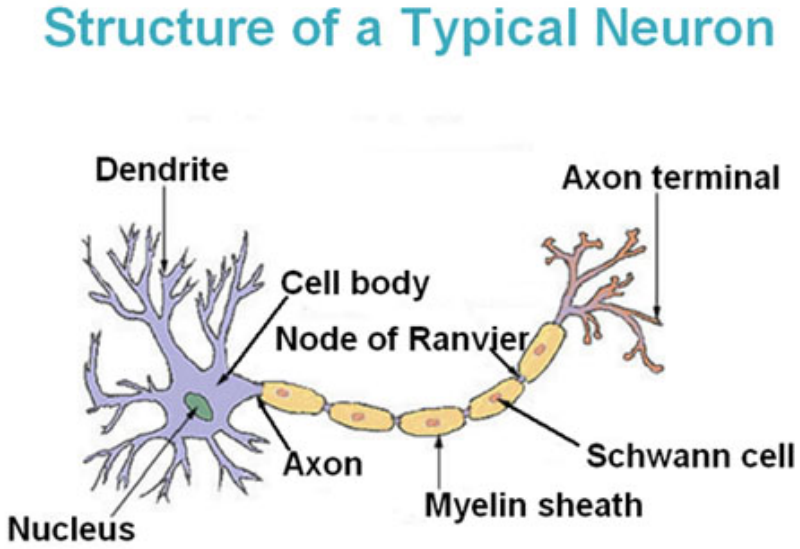
Physiology of Nerve Cells

Introducing the Neuron

Neuron: *is the basic building block of the central nervous system (CNS) and they are specialized cells that transmit chemical and electrical signals to facilitate communication between the CNS and the body*. The CNS is made up entirely of **neurons** and **glia** cells, *which are non-neuronal cells that provide structure and support for the neurons*. Neurons are responsible for most of body functions from consciousness and thought to pain and hunger.

Structures of a Neuron

Neurons have all the normal components of a cell (nucleus, organelles, etc.) and also contain unique structures for receiving and sending the electrical signals that make neuronal communication possible.



This image shows the basic structural components of an average neuron, including the dendrite, cell body, nucleus, Node of Ranvier, myelin sheath, Schwann cell, and axon terminal.

A- Cell Body

Like other cells, each neuron has a **cell body** (or soma) that contains a **nucleus**, **smooth and rough endoplasmic reticulum, Golgi apparatus, mitochondria, and other cellular components**.

B- Dendrite

Dendrites are branch-like structures extending away from the cell body, and their job **is to receive messages from other neurons and allow those messages to travel to the cell body**. Although some neurons do not have any dendrites, other types of neurons have multiple dendrites. Dendrites can have

small protrusions called **dendritic spines**, which further i**ncrease surface area for possible connections with other neurons**.

C- Axon

An axon *is a tube-like structure that carries an electrical impulse from the cell body (or from another cell's dendrites) to the structures at opposite end of the neuron—axon terminals, which can then pass the impulse to another neuron.* The cell body contains a specialized structure, the **axon hillock**, which serves as a j**unction between the cell body and the axon**.

D- Synapse

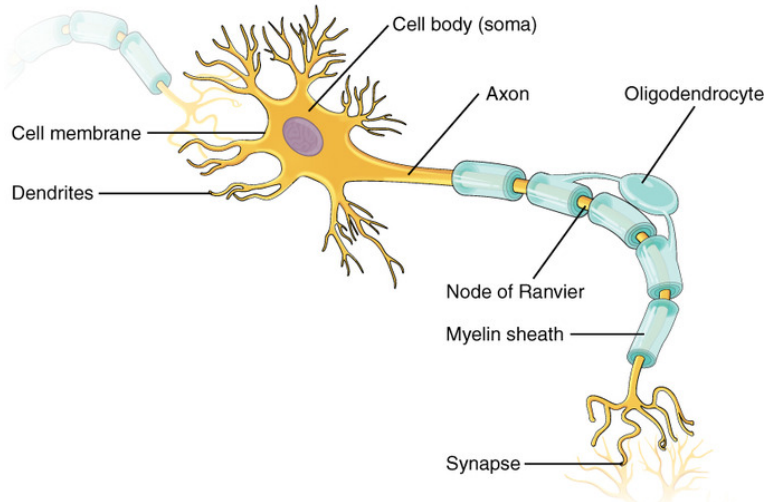
The synapse **is the chemical junction between the axon terminals of one neuron and the dendrites of the next**. It is a gap where specialized chemical interactions can occur, rather than an actual structure.

Myelin Sheath

Myelin sheath *is a fatty material that wraps around the axons of some neurons and functions as insulator to minimize dissipation of the electrical signal as it travels down the axon.* Myelin presence **increases the speed of conduction of the electrical signal, because the fat prevents any electricity from leaking out**. Periodic gaps in the myelin sheath are called **nodes of Ranvier**.

Glia Cells

The myelin sheath **is not actually part of the neuron**. Myelin is produced by **glial cells** (or simply glia, or "glue" in Greek), which are **non-neuronal cells that provide support for the nervous system**. Glia function *to hold neurons in place, supply them with nutrients, provide insulation, and remove pathogens and dead neurons.* In the central nervous system, the glial cells that form the myelin sheath are called **oligodendrocytes**; in the peripheral nervous system, they are called **Schwann cells**.



This neuron diagram also shows the oligodendrocyte, myelin sheath, and nodes of Ranvier.

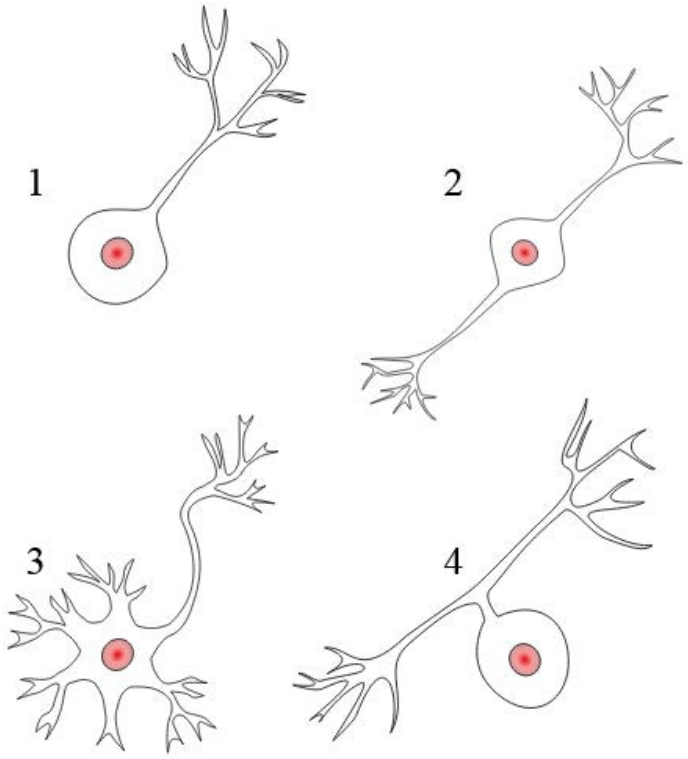
Types of Neurons

There are three major types of neurons: **sensory neurons, motor neurons, and interneurons.**

Sensory Neurons

Sensory neurons a*re neurons responsible for converting external stimuli from the environment into internal stimuli*. They are activated by sensory input, and send projections to other elements of the nervous system, ultimately conveying sensory information to the brain or spinal cord. Sensory neurons are activated by **physical modalities** (such as visible light, sound, heat, physical contact, etc.) or by **chemical signals** (such as smell and taste).

Most sensory neurons are ***pseudounipolar***, meaning they have an axon that branches into two extensions—one connected to dendrites that receive sensory information and another that transmits this information to the spinal cord.



Multipolar and pseudounipolar neurons: This diagram shows the difference between: 1) a unipolar neuron; 2) a bipolar neuron; 3) a multipolar neuron; 4) a pseudounipolar neuron.

Motor Neurons

Motor neurons *are neurons located in the central nervous system (CNS), and they project their axons outside of the CNS to directly or indirectly control muscle*s. The interface between a motor neuron and muscle fiber is a specialized synapse called the **neuromuscular junction**. The structure of **motor neurons is *multipolar***, meaning each cell contains a single axon and multiple dendrites.

Interneurons

Interneurons are **neither sensory nor motor**; rather, they **act connect between the other two nerve types.** Located in the CNS, they operate locally, meaning their axons connect only with nearby sensory or motor neurons. Interneurons can save time and therefore prevent injury by sending messages to the spinal cord and back instead of all the way to the brain. Like motor neurons, they are **multipolar** in structure.

Neural Impulses in the Nervous System

The CNS goes through a **three-step process** when it functions: **sensory input**, **neural processing**, and **motor output**. The sensory input stage is when the neurons (or excitable nerve cells) of the sensory organs are excited electrically. Neural impulses from sensory receptors are sent to the brain and spinal cord for processing. After the brain has processed the information, neural impulses are then conducted from the brain and spinal cord to muscles and glands, which is the resulting motor output.

