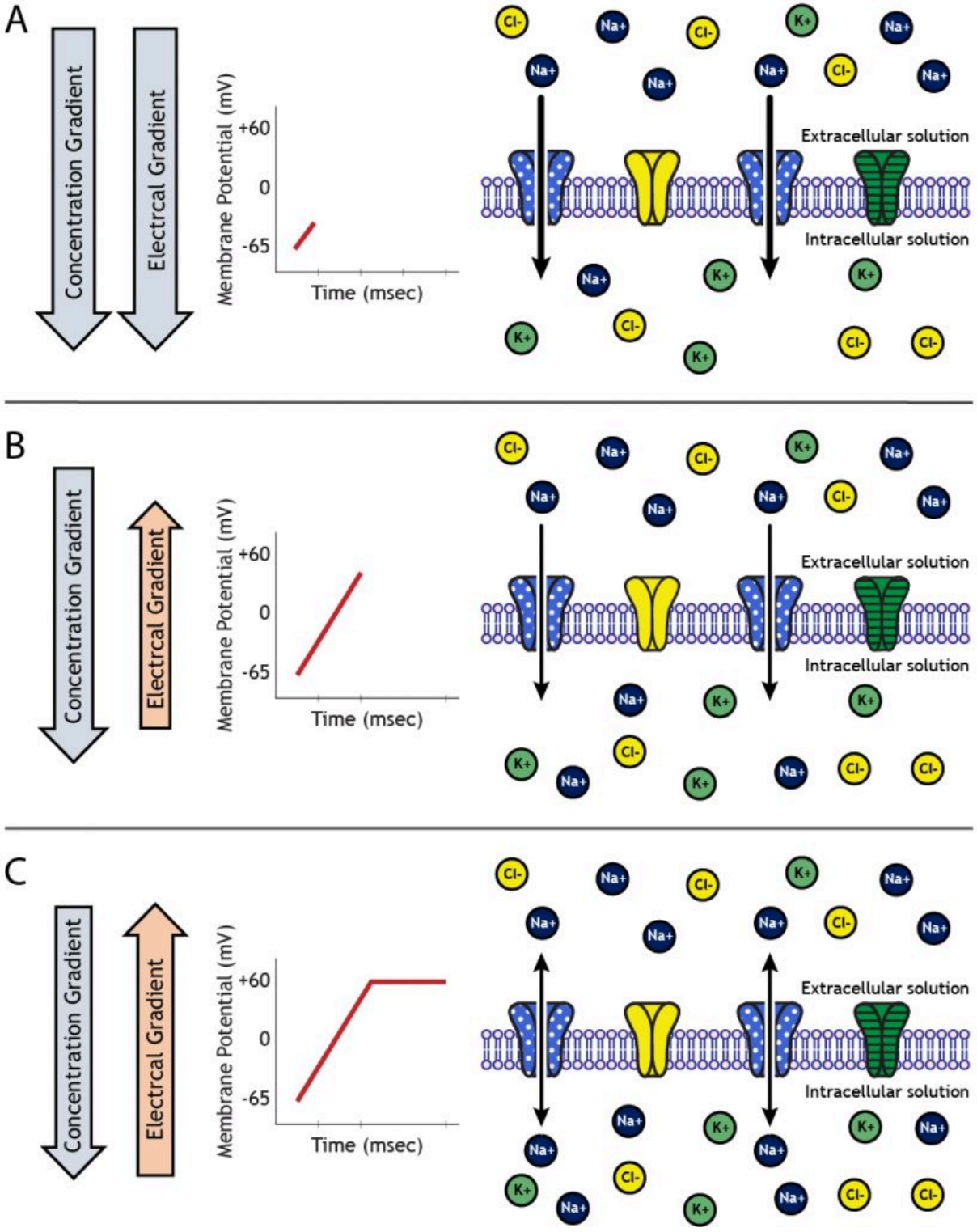


Figure 3.7. A) At rest, both the concentration and electrical gradients for sodium point into the cell.

As a result, sodium flows in. As sodium enters, the membrane potential of the cell decreases and becomes more positive. B) 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. C) 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 Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Chapter 4

Animation 1

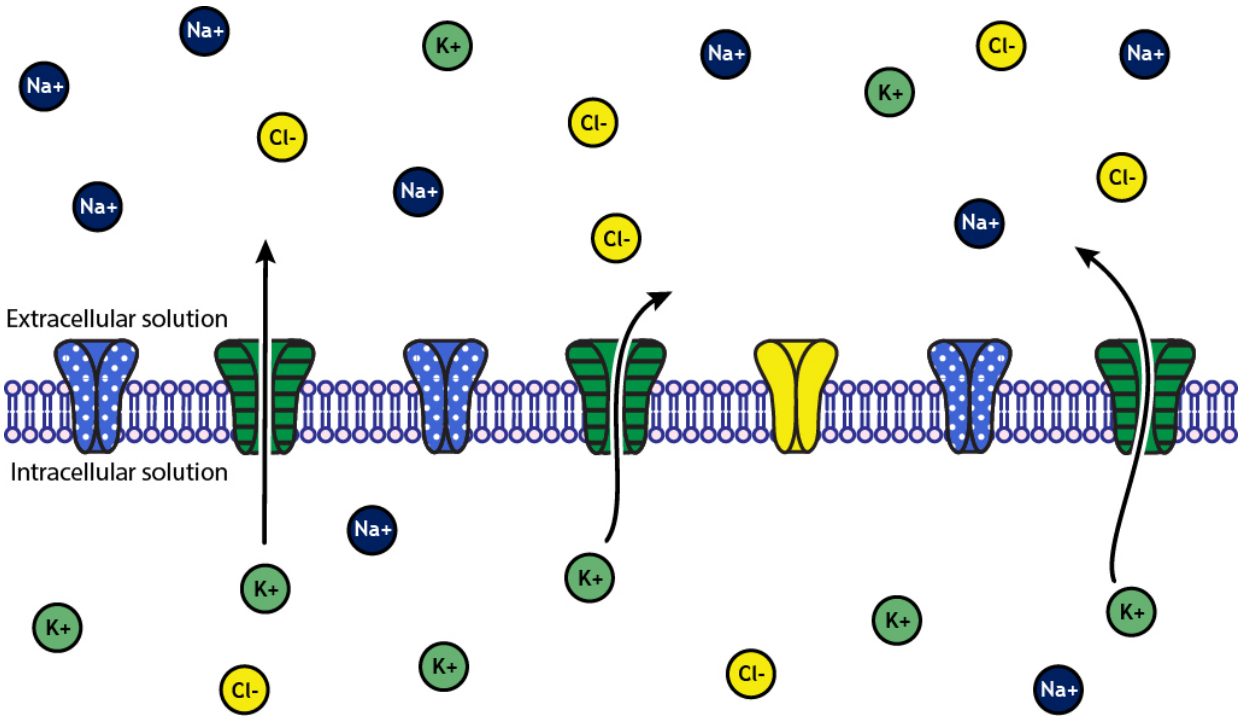


Figure 4.3. Electrochemical gradients drive potassium out of the cell, removing positive charge, making the cell's membrane potential more negative, in the direction of potassium's equilibrium potential. The dotted, blue channels represent sodium leak channels; the striped, green channels represent potassium leak channels; the solid yellow channels represent chloride leak channels. 'Potassium at Rest' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Animation 2

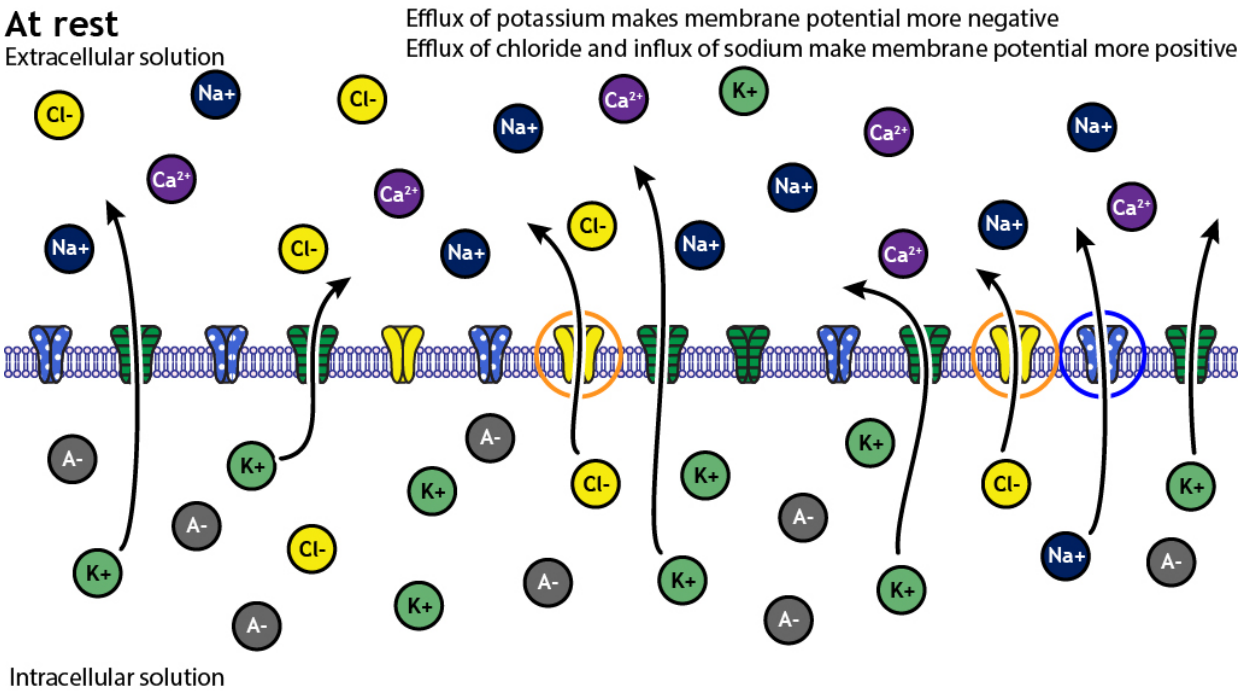


Figure 4.4. The membrane is most permeable to potassium at rest, and this leads to potassium efflux. However, the membrane is also permeable to chloride and sodium, and the flow of these ions keep the resting membrane potential more positive than potassium's equilibrium potential. The dotted, blue channels 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.

Animation 3

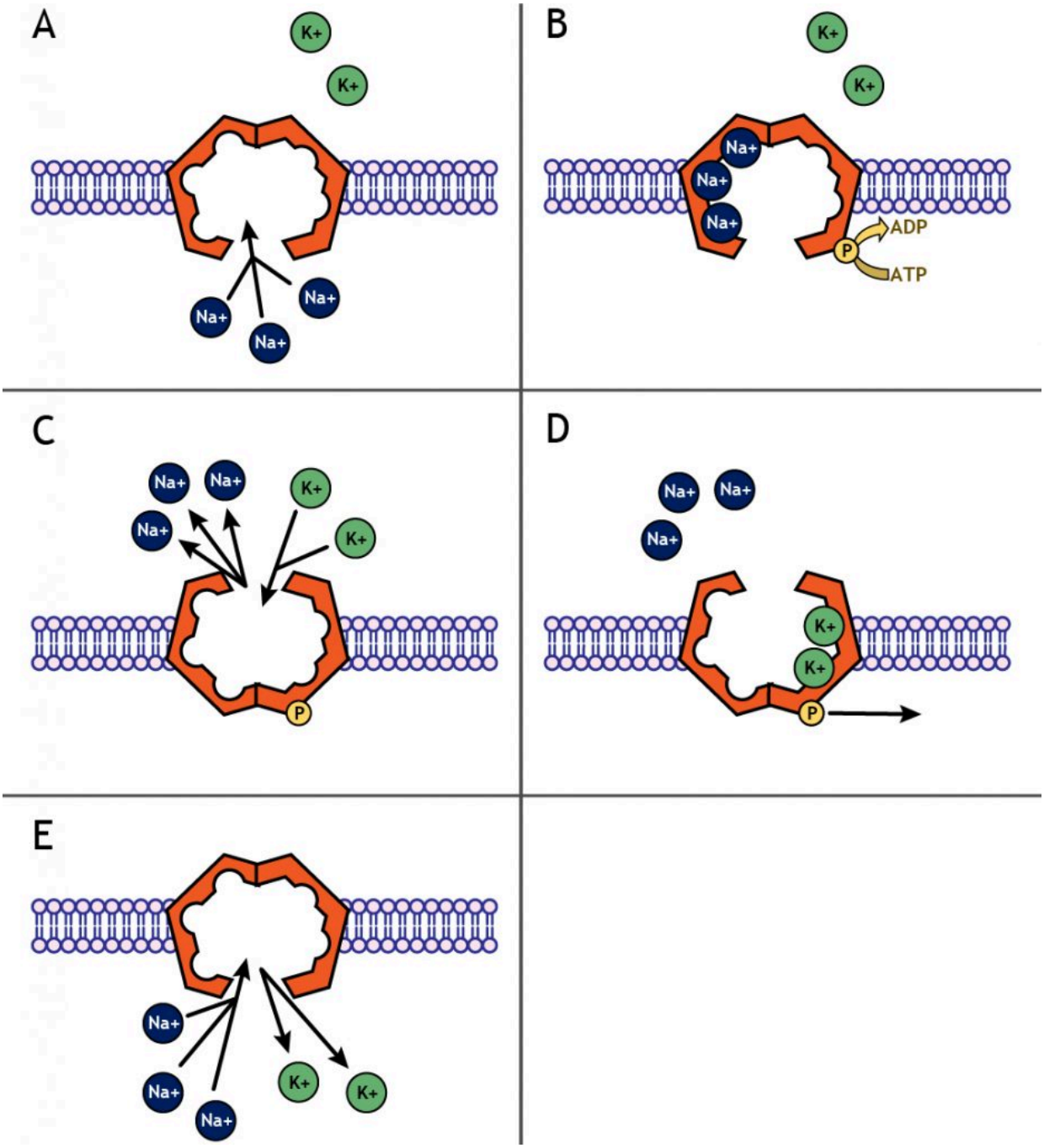


Figure 4.5. The sodium-potassium pump is embedded in the cell membrane and uses ATP to move sodium out of the cell and potassium into the cell, maintaining the electrochemical gradients necessary for proper neuron functioning. A) Three intracellular sodium ions enter the pump. B) ATP is converted to ADP, which leads to a conformational change of the protein, closing the intracellular side and opening the extracellular side. C) The sodium ions leave the pump while two extracellular potassium ions enter. D) The attached phosphate molecule then leaves, causing the pump to again

open toward the inside of the neuron. E) The potassium ions leave, and the cycle begins again. 'Sodium-Potassium Pump' by by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Chapter 5

Animation 1

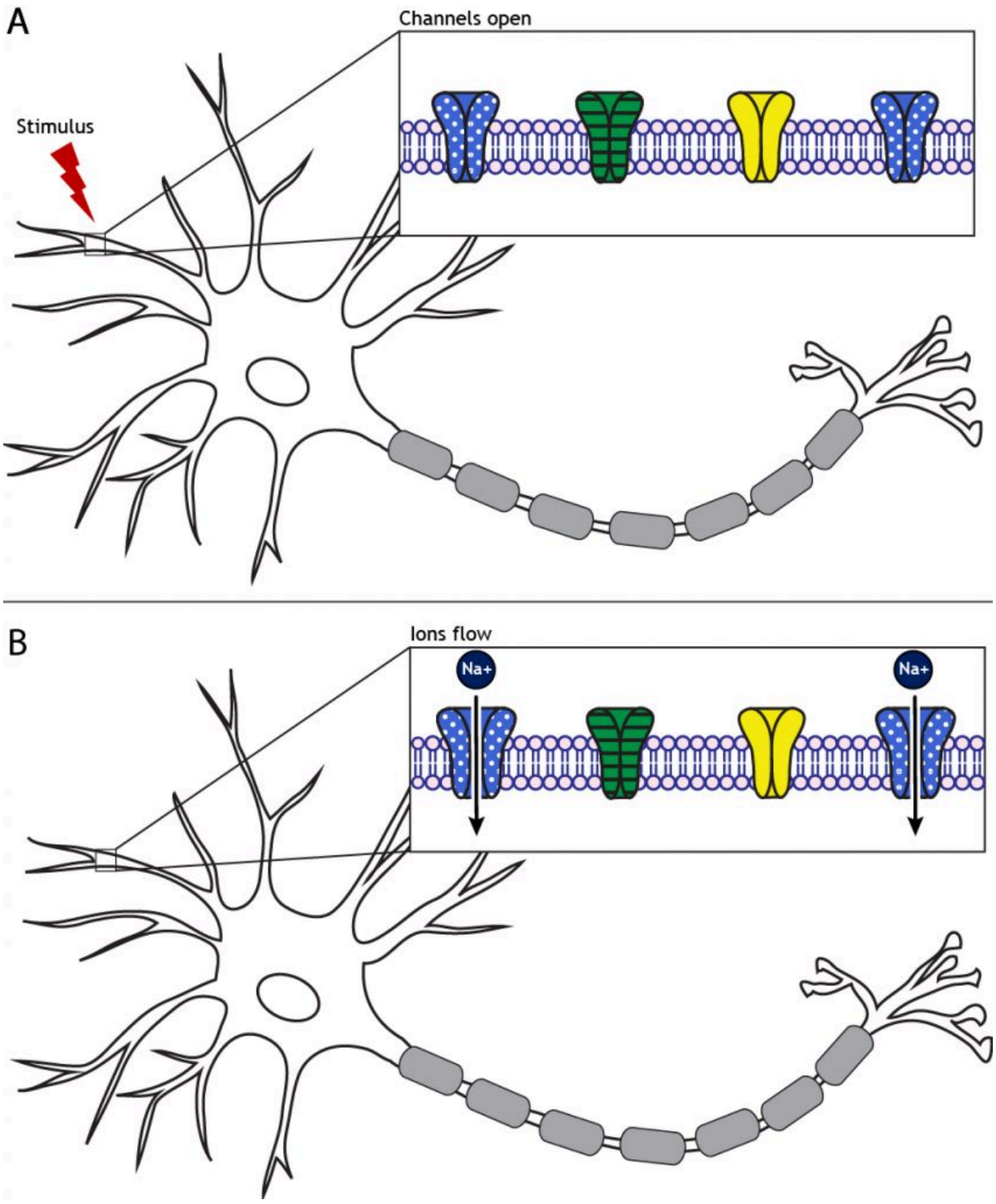


Figure 5.3. Top panel: A stimulus can cause ion channels in the membrane of the cell body or dendrites to open. Bottom panel: The open ion channels allow ion flow across the membrane. The

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.

