BCH 443
Biochemistry of Specialized Tissues

VI. Nerve Tissue and Brain

Nerve Tissue and Brain

- The regulation and integration of body system are regulated by 2 main systems:
  - Nervous System
  - Endocrine System

- The regulatory systems are needed to maintain homoestasis

Comparison between Nervous & Endocrine systems

- Both of them monitor stimuli and react so as to maintain homeostasis.

Nervous system

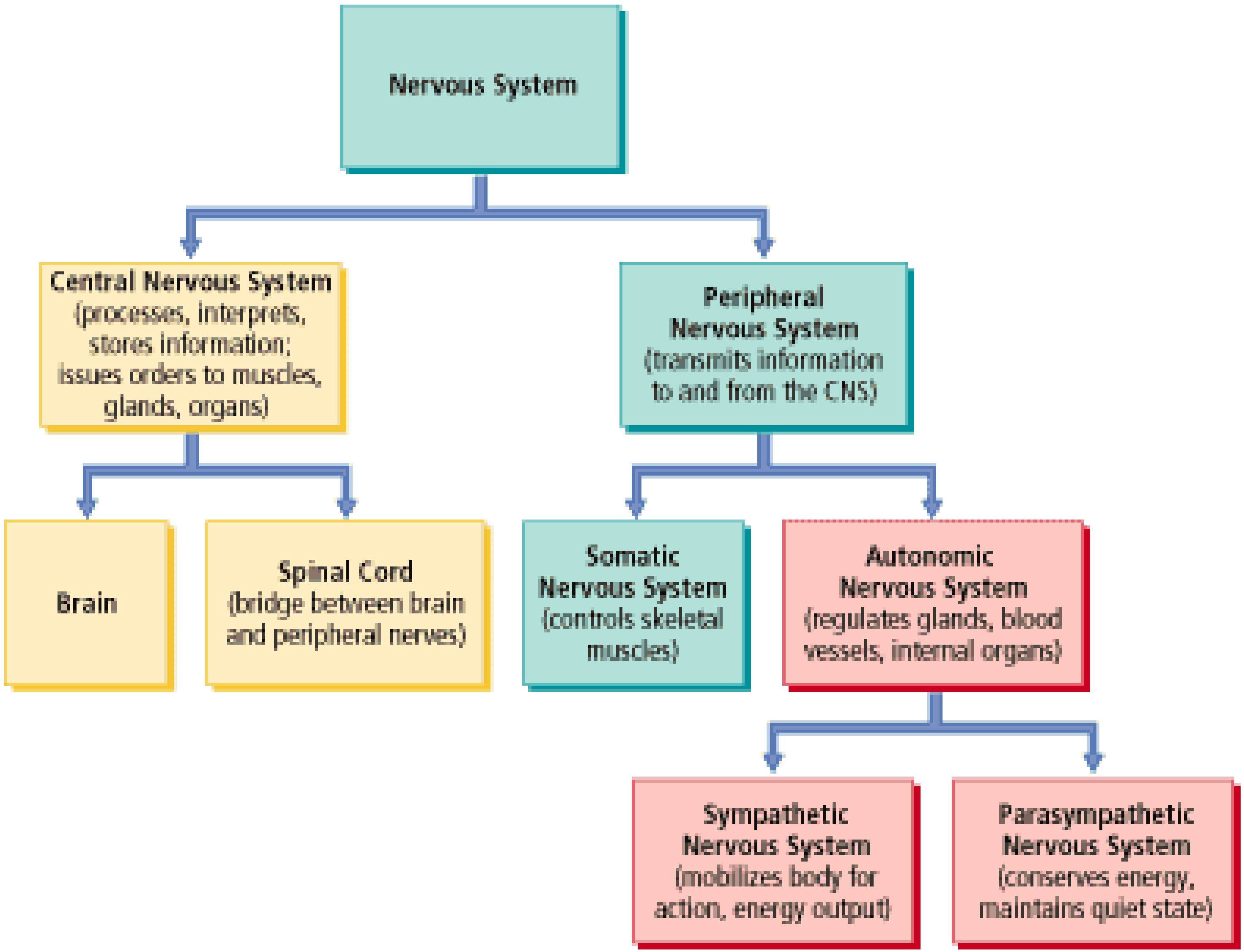
- Rapid acting
- Involved in control of things that change over short time periods (seconds to minutes)
- Examples:
  - Heart rate
  - Respiration
  - Voluntary muscle contractions

