

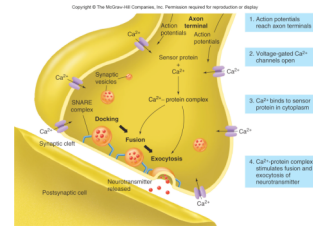
Chapter 7

The Nervous System: Neurons and Synapses

Lecture PowerPoint

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I. Neurons and Supporting Cells



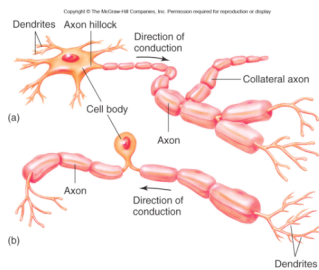
Nervous System

- Divided into:
 - **Central nervous system (CNS)**: brain and spinal cord
 - **Peripheral nervous system (PNS)**: cranial and spinal nerves
- Nervous tissue is composed of *neurons* that conduct impulses and *glial cells (aka, neuroglial, supporting cells)* that support the neurons.

Neurons

- Neurons vary in size and shape, but they (mostly) all have:
 - A **cell body**: cluster in groups called nuclei in the CNS and ganglia in the PNS
 - **Dendrites**: receive signals
 - **Axon**: conducts impulses

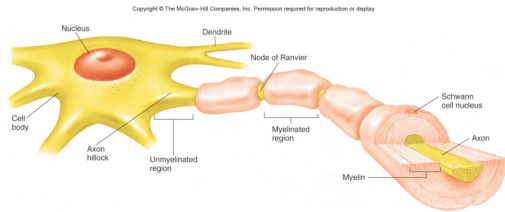
Neurons



Axons

- Axons vary in length from a few millimeters to a meter.
- The region closest to the cell body is the **axon hillock** where action potentials are generated.
- Usually covered in myelin with a node of Ranvier

Axons



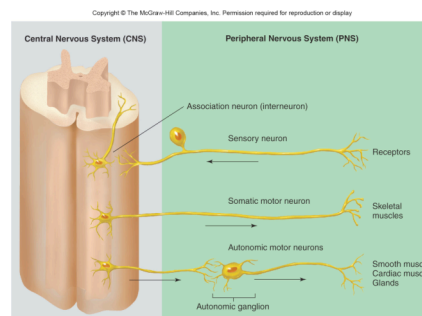
Classification of Neurons

- **Functional** classification:
 - **Sensory neurons**: conduct impulses from sensory receptors to the CNS
 - **Motor neurons**: conduct impulses from the CNS to target organs (muscles or glands)
 - **Association/interneurons**: located completely within the CNS and integrate functions of the nervous system

Motor Neurons

- Two main types of motor neurons:
 - **Somatic** motor neurons: responsible for reflexes and voluntary control of skeletal muscles (**upper motoneurons**, UMN, [innervate lower motoneurons] and **lower motoneurons**, LMN, [directly innervate skeletal muscle])
 - **Autonomic** motor neurons: innervate involuntary targets such as smooth muscle, cardiac muscle, and glands; include...
 - Sympathetic
 - Parasympathetic

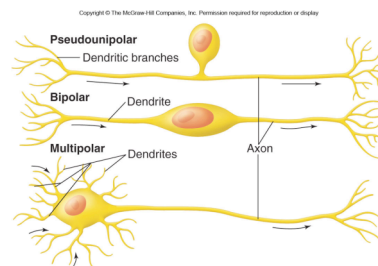
Functional Categories of Neurons



Structural Classification of Neurons

- Based on the number of processes that extend from the cell body:
 - **Pseudounipolar**: single short process that branches like a T to form 2 longer processes
 - Example: sensory neurons
 - **Bipolar neurons**: have two processes, one on either end
 - Example: retina of eye
 - **Multipolar neurons**: several dendrites and one axon; most common type

Structural Classification of Neurons



Nerves

- Are bundles of axons located outside the CNS
- - Most are composed of both sensory and motor neurons and are called [mixed nerves](#).
 - Some of the [cranial nerves](#) have sensory fibers only.
 - A bundle of axons in the CNS is called a [tract](#).

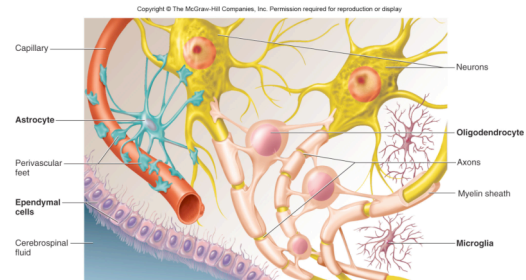
Supporting Cells

- Also called neuroglia or glial cells
- **Two** types are found in the *PNS*:
 - [Schwann cells \(neurolemmocytes\)](#): form myelin sheaths around peripheral axons
 - [Satellite cells \(ganglionic gliocytes\)](#): support cell bodies within the ganglia of the PNS

Supporting Cells

- **Four** types are found in the *CNS*:
 - [Oligodendrocytes](#): form myelin sheaths around the axons of CNS neurons
 - [Microglia](#): migrate around tissue and phagocytize foreign and degenerated material
 - [Astrocytes](#): regulate the external environment of the neurons; important in development of CNS
 - [Ependymal cells](#): line the ventricles and secrete cerebrospinal fluid; part of blood/CSF barrier.