Animation 2

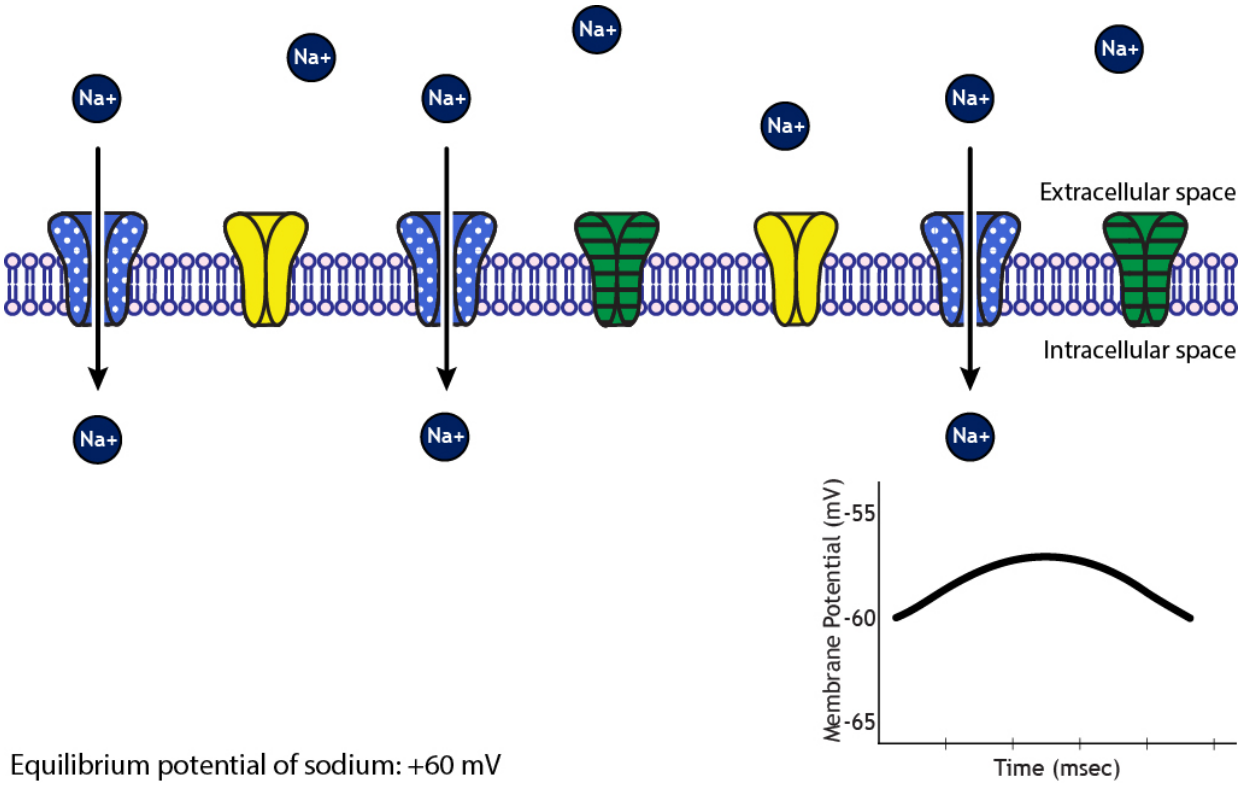


Figure 5.4. When a stimulus opens sodium channels, sodium rushes into the cell because the equilibrium potential of sodium is +60 mV. This causes an excitatory depolarization called an excitatory postsynaptic potential (EPSP). After the stimulus, the ion channels close, and the membrane potential returns 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.

Animation 3

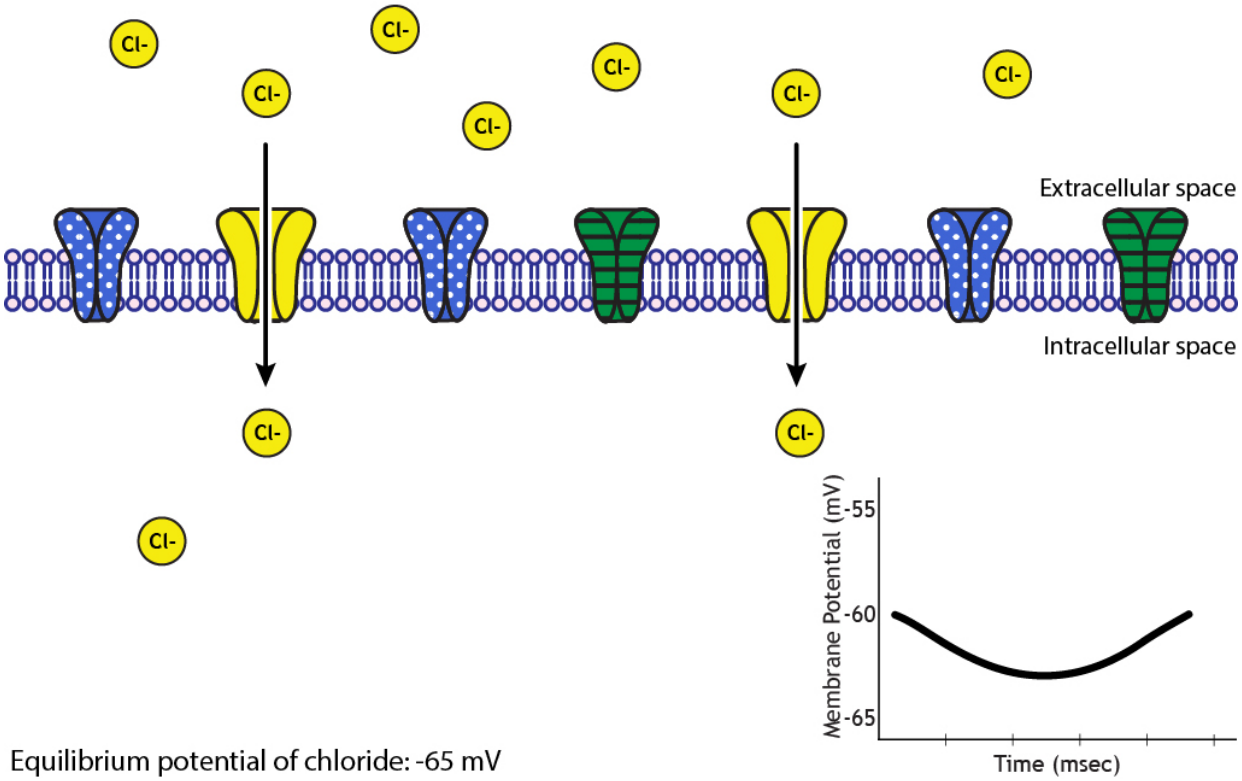


Figure 5.5. When a stimulus opens chloride channels, and the resting membrane potential is more positive than chloride's equilibrium potential of -65 mV, chloride rushes into the cell. This causes an inhibitory hyperpolarization called an inhibitory postsynaptic potential (IPSP). After the stimulus, 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.

Animation 4

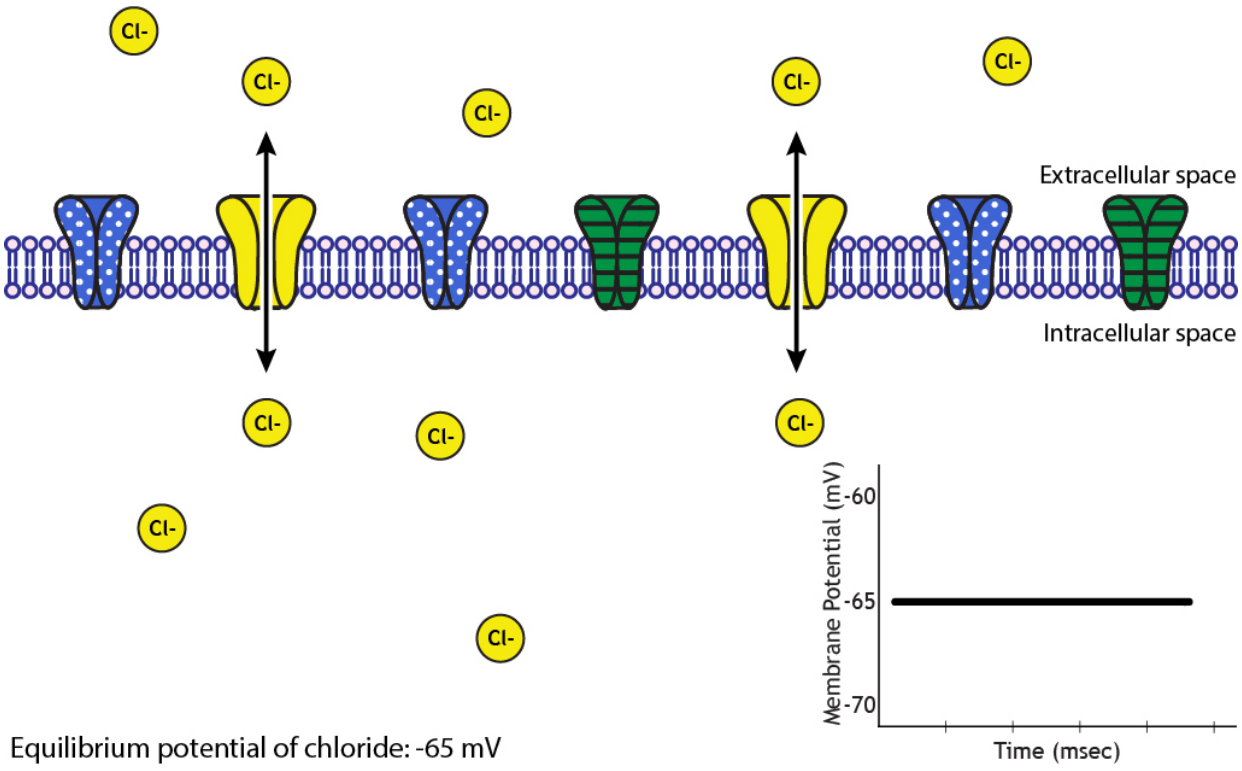


Figure 5.6. If the cell is at rest at chloride's equilibrium potential, when a stimulus opens the chloride channels, there will be no net movement of chloride in either direction because chloride will be at equilibrium. Since there is no net movement, there will also be no change in membrane potential 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.

Animation 5

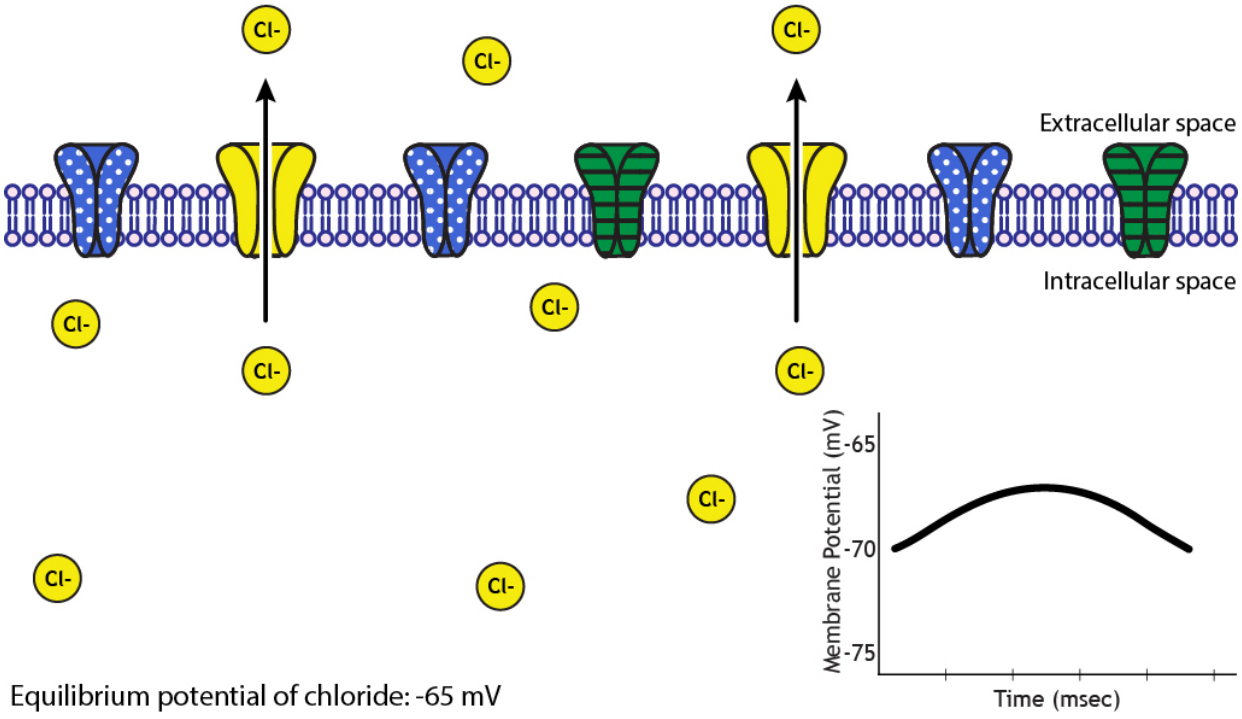


Figure 5.7. If the cell is at rest at chloride's equilibrium potential, when a stimulus opens the chloride channels, chloride will leave the cell, removing its negative charge. This causes a depolarization in the membrane potential, but it is still inhibitory since chloride movement will try to keep 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.

Animation 6

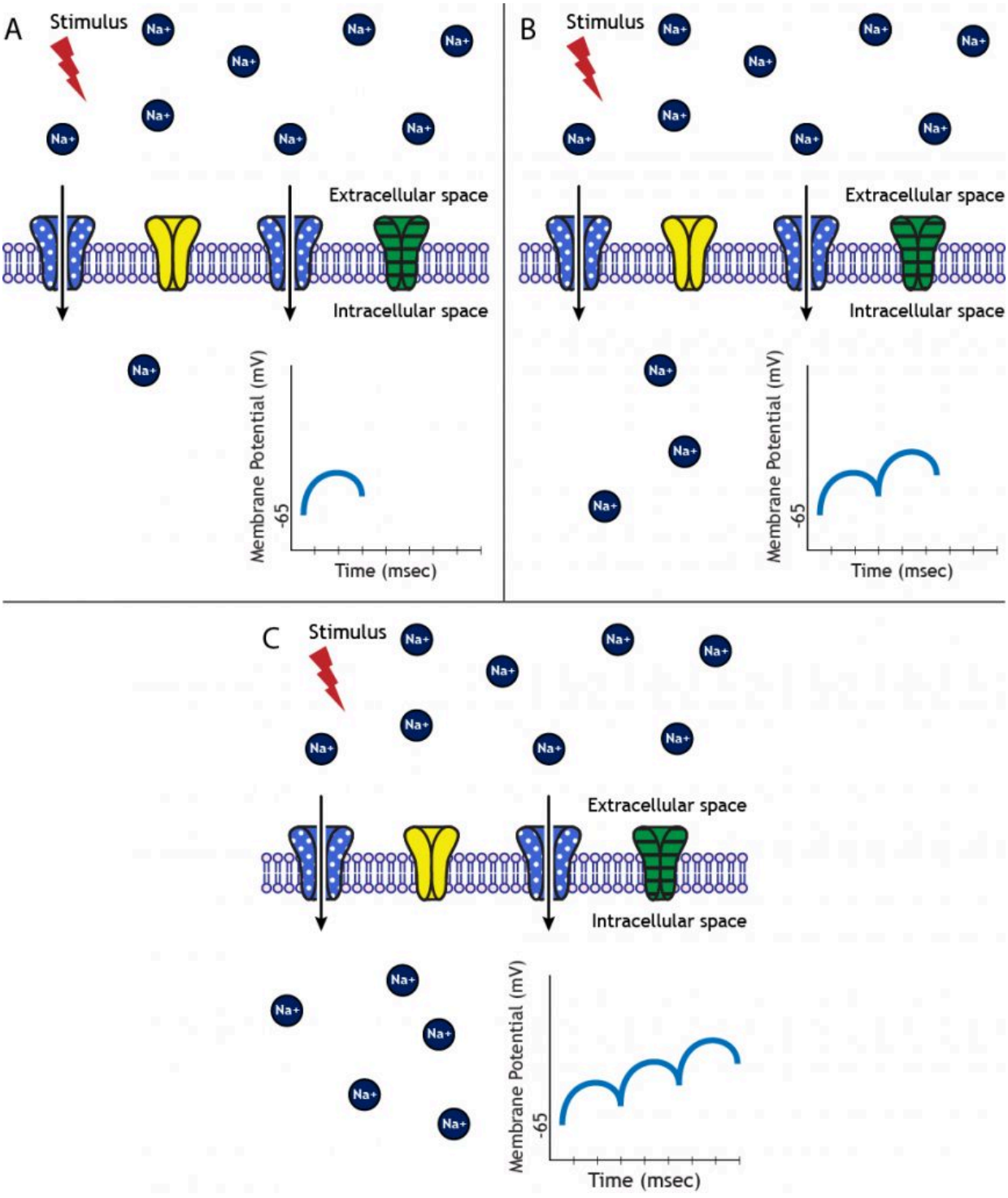


Figure 5.8. Excitatory stimuli that occur quickly in succession lead to summation of EPSPs. This leads to increased depolarization of the membrane potential compared to a single EPSP. The dotted, blue channels represent sodium channels; the striped, green channels represent potassium channels; the

solid yellow channels represent chloride channels. 'Summated EPSPs' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Animation 7