Endocrine system

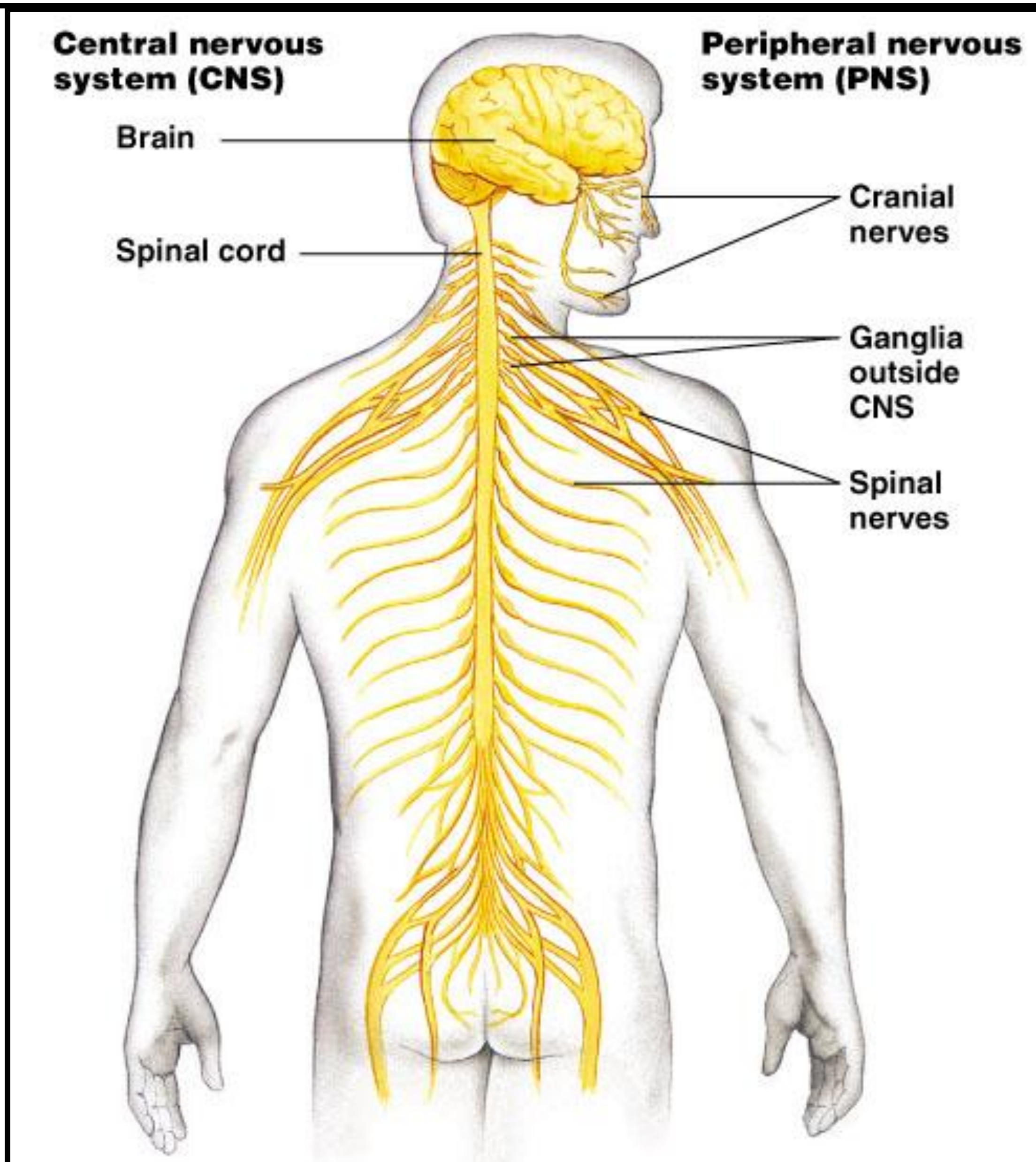
- More slowly acting
- Involved in control of things that change over long time periods (minutes to years)
- Examples:
  - Growth
  - Reproduction

In all vertebrates the nervous system is divided into:

Central nervous system (CNS) & Peripheral nervous system (PNS)



Vertebrate Nervous Systems



Central nervous system

- **Brain**
- **Spinal cord**
  - A collection of neurons and supportive tissue running from the base of the brain down the center of the back.
  - Protected by bone and cerebrospinal fluid (CSF)
  - Neurons in the spinal cord produce reflexes – rapid, automatic motor responses.
  - The spinal cord is the location where the peripheral nervous system and the central nervous system interact.

Peripheral Nervous System (PNS)

- PNS consists of neurons that convey messages to and from the central nervous system.
- The Neural circuit consists of:
  - Sensory neurons (afferent neurons): receptor for stimulus carry information from the sense organs to the brain and spinal cord.
  - Interneurons: integrate signals.
  - Motor neurons (efferent neurons): carry information from the brain and spinal cord to muscles and glands.

Peripheral Nervous System (PNS)

Somatic NS **Autonomic NS**

- **The somatic NS,** sometimes called the skeletal NS, controls the skeletal muscles of the body and permits voluntary actions.
- **The autonomic NS** regulates nonskeletal muscles such as blood vessels, glands and internal organs like the bladder, stomach and heart.
- **Autonomic NS- consists of two parts:**
  - Sympathetic NS mobilizes bodily resources and increases the output of energy during emotion and stress.
  - Parasympathetic NS operates during relaxed states and conserves energy.

Nervous System: Cells and functions

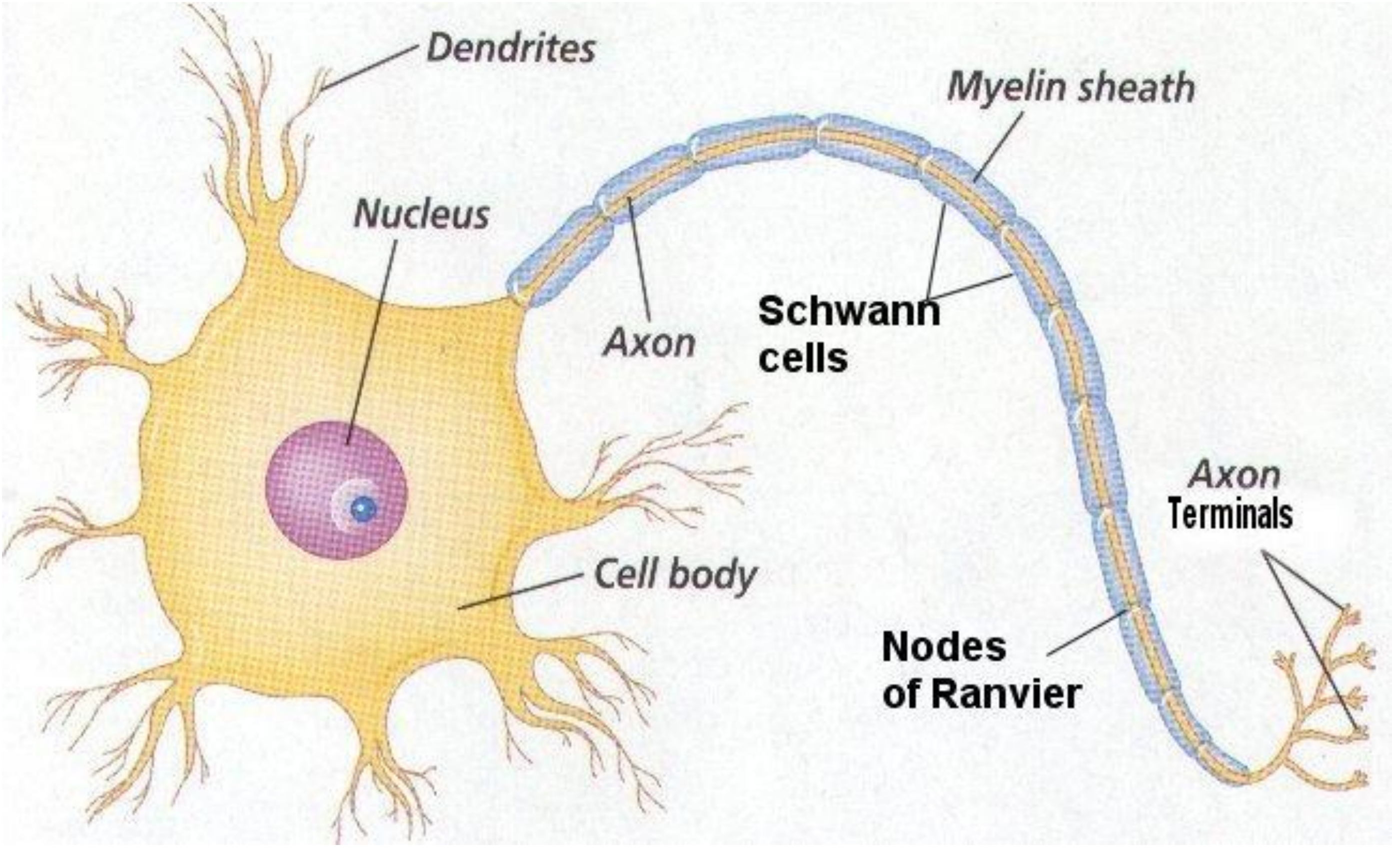
- **Neurons:** are specialized cells of the NS that receive, encode and transmit information.
- Neurons with their support cells (glial cells) make up nervous system.
- Modified neurons called Sensory cells receive information and convert or transduce it into electrical signals that are transmitted and produced by other neurons.
- To cause behavioral or physiological responses, a nervous system communicates these signals to effectors, such as muscles and glands.