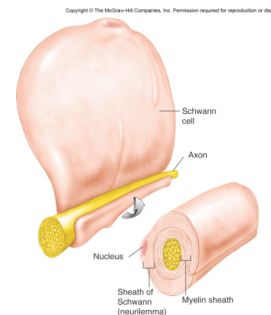
Supporting Cells of the CNS



Neurilemma and Myelin

- **All** axons in the *PNS* are surrounded by a sheath of Schwann cells called the **neurilemma**, or **sheath of Schwann**.
- Most times these cells wrap around axons to form the **myelin sheath** in the PNS.
- **Node of Ranvier** is a **gap between myelin patches** and leaves a piece of axon bare.

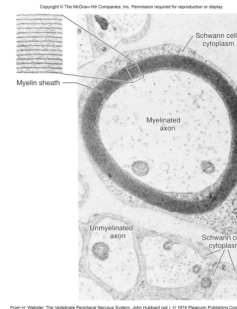
Neurilemma and Myelin



Myelin Sheath

- Small axons (2 micrometers in diameter) are usually unmyelinated.
- But even unmyelinated axons in the PNS have neurilemma.
- Myelinated axons conduct impulses/action potentials more rapidly.

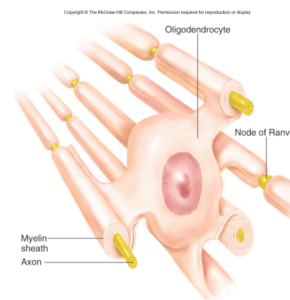
Myelin Sheath



Myelin Sheath in CNS

- In the CNS, the myelin sheath is produced by oligodendrocytes.
- One oligodendrocyte sends extensions to several axons.
- Myelin gives these tissues a white color = white matter of the CNS.
- Gray matter of the CNS is dominated by the cell bodies and dendrites of neurons.

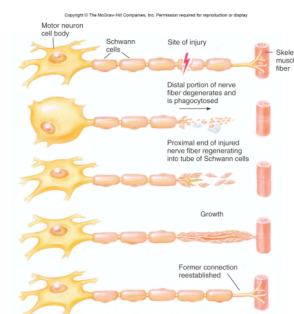
Myelin Sheath in CNS



Regeneration of a Cut Neuron

- When an axon in the PNS is cut, the severed part degenerates, but a regeneration tube formed by Schwann cells remains.
- CNS axons are not as able to regenerate, mainly because apoptosis occurs, scar tissue forms, and inhibitory proteins are produced by oligodendrocytes.

Regeneration of a Cut Neuron



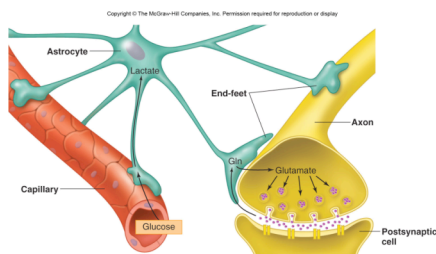
Neurotrophins

- Promote neuronal growth in the fetal brain
 - Nerve growth factor
 - Brain-derived neurotrophic factor
 - Glial-derived neurotrophic factor
 - Neurotrophin-3, neurotrophin-4/5
- In adults, neurotrophins aid in the maintenance of sympathetic ganglia and the regeneration of sensory neurons.

Astrocytes

- Most abundant glial cell
- Processes with **end-feet** associate with blood capillaries and axon terminals

Astrocytes



Astrocyte Functions

- Take up K^+ from the extracellular environment to maintain ionic environment for neurons
- Take up extra neurotransmitter released from axon terminal. Chemicals are recycled.
- End-feet around capillaries take up glucose from blood for use by neurons to make ATP.

Astrocyte Functions

- Needed for the formation of synapses in the CNS
- Regulate neurogenesis in regions of the adult brain
- Form the blood-brain barrier
- Release transmitter molecules that can stimulate or inhibit neurons

Astrocytes

- Although astrocytes do not produce action potentials, they are excited by changes in intracellular Ca^{2+} concentration.
 - When some neurons are active, they release ATP, which increases the Ca^{2+} of adjacent astrocytes.
 - This makes the astrocyte release prostaglandin E_2 from the end-feet on a blood capillary, *increasing blood flow*.

Blood-Brain Barrier

- Capillaries in the brain do not have pores between adjacent cells but are joined by tight junctions.
 - Substances can only be moved by a very selective process.
 - *Astrocytes* influence the production of ion channels and enzymes that can destroy toxic substances by secreting glial-derived **neurotrophic factor**.

II. Electrical Activity in Axons

Resting Membrane Potential

- Neurons have a **resting membrane potential** (rmp) of (approximately) -70mV , inside negative wrt the outside.
 - RMP is established and maintained by :
 - large negative molecules inside the cell
 - Na^+/K^+ pumps
 - Permeability of the membrane to ions
- At rest, there is a high concentration of K^+ inside the cell and Na^+ outside the cell.

Altering Membrane Potential

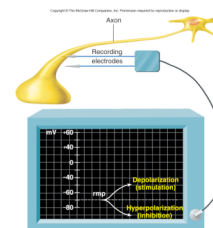
- Neurons and muscle cells can change their membrane potentials--**this is their way of signaling**.
 - Called **excitability** or **irritability**
 - Caused by changes in the permeability to certain ions
 - Ions will follow their **electrochemical gradient** (= combination of concentration gradient and attraction to opposite charges).
 - Flow of ions is called **ion current**.