Stages of Neural Impulses

"**Resting potential**" is the name for the electrical state when a neuron is not actively being signaled. A neuron at resting potential has a membrane with established amounts of sodium (Na+) and potassium (K+) ions on either side, leaving the inside of the neuron negatively charged relative to the outside.
The **action potential** is *a rapid change in polarity that moves along the nerve fiber from neuron to neuron.* In order for a neuron to move from resting potential to action potential, the neuron must be stimulated by pressure, electricity, chemicals, or another form of stimuli. *The level of stimulation that a neuron must receive to reach action potential is known as the* **threshold** of excitation, and until it reaches that threshold, no action potential occur.

Action Potential

It is a short-term change in the electrical potential (cell membrane charge) that travels along a cell and to be passed to another cell, such as a nerve or muscle fiber, and allows nerves to communicate.

Stages of the Action Potential

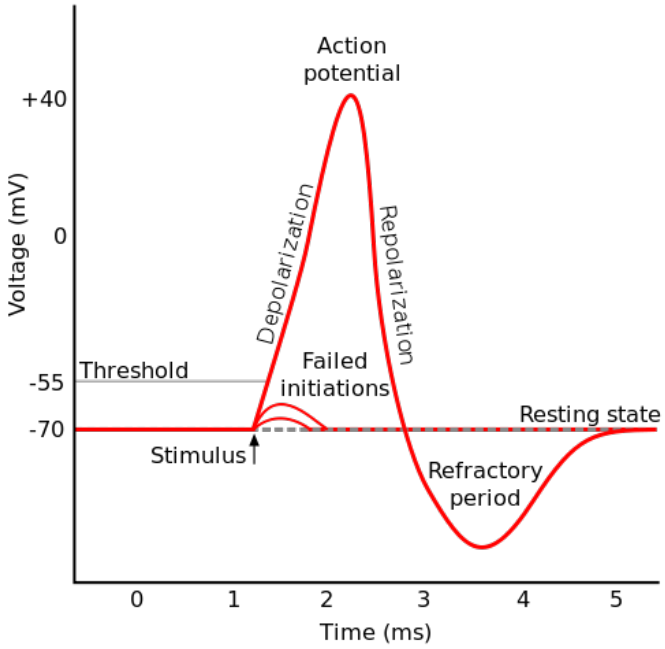
Neural impulses occur when a stimulus depolarizes a cell membrane, prompting an action potential which sends an "all or nothing" signal.

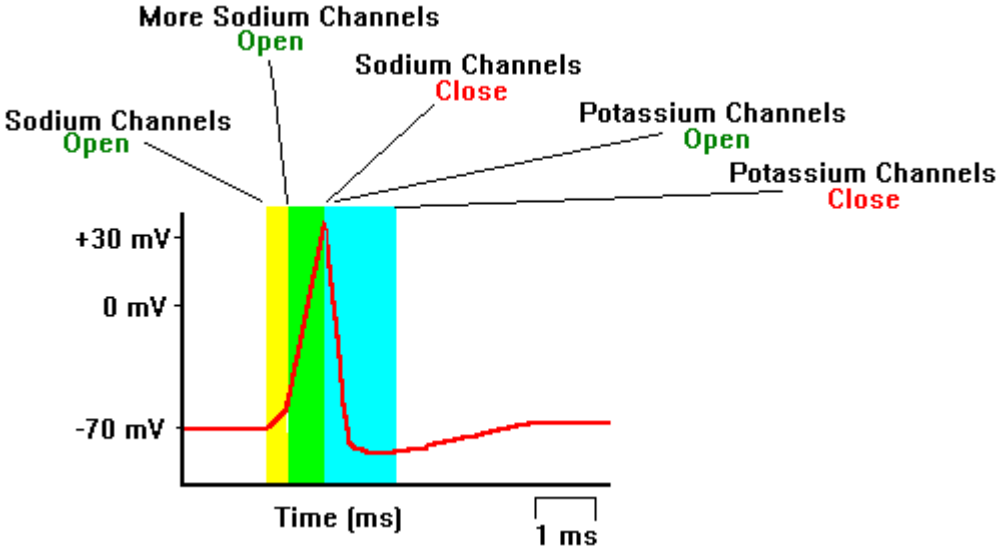
The action potential has several stages:

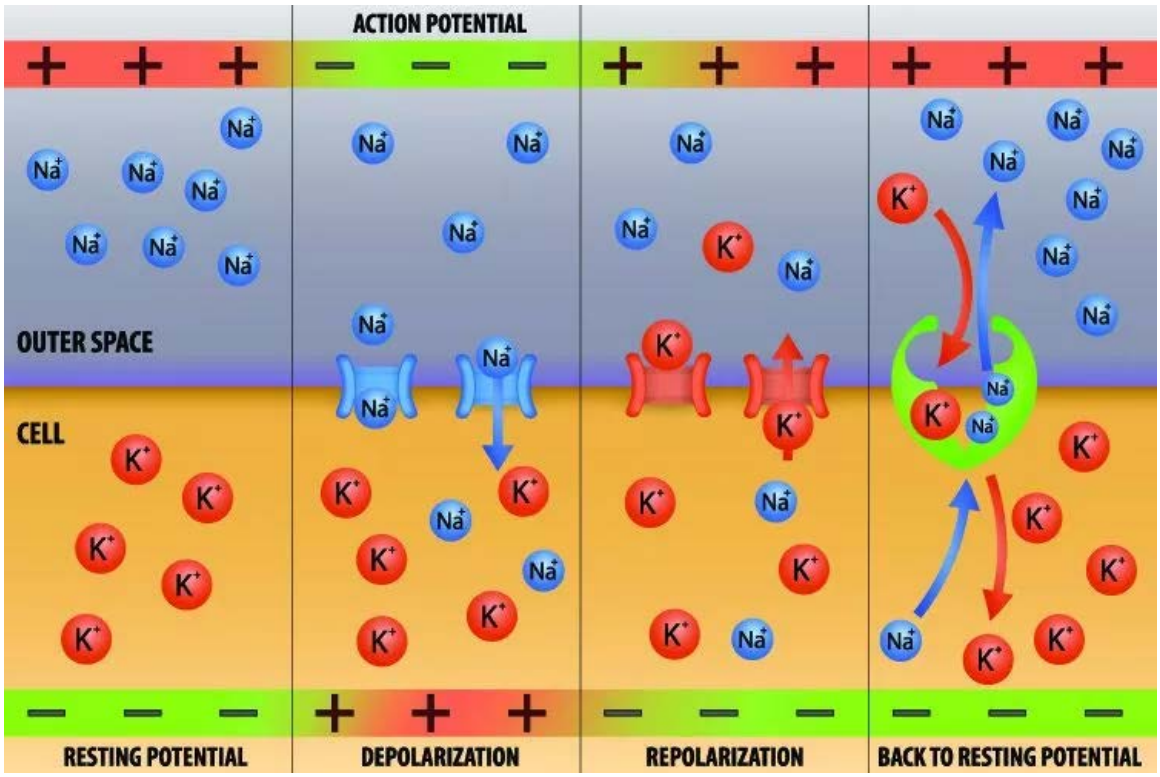
1. **Depolarization**: A stimulus starts the depolarization of the membrane. Depolarization is caused when positively charged **sodium ions** rush into a nerve cell. As these positive ions rush in, the membrane of the stimulated cell reverses its polarity so that the outside of the membrane is negative relative to the inside.
2. **Repolarization**: Once the electric gradient has reached the threshold of excitement, the repolarization begins. The channels that let the positive sodium ion channels through close up, while channels that allow positive **potassium ions** open, resulting in the release of positively charged potassium ions from

the neuron. This expulsion *acts to restore the localized negative membrane potential of the cell, bringing it back to its normal charge.*