Nervous System: Cells and functions

- **In vertebrates,** most of the cells of the nervous system are found in the brain and the spinal cord, which together are called the central nervous system (CNS)
- Information is transmitted from sensory cells to the CNS and from the CNS to effectors via neurons, which extend or reside outside of the brain and spinal cord.
- Neurons and supporting cells found outside the CNS are called the Peripheral Nervous System (PNS)

Nervous System: Cells and functions

- **Neurons** function similarly in animals as different as humans. In addition to neurons, nervous systems also contain Glial cells, which also vary in their forms and functions.
- The neuron's plasma membrane generates electrical signals called **nerve impulses** (or **action potentials**) and conducts the signals from one location on a cell to the most distant reaches of that cell.
- **Most neurons (Cell) have four regions:**
  - a cell body,
  - dendrites,
  - an axon,
  - axon terminals.


Dendrites
Myelin sheath
Nucleus
Axon
Schwann
cells
Axon
Terminals
Cell body
Nodes
of Ranvier

Nervous System: Cells and functions

- **The neuron's cell body** contains the nucleus and most of the cell's organelles.
- **Dendrites,** many projections sprout from the neuron cell body; most of them are which bring information from other neurons or sensory cells to the cell body.
- **The axon** usually carries information away from the cell body.

Nervous System: Cells and functions

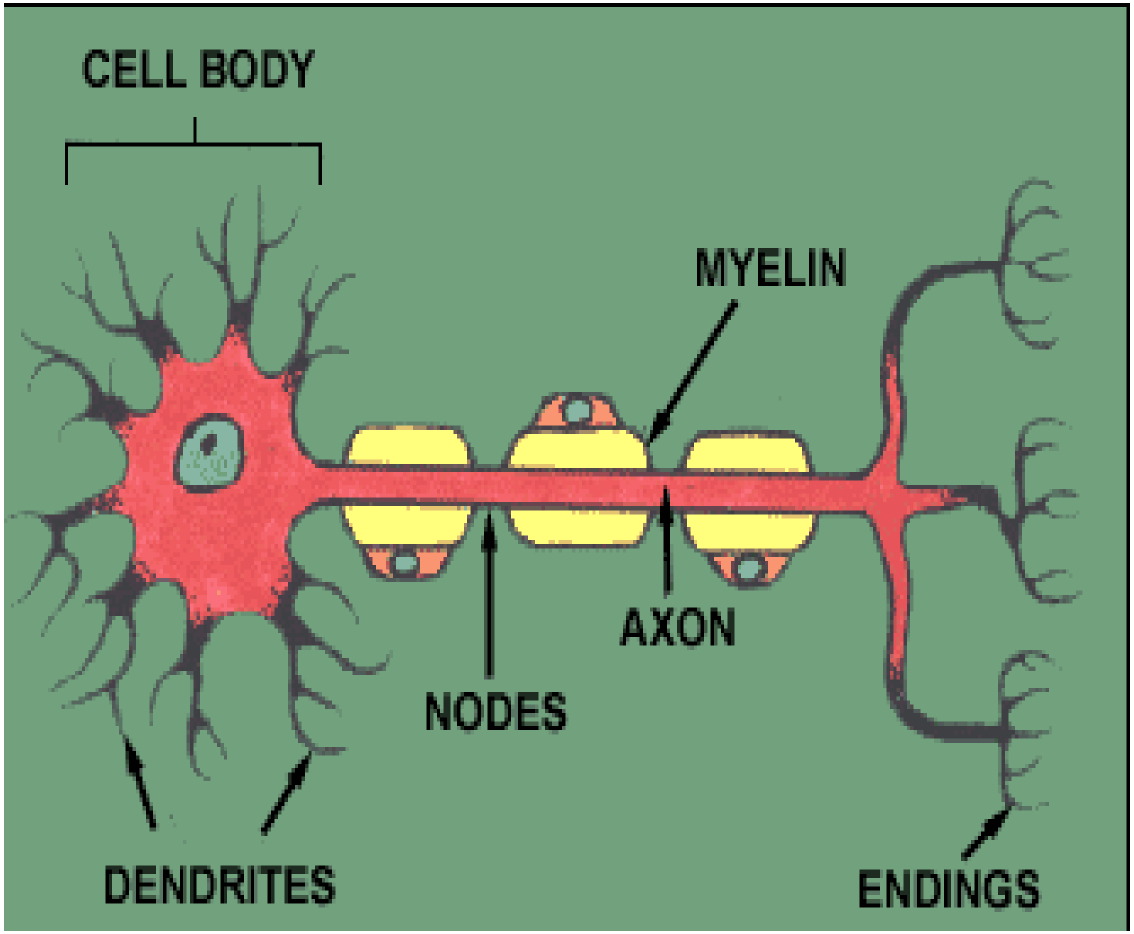
- **Axons** conduct information to target cells, which can be other neurons, muscle cells, or gland cell.
- At its end, the axon divides into many fine nerve endings. At the tip of each nerve endings is a swelling called the **axon terminal**.
- The axon terminal is positioned very close to the target cell.