Changes in Membrane Potential

- At rest, a neuron is considered **polarized** when the inside is more negative than the outside.
- When the membrane potential difference across the cell membrane **decreases** (becomes less negative inside), this is called **depolarization**.
- A return to resting potential is called **repolarization**.
- When the membrane potential difference across the cell membrane **increases** (usually, beyond the RMP), this is called **hyperpolarization**.

Changes in Membrane Potential

- Changes can be recorded on an oscilloscope by recording the voltage inside and outside the cell.



Changes in Membrane Potential

- **Depolarization** occurs when positive ions enter the cell (usually Na^+).
- **Hyperpolarization** occurs when positive ions leave the cell (usually K^+) or negative ions (Cl^-) enter the cell.
- **Depolarization** of the cell is **excitatory** --> more likely to generate an action potential (or other) signal.
- **Hyperpolarization** is **inhibitory** --> less likely to generate an action potential (or other) signal.

Ion Gating in Axons

- **Changes in membrane potential (signals)** are controlled by changes in the flow of ions through channels-- so **opening or closing channels is the key**.
 - K^+ has two types of channels:
 1. **Not gated** (always open); sometimes called "leaky" K^+ channels
 2. **Voltage-gated** K^+ channels; open when a particular membrane potential is reached

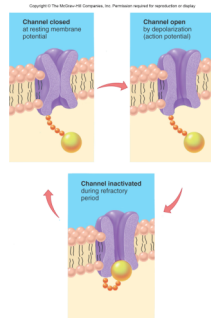
Ion Gating in Axons

- **Changes in membrane potential** are controlled by changes in the flow of ions through channels.
 - Na^+ has only **voltage-gated** channels that are closed at rest.
 - The membrane is less permeable to Na^+ at rest than it is to K^+ .

Voltage-Gated Na^+ Channels

- These channels open if the membrane potential depolarizes to -55mV .
 - This voltage level is called the **threshold level**.
 - Na^+ rushes in due to the electrochemical gradient.
 - Membrane potential climbs toward Na^+ **equilibrium potential**.
 - These channels are then deactivated at about $+30\text{mV}$.

A Voltage-Gated Ion Channel



Voltage-Gated K^+ Channels

- At around $+30\text{mV}$, voltage-gated K^+ channels open, and K^+ rushes out of the cell following the electrochemical gradient.
 - This makes the cell **repolarize** back toward the RMP and even **hyperpolarize** to the K^+ equilibrium potential.

Action Potentials

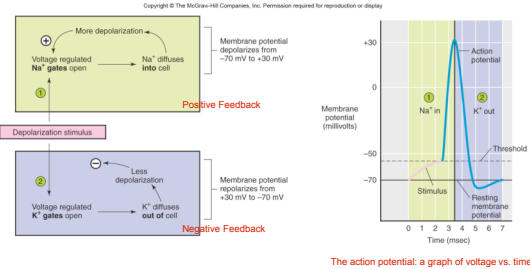
- Summary:

At threshold potential (-55mV), voltage-gated Na^+ channels open, and Na^+ rushes in.

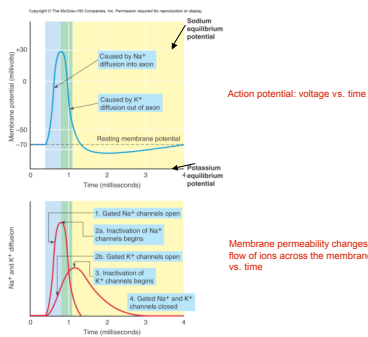
As the cell depolarizes, more voltage-gated Na^+ channels are open, and the cell becomes more and more permeable to Na^+ and Na^+ rushes in..., etc.

- This is a **positive feedback loop**.
- Membrane potential reaches $+30\text{mV}$.
- This is called the **action potential**.

Action Potential



Action Potentials



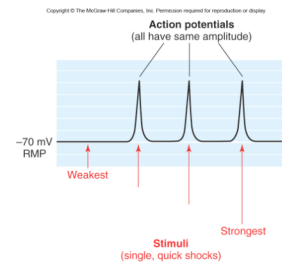
After-Hyperpolarization

- Repolarization actually overshoots resting potential and gets down to -85mV , or so-- called after-hyperpolarization or just hyperpolarization.
 - This does not reach K^+ equilibrium potential because voltage-gated K^+ channels are **inactivated** as the membrane potential falls.
- The **slowing of current flow decreases stops the voltage changes** and quickly reestablishes the resting potential
 - (the Na^+/K^+ pumps, which are constantly working through all this, move the relatively few ions that flowed through channels back across the membrane).

All-or-None Law

- This law says once threshold has been reached, action potential will happen.
 - The size of the stimulus that caused threshold to be reached will not affect the **size** of the action potential; it will always reach $+30\text{mV}$.
 - The size of the stimulus will not affect action potential **duration**.