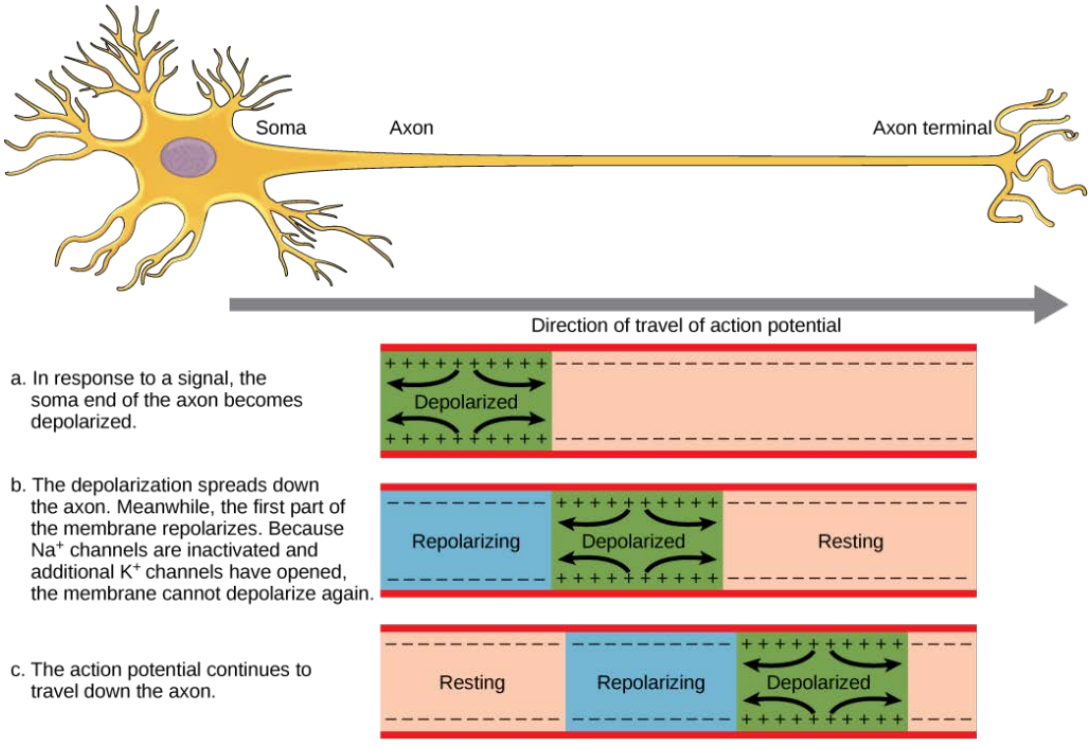
3. **Refractory Phase**: The refractory phase takes place over a short period of time after the depolarization stage. Shortly after the s**odium gates open**, they close and go into an inactive conformation. The sodium gates cannot be opened again until the membrane is returned to its normal resting potential. The **sodium-potassium pump** returns sodium ions to the outside and potassium ions to the inside. During the refractory phase this particular area of the nerve cell membrane cannot be depolarized. *Therefore, the neuron cannot reach action potential during this "rest period."*



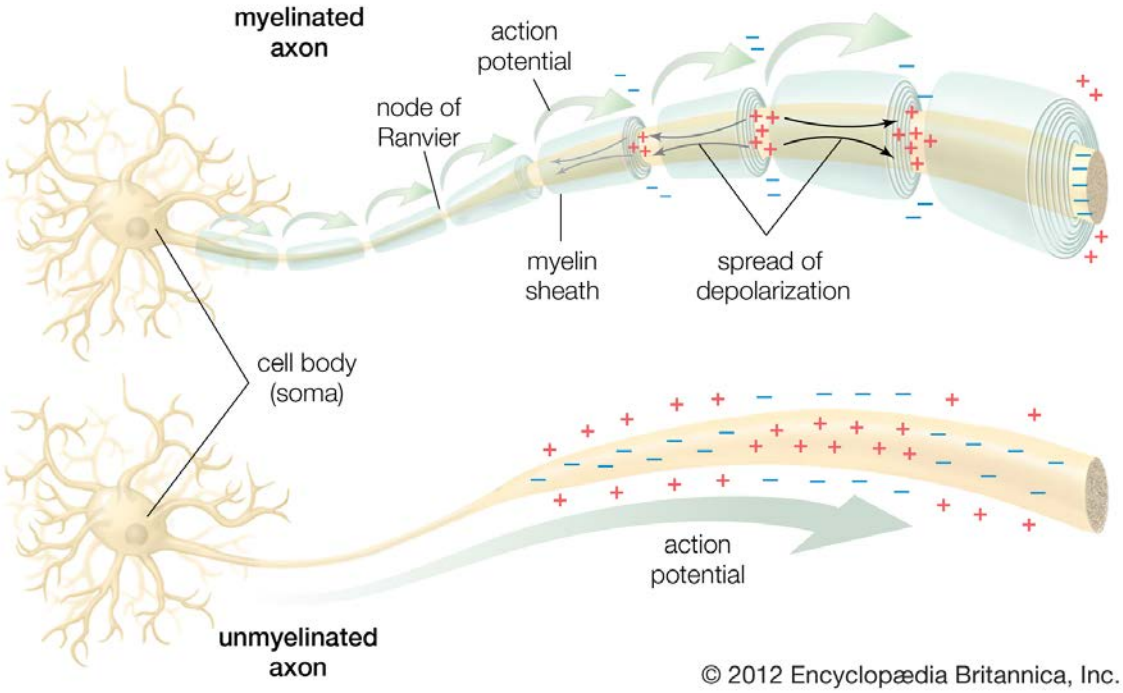




The process of depolarization, repolarization, and recovery moves along a nerve fiber from neuron to neuron like a very fast wave. In **unmyelinated** axons (axons that are not covered by a myelin sheath), this happens in a continuous fashion *because there are voltage-gated channels throughout the membrane.*



In **myelinated** axons (axons covered by a myelin sheath), this process is described as **saltatory conduction** *because voltage-gated channels are only found at the nodes of Ranvier*, and the electrical events seem to "jump" from one node to the next. **Saltatory conduction** is ***faster*** than continuous conduction.



Saltatory conduction *is the propagation of action potentials along myelinated axons from one node of Ranvier to the next node, increasing the conduction velocity of action potentials*. The uninsulated nodes of Ranvier are the only places along the axon where ions are exchanged across the axon membrane, regenerating the action potential between regions of the axon that are insulated by myelin.

All-or-none Signals

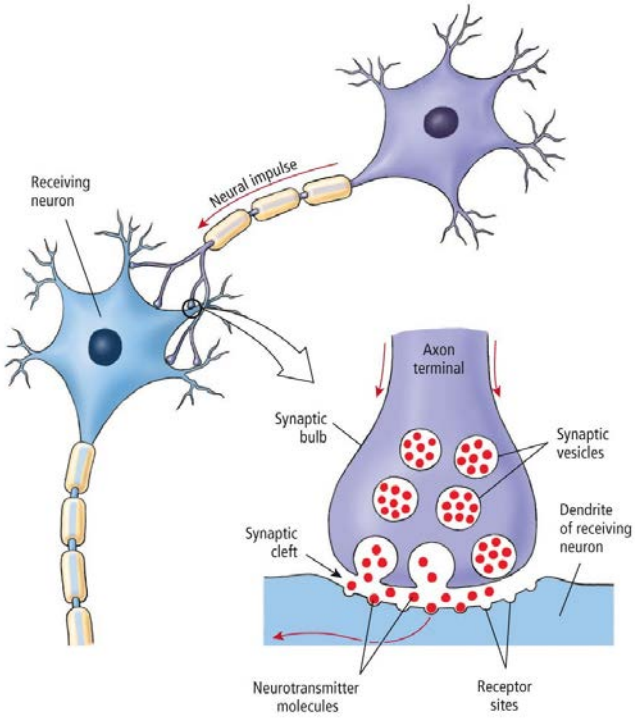
The amplitude of an action potential is independent of the amount of current that produced it. In other words, larger currents do not create larger action potentials. Therefore, action potentials are said to be all-or-none signals, since either they occur fully, or they do not occur at all. The frequency of action potentials is correlated with the intensity of a stimulus.

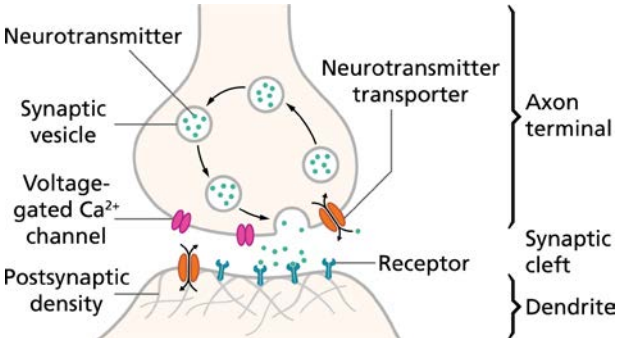
Synapses

The **synapse** *is the site at which a chemical or electrical exchange occurs between the* ***presynaptic*** *and* ***postsynaptic*** *regions of nerve cells.*

The synapse is the junction where neurons trade information. The presynaptic cell (**giving the signal**) and the postsynaptic cell (**receiving the signal**). There are two types of possible reactions at the synapse—**chemical** or **electrical**. During a **chemical reaction**, a chemical called a **neurotransmitter**

is released from one cell into another. In an **electrical reaction**, the electrical charge of one cell is influenced by the charge an adjacent cell.





All synapses have a few common characteristics:

- Presynaptic cell: a specialized area within the axon of the giving cell that transmits information to the dendrite of the receiving cell.
- Synaptic cleft: the small space at the synapse that receives neurotransmitters.
- G-protein coupled receptors: receptors that sense molecules outside the cell and thereby activate signals within it.
- Ligand-gated ion channels: receptors that are opened or closed in response to the binding of a chemical messenger.
- Postsynaptic cell: a specialized area within the dendrite of the receiving cell that contains receptors designed to process neurotransmitters.