Nervous System: Cells and functions

- At the axon, terminal nerve impulses cause the release of **neurotransmitters** (chemical messengers) into the **Synapse**.
- Variation between different types of neurons is considerable.
- Length of the axon differs in different cell types. Some axons can be very long.

Nervous System: Cells and functions

- Some **glial cells** physically support and orient neurons. Others provide insulation for axons.
- **Schwann cells** are a type of glial cells that wraps around the axons of neurons in the peripheral nervous system, providing electrical insulation.
- **Oligodendrocytes** have a similar function of Schwann cells for axons in the CNS.
- **Myelin** is the covering produced by schwann cells and oligodendrocytes.


CELL BODY
MYELIN
AXON
NODES
DENDRITES
ENDINGS

Nervous System: Cells and functions

- **The function of Glial cells:**
  - supply neurons with nutrients.
  - some consume foreign particles, and
  - some maintain ionic balance around neurons
  - Forms brain blood barrier.
- Some glial cells communicate electrically through gap junctions.
- Glial cells called astrocytes contribute to the blood-brain barrier, which protects the brain from toxic chemicals in the blood.

Nervous System: Cells and functions

- ***Astrocytes*** surround the smallest blood vessels in the brain. They are permeable to fat-soluble molecules such as alcohol.
- It is important to remember that nervous systems depend on neurons working together.

- **The simplest *neural network* consists of three cells:**
  - A sensory neuron connected to:
  - A motor neuron connected to:
  - A muscle cell.

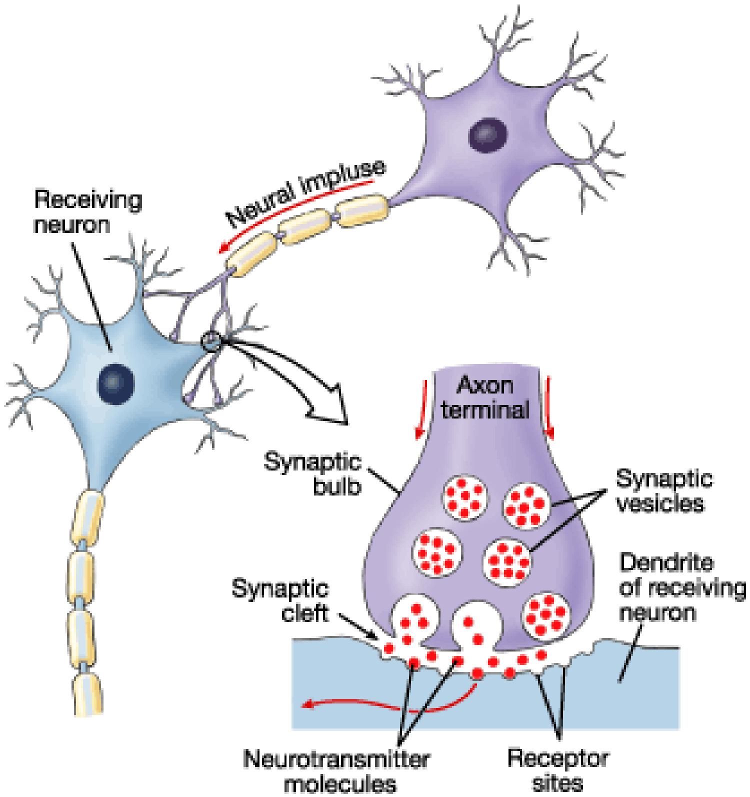
Structure of a Neuron

- The axons of most neurons are covered with a **myelin sheet** – a coat of cells composed primarily of fats that facilitates transmission of information to other neurons.
- Myelinated axons give some portions of the brain a white appearance – hence the term **White matter**
- When an impulse travels down the axon, it hops from one break in the string to another
- This allows the impulse to travel faster than it could if it had to move along the entire axon.
- These small gaps are called the **Nodes of Ranvier**