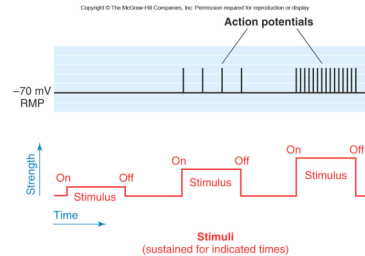
All-or-None Law



Coding for Stimulus Intensity

- So, if the a.p. is all-or-none, how does the a.p. relay info about the stimulus intensity?
 - A stronger stimulus will make action potentials occur more frequently--- aka, **Frequency Code**.
 - A stronger stimulus may also activate more neurons in a nerve. This is called **recruitment**--- aka, **Population Code**.

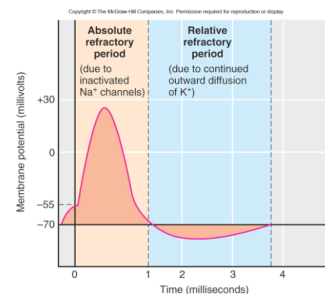
Coding for Stimulus Intensity



Refractory Periods

- Action potentials can only increase in frequency to a certain point.
- There is a **refractory period** after an action potential when the neuron cannot become excited again or it takes a bigger stimulus.
 - The **absolute refractory period** occurs during the first part of the action potential. Na⁺ channels are inactive.
 - The **relative refractory period** is when K⁺ channels are still open. Only a **very strong** stimulus can overcome this.

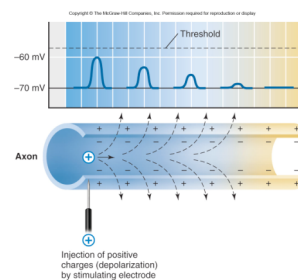
Refractory Periods



Cable Properties of Neurons

- ...Refers to the ability of neurons to conduct charges through their cytoplasm
 - Conduction is poor due to high internal resistance to the spread of charges and leaking of charges through the membrane
 - Neurons could not depend on cable properties to move or conduct an impulse down the length of an axon.

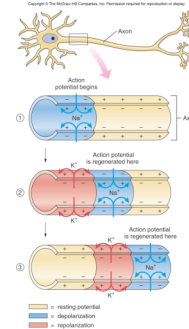
Cable Properties of Neurons



Conduction of Nerve Impulses

- So, when an action potential occurs at a given point on a neuron membrane, voltage-gated Na^+ channels open in a wave-like process down the length of the axon, by exciting the area in front of it to threshold.

Conduction of Nerve Impulses



Conduction in an Unmyelinated Neuron

In unmyelinated axons...

- Axon potentials are produced down the entire length of the axon.
- The conduction rate is slow because so many action potentials are generated.

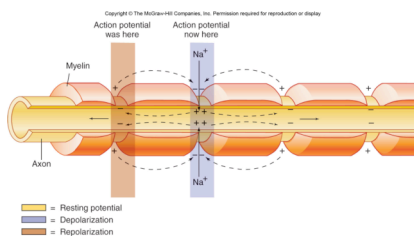
Conduction in a Myelinated Neuron

In myelinated axons...

Myelin provides insulation, improving the cable properties and the speed of the a.p.s.

- Nodes of Ranvier allow Na^+ and K^+ to cross the membrane every 1–2 mm.
- Action potentials seem to "leap" from node to node.
- This is called [saltatory conduction](#).

Conduction in a Myelinated Neuron



Action Potential Conduction Speed

- Increased by:
 - Increased diameter of the neuron. This reduces resistance to the spread of charges via cable properties.
 - Presence of myelination. This forces current to concentrate at Nodes and results in saltatory conduction.

III. The Synapse

Synapse

- Def: The functional connection between a neuron and the cell it is signaling.
- - In the CNS, this second cell will be another neuron.
 - In the PNS, the second cell will be in a muscle or gland cell.
 - At a muscle, often called **myoneural** or **neuromuscular junctions (NMJs)**

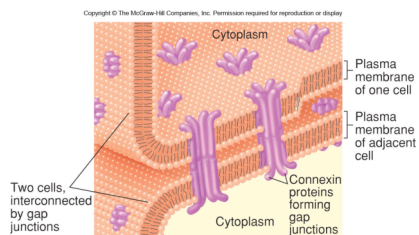
Synapses

- If one neuron is signaling another neuron, the first is called the **presynaptic neuron**, and the second is called the **postsynaptic neuron**.
 - A presynaptic neuron can signal the dendrite, cell body, or axon of a second neuron.
 - There are **axodendritic**, **axosomatic**, and **axoaxonic synapses**.
 - Most synapses are **axodendritic**.

Electrical Synapses

- Electrical synapses occur in:
 - smooth muscle and cardiac muscle,
 - between some neurons of the brain, and
 - between glial cells.
- Cells are joined by gap junctions.

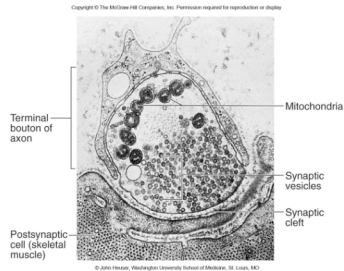
Electrical Synapses



Chemical Synapses

- Chemical synapses are more common.
- Chemical synapses involve the release of a chemical called a neurotransmitter from the axon's **terminal boutons**.
- The synaptic cleft is very small, and the presynaptic and postsynaptic cells are held close together by **cell adhesion proteins**.