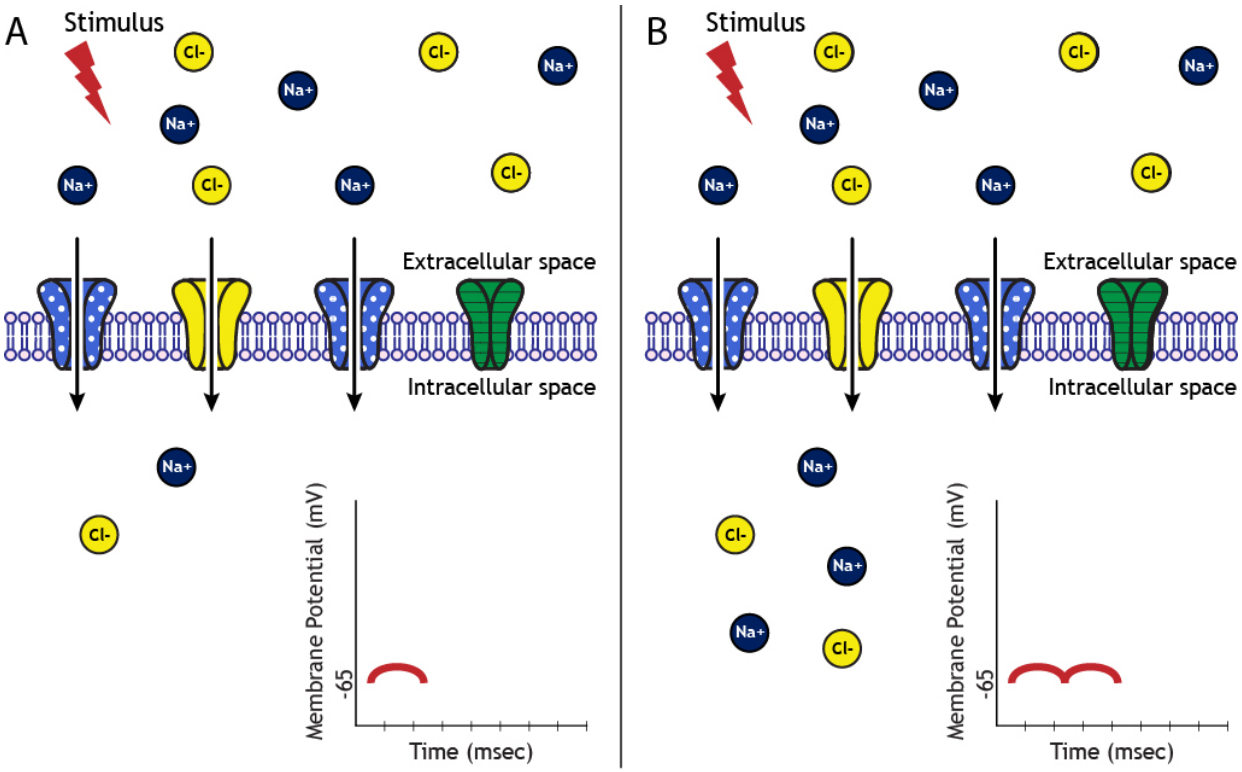
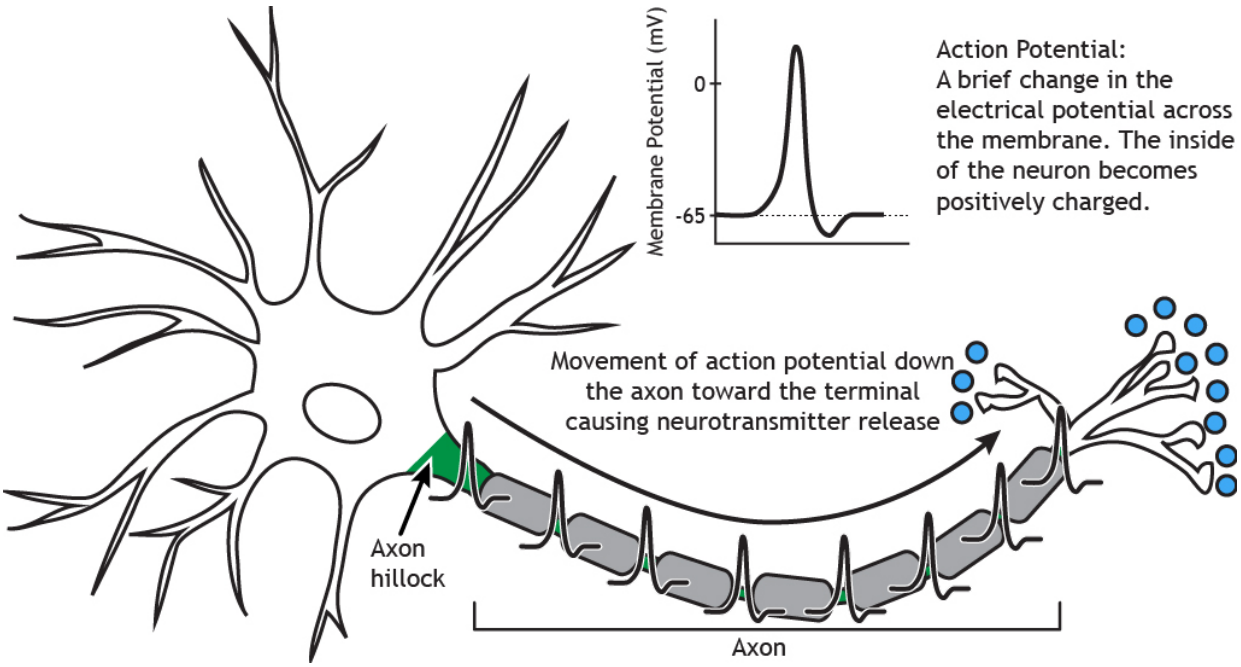


Figure 5.9. When an inhibitory input and an excitatory input stimulate a postsynaptic neuron at the same time, chloride and sodium channels open. Due to the equilibrium potentials of the two ions, both will flow into the cell. Sodium tries to depolarize the cell, whereas chloride tries to keep the cell 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.

Chapter 6

Animation 1



Animation 6.9. 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 in 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.

Animation 2

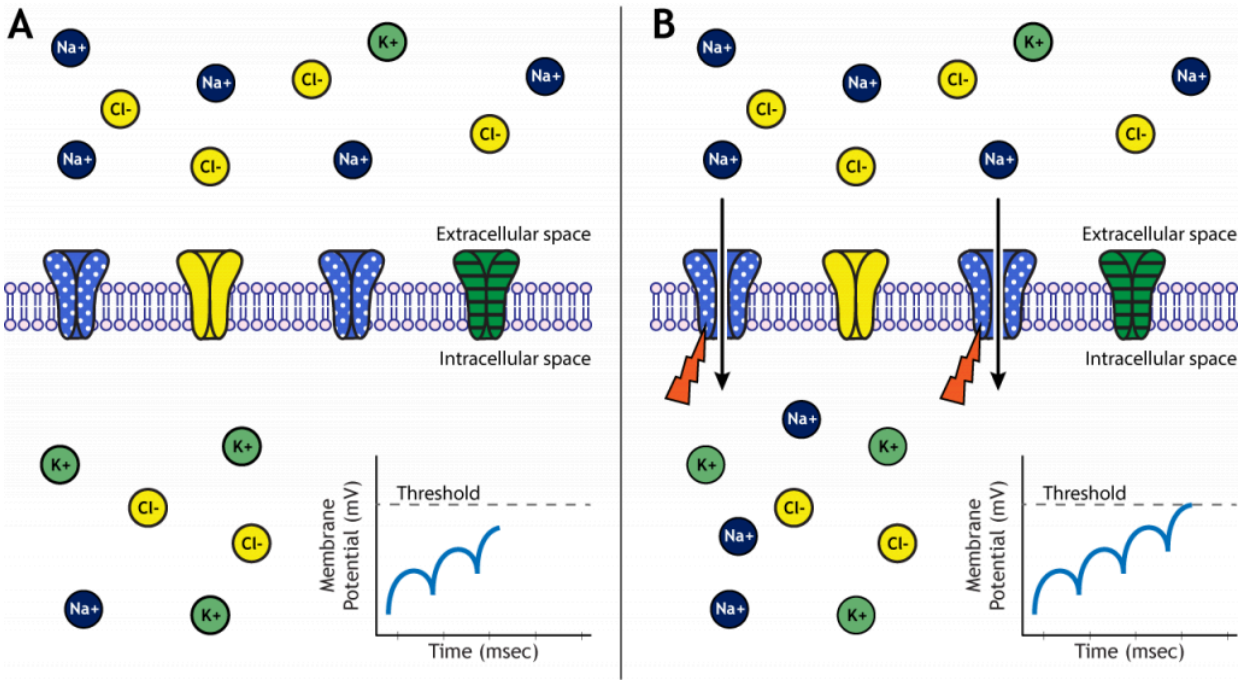


Figure 6.10. A. As EPSPs summate, a result of ion movement not shown in the figure, the cell's membrane potential will depolarize. B. Reaching threshold causes voltage-gated ion channels to open. Once the channels are open, ions will move toward equilibrium. In the figure, sodium ions flow inward. The 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.

Animation 3

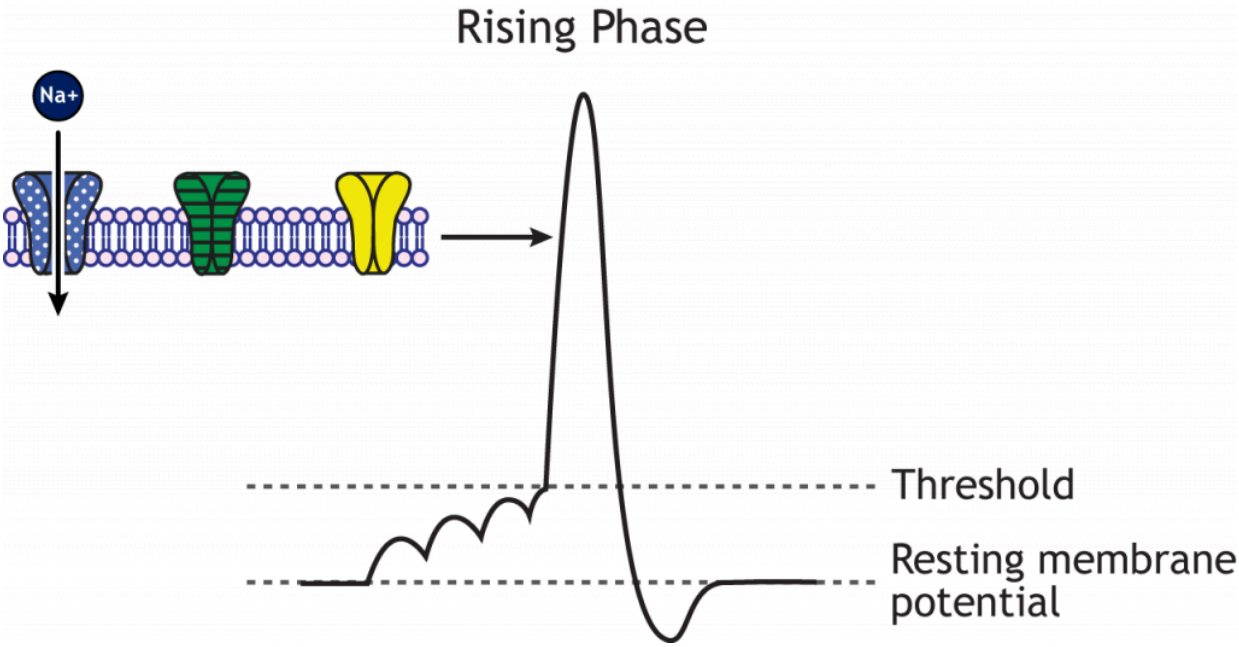


Figure 6.11. Voltage-gated sodium channels open once the cell's membrane potential reaches threshold. The rapid influx of sodium results in a large depolarization called the rising phase. The dotted, blue channels represent voltage-gated sodium channels; the striped, green channels represent voltage-gated 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.

Animation 4

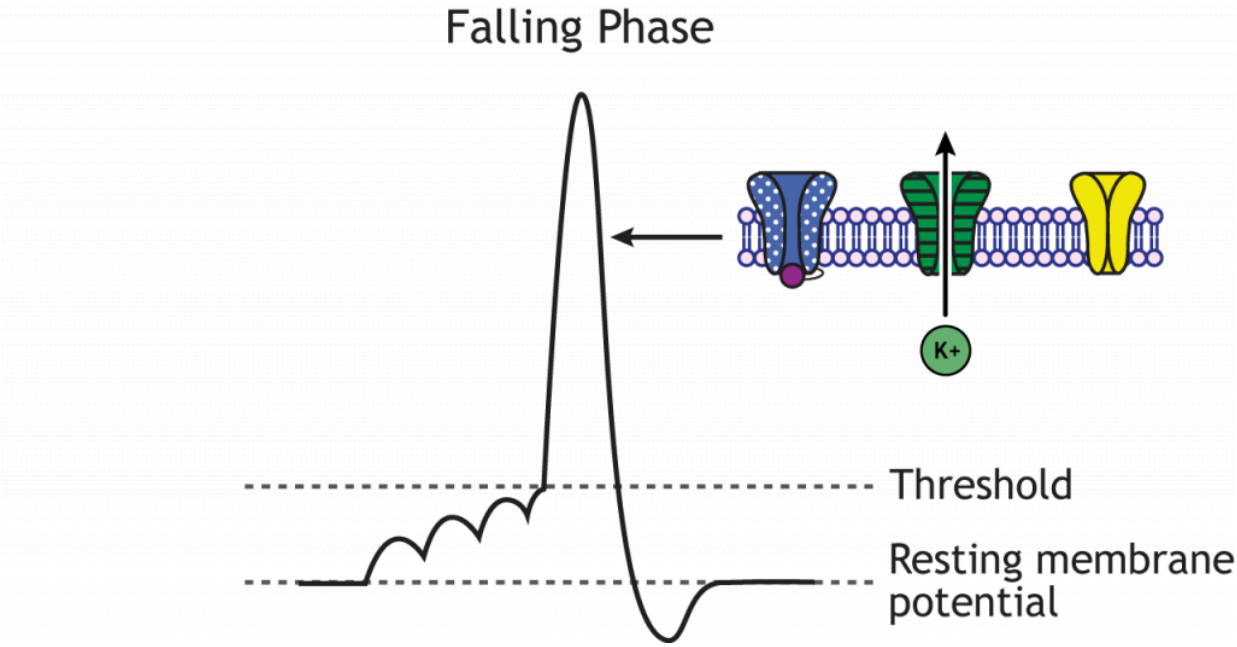


Figure 6.12. After approximately 1 msec, the voltage-gated sodium channels inactivate, which prevents any further ion flow into the cell. Although the voltage-gated potassium channels are activated in response to the cell reaching threshold, their opening is delayed and occurs alone with the sodium channel 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.

Animation 5

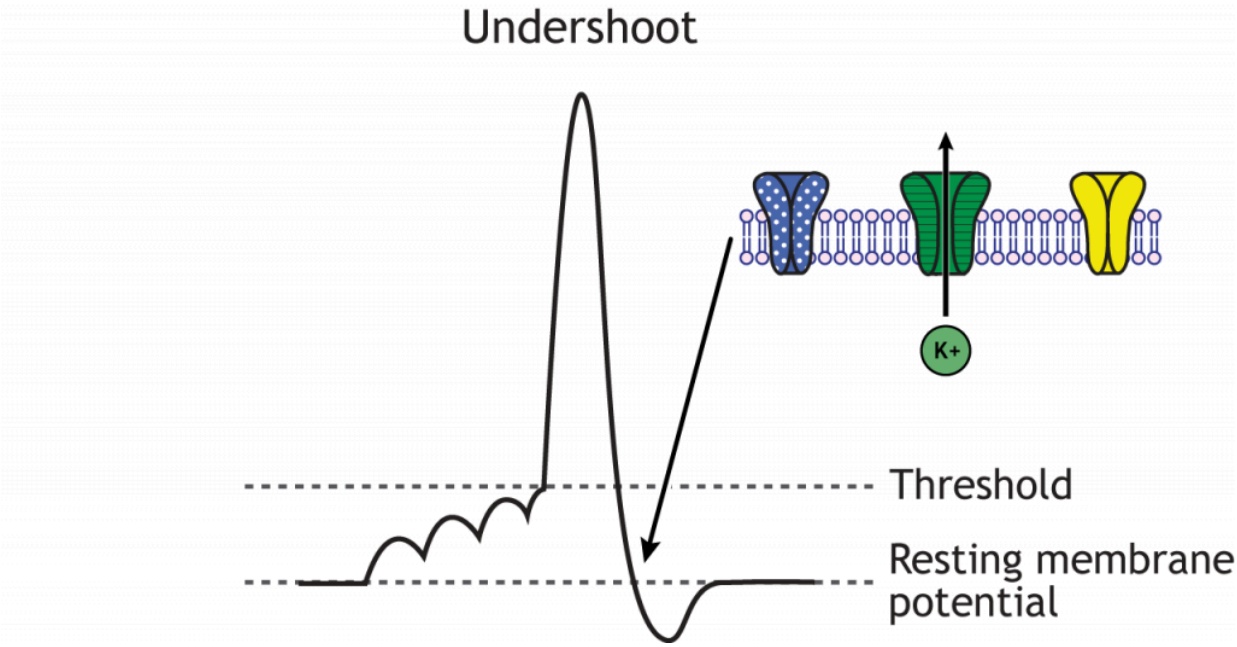


Figure 6.13. Once the cell's membrane potential repolarizes, the voltage-gated sodium channels de-inactivate and return to their closed state. The voltage-gated potassium channels remain open long enough for the undershoot to occur as potassium continues to flow out of the cell. The dotted, blue channels 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.