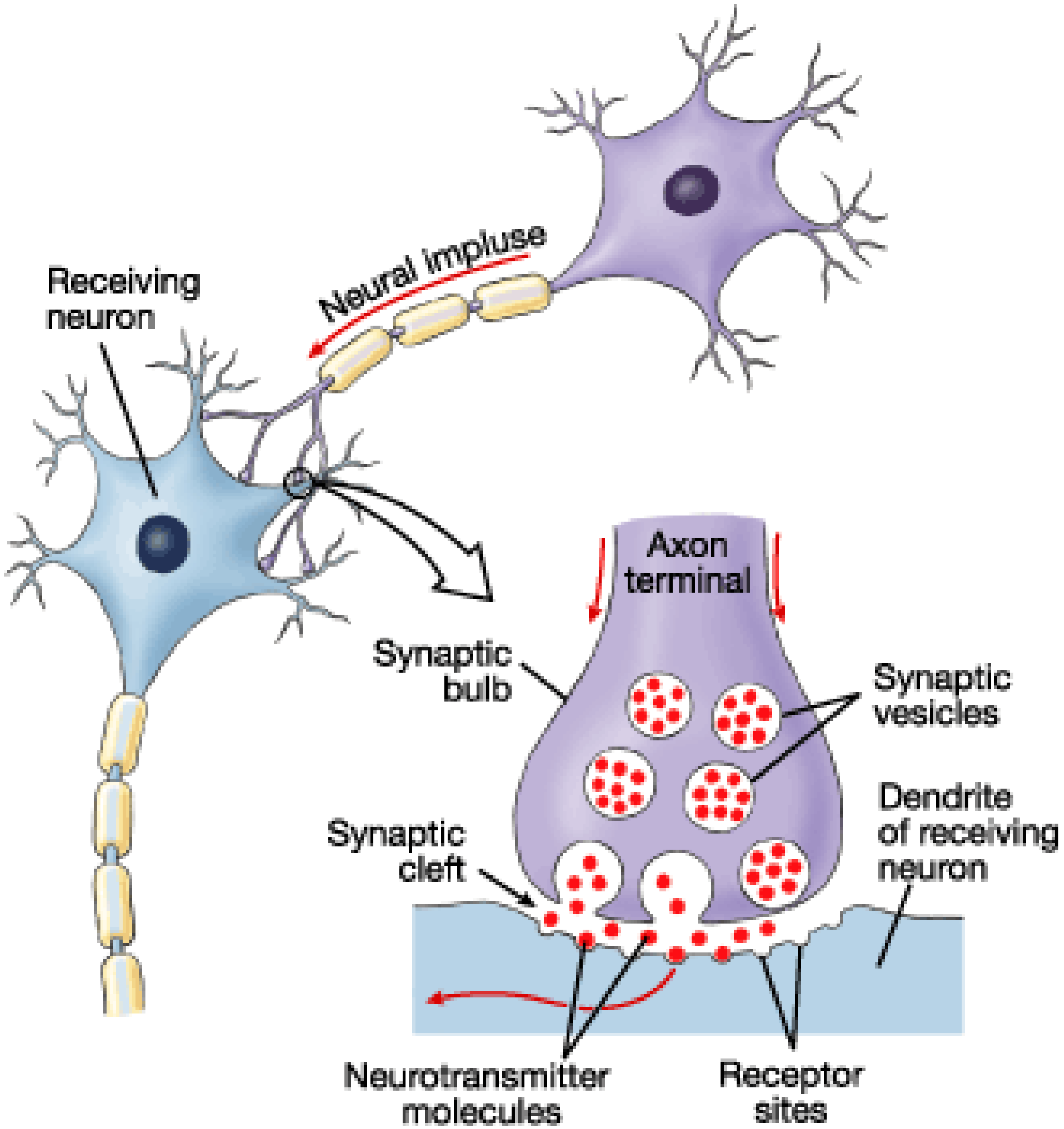
Structure of a Neuron

- At the end of an axon located terminal buttons which send signals from a neuron to adjacent cells.

- Connection between neurons occur at Synapses.
- The two cells do not actually touch at a synapse, instead a space exists between the two neurons known as th synaptic gap.



Structure of a Neuron



How neurons communicate?

- Throughout life, new learning results in new connections in the brain.
- Conversely, some unused synaptic connections may be lost as cells or their branches die.
- So the brain is not exactly hardwired, but is continually changing in response to challenges and changes in the environment.

Membrane potential

- Most cells have a difference in electrical charge across the plasma membrane
  - A more negative electrical charge inside the cell
  - A positive electrical charge of the extracellular fluid
- The plasma membrane is said to be electrically **polarized**
  - Meaning that one side or (pole) has a different charge from the other.
  - This difference in charge gives rise to an electrical voltage gradient
  - The voltage measured across the plasma membrane is referred to as **membrane potential**

Resting potential

- The membrane potential in a resting neuron is called its **resting potential.**
- The resting potential is generally expressed in units called millivolts (mV).
- Voltage is the force that causes charged particles to flow between two points.

- Magnitude of the resting potential is determined by:
  - Differences in concentrations of specific ions inside the cell relative to the extracellular fluid
    - Mainly sodium and potassium
  - Selective permeability of the plasma membrane to these ions

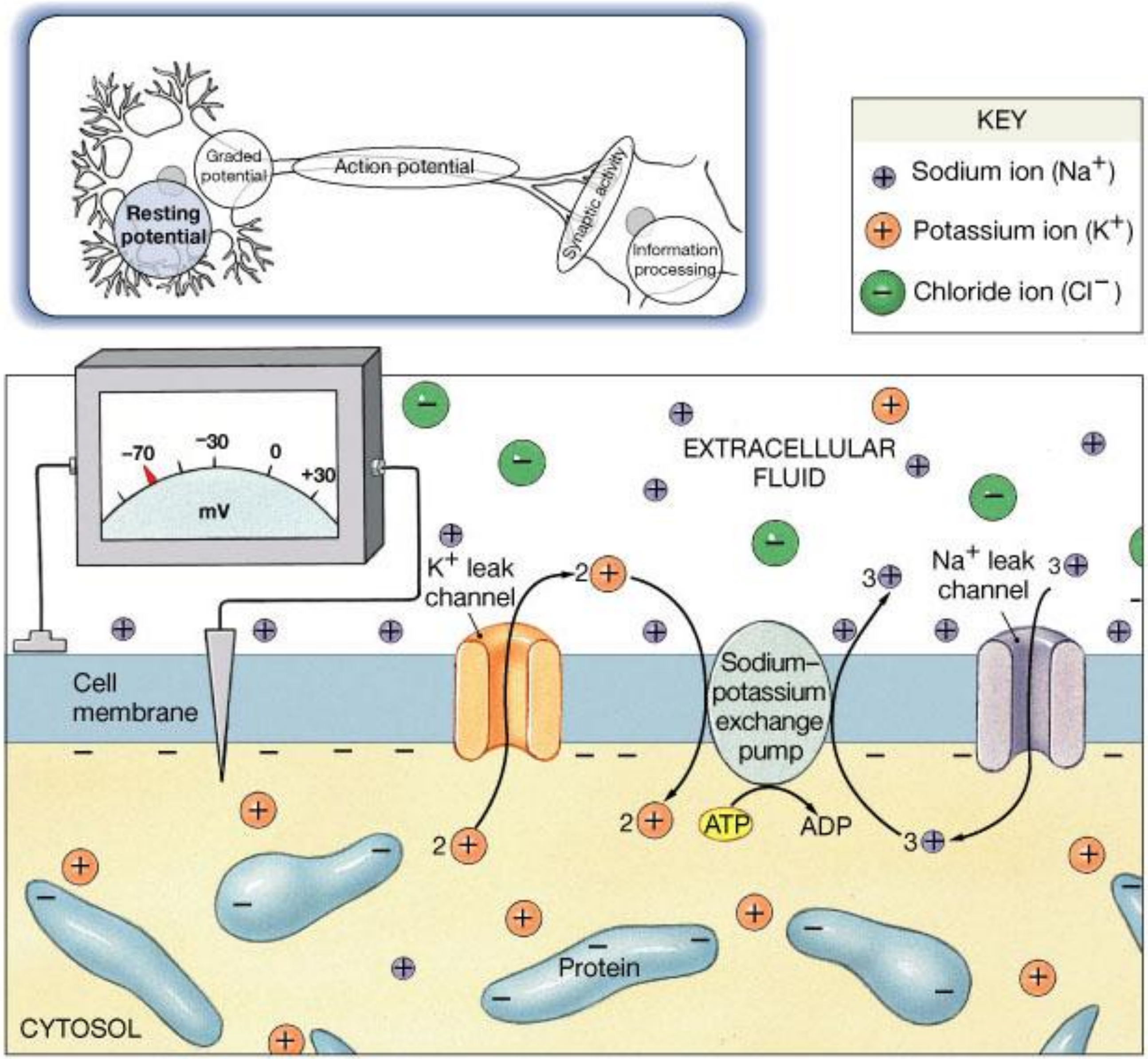
Resting Membrane Potential

- **<u>Characteristics:</u>**
- Number of charged molecules and ions inside and outside cell nearly equal (meanly K^+ and Na^+).
- Concentration of K^+ is higher inside than outside cell.
- Concentration of Na^+ is higher outside than inside cell.
- At equilibrium, there is very little movement of K^+ or other ions across plasma membrane.