Chemical Synapses



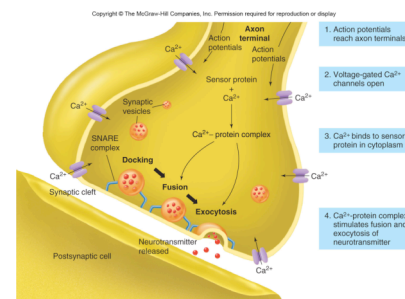
Release of Neurotransmitter

- The neurotransmitter is enclosed in synaptic vesicles in the axon terminal.
 - When the action potential reaches the end of the axon, voltage-gated Ca^{2+} channels open.
 - Ca^{2+} stimulates the fusing of synaptic vesicles to the plasma membrane and exocytosis of neurotransmitter.
 - A greater frequency of a.p.s results in more stimulation of the postsynaptic neuron.

Ca^{2+} and Synaptic Vesicles

- When Ca^{2+} enters the cell, it binds to a protein called **synaptotagmin**.
- Vesicles are docked at the plasma membrane by **SNARE** proteins.
- The **Ca^{2+} synaptotagmin complex** displaces part of SNARE, and the vesicle fuses.

Release of Neurotransmitter



Action of Neurotransmitter

- Neurotransmitter diffuses across the synapse, where it binds to a specific **receptor** protein.
 - The neurotransmitter is referred to as the **ligand**.
 - This results in the opening of **ligand-gated ion channels** (also called chemically regulated ion channels).

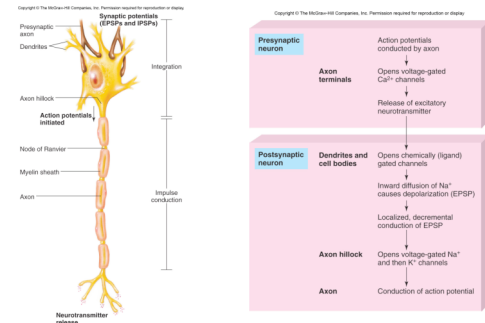
Graded Potential

- When **ligand-gated** ion channels open, the membrane potential changes depending on *which* ion channel is open.
 - Opening Na^+ or Ca^{2+} channels results in a **graded** depolarization called an **excitatory postsynaptic potential (EPSP)**.
 - Opening K^+ or Cl^- channels results in a **graded** hyperpolarization called an **inhibitory postsynaptic potential (IPSP)**.

EPSPs and IPSPs

- EPSPs move the membrane potential closer to threshold.
 - May require EPSPs from several neurons to actually produce an action potential
- IPSPs move the membrane potential farther from threshold.
 - Can counter (negate) EPSPs occurring at other synapses on the neuron
- Summation of EPSPs and IPSPs determines whether an action potential occurs.

Summary of Neurotransmitter Action



IV. Acetylcholine

Acetylcholine (ACh)

- **ACh** is a neurotransmitter that directly opens ion channels when it binds to its receptor.
 - In some cases, ACh is excitatory, and in other cases it is inhibitory, depending on which ion channels are open.
 - Excitatory in some areas of the CNS, in some autonomic motor neurons, and in all somatic motor neurons
 - Inhibitory in some autonomic motor neurons

Two Types of Acetylcholine Receptor

1. Nicotinic ACh receptors

- Can be stimulated by nicotine
- Found on the motor end plate of muscle cells, in autonomic ganglia, and in some parts of the CNS

Two Types of Acetylcholine Receptor

2. Muscarinic ACh receptors

- Can be stimulated by muscarine (from poisonous mushrooms)
- Found in CNS and plasma membrane of smooth and cardiac muscles and glands innervated by autonomic motor neurons

Agonists and Antagonists

- **Agonists:** drugs that can stimulate a receptor
 - eg., *Nicotine* for nicotinic ACh receptors
 - eg., *Muscarine* for muscarinic ACh receptors
- **Antagonists:** drugs that inhibit or block a receptor
 - eg., *Atropine* is an antagonist for muscarinic receptors.
 - eg., *Curare* is an antagonist for nicotinic receptors.

Chemically Regulated Channels

- Binding of a neurotransmitter to a receptor can open an ion channel in one of two ways--- through...
 - Ligand-gated channels
 - or
 - G-protein coupled channels

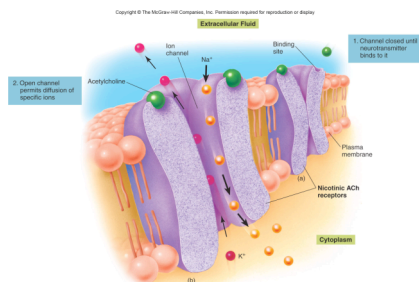
Ligand-Gated Channels

- In ligand-gated channels, the receptor protein is also an ion channel.
 - Binding of the neurotransmitter directly opens the ion channel.
 - Nicotinic ACh receptors are ligand-gated channels.