Types of Synapses

A- The Electrical Synapse

The stages of an electrical reaction at a synapse are as follows:

1. Resting potential. The membrane of a neuron is normally at rest with established concentrations of sodium ions (Na+) and potassium ions (K+) on either side. The membrane potential (or, voltage across the membrane) at this state is -70 mV, with the inside being negative relative to the outside.

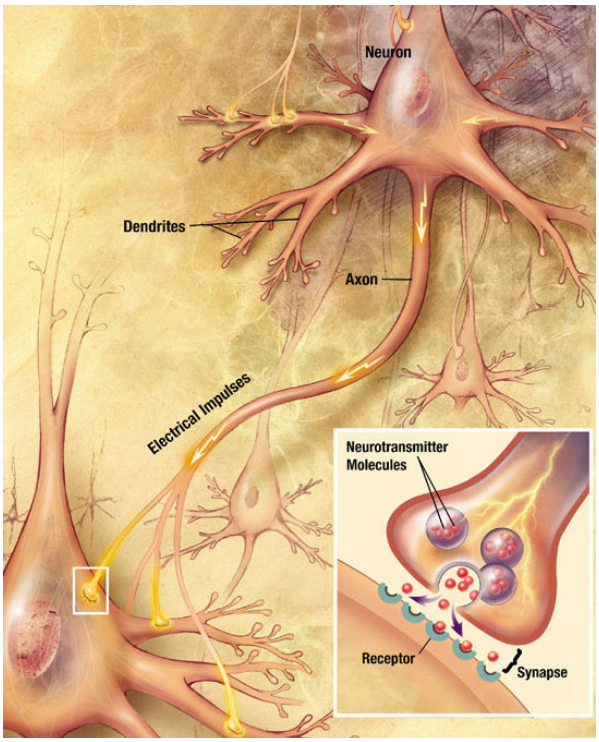
2. Depolarization. A stimulus begins the depolarization of the membrane. Depolarization occurs when positively charged sodium ions (Na+) suddenly rush through open sodium gates into a nerve cell. If the membrane potential reaches -55 mV, it has reached the threshold of excitation. Additional sodium rushes in, and the membrane of the stimulated cell actually reverses its polarity so that the outside of the membrane is negative relative to the inside. The change in voltage stimulates the opening of additional sodium channels (called a voltage-gated ion channel), providing what is known as a positive feedback loop. Eventually, the cell potential reaches +40 mV, or the action potential.

3. Repolarization is caused by the closing of sodium ion channels and the opening of potassium ion channels, resulting in the release of positively charged potassium ions (K+) from the nerve cell. This expulsion acts *to restore the localized negative membrane potential of the cell*.

4. Refractory Phase. The refractory phase is a short period of time after the repolarization stage. Shortly after the sodium gates open, they close and go into an inactive conformation where the cell's membrane potential is actually even lower than its baseline -70 mV. The sodium gates cannot be opened again until the membrane has completely repolarized to its normal resting potential, -70 mV. The sodium-potassium pump returns sodium ions to the outside and potassium ions to the inside.

B- The Chemical Synapse

The process of a chemical reaction at the synapse has some important differences from an electrical reaction. Chemical synapses are much more complex than electrical synapses, which makes them **slower**, but also allows them to generate different results. Like electrical reactions, chemical reactions involve electrical modifications at the postsynaptic membrane, but chemical reactions also require chemical messengers, such as **neurotransmitters**, to operate.



This image shows electric impulses traveling between neurons; the inset shows a chemical reaction occurring at the synapse.

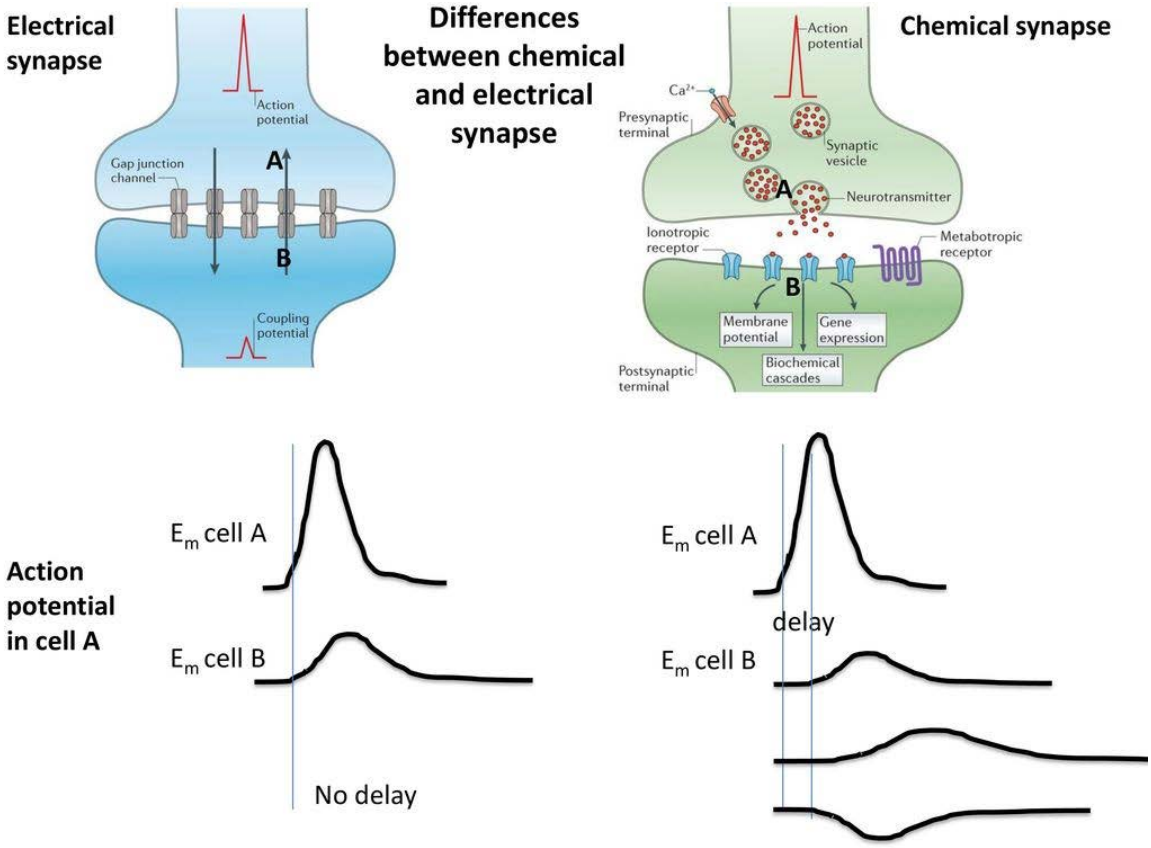
A basic chemical reaction at the synapse undergoes a few additional steps:

1. The action potential (which occurs as described above) travels along the membrane of the presynaptic cell until it reaches the synapse. The electrical depolarization of the membrane at the synapse causes channels to open that are **selectively permeable**, meaning they specifically only allow the entry of positive sodium ions (Na+).
2. The ions flow through the presynaptic membrane, rapidly increasing their concentration in the interior.
3. The high concentration activates a set of ion-sensitive proteins attached to **vesicles**, which are small membrane compartments that contain a neurotransmitter chemical.
4. These proteins change shape, causing the membranes of some "**docked**" vesicles to fuse with the membrane of the presynaptic cell. This opens the vesicles, which releases their neurotransmitter contents into the **synaptic cleft**, the narrow space between the membranes of the pre- and postsynaptic cells.
5. The neurotransmitter diffuses within the cleft. Some of it escapes, but the rest of it binds to chemical receptor molecules located on the membrane of the postsynaptic cell.
6. The binding of neurotransmitter causes the receptor molecule to be activated. Several types of activation are possible, depending on what kind of neurotransmitter was released. In any case, this is the key step by which the synaptic process affects the behavior of the postsynaptic cell.

7. Due to thermal shaking, neurotransmitter molecules eventually break loose from the receptors and drift away.
8. The neurotransmitter is either **reabsorbed by the presynaptic cell** and **repackaged** for future release, or else it is **broken down metabolically**.

Differences Between Electrical and Chemical Synapses

- Electrical synapses are faster than chemical synapses because the receptors do not need to recognize chemical messengers. The synaptic delay for a chemical synapse is typically about **2 msec**, while the synaptic delay for an electrical synapse may be about **0.2 msec**.
- Because electrical synapses do not involve neurotransmitters, electrical neurotransmission is less modifiable than chemical neurotransmission.
- The response is always the same sign as the source. For example, depolarization of the presynaptic membrane will always induce a depolarization in the postsynaptic membrane.
- The response in the postsynaptic neuron is generally smaller in amplitude than the source. The amount of attenuation of the signal is due to the membrane resistance of the presynaptic and postsynaptic neurons.



Neurotransmitters

Neurotransmitters are chemicals that transmit signals from a neuron across a synapse to a target cell.