Resting potential

- Ions pass through **passive ion channels** in the plasma membrane
- Potassium (K^+) ions leak out more readily than sodium (Na^+) ions can leak in
- Chloride (Cl^-) ions accumulate along the surface of the cell membrane
- The gradients that determine resting potential are determined by sodium-potassium pumps in the plasma membrane
- These pumps continuously transport sodium ions out of the neuron and potassium ions in

An Introduction to the Resting Potential



Action potential

- Neurons are excitable cells.
- They have ability to respond to stimuli and convert stimuli into nerve impulses.
- An electrical, chemical, or mechanical stimulus may alter the resting potential by increasing the membrane's permeability to sodium.
- If the neuron membrane is only slightly stimulated, only a local excitation may occur in the membrane.
- When a stimulus causes sodium ions to move into the neuron, the membrane potential becomes less negative (closer to zero) than the resting potential.
- The membrane is described as **depolarized.**

Action potential

- Because depolarization brings a neuron closer to transmitting a neural impulse it is **excitatory.**
- In contrast, when a stimulus affects the permeability of the neuron plasma membrane in a way that causes the membrane potential to become more negative than the resting potential, the membrane is hyperpolarized.

- **Hyperpolarization** decreases the ability of the neuron to generate a neural impulse.
  - It is therefore described as **inhibitory**

Action potential

- When a stimulus is sufficiently strong, voltage activated ion channels in the plasma membrane open;
  - Sodium enters the neuron
  - Potassium leaves the neuron
- This depolarizes the membrane.
- When the voltage across the membrane is decreased to a critical point, called the **threshold level**, an **action potential** is generated.

Generating and Conducting Nerve Impulses (1)

- The difference in electrical charge (measured as voltage) across the plasma membrane of a neuron is called membrane potential.
- In an unstimulated neurons, this voltage is called a resting potential.
- Membrane potential can be measured with electrodes,
- The membrane potential of a resting axon is about - 60 millivolts (mV). The inside of the cell is more **negative** than the outside.

Generating and Conducting Nerve Impulses (2)

- A neuron is sensitive to chemical or physical factors that cause a change in the resting potential.
- An <u>action potential</u> (electrical impulse) is the sudden and rapid reversal in voltage across a portion of the plasma membrane.
- For 1 to 2 milliseconds, the inside of the cell becomes more **<u>positive</u>** than the outside.
- **<u>Nerve impulses</u>** are action potentials that travel along axons.

Generating and Conducting Nerve Impulses (3)

- **Voltage** (potential or electric charge difference) is the tendency for electrically charged particles like electrons or ions to move between two points.
- Electrical charges move across cell membranes not as electrons, but as charged ions.
- The major ions that carry electric charges across the plasma membranes of the neurons are Na^+, Cl^-, K^+ and Ca^{2+}.

Generating and Conducting Nerve Impulses (4)

- Ions with opposite charges attract one another.
- Ions with like charges repel.
- Ions pumps use energy to move ions or other molecules against their concentration gradients.
- The major ion pump in neuronal membranes is the **Sodium-potassium pump,** which expels Na^+ from the cell, exchanging them for K^+ from outside the cell.
- This keeps the concentration of K^+ greater inside the cell than outside.
- **Ion channel** are pores formed by proteins in the lipid bilayer that selectively allow ions to pass through.
- **Potassium channels** are the most common open channels in the plasma membranes of resting neurons, and resting neurons are more permeable to K^+ than any other ion.

Generating and Conducting Nerve Impulses (5)

- The sodium-potassium pump keeps K^+ concentration high inside the cell, but K^+ can diffuse out the open channels.
- The membrane potential at which the tendency of K^+ ions to diffuse into the cell is equal to their tendency to diffuse out is called the potassium equilibrium potential.
- The value of the potassium equilibrium potential can be calculated with the **Nernst equation.**
- The Nernst equation predicts a resting potential of about -84 mV. The actual resting potential is a little less negative because resting neurons are also slightly permeable to other ions, such as Na^+ and Cl^-.

Generating and Conducting Nerve Impulses (6)

- Many ion channels in the plasma membranes of neurons are gated; they open under some conditions but close under other conditions.
- **There are two types of gated channels:**
- **Voltage-gated channels** open or close in response to a change in the voltage across a plasma membrane.
- **Chemically gated channels** open or close depending on the presence or absence of a specific chemical that binds to the channel protein.

Generating and Conducting Nerve Impulses (7)

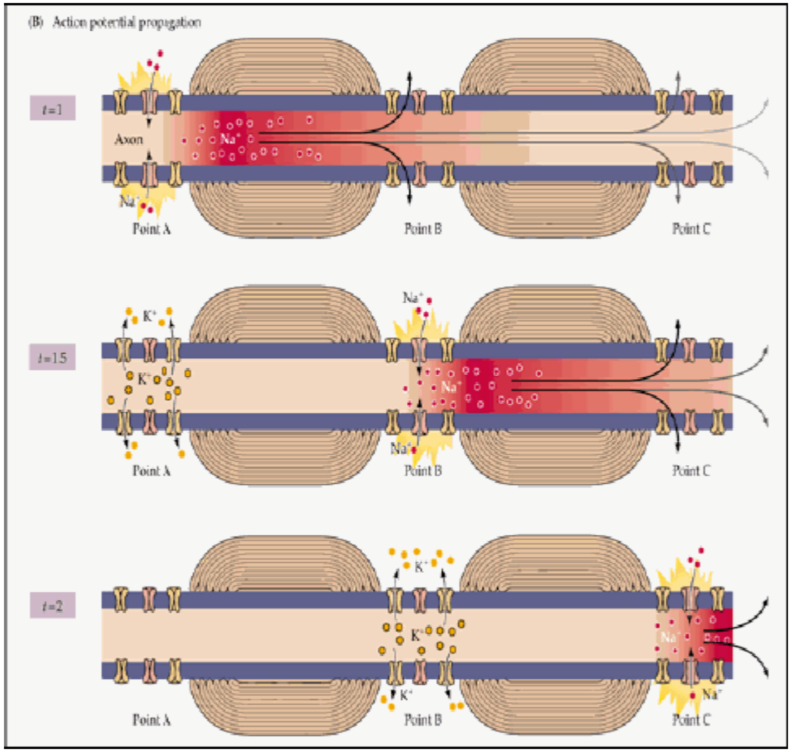
- When the inside of a neuron becomes less negative in comparison to its resting condition, its plasma membrane is said to be **depolarized.**
- Conversely, when the inside of a neuron becomes more negative in comparison to its resting conditions, its plasma membrane is said to be **hyperpolarized.**
- Opening and closing of ion channels, which result in changes in the polarity of the plasma membrane, are the basic mechanisms by which neurons respond to stimuli.
- Local changes in membrane potential cause a flow of electrically charged ions, which tends to spread the change in membrane potential to adjacent regions of the membrane.