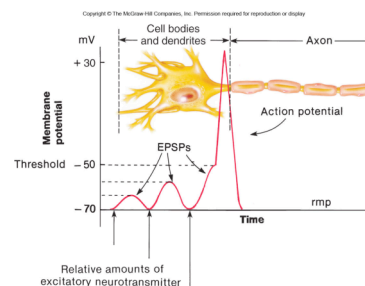
Nicotinic ACh Receptors

- Binding of acetylcholine opens a channel that allows both Na^+ and K^+ passage.
 - Na^+ flows in, and K^+ flows out.
 - Due to electrochemical gradient, more Na^+ flows in than K^+ out.
 - This inward flow of Na^+ depolarizes the cell, creating an **EPSP**.
 - EPSPs occur in the dendrites and cell bodies.
 - EPSPs from the binding of several ACh molecules can be added together to produce greater depolarization.
 - This may reach the threshold for voltage-gated channels in the axon hillock, leading to action potential.

Nicotinic ACh Receptors



Nicotinic ACh Receptors



Comparison of EPSPs and Action Potentials

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Table 7.4 | Comparison of Action Potentials and Excitatory Postsynaptic Potentials (EPSPs)

Characteristic	Action Potential	Excitatory Postsynaptic Potential
Stimulus for opening of ionic gates	Depolarization	Acetylcholine (ACh) or other excitatory neurotransmitter
Initial effect of stimulus	Na ⁺ channels open	Common channels for Na ⁺ and K ⁺ open
Cause of repolarization	Opening of K ⁺ gates	Loss of intracellular positive charges with time and distance
Conduction distance	Regenerated over length of the axon	1–2 mm; a localized potential
Positive feedback between depolarization and opening of Na ⁺ gates	Yes	No
Maximum depolarization	+40 mV	Close to zero
Summation	No summation—all-or-none event	Summation of EPSPs, producing graded depolarizations
Refractory period	Yes	No
Effect of drugs	ACh effects inhibited by tetrodotoxin, not by curare	ACh effects inhibited by curare, not by tetrodotoxin

Drugs and Skeletal Muscle

ACh Receptors

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Table 7.5 | Drugs That Affect the Neural Control of Skeletal Muscles

Drug	Origin	Effects
Botulinum toxin	Produced by <i>Clostridium botulinum</i> (bacteria)	Inhibits release of acetylcholine (ACh)
Curare	Resin from a South American tree	Prevents interaction of ACh with its nicotinic receptor proteins
α -Bungarotoxin	Venom of Bungarus snakes	Binds to ACh receptor proteins and prevents ACh from binding
Saxitoxin	Red tide (<i>Gonyaulax</i>) algae	Blocks voltage-gated Na ⁺ channels
Tetrodotoxin	Pufferfish	Blocks voltage-gated Na ⁺ channels
Nerve gas	Artificial	Inhibits acetylcholinesterase in postsynaptic membrane
Neostigmine	Nigerian bean	Inhibits acetylcholinesterase in postsynaptic membrane
Strychnine	Seeds of an Asian tree	Prevents IPSPs in spinal cord that inhibit contraction of antagonistic muscles

G-Protein Coupled Channels

- In this case, the neurotransmitter receptor is separate from the protein that serves as the ion channel.
 - Binding at the receptor opens ion channels indirectly by using a G-protein.
 - Muscarinic ACh receptors interact with ion channels in this way.

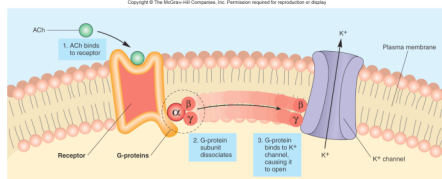
Muscarinic ACh Receptors

- Associated with a G-protein
 - G-proteins have three subunits (alpha, beta, and gamma).
 - Binding of ACh results in the dissociation of the alpha subunit.
 - Either the alpha or the beta-gamma diffuses through the cytoplasm to the ion channel.
 - This opens the channel for short period of time.

Muscarinic ACh Receptors

Binding of acetylcholine opens K⁺ channels in some tissues (IPSP) or closes K⁺ channels in others (EPSP).

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Muscarinic ACh Receptors

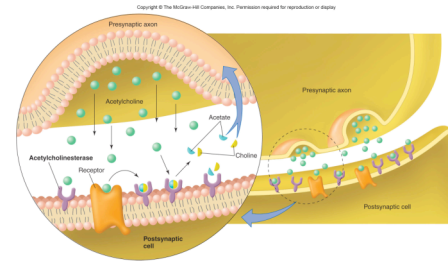
- In the heart, K⁺ channels are opened, creating IPSPs (hyperpolarization) that slow the heart rate.
- In the smooth muscles of the stomach, K⁺ channels are closed, producing EPSPs (depolarization) and the contraction of these muscles.

Acetylcholinesterase (AChE)

How do you STOP the activity once it is started?

- AChE is an enzyme that inactivates ACh activity shortly after it binds to the receptor.
 - AChE hydrolyzes ACh into acetate and choline, which are taken back into the presynaptic cell for later reuse.

Acetylcholinesterase (AChE)



ACh in the PNS

- **Somatic motor neurons** form interactions called **neuromuscular junctions** with muscle cells.
- The area on the muscle cell with receptors for neurotransmitter is called the **motor end plate**.
 - EPSPs formed here are often called **end plate potentials (epp's)**.

Neuromuscular Junctions

- **End plate potentials** depolarize to threshold, open voltage-gated Na^+ channels, which results in an action potential.
 - This eventually produces muscle contraction.