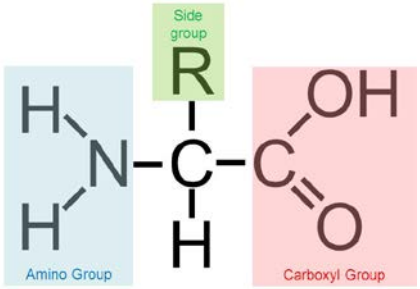
There are several systems of neurotransmitters found at various synapses in the nervous system. The following groups refer to the specific chemicals and within each group are specific systems.

Cholinergic System

The cholinergic system is a neurotransmitter system of its own, and is based on the neurotransmitter **acetylcholine** (ACh). The cholinergic system has two types of receptors: the **nicotinic receptor** and **the acetylcholine receptor**, which is known as the **muscarinic receptor**. Both of these receptors are named for chemicals that interact with the receptor in addition to the neurotransmitter acetylcholine. Nicotine, the chemical in tobacco, binds to the nicotinic receptor and activates it similarly to acetylcholine. **Muscarine**, a chemical product of certain mushrooms, binds to the muscarinic receptor. However, they cannot bind to each others' receptors.

Amino Acids

Another group of neurotransmitters are amino acids, including **glutamate** (Glu), gamma-aminobutyric acid (GABA) and glycine (Gly). These amino acids have an **amino group** and a **carboxyl group** in their chemical structures.



Biogenic Amines

Another class of neurotransmitter is the biogenic amine, a group of neurotransmitters made enzymatically from amino acids. They **have amino groups** in them, but **do not have carboxyl groups** and are therefore no longer classified as amino acids.

Neuropeptides

A neuropeptide is a neurotransmitter molecule **made up of chains of amino acids** connected by peptide bonds, similar to proteins. However, **proteins are long molecules** while some **neuropeptides are quite short**.

Catecholamine Group

Dopamine is the best-known neurotransmitter of this group.

Neuromuscular Junction

The neuromuscular junction (NMJ) is a synaptic connection between the terminal end of a motor nerve and a muscle (skeletal/ smooth/ cardiac). It is the site for the transmission of action potential from nerve to the muscle.

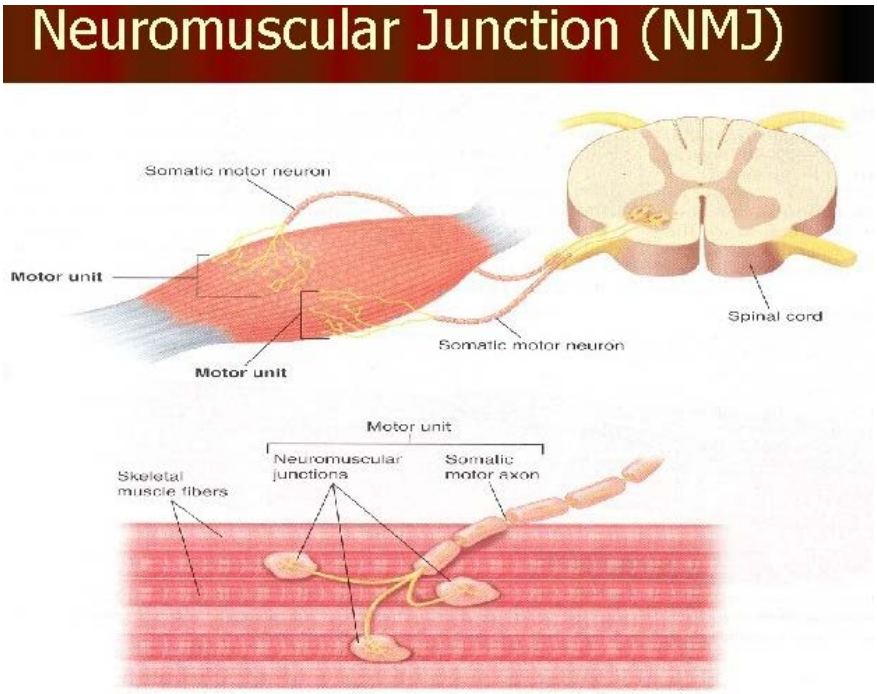
Structure of NMJ

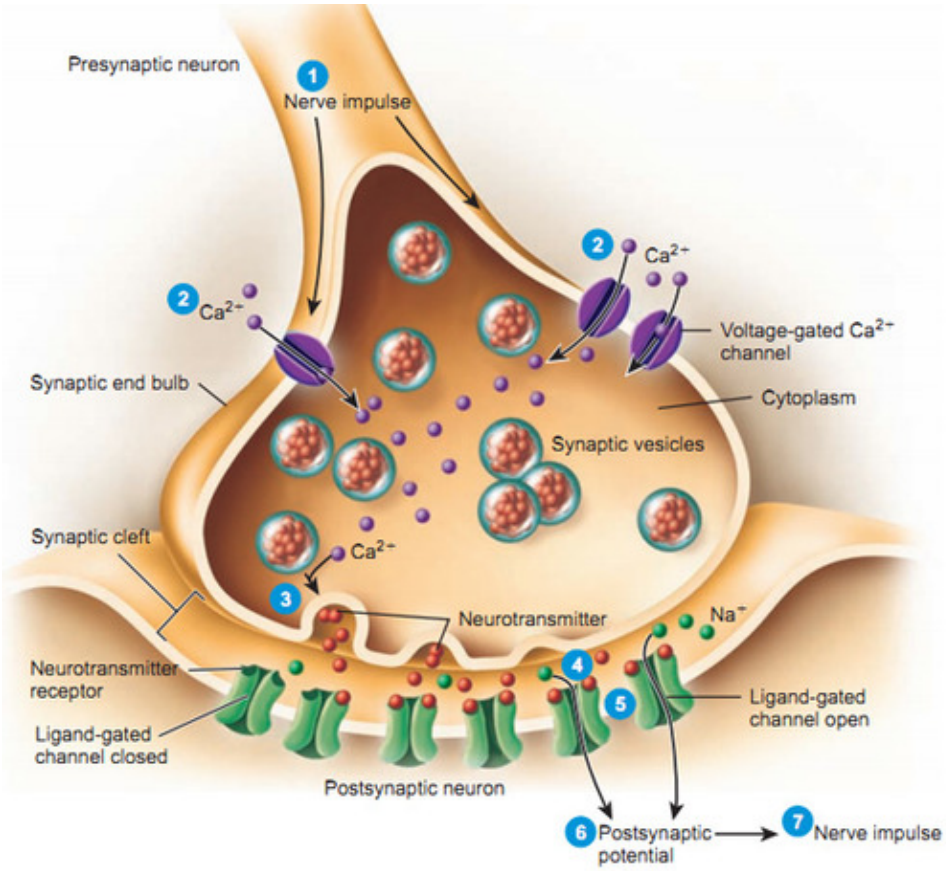
NMJ can be divided into three main parts: a **presynaptic part** (nerve terminal), the **postsynaptic part** (motor endplate), and **synaptic cleft** which is an area located between the nerve terminal and motor endplate.

Nerve Terminal: A myelinated motor neuron, on reaching the target muscle, loses its myelin sheath to form a complex of 100-200 branching nerve endings. These nerve endings are called **nerve terminals** or **terminal boutons**. The nerve terminal membrane has areas of membrane thickening called active zones. Active zones have a family of synaptosomal-associated proteins (syntaxins and synaptosomal-associated protein 25) and rows of voltage-gated calcium (Ca^{++}) channels. A nerve terminal also has potassium channels on its membrane and contains mitochondria, endoplasmic reticulum, and synaptic vesicles (SVs). Each SV stores around 5000-10000 molecules of acetylcholine (ACh), the neurotransmitter at NMJ. The SVs are concentrated around the active zone. The membrane of SVs has synaptotagmin and synaptobrevin proteins. These proteins are essential for fusion and docking of SVs at active zones. On arrival of an action potential at the nerve terminal, Ca^{++} channels open to cause influx. Increased Ca^{++} inside the nerve terminal causes a series of events leading to docking of SVs at active zones and exocytosis of the ACh from the synaptic vesicles into the synaptic cleft.

Synaptic Cleft or **Junctional Cleft**: The space between the nerve terminal and the plasma membrane of muscle is called synaptic/junctional cleft and measures ~50 nm. It is the site where presynaptic neurotransmitters, ACh is released before it interacts with nicotinic ACh receptors on the motor endplate. Synaptic cleft of NMJ contains **acetylcholinesterase enzyme**, responsible for the catabolism of released ACh so that its effect on the post-synaptic receptors is not prolonged.

Motor End Plate (the postsynaptic part of NMJ): It is the thickened portion of the muscle plasma membrane (sarcolemma) that is folded to form depressions called **junctional folds**. The terminal nerve endings do not penetrate the motor endplate but fit into the junctional folds. Junctional folds have nicotinic ACh receptors concentrated at the top. These receptors are ACh gated ion channels. Binding of ACh to these receptors opens the channels allowing the influx of sodium ions from the extracellular fluid into the muscle membrane. This creates endplate potential and generates and transmits AP to the muscle membrane.