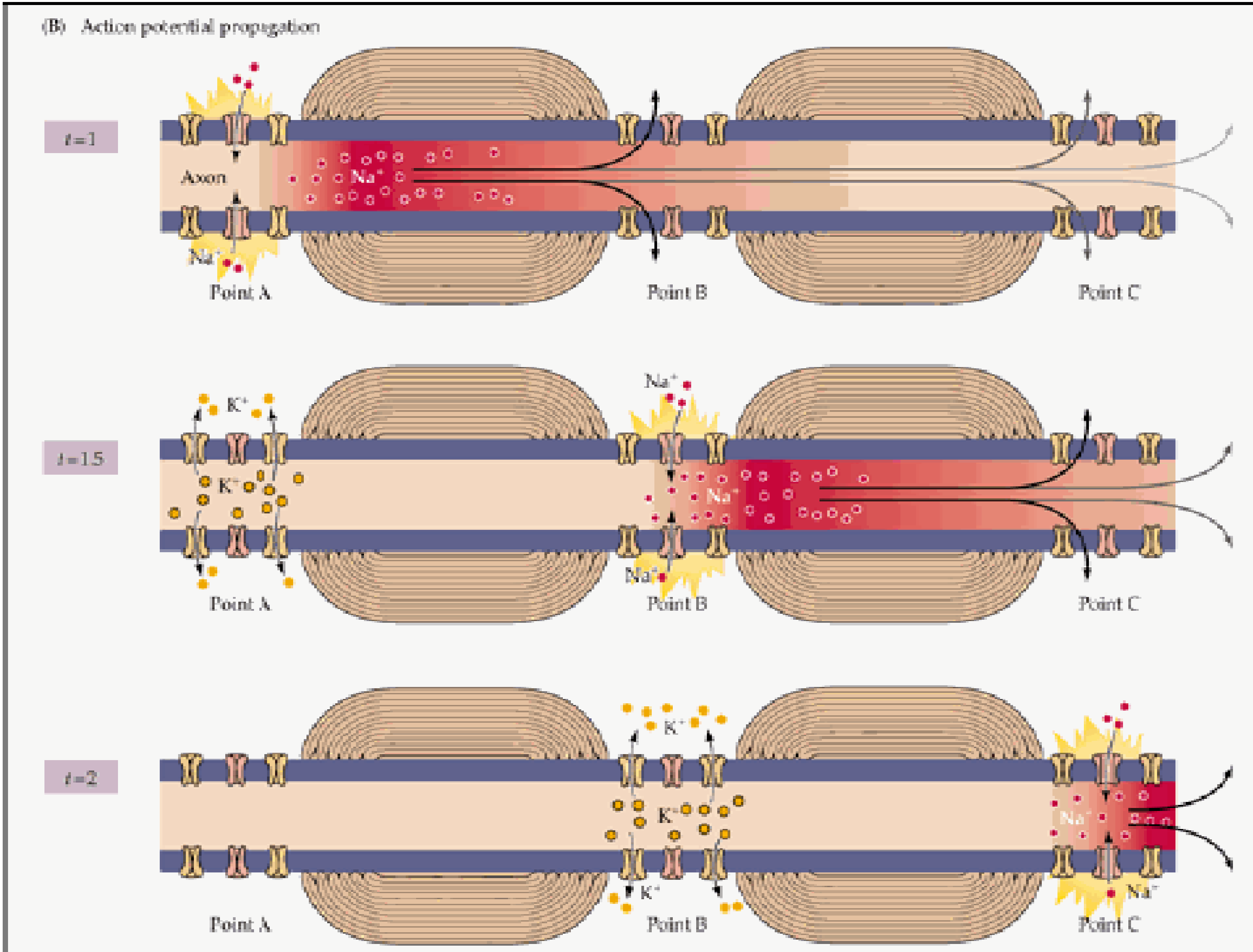
Generating and Conducting Nerve Impulses (8)

- This flow of ions is an electrical current. It does not travel very far before it diminishes because the membranes are permeable to ions.
- Hence, the axon doesn't transmit information as a continuous flow of electrical current.
- Local flow of electric current is part of the mechanism that generates the signals that axons do transmit: **Action potentials.**
- An action potential is a sudden and major change in membrane potential that lasts for about 1-2 milliseconds.
- Action potentials are conducted along axons at speeds of up to 100 meter per second.
- If the membrane potential of an axon is measured when an action potential passes, the voltage changes from the resting potential of -70 mV to +50 mV, then rapidly returns to the resting potential.

Generating and Conducting Nerve Impulses (9)

- Voltage-gated sodium channels are primarily responsible for action potentials.
- At resting potential, most of the sodium channels are closed.
- A specific membrane potential called the **threshold potential** opens voltage-gated ion channels.