Interruption of Neuromuscular Transmission

- Certain **drugs** can block neuromuscular transmission.
 - **Curare** is an antagonist of acetylcholine. It blocks ACh receptors so muscles do not contract.
 - Leads to paralysis and death (due to paralyzed diaphragm)
 - Used clinically as a muscle relaxant

Alzheimer Disease

- Associated with loss of **cholinergic neurons** (neurons that release ACh) that synapse on the areas of the brain responsible for **memory** (eg., the hippocampus).

V. Monoamines

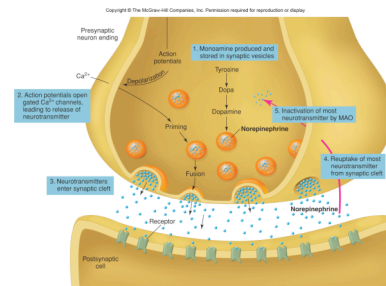
Monoamines

- Regulatory molecules derived from amino acids
 - **Catecholamines**: derived from tyrosine
 - Include **dopamine**, **norepinephrine** (=noradrenalin), and **epinephrine** (=adrenalin).
 - **Serotonin**: derived from tryptophan
 - **Histamine**: derived from histidine
 - Serotonin, dopamine, and norepinephrine are major neurotransmitters.

Monoamine Action and Inactivation

- Like ACh, monoamines are made in the presynaptic axon, released via exocytosis, diffuse across the synapse, and bind to specific receptors.
- They are quickly taken back into the presynaptic cell (called reuptake) and degraded by monoamine oxidase (MAO).

Monoamine Action and Inactivation



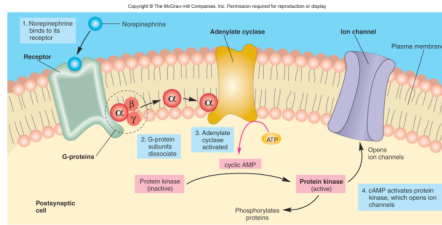
Monoamine Action

- None of the receptors for these signals are direct ion channels.
- All use a second messenger system.
 - Cyclic adenosine monophosphate (cAMP) is the most common second messenger for catecholamines.

Monoamines and cAMP

- Binding of a catecholamine to its receptor activates a G-protein to dissociate and send the alpha subunit to an enzyme called adenylate cyclase.
 - Converts ATP to cAMP
- cAMP activates an enzyme called protein kinase, which **phosphorylates** other proteins.
- *Then*, an ion channel opens.

Monoamines and cAMP



Serotonin

- Used by neurons in the raphe nuclei (middle region of brain stem)
 - Implicated in mood, behavior, appetite, and cerebral circulation
 - The drug LSD may be an agonist.
- Serotonin specific reuptake inhibitors (SSRIs) are used to treat depression.
 - Prozac, Paxil, Zoloft

Serotonin Receptors

- Over a dozen known receptors allow for diversity of serotonin function.
 - Different drugs that target specific serotonin receptors could be given for anxiety, appetite control, and migraine headaches.

Dopamine

- Neurons that use dopamine are highly concentrated in the midbrain. Two main areas:
 - Nigrostriatal dopaminergic system: involved in motor control
 - Mesolimbic dopaminergic system: involved in emotional reward

Nigrostriatal Dopamine System

- Neurons from the **substantia nigra** of the brain send dopaminergic neurons to the **corpus striatum**.
 - Important step in the control and initiation of movements
 - Parkinson disease is caused by degeneration of these neurons.
 - Patients are treated with L-dopa and MAO-Is (monoamine oxidase inhibitors).

Mesolimbic Dopamine System

- Regions of the midbrain send dopaminergic neurons to regions of the forebrain.
 - Involved in emotional reward systems and associated with addictions
 - Schizophrenia is associated with too much dopamine in this system.
 - Drugs that treat schizophrenia are dopamine antagonists.

Norepinephrine

- Used in both the CNS and PNS
 - Sympathetic neurons of the PNS use norepinephrine on smooth muscles, cardiac muscles, and glands.
 - Used by neurons of the CNS in brain regions associated with *arousal*
 - Amphetamines work by stimulating norepinephrine pathways in the brain.

VI. Other Neurotransmitters

Glutamate

- An amino acid used as the most important excitatory neurotransmitter in the brain
 - Produces EPSPs in 80% of the synapses in the cerebral cortex
 - Energy required for all the EPSPs constitutes the major energy use in the brain
 - All glutamate receptors also serve as ion channels

Glutamate Receptors

- Three types:
 - NMDA (N-methyl-D-aspartate) receptors
 - AMPA (α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptors
 - kainate receptors
- NMDA and AMPA receptors work together in memory storage.

Glycine

- Amino acid used as a neurotransmitter to produce IPSPs
 - Binding of glycine opens Cl^- channels, causing an influx of Cl^- .
 - Makes it harder to reach threshold
 - Important in the spinal cord for regulating skeletal muscle movement. This allows antagonistic muscle groups to relax while others are contracting (e.g., biceps relax while triceps contract).

Glycine

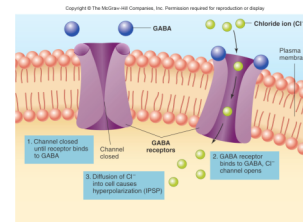
- Also important in the relaxation of the diaphragm, which is necessary for breathing
 - The poison [strychnine](#) blocks glycine receptors, which produces death by asphyxiation.