Animation 6

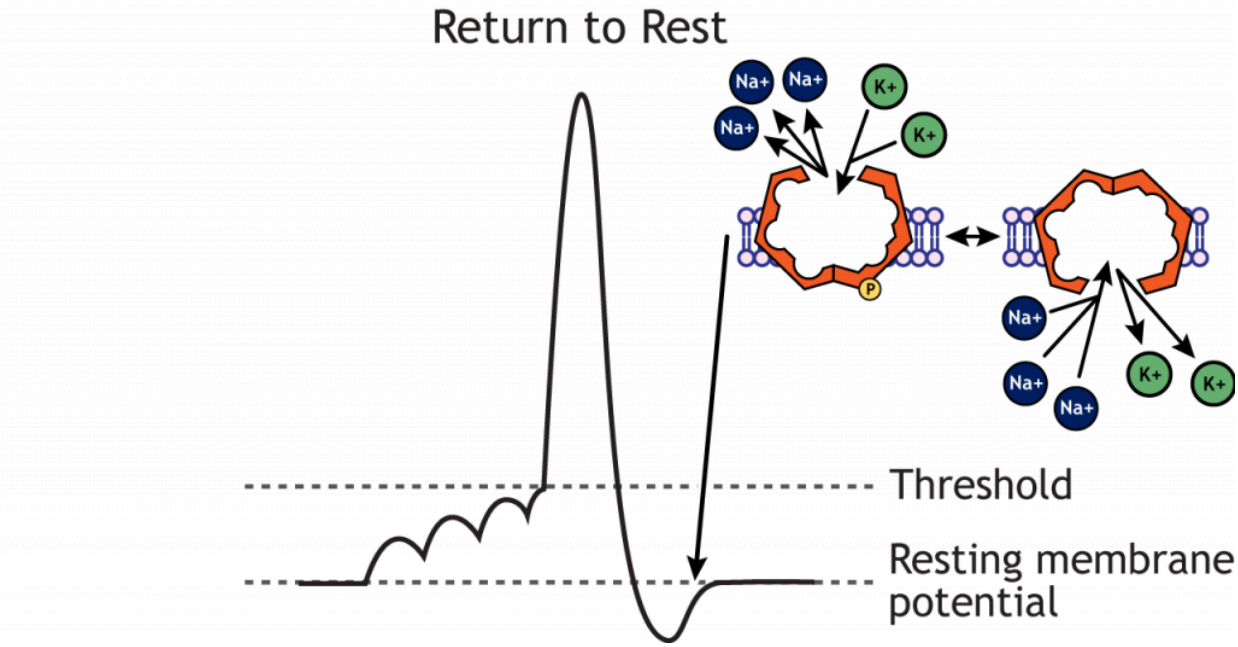


Figure 6.14. Once the voltage-gated potassium channels close, the sodium-potassium pump will work to re-establish the electrochemical gradients and return the cell to its resting membrane potential. 'Return to Rest' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Animation 7

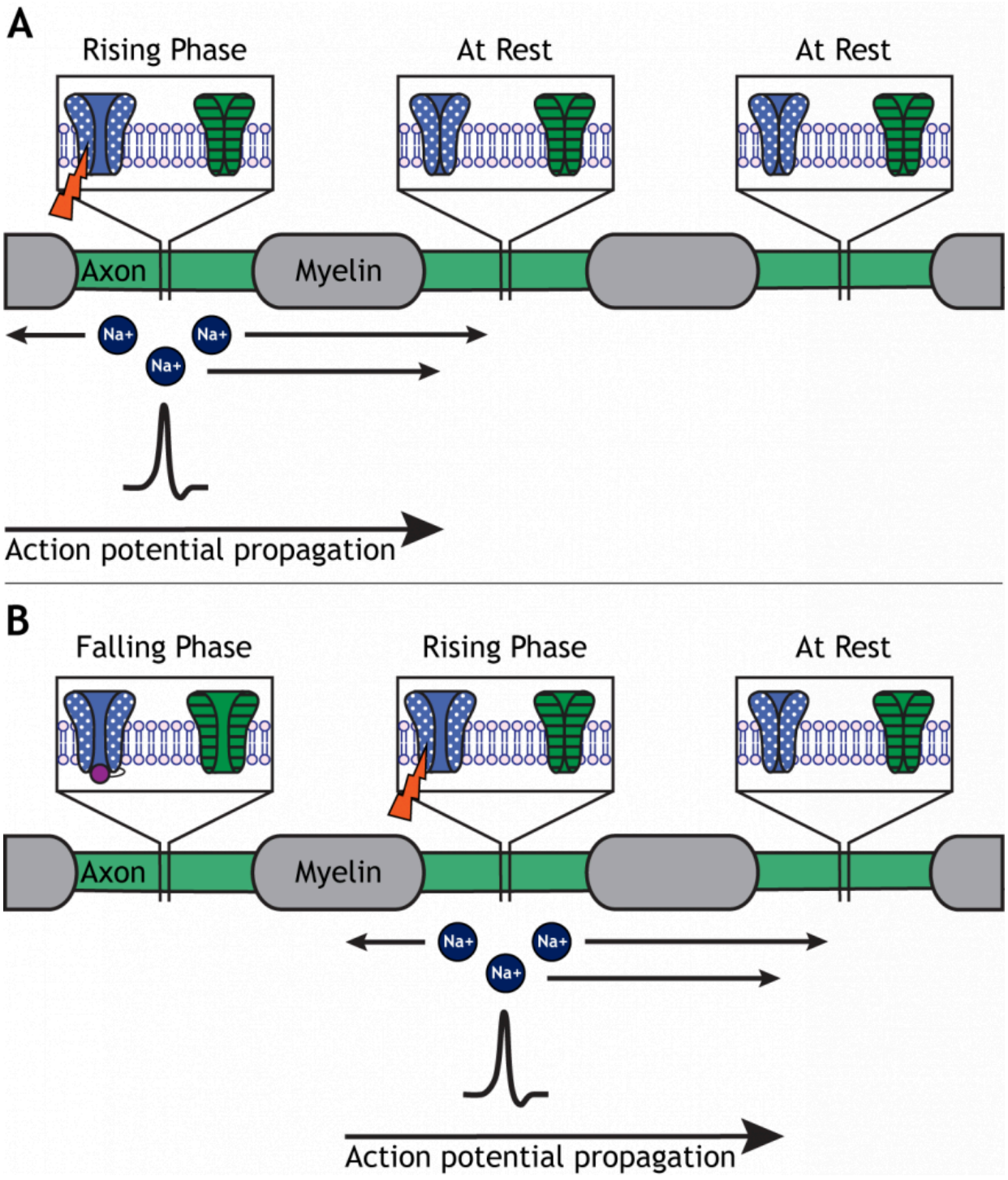


Figure 6.15. A) A voltage change that reaches threshold will cause voltage-gated sodium channels to open in the axonal membrane. The influx of sodium causes the rising phase of the action potential, but the ion flow also depolarizes nearby axon regions. B) As the depolarization reaches threshold,

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.

Animation 8

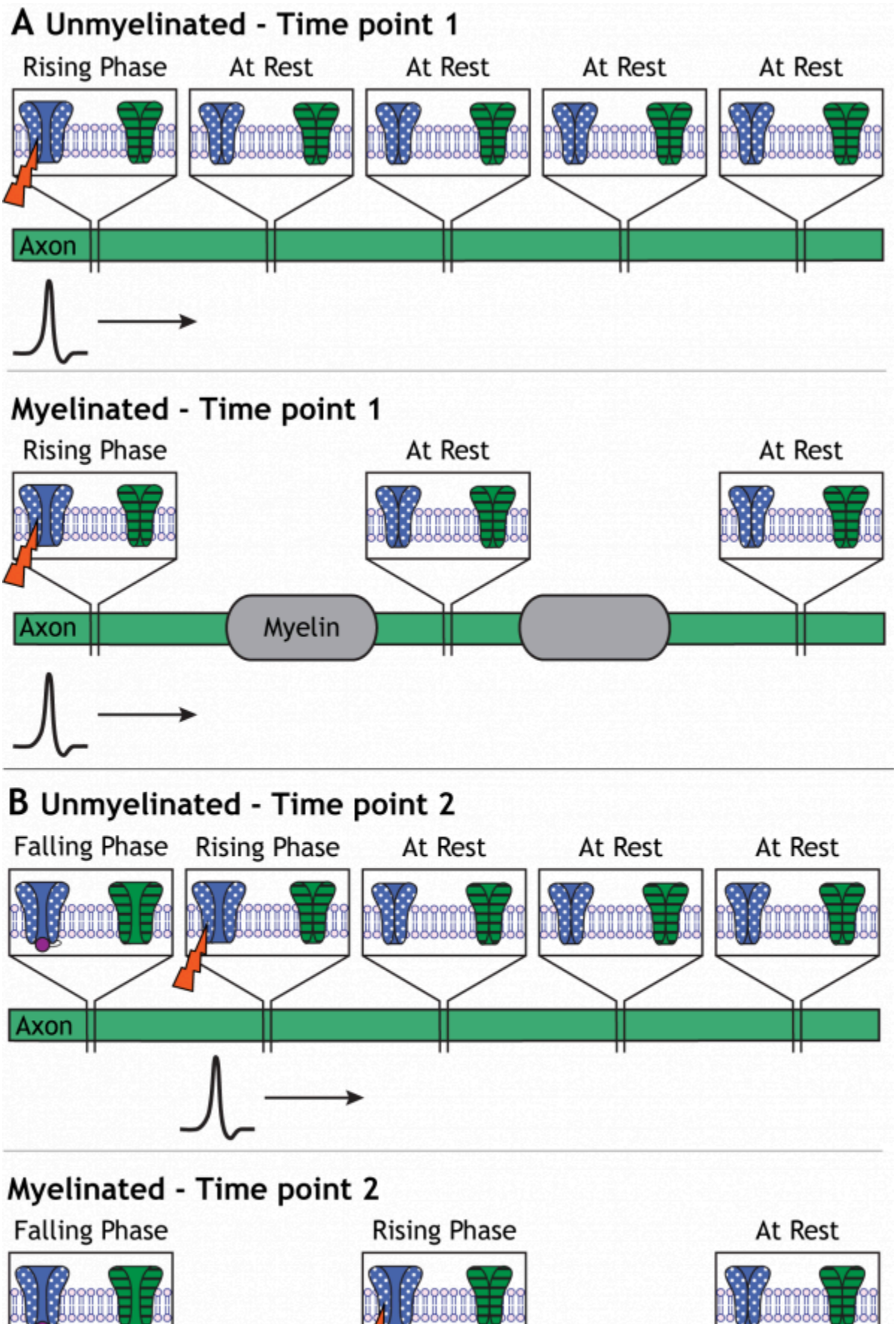

A Unmyelinated - Time point 1
Rising Phase
At Rest
At Rest
At Rest
At Rest
Axon
Myelinated - Time point 1
Rising Phase
At Rest
At Rest
Axon
Myelin
B Unmyelinated - Time point 2
Falling Phase
Rising Phase
At Rest
At Rest
At Rest
Axon
Myelinated - Time point 2
Falling Phase
Rising Phase
At Rest

Figure 6.16. 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.

Chapter 7

Animation 1

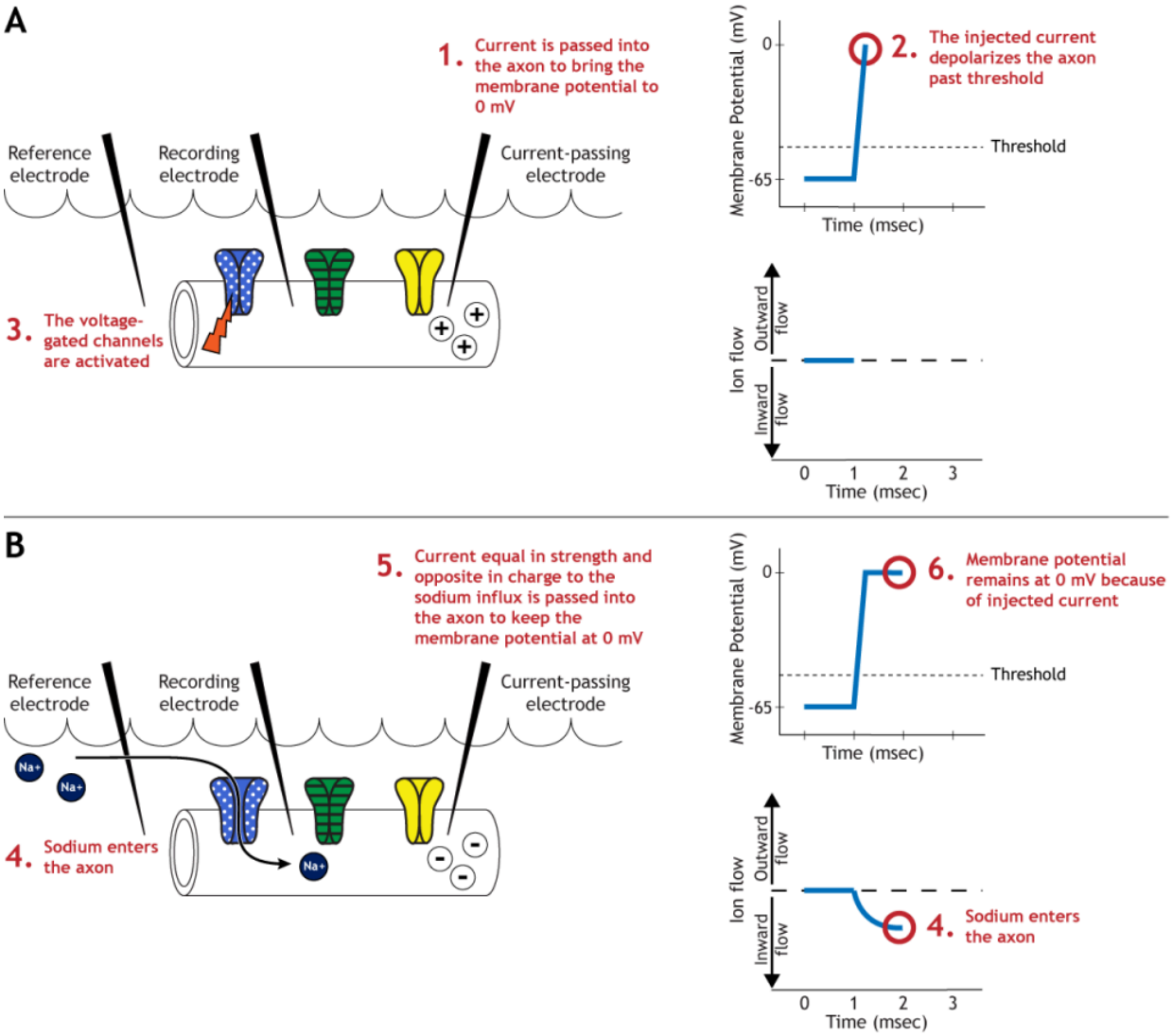


Figure 7.9. A) Clamping the cell at 0 mV will result in current being passed into the axon to depolarize the membrane potential. This depolarization is above threshold, so the voltage-gated ion channels in the membrane will be activated. B) Sodium will enter the axon through the open sodium channels. 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.

Animation 2

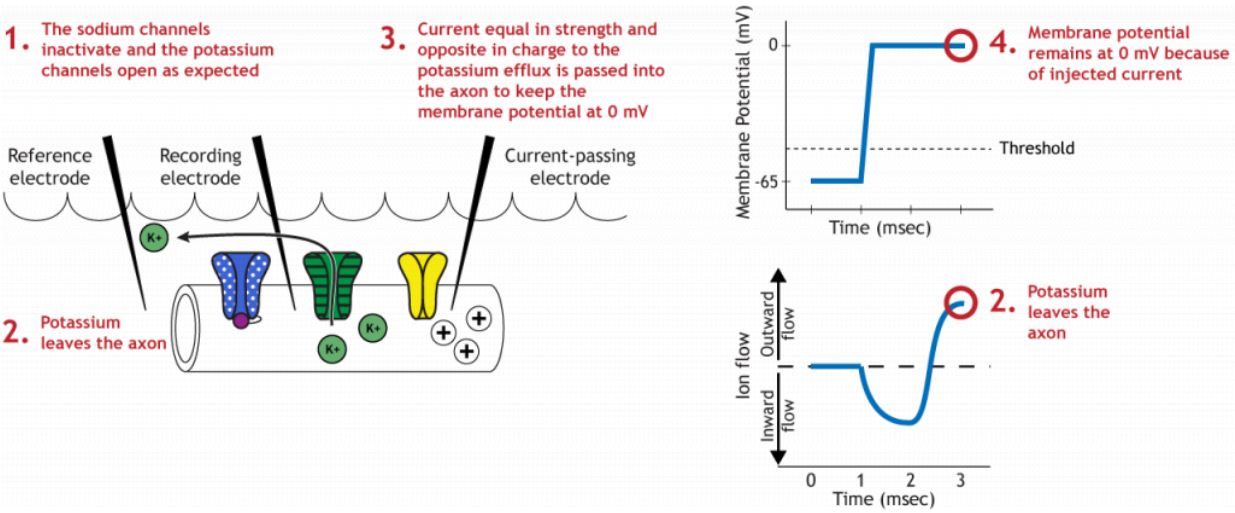


Figure 7.10. The voltage-gated sodium channels will inactivate, and the potassium channels will open. Potassium will then flow out of the axon. Similar to the sodium influx, the voltage clamp equipment will inject current equal in strength and opposite in charge to the potassium efflux in order to keep the membrane potential of the axon at 0 mV. 'Voltage Clamp Potassium Flow' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Chapter 8

Animation 1

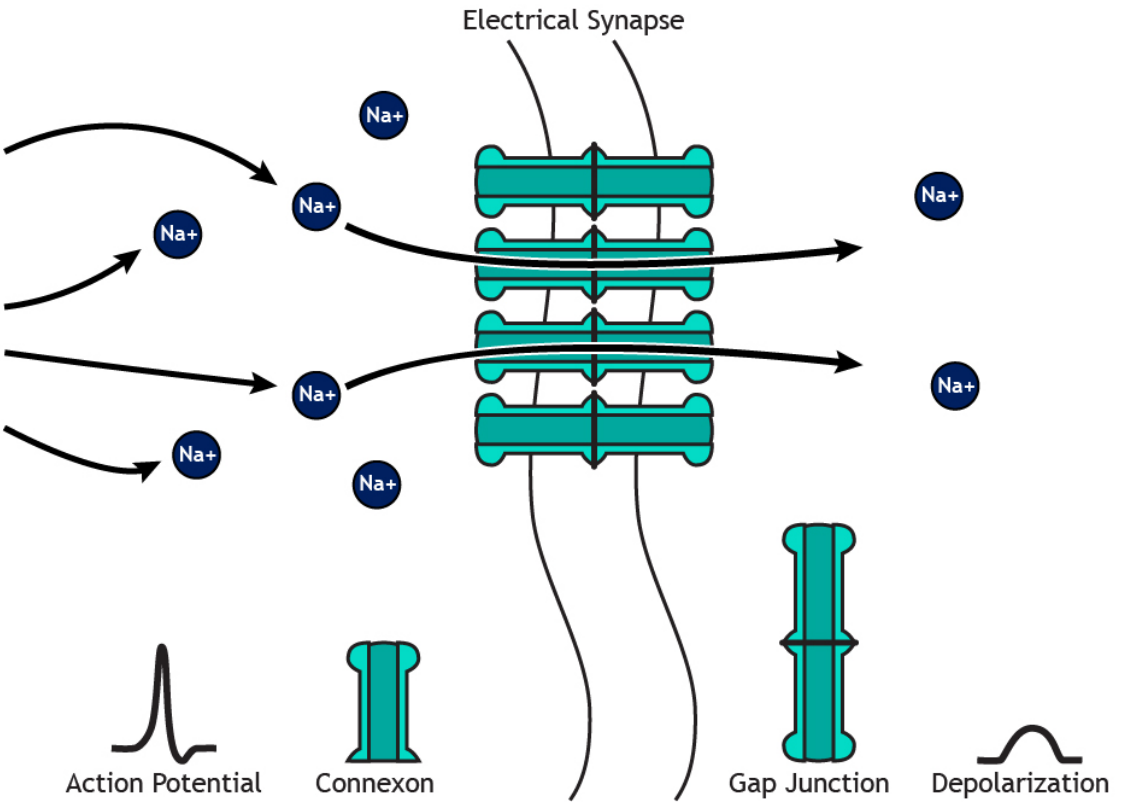


Figure 8.4. Membrane-bound proteins called connexons form gap junctions between presynaptic and postsynaptic neurons. This allows for direct exchange of ions between neurons. An action potential in the presynaptic neuron will cause an immediate depolarization of the postsynaptic membrane because the sodium ions will cross the membrane through the gap junctions. 'Electrical Synapse – Ion Flow' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Animation 2