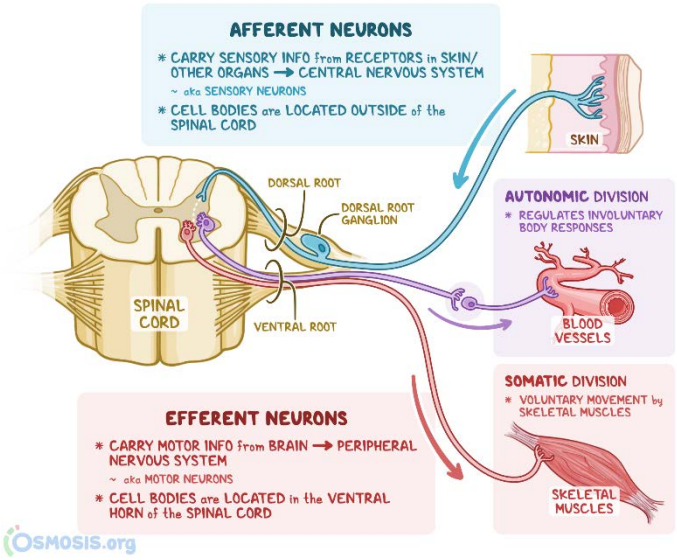


Neuromuscular junction

Autonomic Nervous System Physiology

Nervous System

The nervous system is a complex network of nerve cells (neurons) that carry signals to and from the brain and spinal cord to different parts of the body. **Afferent neurons** carry information from **sensory** receptors of the skin and other organs to the central nervous system (i.e., brain and spinal cord), whereas **efferent neurons** carry **motor** information away from the central nervous system to the muscles and glands of the body.



Components and Functions of the Nervous System

The nervous system has two major components: the **central nervous system** (CNS) and the **peripheral nervous system** (PNS). The CNS is composed of the **brain** and the **spinal cord**. The PNS includes nerves outside the CNS (brain and spinal cord) and consists of **sensory neurons** and **motor neurons**. Sensory neurons *sense the environment and conduct signals to the brain* that become a conscious perception of that stimulus. This conscious perception may *lead to a motor response that is conducted from the brain to the PNS* via motor neurons to cause a movement. Motor neurons consist of the **somatic nervous system** (SNS) that stimulates **voluntary** movement of muscles and the **autonomic nervous system** (ANS) that controls **involuntary** responses.

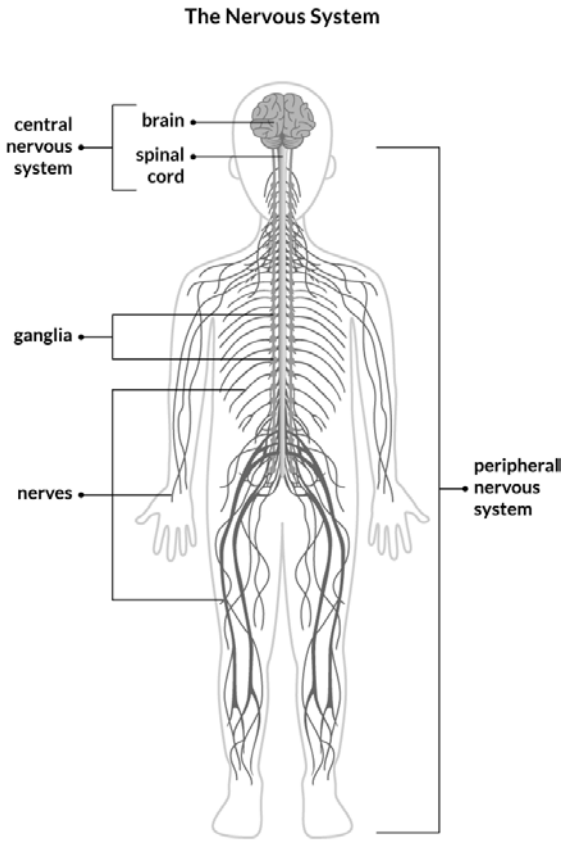


Diagram of the nervous system

What is the Autonomic Nervous System?

Many bodily functions proceed without any conscious supervision from our CNS. For example, we don't have to remember to digest our food after a meal, or sweat when too warm. These functions are controlled subconsciously, with a degree of automaticity, by a branch of the nervous system – The autonomic nervous system (ANS).

There are *two* divisions of the ANS: the **sympathetic nervous system** (SyNS) and **parasympathetic nervous system** (PaNS). The SyNS contains **alpha** and **beta receptors**, and the PaNS contains **nicotinic** and **muscarinic receptors**. Each type of receptor has a specific action when stimulated. See Figure 2 below for an image of the divisions of the nervous system and the receptors in the ANS.

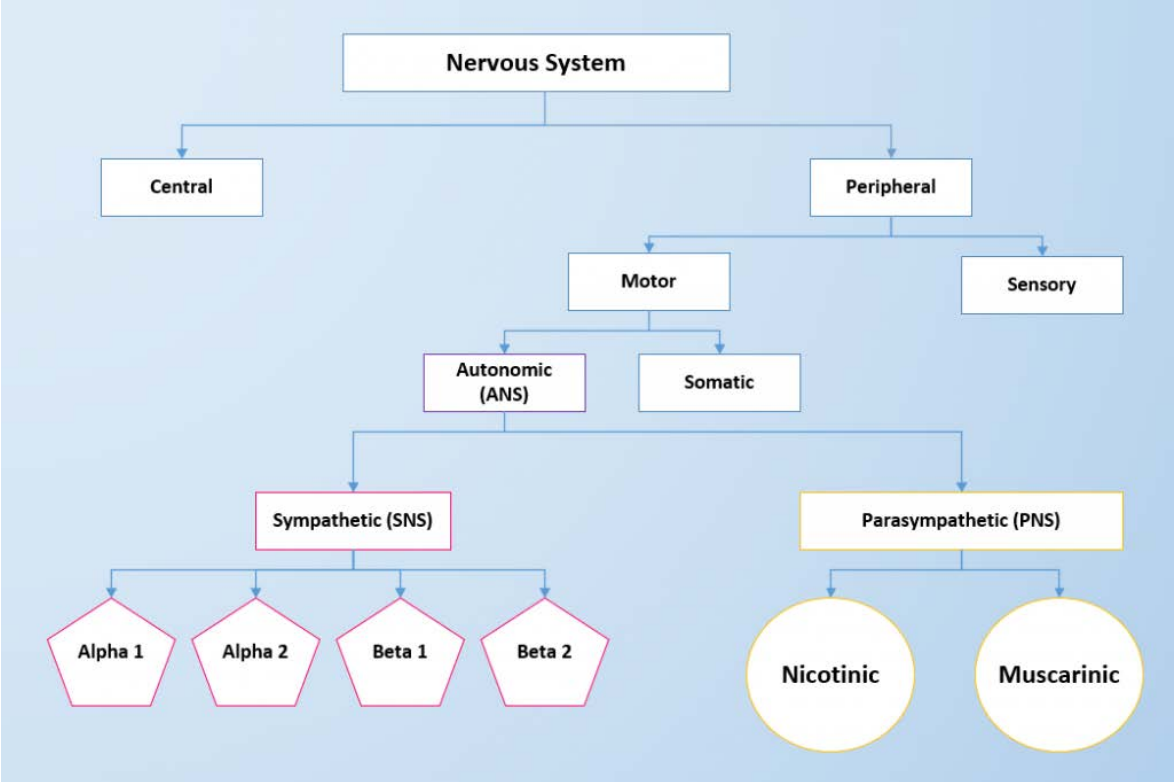


Figure 2 Components of the Nervous System and ANS receptors

SyNS and PaNS Functions

The ANS regulates several internal organs through a balance of these two divisions and is instrumental in homeostatic mechanisms in the body.

Stimulation of SyNS primarily produces increased heart rate, increased blood pressure via the constriction of blood vessels, and bronchial dilation. In comparison, stimulation of the PaNS causes slowing of the heart, lowering of blood pressure due to vasodilation, bronchial constriction.

Homeostasis: is the balance between the two systems. At each target organ, dual innervations determine the organ activity. For example, the heart receives connections from both the sympathetic and parasympathetic divisions. SyNS stimulation causes the heart rate to increase, whereas PaNS stimulation causes the heart rate to decrease. See Figure 3 to compare the effects on PaNS and SyNS stimulation on target organs.