GABA

- γ -aminobutyric acid is the most common neurotransmitter in the brain and is used by 1/3 of the brain's neurons.
 - It is **inhibitory**: opening Cl^- channels when it binds to its receptor.
 - It is involved in motor control.
 - Degeneration of GABA-secreting neurons in the cerebellum results in [Huntington's disease](#).

GABA

- The actions of GABA and glycine are very similar.



Neuropeptides

- Many chemicals used as hormones or paracrine signals are also found in the brain acting as neurotransmitters.
 - **CCK**: involved in a feeling of satiety after a meal
 - **Substance P**: mediates sensations of pain

Endogenous Opioids

- Opioid receptors were discovered to bind with drugs such as opium and morphine, resulting in pain relief.
- Endogenous opioids are polypeptides produced by the brain and pituitary gland.
 - B-endorphin, enkephalin, and dynorphin

Neuropeptide Y

- Most abundant neuropeptide in the brain
 - Plays a role in stress response, circadian rhythms, and cardiovascular control
 - Powerful stimulator of hunger

Endocannabinoids

- Neurotransmitters that bind to the same receptors that bind to the active ingredient in marijuana (THC or tetrahydrocannabinol)
 - Short fatty acids produced in the dendrites and cell bodies and released directly from the plasma membrane (no vesicle)
 - **Retrograde neurotransmitters** released from the postsynaptic neuron--- inhibit further neurotransmitter release from the presynaptic axon

Endocannabinoids

- Endocannabinoids can inhibit IPSP-producing NTs from one neuron so EPSP-producing NTs from another neuron can have a greater effect.
- Endocannabinoids may enhance learning and memory and have been shown to induce appetite.
- Marijuana use impairs learning and memory because the action of THC is widespread and not controlled.

• THC has mild to moderate analgesic effects, and cannabis can be used to treat pain by altering transmitter release on dorsal root ganglion of the spinal cord and in the periaqueductal gray. Other effects include relaxation, altered space-time perception, alteration of visual, auditory, and olfactory senses, fatigue, and appetite stimulation (colloquially known as "the munchies"). It also has antiemetic properties, and also may reduce aggression in certain subjects. (Wikipedia)

Nitric Oxide

- A gas produced by some neurons in the CNS and PNS
 - Diffuses across the presynaptic axon plasma membrane (needs no vesicle)
 - Diffuses into the target cell and activates the production of cGMP as a second messenger

Nitric Oxide

- In the PNS, nitric oxide (NO) is secreted by autonomic neurons onto cells in the digestive tract, respiratory passages, and the penis, causing smooth muscle relaxation, including smooth muscle in walls of blood vessels.
 - Responsible for an erection
 - The drug Viagra works by increasing NO release.

Carbon Monoxide

- CO is another gas used as a neurotransmitter
 - Also activates the production of cGMP in target cells
 - Used in the olfactory epithelium and cerebellum

ATP

- Used as a [cotransmitter](#) --- released via vesicles with another neurotransmitter
 - Binds to purinergic receptors
 - Released with norepinephrine to stimulate blood vessel constriction and with ACh to stimulate intestinal contraction

VII. Synaptic Integration

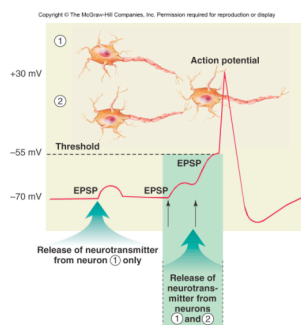
Neural Pathways

- **Divergence** of neural pathways: Axons have collateral branches, so one presynaptic neuron can form synapses with several postsynaptic neurons. (amplifies signal)
- **Convergence** of neural pathways: Several different presynaptic neurons (up to a thousand) can synapse on one postsynaptic neuron.

Summation

- **Spatial** summation occurs due to convergence of signals from different neurons onto a single postsynaptic neuron.
 - All of the EPSPs and IPSPs are added together at the axon hillock.
- **Temporal** summation is due to successive waves of neurotransmitter release from a single source.

Summation



Synaptic Plasticity

- Repeated use of a neuronal pathway may strengthen or reduce synaptic transmission in that pathway.
 - When repeated stimulation enhances excitability, it is called **long-term potentiation (LTP)**.
 - Found in the hippocampus of the brain where memories are stored
 - Associated with NMDA and AMPA glutamate receptors

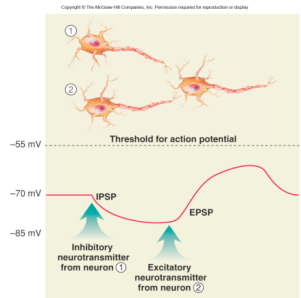
Synaptic Plasticity

- **Long-term depression (LTD)** occurs when glutamate-releasing presynaptic neurons stimulate the release of endocannabinoids.
 - This suppresses the further release of neurotransmitter.

Synaptic Inhibition

- Postsynaptic inhibition is produced by inhibitory neurotransmitters such as glycine and GABA.
 - Hyperpolarizes the postsynaptic neuron and makes it less likely to reach threshold voltage at the axon hillock

Synaptic Inhibition



Presynaptic Inhibition

- Sometimes a neuron synapses on the axon of a second neuron, inhibiting the release of excitatory neurotransmitter from the second neuron--- called **PREsynaptic** inhibition.

– Eg., action of endogenous opioids in pain reduction