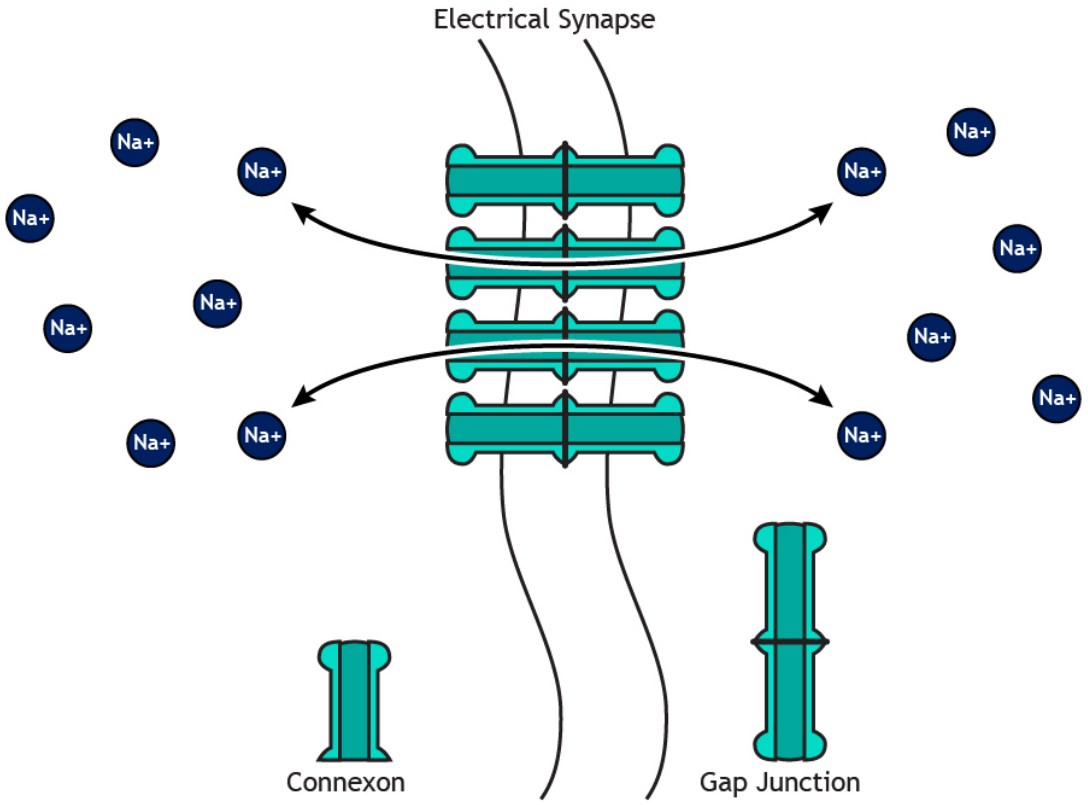


Figure 8.5. Since an electrical synapse is a direct, physical connection between two neurons, ions are able to flow either direction across the gap junction. 'Bidirectional Electrical Synapse' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Animation 3

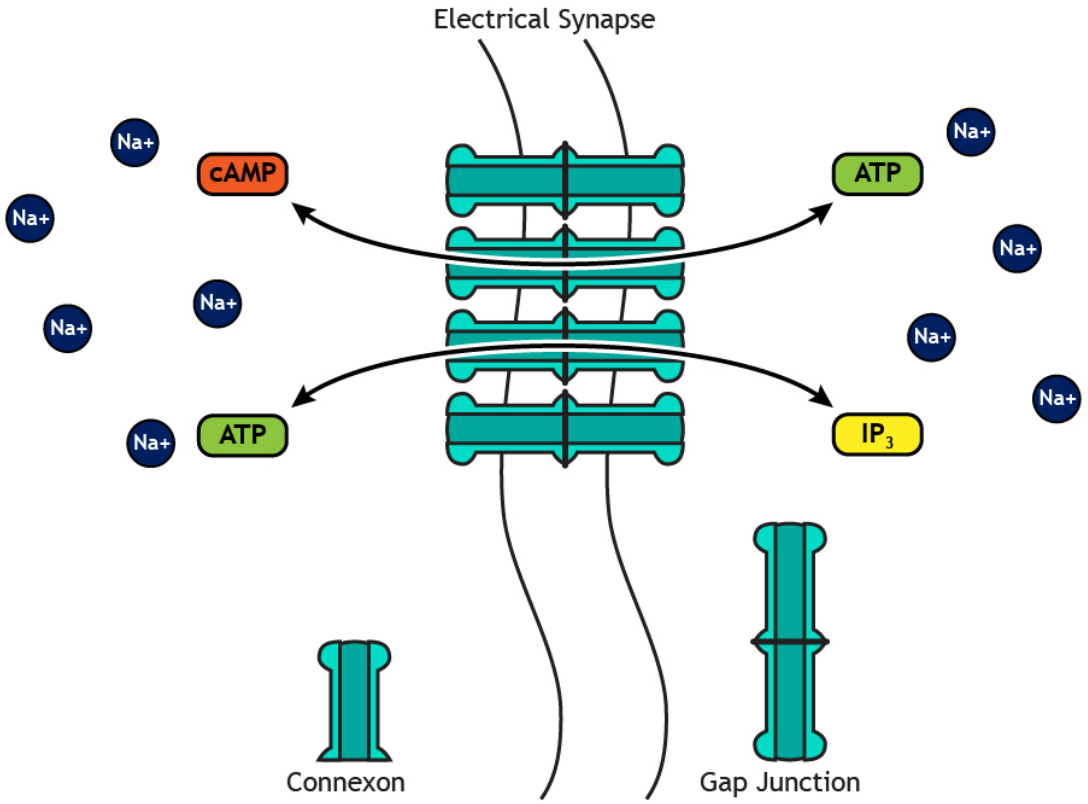


Figure 8.6. Gap junctions are large enough to allow the flow of small cellular molecules like ATP or second messengers. 'Electrical Synapse – Small Molecules' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Animation 4

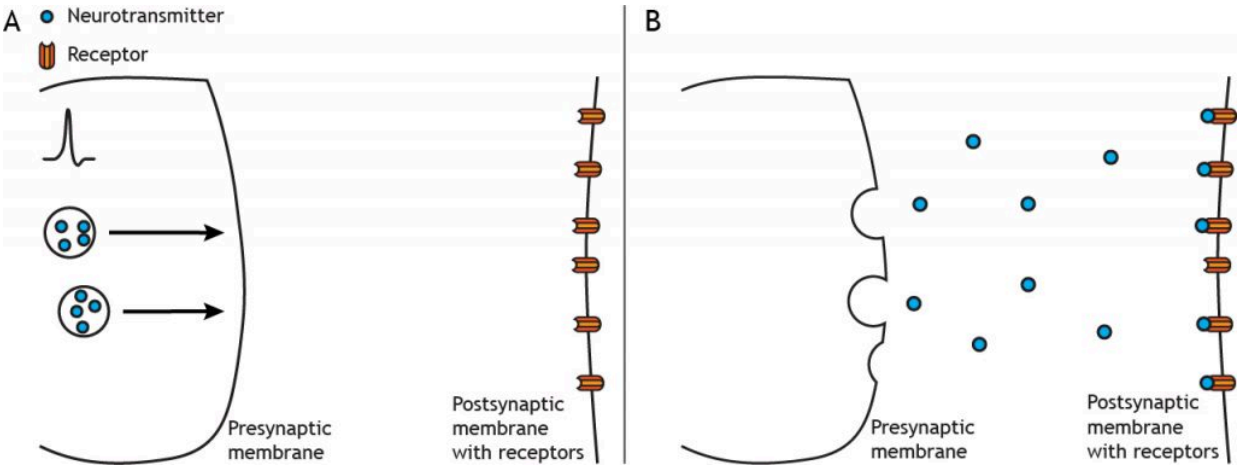
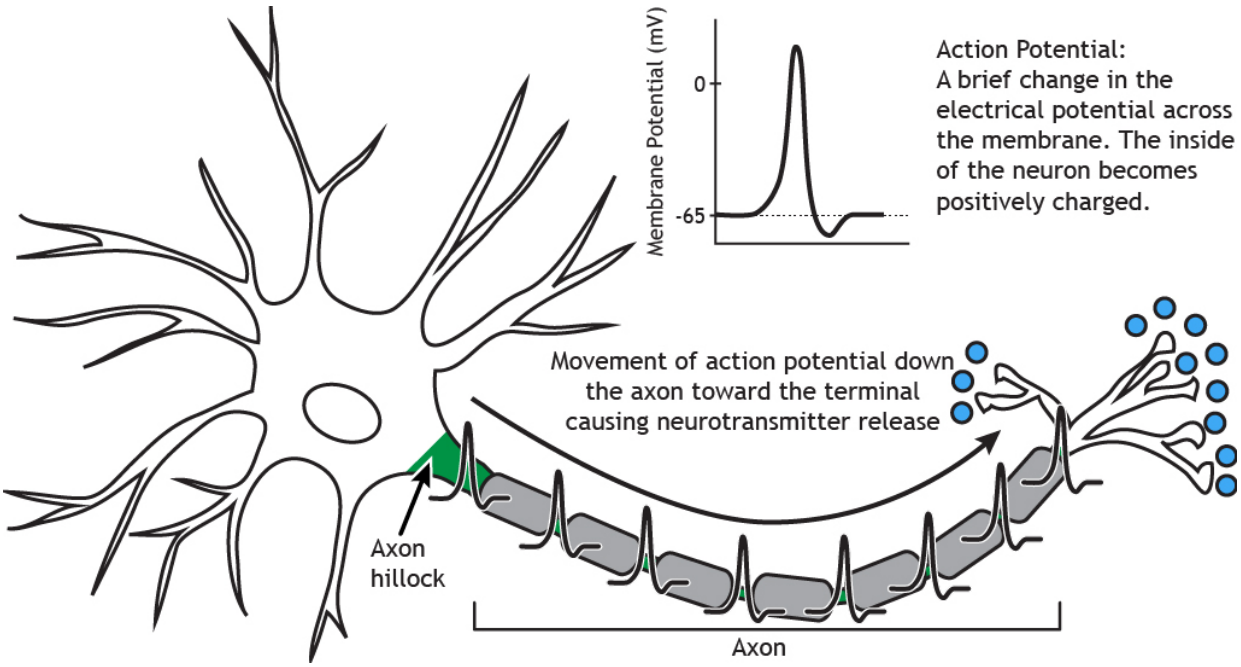


Figure 8.7 When an action potential arrives in the presynaptic terminal, neurotransmitters are released into the synaptic cleft where they can act on neurotransmitter receptors in the postsynaptic membrane. 'Chemical Synapse – Neurotransmitter Release' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Chapter 10

Animation 1



Animation 10.5. 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.

Animation 2

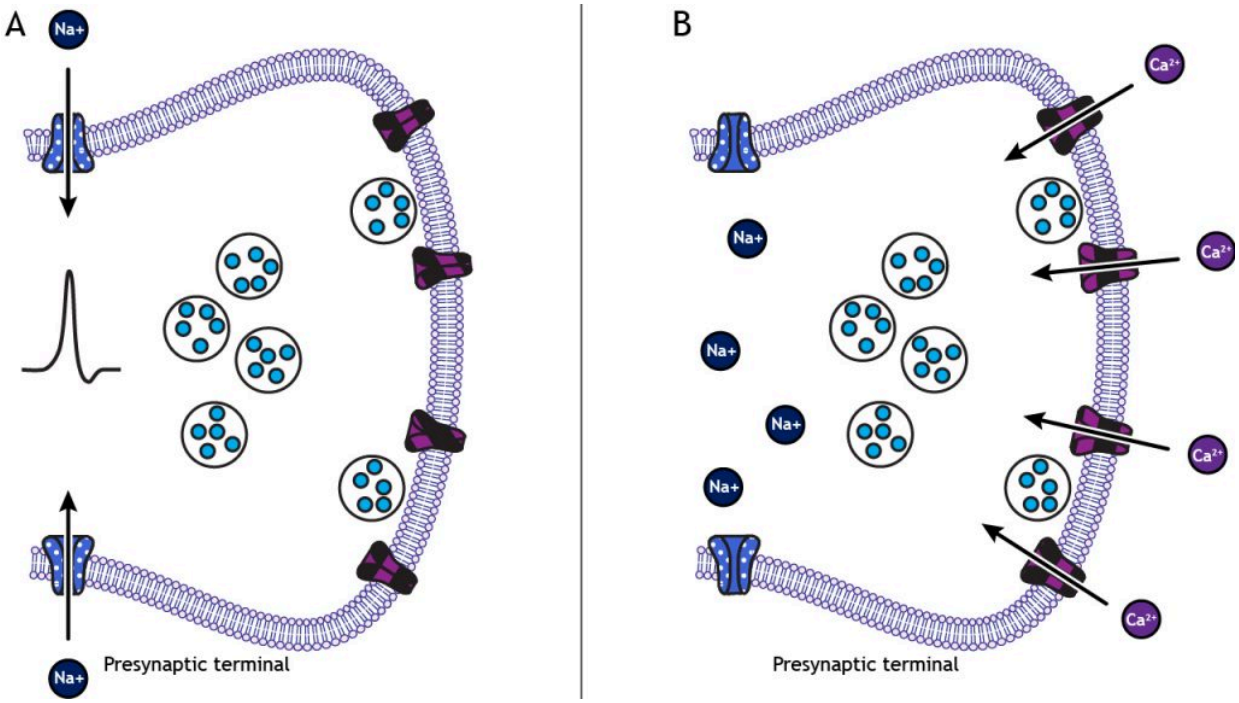


Figure 10.6. A) An action potential causes an influx of sodium in the terminal. B) The depolarization opens voltage-gated calcium channels, and calcium ions flow into the terminal down their electrochemical gradient. The blue, dotted channels represent voltage-gated sodium channels, and the purple, striped channels represent voltage-gated calcium channels. 'Terminal Calcium Influx' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Animation 3

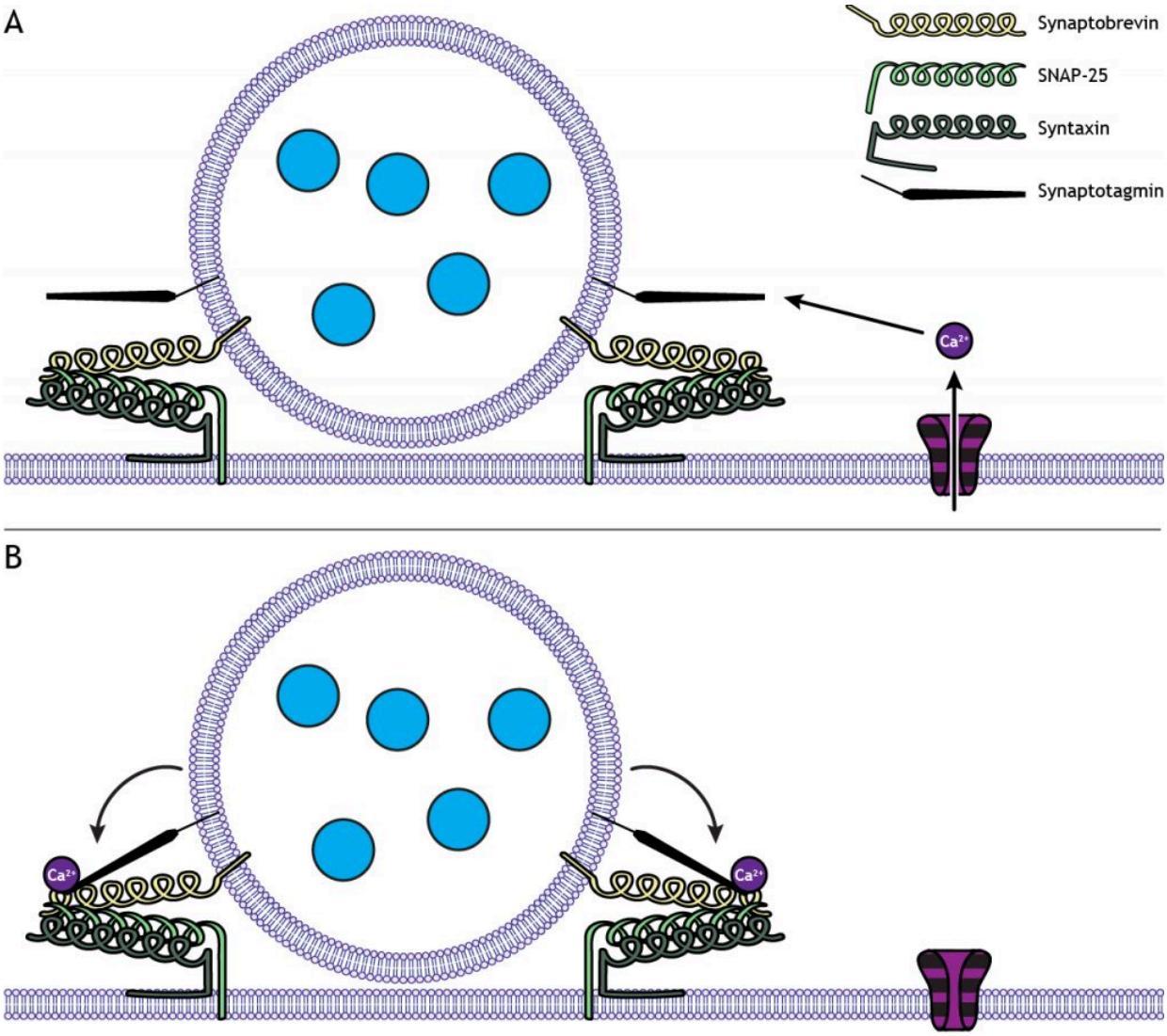


Figure 10.7. A) Calcium enters the cell when the voltage-gated channels open. B) In the presence of calcium, synaptotagmin, a protein bound to the vesicular membrane interacts with the SNARE proteins. The purple, striped channels represent voltage-gated calcium channels. 'Synaptotagmin' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Animation 4