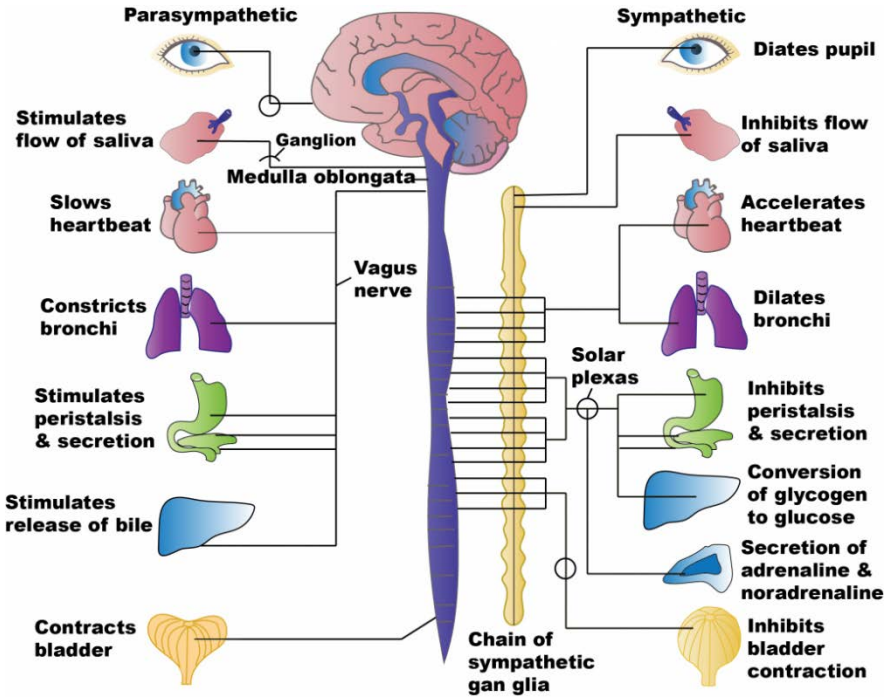


Figure 3. Effects of PaNS and SyNS Stimulation on Target Organs

The SyNS is associated with the "**fight** or **flight**" response, and PaNS activity is often referred to as "**rest** and **digest**."

To respond to a threat – to "fight or flight" – the sympathetic system stimulates many different target organs to achieve this purpose. For example, if a person sees a grizzly bear in the wilderness, the individual has the choice to stand and fight the bear or to run away. For either choice, several things must occur for additional oxygen and glucose to be delivered to skeletal muscle to fight or run. The respiratory, cardiovascular, and musculoskeletal systems are all activated to breathe rapidly, cause bronchodilation in the lungs to inhale more oxygen, stimulate the heart to pump more blood, and increase blood pressure to deliver it to the muscles. The liver creates more glucose for energy for the muscles to use. The pupils dilate to see the threat (or the escape route) more clearly. Sweating prevents the body from overheating from excess muscle contraction. Since the digestive system is not needed during this time of threat, the body shunts oxygen-rich blood to the skeletal muscles. To coordinate all these targeted responses, catecholamines such as **epinephrine** and **norepinephrine** are released in the sympathetic system and disperse to many neuroreceptors on the target organs simultaneously.

Chemical Signaling in the Autonomic Nervous System

Neurones conduct impulses to the synapse of a target organ. The synapse is a connection between two neuronal cells. See Figures 4 and 5 for images of synapse connections.

Ganglia

A ganglion is a cluster of neuronal cell bodies that house millions of synapses. *Synapse* is located in the ganglion. The key difference between ganglion and synapse is *ganglion houses millions of synapses while synapse is a small junction where two neurons come closer during the signal transmission.*

The ganglion is composed of **preganglionic** (presynaptic) neurons and **postganglionic** (postsynaptic) neurons.

Preganglionic neurones release **acetylcholine** (ACh) onto **nicotinic receptors** on the postganglionic neuron. Nicotine, found in *tobacco* products, also binds to and activates nicotinic receptors, mimicking the effects of ACh.

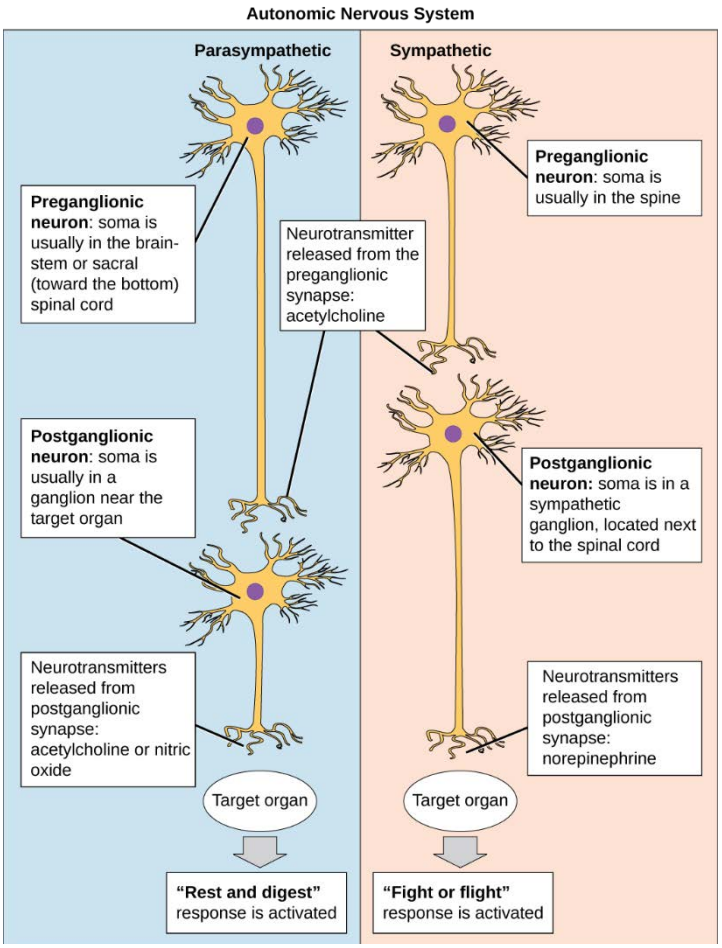


Figure 4 Autonomic System neurons conduct signals via the preganglionic neurons to postganglionic neurons to the target organs

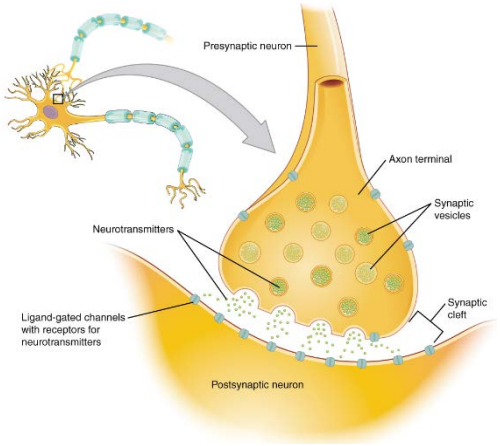


Figure 5 The synapse is the connection between a neuron and its target cell

Postganglionic Neurons

There are different types of postganglionic neurons in the SyNS and PaNS branches of the ANS. *Postganglionic neurons of the PaNS* branch are classified as **cholinergic neurons**, meaning that **ACh** is released, whereas *postganglionic neurons of the SyNS* are classified as **adrenergic neurons**, meaning that **norepinephrine** (NE) is released. (See Figure 6 for an image of the release of ACh and NE and their attachment to the corresponding adrenergic or nicotinic receptors.)

The cholinergic system of the PaNS includes two classes of postganglionic neuroreceptors: the **nicotinic receptors** and the **muscarinic receptors**. *Both receptor* types bind to **ACh** and cause changes in the target cell.

The adrenergic system of the SyNS has *two* major types of neuroreceptors: the **alpha (α)-adrenergic receptor** and **beta (β)-adrenergic receptor**. There are *two* types of α-adrenergic receptors, termed **α1** and **α2**, and there are *two* types of β-adrenergic receptors, termed **β1** and **β2**. These receptors bind to **norepinephrine** (noradrenalin) and **epinephrine** (adrenalin) that are secreted from *adrenal glands* and these are associated with **fight** and **flight** response.

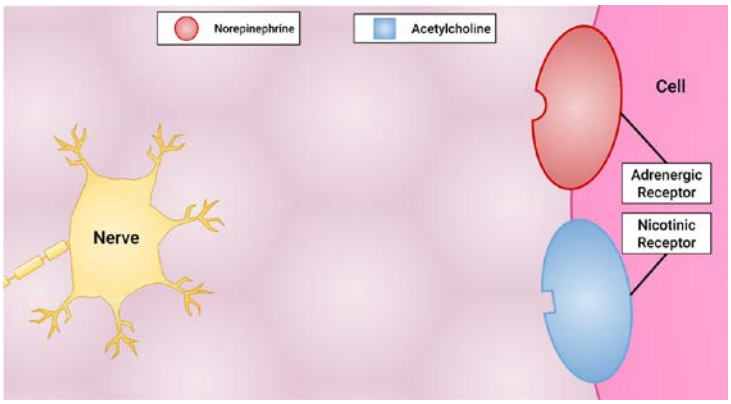


Figure 6 Sympathetic and Parasympathetic Pre-and Postganglionic Fibers and Neuroreceptors

ANS Neuroreceptors and Effects

The effects of stimulating each type of neuroreceptor are outlined in this section and sample uses of medications are provided.