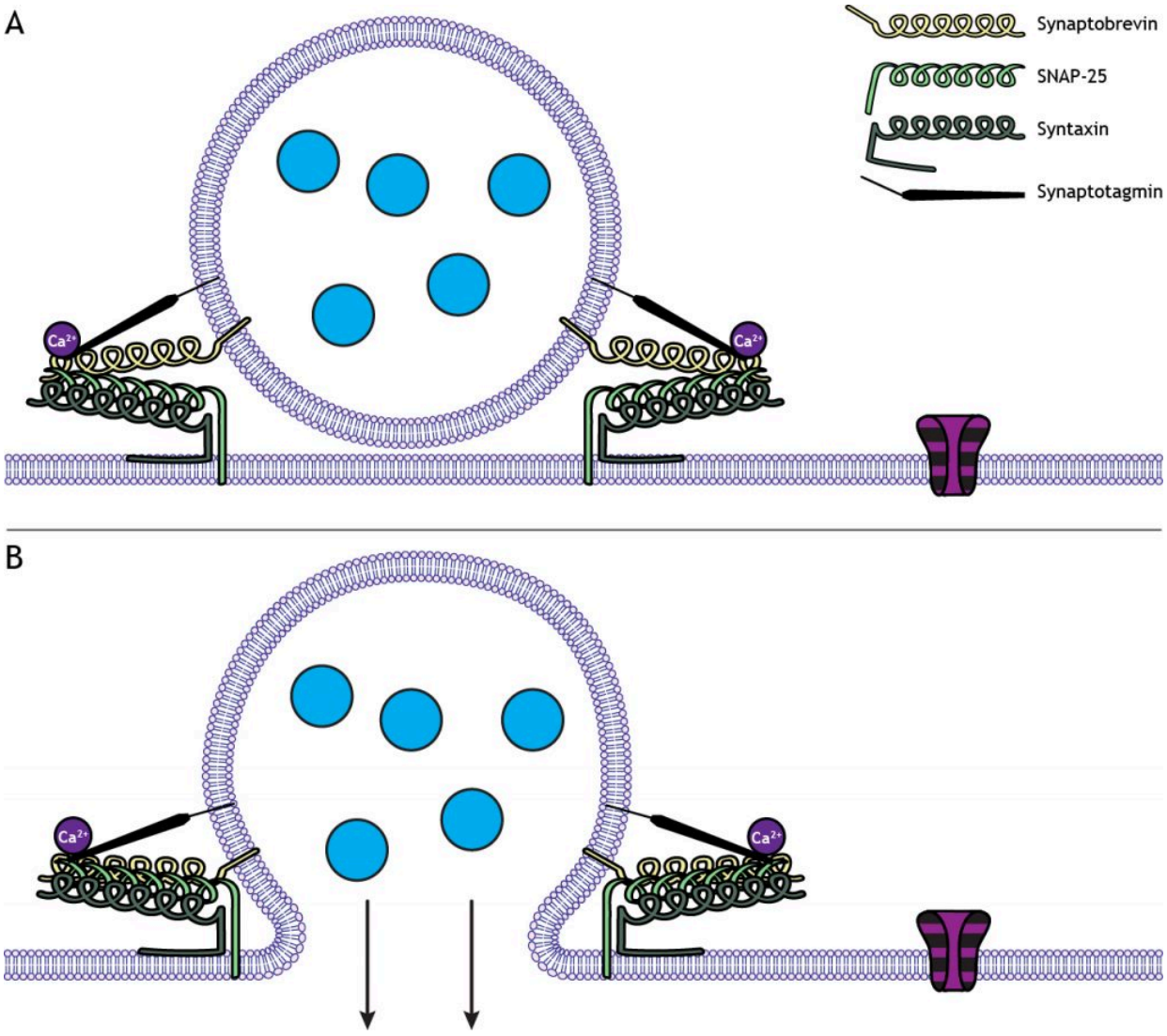


Figure 10.8. Once the synaptotagmin-SNARE protein complex forms, the synaptic vesicle membrane fuses with the terminal membrane, and the neurotransmitters are released into the synaptic cleft through exocytosis. The purple, striped channels represent voltage-gated calcium channels. 'Transmitter Exocytosis' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Chapter 11

Animation 1

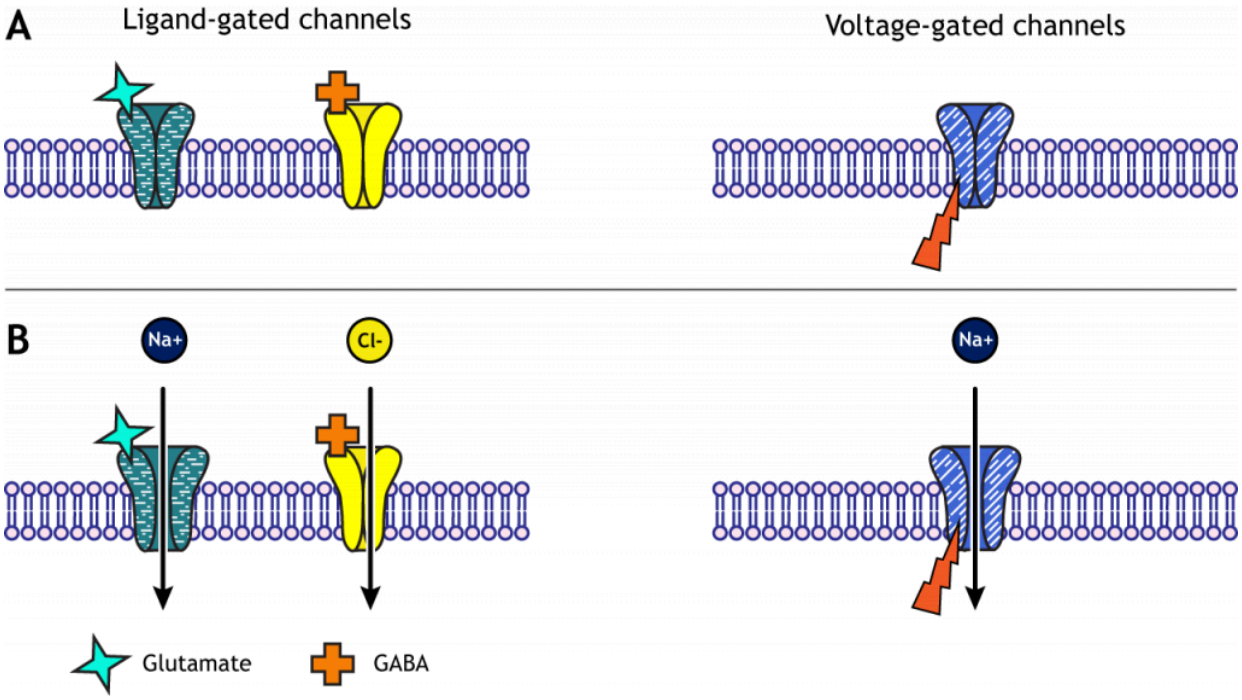


Figure 11.2. A) Ionotropic receptors, also called ligand-gated channels, are ion channels that are opened by the binding of neurotransmitters. Voltage-gated channels are opened by the membrane potential of the cell reaching threshold. B) Both types of channels allow ions to diffuse down their electrochemical gradient. The lined, teal channels represent glutamate receptors; the solid yellow channels represent GABA receptors; the dotted, blue channels represent voltage-gated sodium channels. 'Ion Channel Gating' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Animation 2

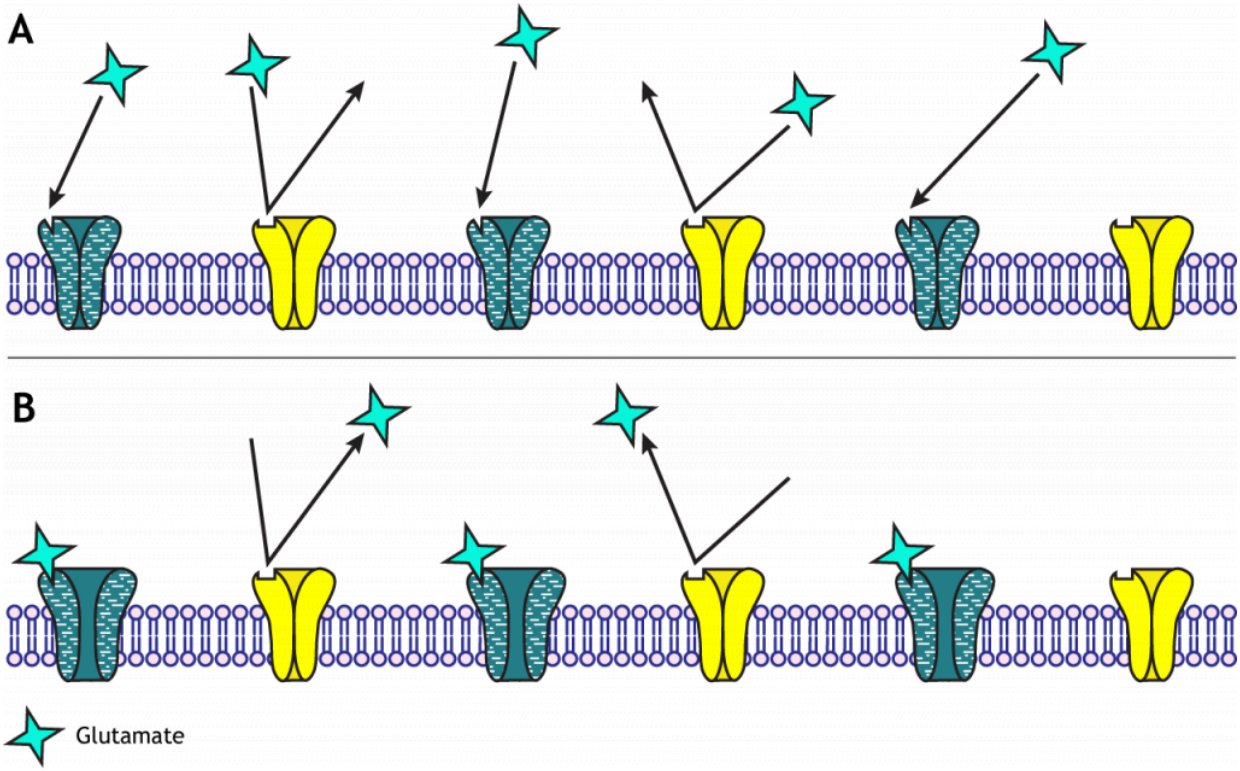


Figure 11.3. Since neurotransmitter receptors can only bind specific neurotransmitters. glutamate binds to (A) and opens (B) glutamate receptors but has no effect on GABA receptors. The lined, teal channels represent glutamate receptors; the solid yellow channels represent GABA receptors. 'Ligand and Receptor' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Animation 3

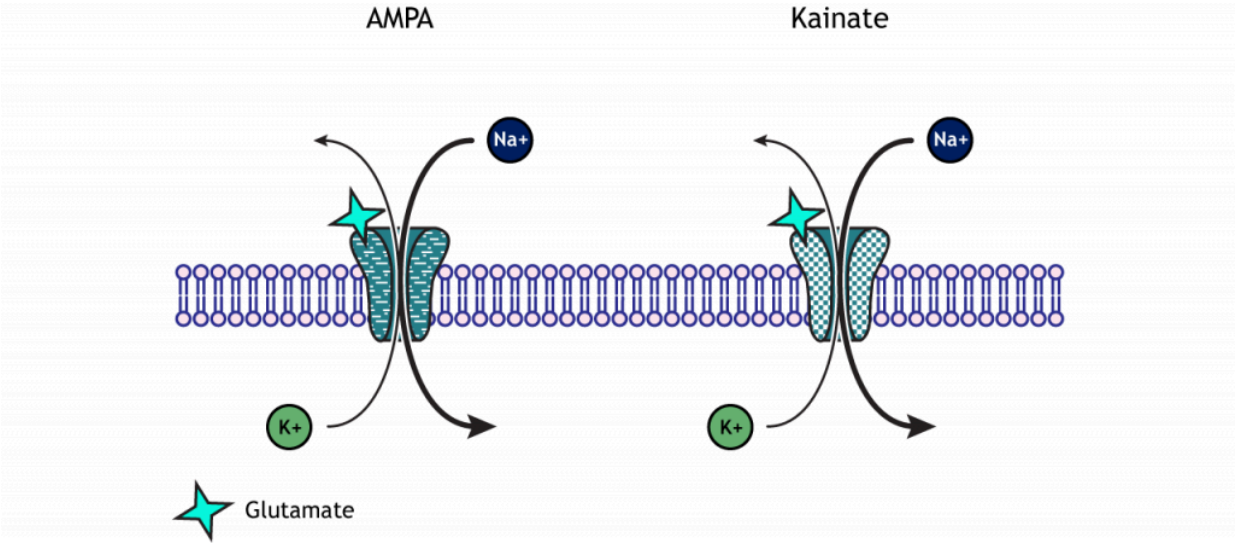


Figure 11.4. AMPA and kainate glutamate receptors are non-selective ion channels that allow both sodium and potassium to flow across the membrane. When glutamate binds, sodium flows in and potassium flows out. The lined, teal channel represents AMPA receptors; the checkered, teal channel represents kainate receptors. 'AMPA and Kainate' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Animation 4

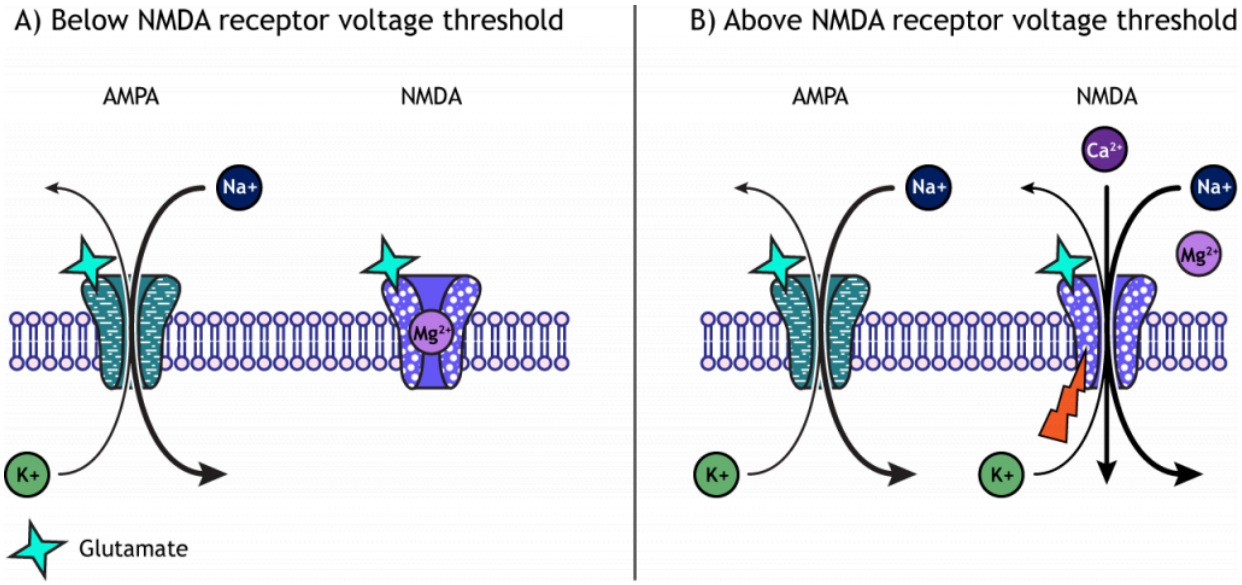


Figure 11.5. NMDA receptors are opened by a combination of glutamate binding and a voltage trigger. A) At low levels of stimulation when the the membrane potential is near rest and below the NMDA receptor voltage threshold, a magnesium ion blocks the open NMDA receptor channel preventing ion flow. Ions can flow through open AMPA receptors, which begins to depolarize the membrane. B) Once the NMDA receptor voltage threshold has been reached, the magnesium ion is expelled from the channel, allowing sodium, potassium, and calcium to cross the membrane. The lined, teal channels represent AMPA receptors; the dotted, violet channels represent NMDA receptors. 'AMPA and NMDA' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Animation 5

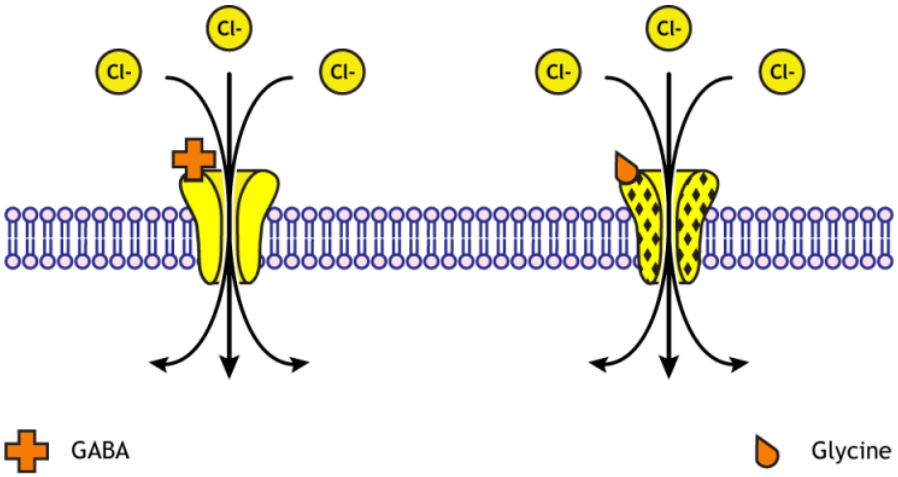


Figure 11.6. GABA and glycine are inhibitory receptors that are selective to chloride. The solid yellow channel represents a GABA receptor; the patterned, yellow channel represents a glycine receptor. 'GABA and Glycine' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Animation 6

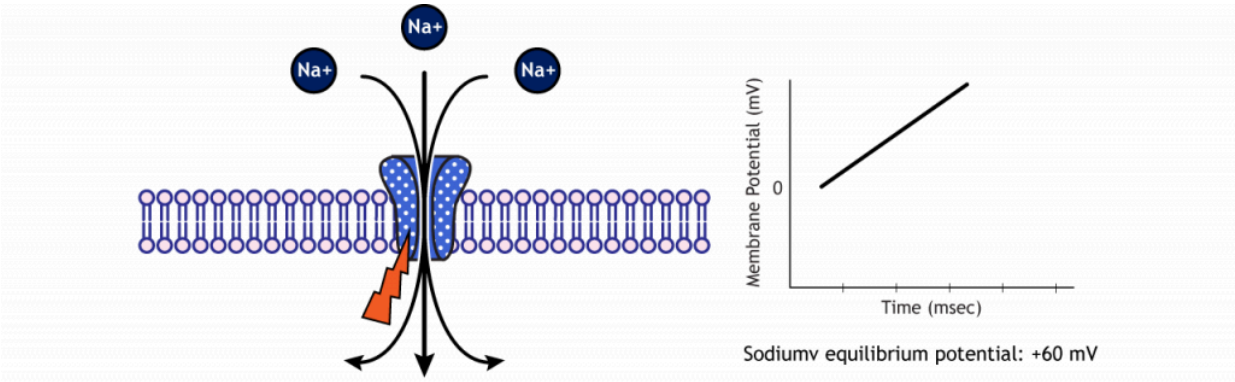


Figure 11.7. Ions move through open voltage-gated channels trying to reach equilibrium. As the ions cross the membrane, the neuron's membrane potential moves closer to the ion's equilibrium potential. In the figure, a voltage-gated sodium channel opens, and sodium flows in until the membrane potential equals approximately +60 mV, sodium's equilibrium potential. The blue, dotted channel represents a voltage-gated sodium channel. 'Equilibrium Potential' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Animation 7

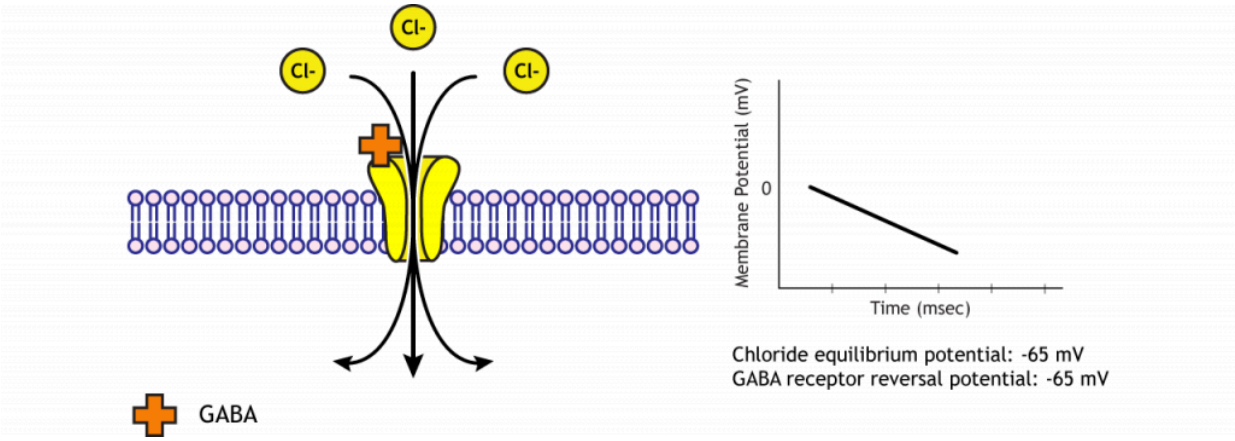


Figure 11.8. Ions move through open ligand-gated channels trying to reach equilibrium. As the ions cross the membrane, the neuron's membrane potential moves closer to the receptor's reversal potential. When the ionotropic receptor only increases permeability for one ion, the receptor's reversal potential is the same as the ion's equilibrium potential. In the animation, a GABA receptor open, and chloride flows in until the membrane potential equals approximately -65 mV, GABA's reversal potential and chloride's equilibrium potential. The yellow, checkered channel represents a GABA receptor. 'GABA Reversal Potential' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Animation 8

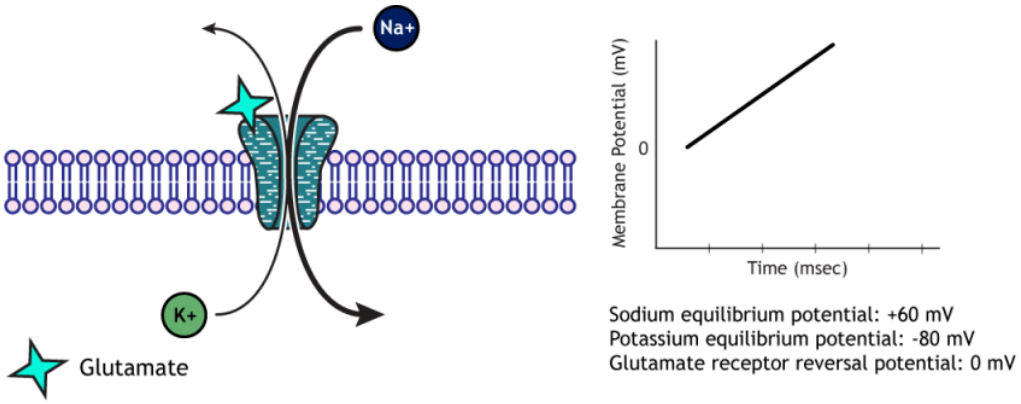


Figure 11.9. The reversal potential of an ionotropic receptor that is not selective to one ion will fall between the equilibrium potentials of the permeable ions. Glutamate receptors allow the flow of both sodium and potassium ions, so the reversal potential for the receptor is approximately 0 mV. More sodium will flow into the cell than potassium flows out, resulting in a depolarization of the membrane. The line, teal channel represents a glutamate receptor. 'Glutamate Reversal Potential – Rest' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Animation 9

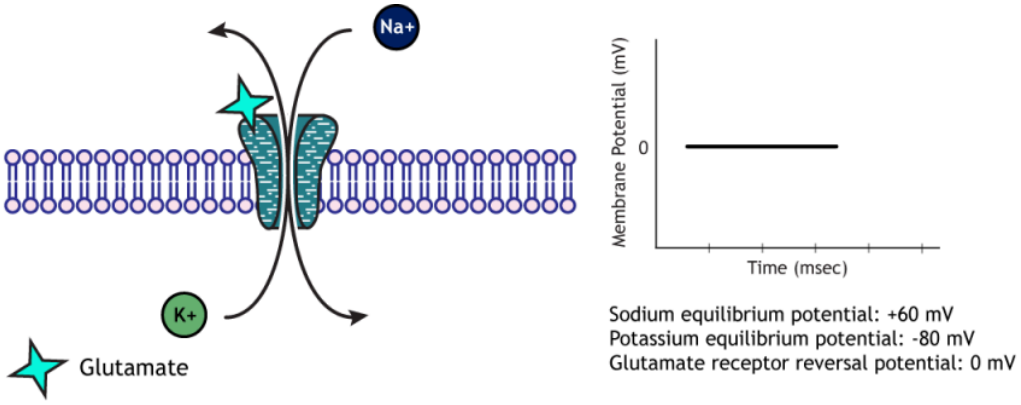


Figure 11.10. At the reversal potential, there is no net ion flow in either direction. An equal number of sodium ions enter the cell as potassium ions leave. Since there is no change in voltage at the reversal potential, if the receptor remained open, the membrane potential would stay at 0 mV. 'Glutamate Reversal Potential – 0 mV' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC-BY-NC-SA) 4.0 International License.

Chapter 12

Animation 1

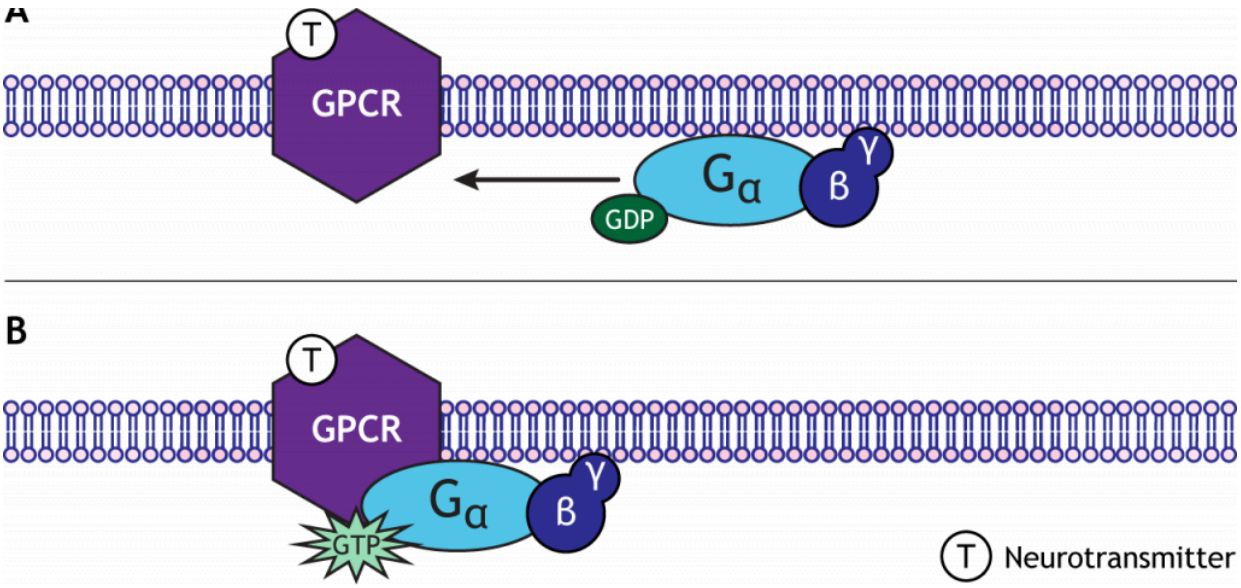


Figure 12.5. A) Neurotransmitter binding to a G-protein-coupled receptor causes the inactivated G-protein complex to interact with the receptor. B) The GDP molecule is then exchanged for a GTP molecule, which activates the G-protein complex. 'G-protein Binding' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Animation 2

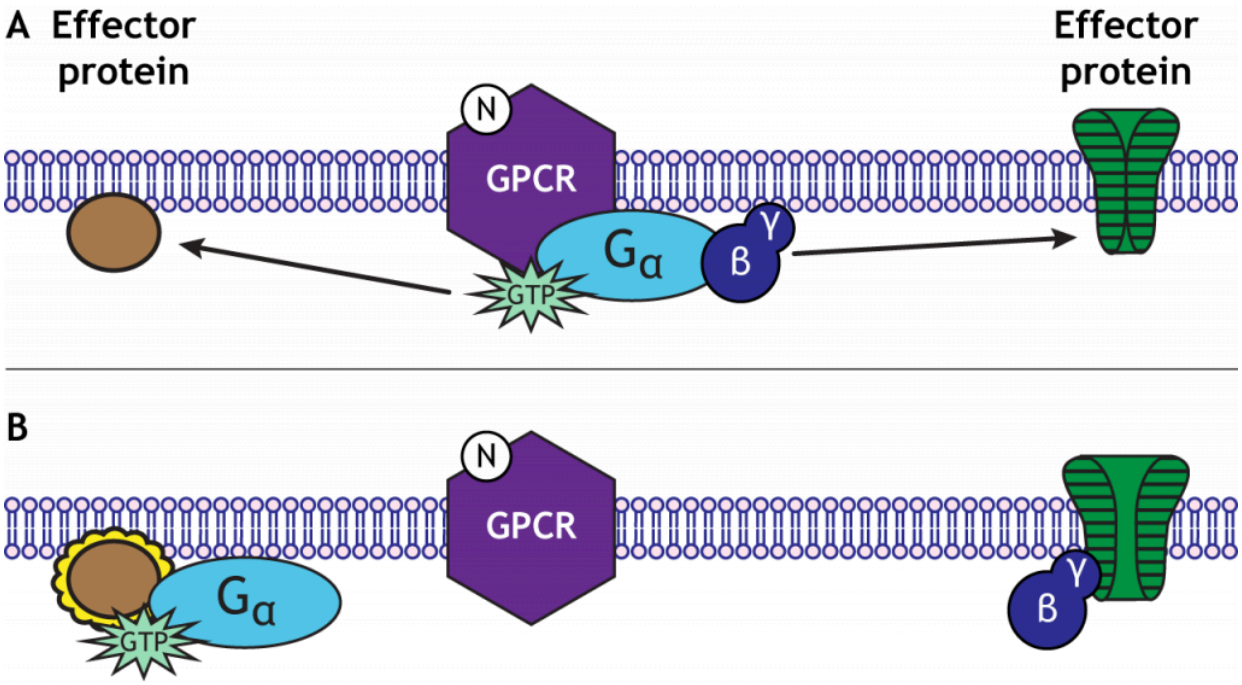


Figure 12.6. A) Once activated, the G-protein complex will separate into the alpha-GTP subunit and the beta-gamma subunit. B) These subunits can stimulate or inhibit effector proteins within the cell. 'G-protein Effects' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Animation 3

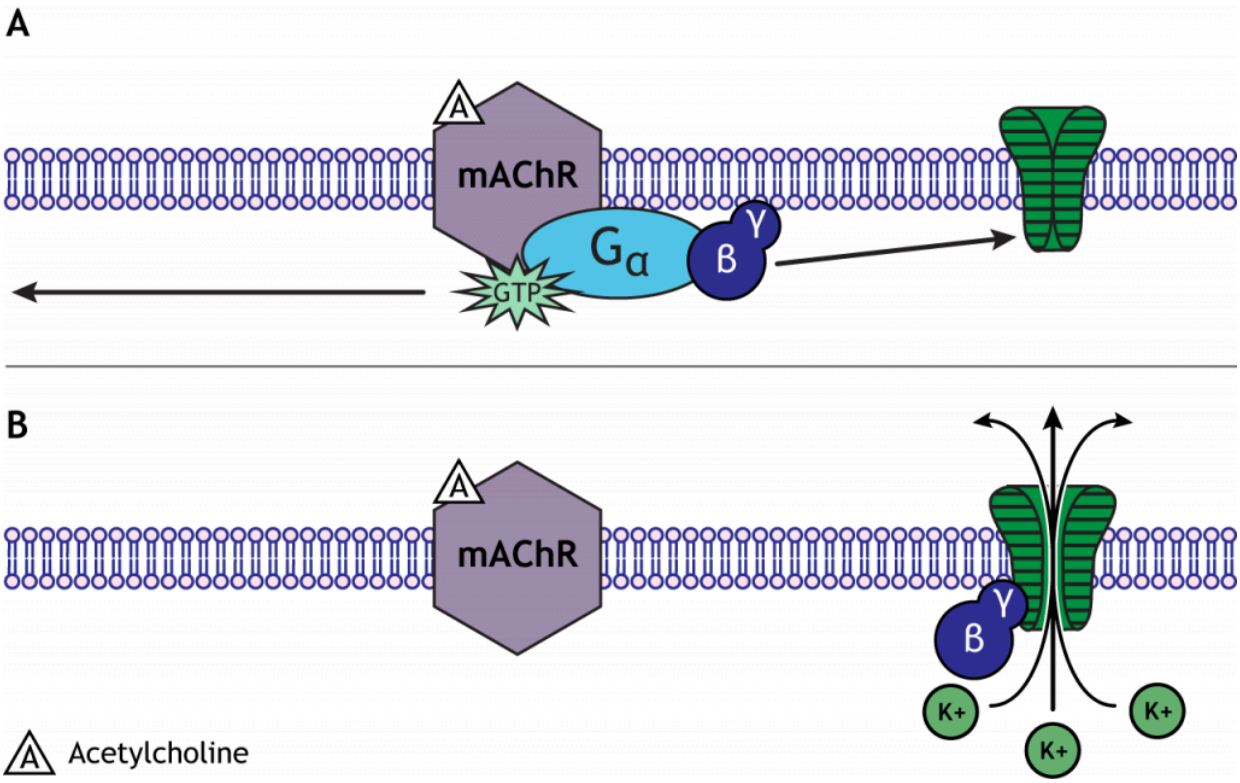


Figure 12.7. Some GPCRs, like the muscarinic acetylcholine receptors in the heart, alter cellular permeability by opening ion channels. The activated beta-gamma subunit of the muscarinic receptor (A) opens GIRK potassium channels and allows the efflux of potassium (B). 'Beta-Gamma Ion Channels' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Animation 4

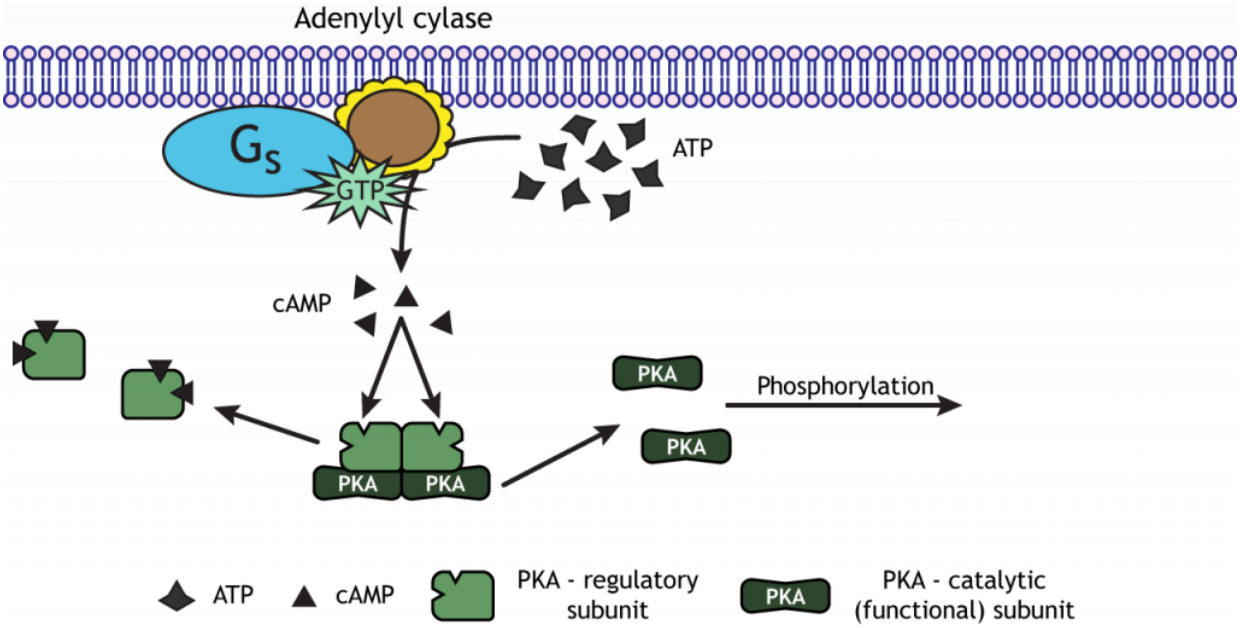


Figure 12.8. GPCRs that couple to the Gs alpha subunit initiate the adenylyl cyclase / cAMP pathway. The Gs subunit activates adenylyl cyclase, which then converts ATP to cAMP. cAMP binds to and activates protein kinase A (PKA), which phosphorylates proteins in the cell. 'Adenylyl Cyclase Pathway' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Animation 5