Sympathetic Nervous System

SyNS receptors include Alpha-1, Alpha-2, Beta-1, and Beta-2 receptors. **Epinephrine and norepinephrine stimulate these receptors**, causing the overall fight-or-flight response in various target organs. Medications causing similar effects are called **adrenergic agonists** or **sympathomimetics**, because they mimic the effects of the body's natural SyNS stimulation. On the other hand, adrenergic **antagonists** block the effects of the SyNS receptors. **Dopamine** also stimulates these receptors, but it is dosage-based. Dopamine causes vasodilation of arteries in the kidney, heart, and brain, depending on the dosage. See Table 4.1 for a comparison of stimulation and inhibition of these SNS receptors.

Table 1 Comparison of Medication Effects of Adrenergic Receptor Stimulation and Inhibition

Receptor	Effects of Stimulation	Effects of Inhibition
Alpha-1	Contract smooth muscle CNS stimulation Blood vessels: vasoconstriction to nonessential organs Gastrointestinal tract (GIT): relax smooth muscle and decrease motility Liver: increase glyconeogenesis Bladder: muscle contraction Uterus: muscle contraction Pupils: dilation Medication example: Pseudoephedrine to treat nasal congestion by vasoconstriction	Relax smooth muscle Vasodilation Bladder: Increase urine flow Medication example: Tamsulosin to improve urine flow
Alpha-2	Vasodilation Medication Example: Clonidine to treat hypertension	Not used clinically

Beta-1	Primarily stimulates heart with increased heart rate and contractility Also causes kidneys to release renin Medication example: Dobutamine to treat acute heart failure to increase cardiac output	"Selective Beta blocker" used to decrease heart rate and blood pressure Medication example: Metoprolol to decrease heart rate and blood pressure
Beta-2	Primarily relax smooth muscle Blood vessels: vasodilation Lungs: bronchodilation GIT: decreased motility Liver: glyconeogenesis Uterus: relaxation Medication example: Albuterol for bronchodilation	"Nonselective Beta Blockers" block Beta-1 and Beta-2 receptors so also cause bronchoconstriction Medication example: Propranolol blocks Beta-1 and Beta-2 receptor so lowers blood pressure but inadvertently causes bronchoconstriction

Parasympathetic Nervous System

Acetylcholine (ACh) stimulates *both* **nicotinic** and **muscarinic** receptors. Drugs that stimulate nicotinic and muscarinic receptors are called **cholinergics**. Medications are primarily designed to stimulate muscarinic receptors. **Nicotine** stimulates pre- and post-ganglionic nicotinic receptors, causing muscle relaxation and other CNS effects. An example of a medication designed to stimulate nicotinic receptors is the *nicotine patch*, used to assist with smoking cessation.

Muscarinic agonists are also called **parasympathomimetics** and primarily cause smooth muscle contraction, resulting in decreased heart rate, bronchoconstriction, increased gastrointestinal/genitourinary tone, and pupillary constriction. *There are two types of muscarinic agonists:* **direct-acting and indirect-acting**. Direct-acting agonists bind to the muscarinic receptor. Indirect-acting muscarinic agonists work by preventing the breakdown of ACh, thus increasing the amount of acetylcholine available to bind receptors.

Examples of direct-acting muscarinic agonist medications include:

- Pilocarpine**:** Used to treat glaucoma by causing the ciliary muscle to contract and allow for the drainage of aqueous humor
- Bethanechol**:** Used for urinary retention by stimulating the bladder causing urine output

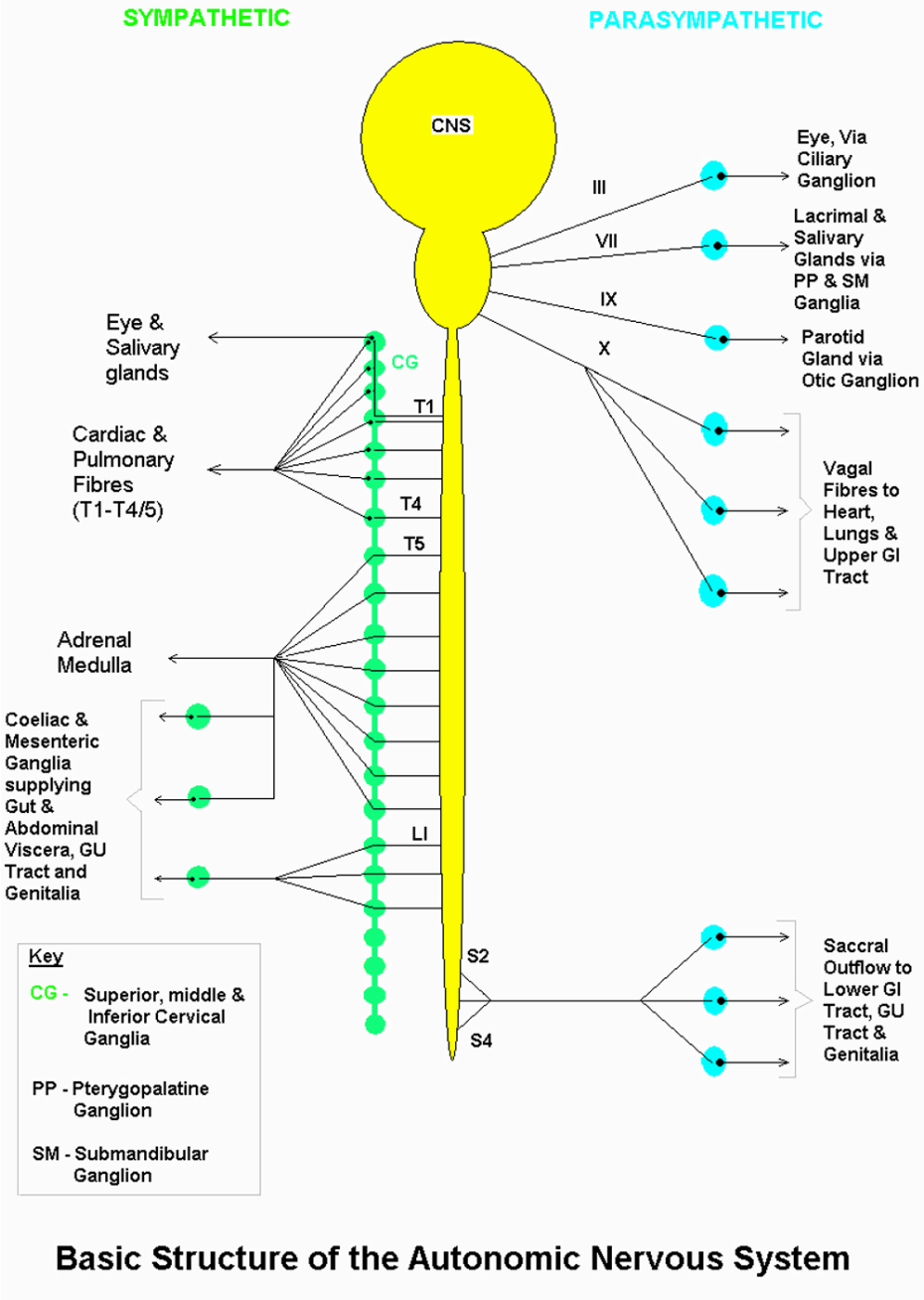
Examples of indirect-acting muscarinic agonist medications include:

- Pyridostigmine**:** Used to reverse muscle weakness in patients with myasthenia gravis
- Physostigmine**:** Used to treat organophosphate insecticide poisoning
- Donepezil**:** Enhances memory in some patients with early Alzheimer's disease

Muscarinic **antagonists** are referred to as **anticholinergics** or "**parasympatholytics**." Anticholinergics inhibit ACh and allow the SyNS to dominate, creating similar effects as adrenergics. Their overall use is to relax smooth muscle. "SLUDGE" is a mnemonic commonly used to recall the effects of anticholinergics: **S**alivation decreased, **L**acrimation decreased, **U**rinary retention, **D**rowsiness/dizziness, **G**IT upset, **E**yes (blurred vision/dry eyes).

Examples of anticholinergic medications include:

- Atropine**:** Specific anticholinergic responses are dose-related. Small doses of atropine inhibit salivary and bronchial secretions and sweating; moderate doses dilate the pupil, inhibit accommodation, and increase the heart rate (vagolytic effect); larger doses will decrease motility of the gastrointestinal (GI) and urinary tracts; very large doses will inhibit gastric acid secretion
- Oxybutynin**:** Relaxes overactive bladder
- Benztropine**:** Reduces tremor and muscle rigidity in Parkinson's disease or in treatment of extrapyramidal reactions from antipsychotic medications
- Scopolamine**:** Decreases GI motility and GI secretions; used for motion sickness and post-operative nausea and vomiting



Basic Structure of the Autonomic Nervous System