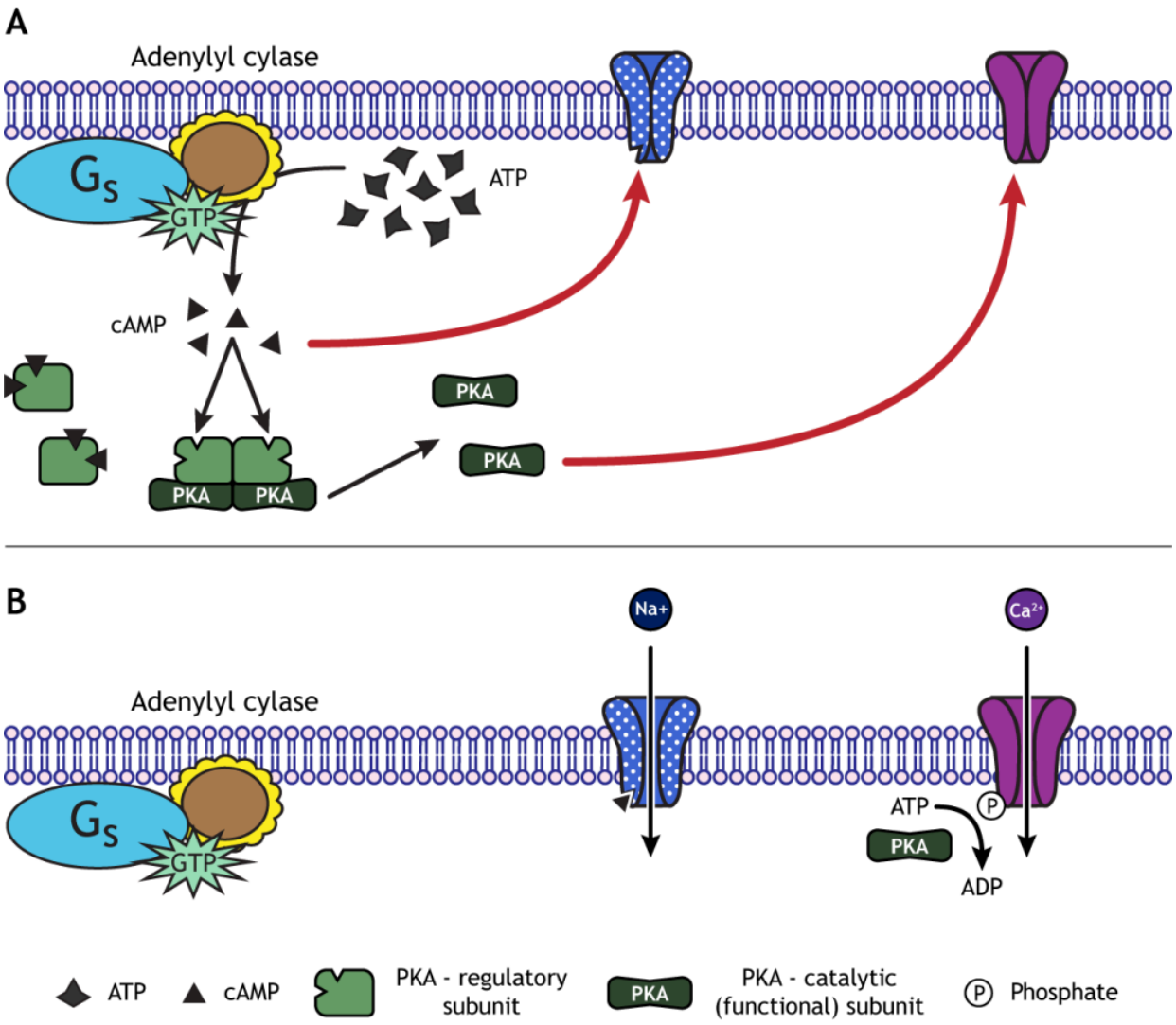


Figure 12.9. A) The adenylyl cyclase / cAMP pathway can alter many cellular functions. One example is that both cAMP and PKA can open ion channels. B) Like ligand-gated channels, there are also cAMP-gated channels, which open after cAMP binding. PKA is able to phosphorylate and modulate ion channel function by converting ATP to ADP. 'Second Messenger Ion Channel Action' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Animation 6

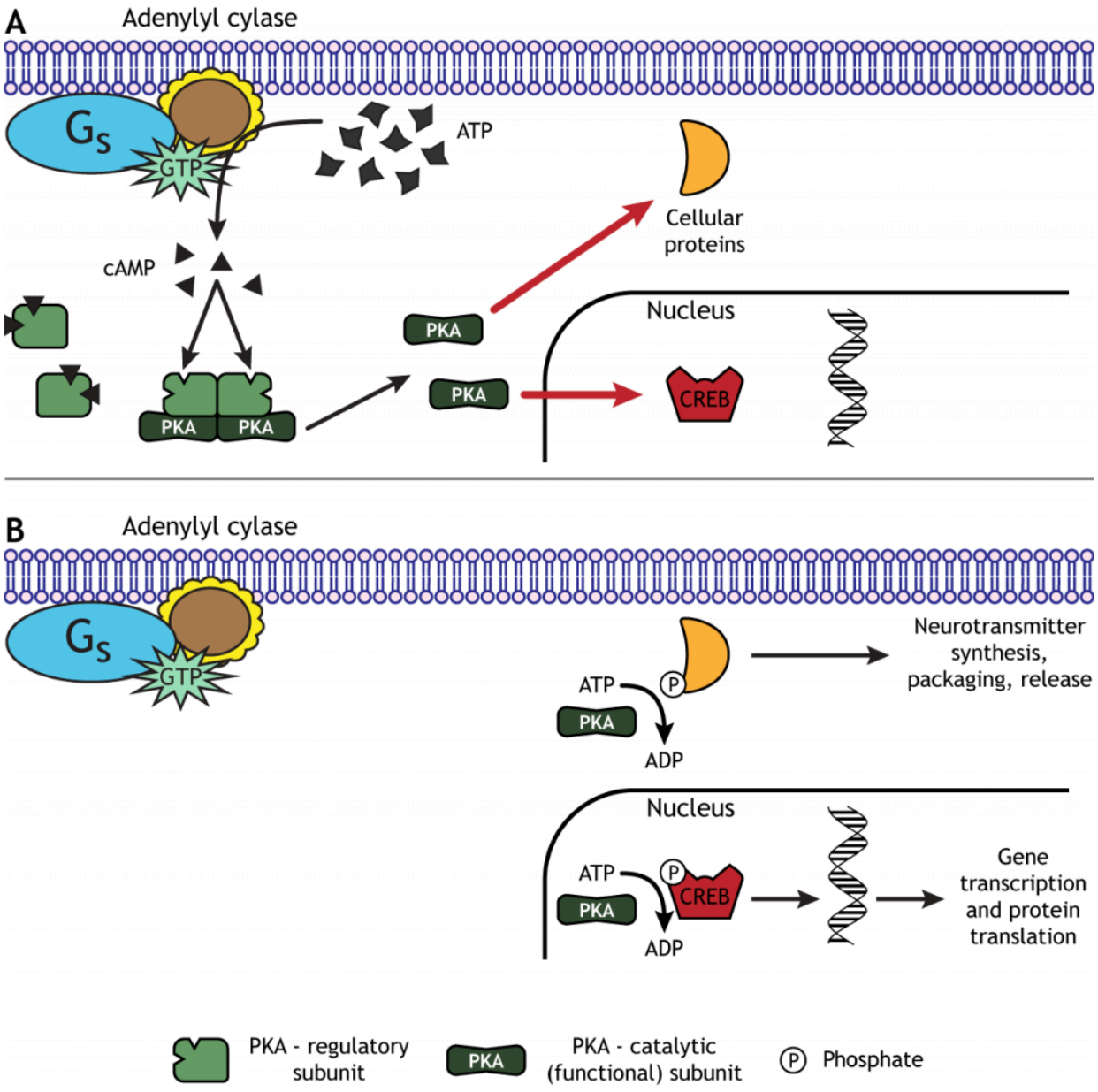


Figure 12.10. A) PKA can phosphorylate a number of proteins involved with neuron function. B) It can target proteins involved with neurotransmitter synthesis, packing, and release, or it can enter the nucleus and phosphorylate CREB, a transcription factor that can initiate gene transcription and protein synthesis. 'PKA Targets' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Animation 7

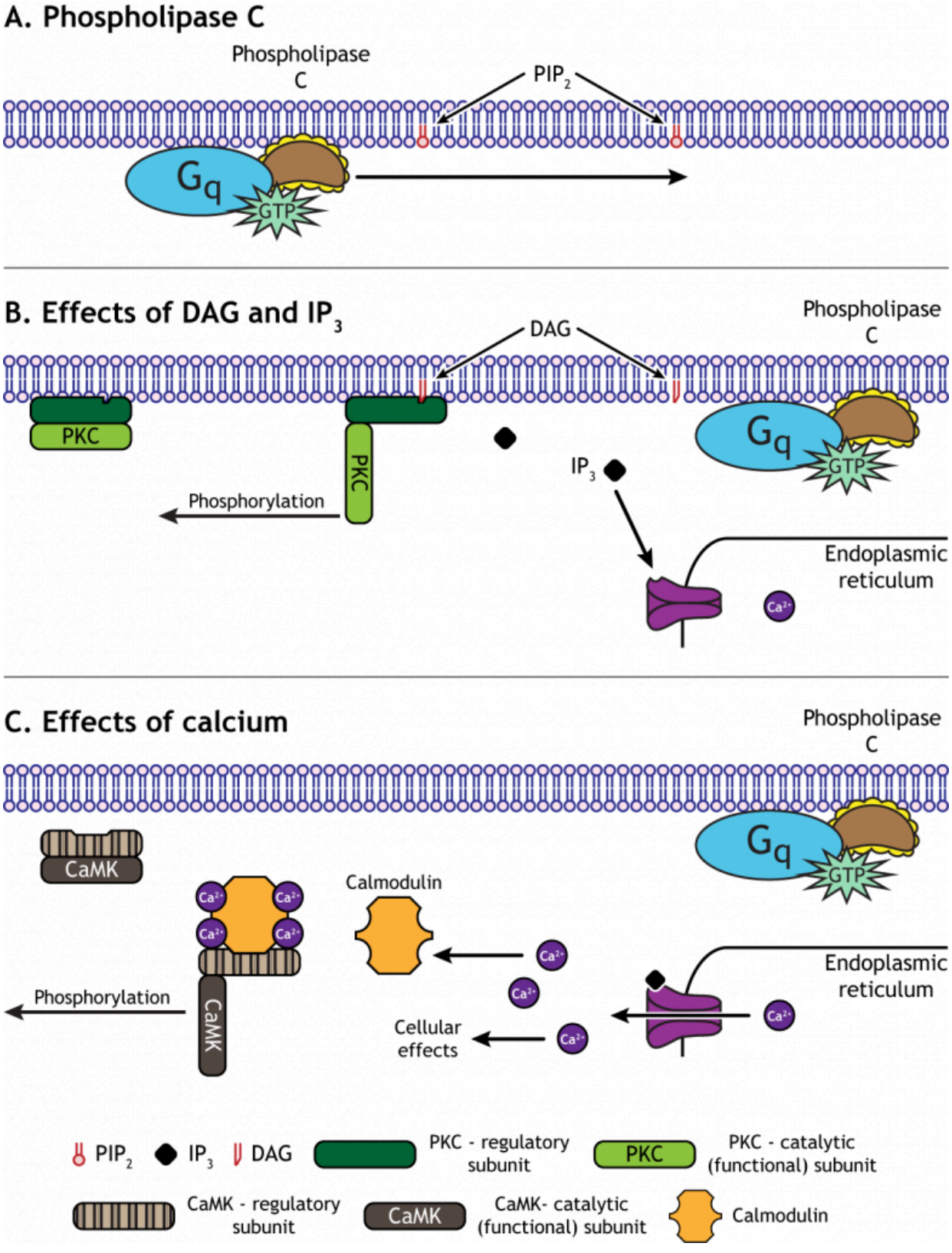

A. Phospholipase C
Phospholipase C
PIP2
Gq
GTP
B. Effects of DAG and IP3
DAG
Phospholipase C
PKC
PKC
Phosphorylation
IP3
Gq
GTP
Endoplasmic reticulum
Ca2+
C. Effects of calcium
Phospholipase C
CaMK
Calmodulin
Ca2+
Phosphorylation
CaMK
Gq
GTP
Endoplasmic reticulum
Cellular effects
PIP2
IP3
DAG
PKC - regulatory subunit
PKC
PKC - catalytic (functional) subunit
CaMK - regulatory subunit
CaMK
CaMK- catalytic (functional) subunit
Calmodulin

Figure 12.11. A) The Gq G-protein subunit activates phospholipase C, which converts the phospholipid PIP2 in the cell membrane into DAG, another membrane-bound molecule, and IP3, a cytoplasmic molecule. B) DAG can interact with PKA, initiating phosphorylation of cellular proteins. IP3 opens calcium channels in the endoplasmic reticulum, allowing calcium to flow into the cytoplasm. C) Calcium, another second messenger can have many cellular effects. It can bind to calmodulin, which then activates CaMK, causing phosphorylation of more protein targets. 'IP3-DAG Pathway' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.

Chapter 19

Animation 1

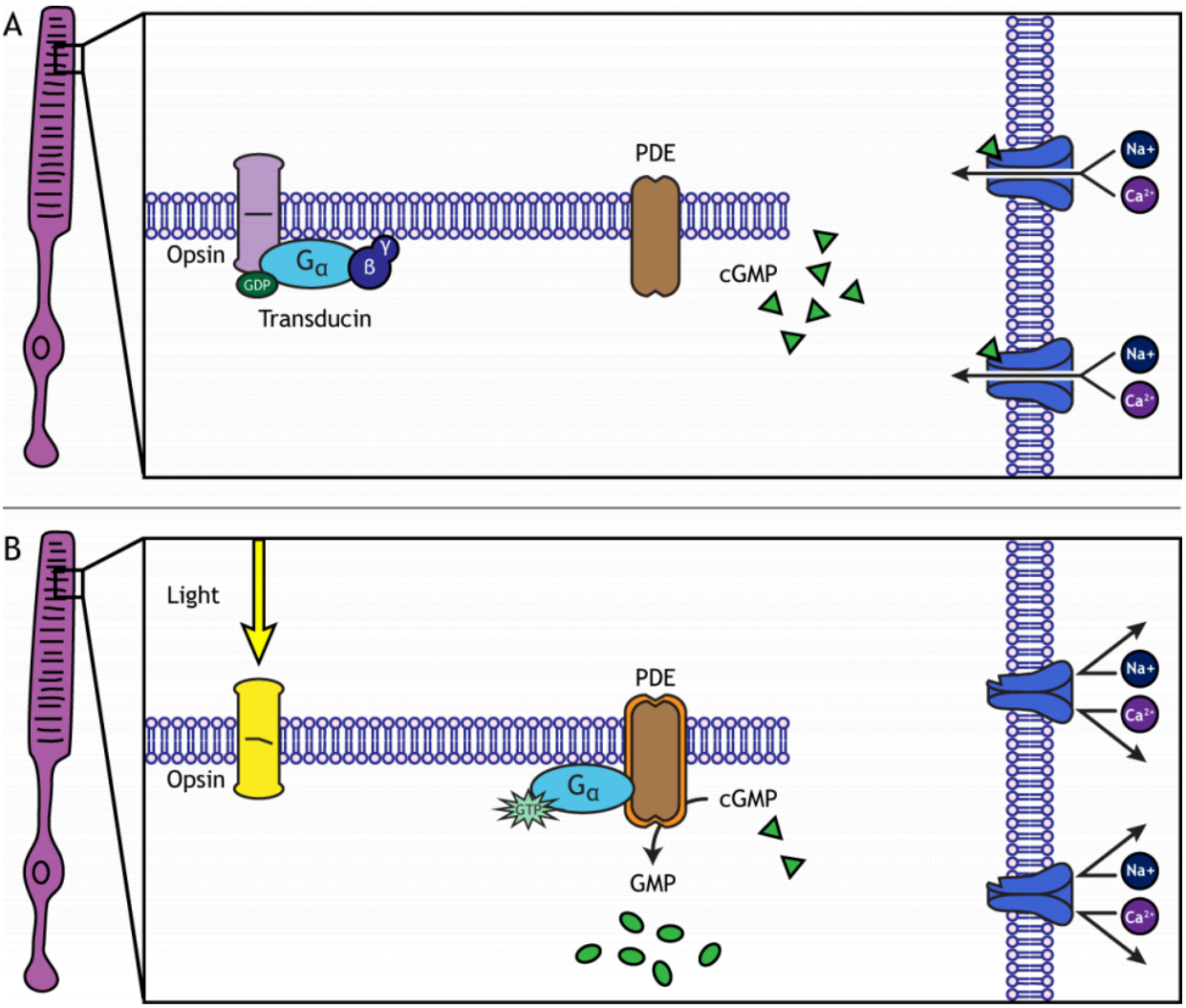


Figure 19.16. A) In the dark, the photoreceptor is depolarized due to an influx of sodium and calcium through open ion channels that are gated by cGMP. The photoreceptor has high levels of cGMP when it is in the dark. Additionally, the opsin proteins, the G-protein transducin, and phosphodiesterase (PDE) are all inactivated. B) Light reaching the photoreceptor causes a conformational change in the opsin protein, which activates the G-protein transducing. Transducin activates phosphodiesterase (PDE), which converts cGMP to GMP. Without cGMP, the cation channels close, stopping the influx of positive ions. This results in a hyperpolarization of the cell. 'Phototransduction' by Casey Henley is licensed under a Creative Commons Attribution Non-Commercial Share-Alike (CC BY-NC-SA) 4.0 International License.