(B) Action potential propagation
t = 1
Axon
Na+
Na+
Point A
Point B
Point C
t = 1.5
K+
K+
Na+
Na+
Na+
Point A
Point B
Point C
t = 2
K+
K+
K+
Na+
Na+
Point A
Point B
Point C

Generating and Conducting Nerve Impulses (10)

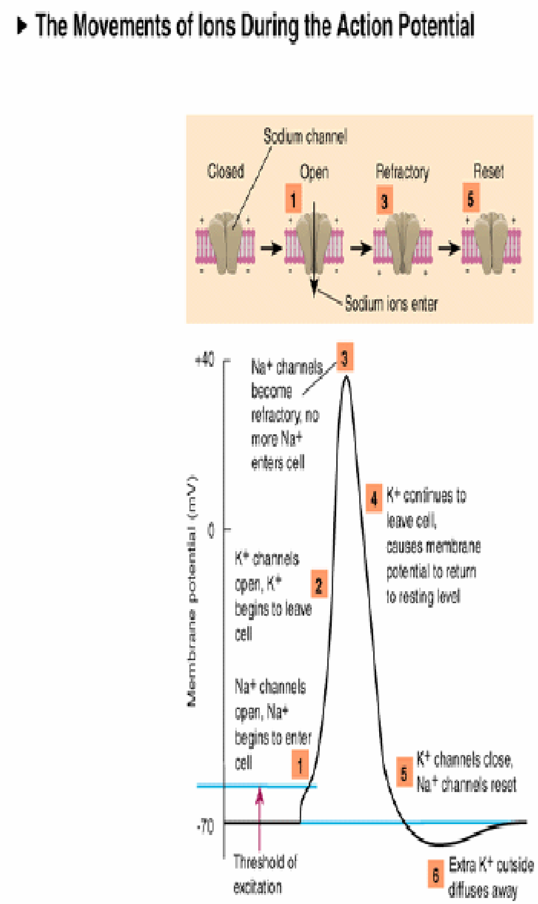
- During the transmission of an action potential, the sodium channels stay open or for less than a millisecond; in that time sodium rushes into the cell.
- The opening of sodium channels causes the rising phase (spike) of the action potential.
- Potassium channels open more slowly than the sodium channels and stay open longer; this allows potassium ions to carry excess positive charges out of the axon.
- Potassium channels thus help the plasma membrane return to its resting potential, falling phase (Repolarization).
- Another feature of voltage-gated sodium channels is that once they open and close, they can be triggered again only after a short delay of 1-2 milliseconds.

Generating and Conducting Nerve Impulses (11)

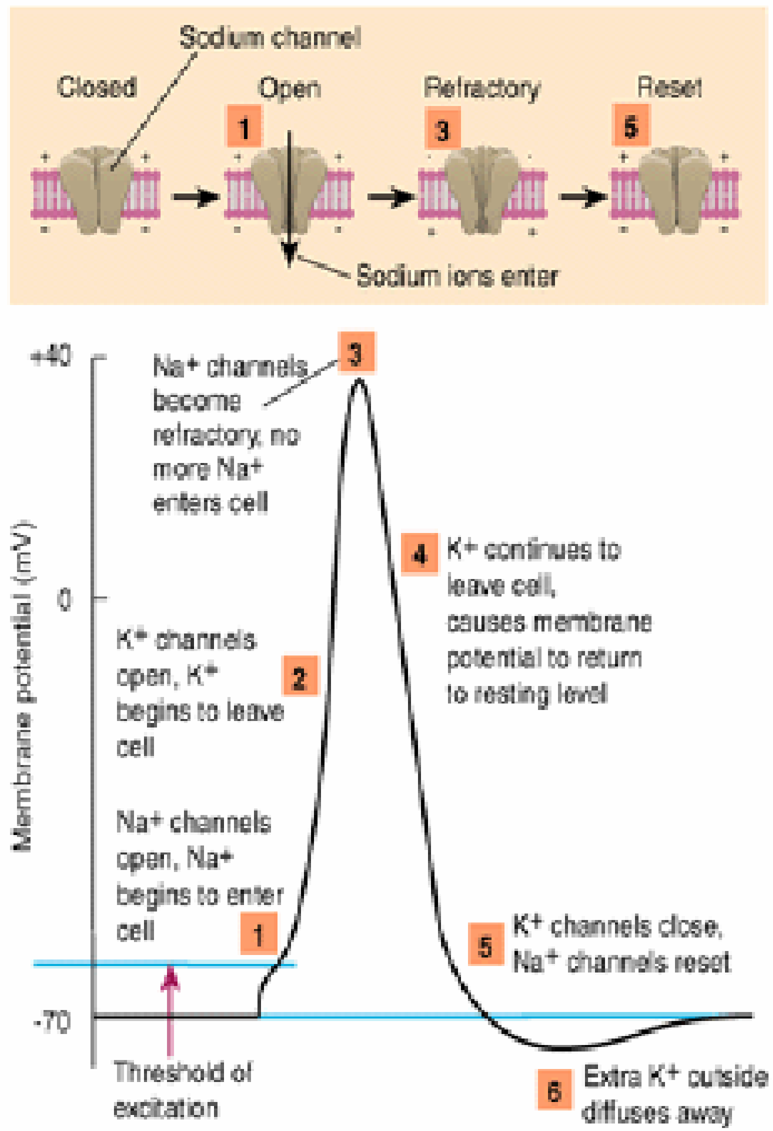
- This delay is the **refractory period,** the time when a plasma membrane cannot propagate an action potential.
- The concentration of K^+ and Na^+ ions on opposite sides of the plasma membrane is the "Battery" that drives action potentials.
- Since only a small fraction of the total amount of Na^+ ions moves down their concentration gradient when sodium channels open, the overall ratio of K^+ to Na^+ is not changed very much.

Generating and Conducting Nerve Impulses (12)

- Therefore, the “battery” can be recharged without difficulty even when many action potentials are being transmitted.
- Action potentials travel long distances with no loss of signal.
- Action potentials are **<u>all-or-nothing</u>** due to the interaction between the voltage-gated sodium channels and the membrane potential.



► The Movements of Ions During the Action Potential



Generating and Conducting Nerve Impulses (13)

- All-or-none response: An individual neuron either fires (once threshold is reached) or does not.
- Strength of stimuli cannot cause a single neuron to fire stronger or faster, but it can cause more neurons to fire and/or fire more often.
- The action potential is **Self-regenerating** because it spreads by current flow to adjacent regions of the membrane.
- The action potential propagates in one direction and cannot be reversed because the part of the membrane it came from it in its refractory period.
- Action potentials travel faster in large-diameter axons than in small-diameter ones.

Generating and Conducting Nerve Impulses (15)

- The electrical difference between the inside and outside of the axon is -70 mV
- When a neuron is stimulated by another neuron, one of two things can happen.
- The neuron become:
  - excited (depolarized) or
  - Inhibited (hyperpolarized).

Excited (Depolarization)

- Stimulation reduces the polarization (e.g. from -70 to -60 mV). <u>**More likely**</u> to fire

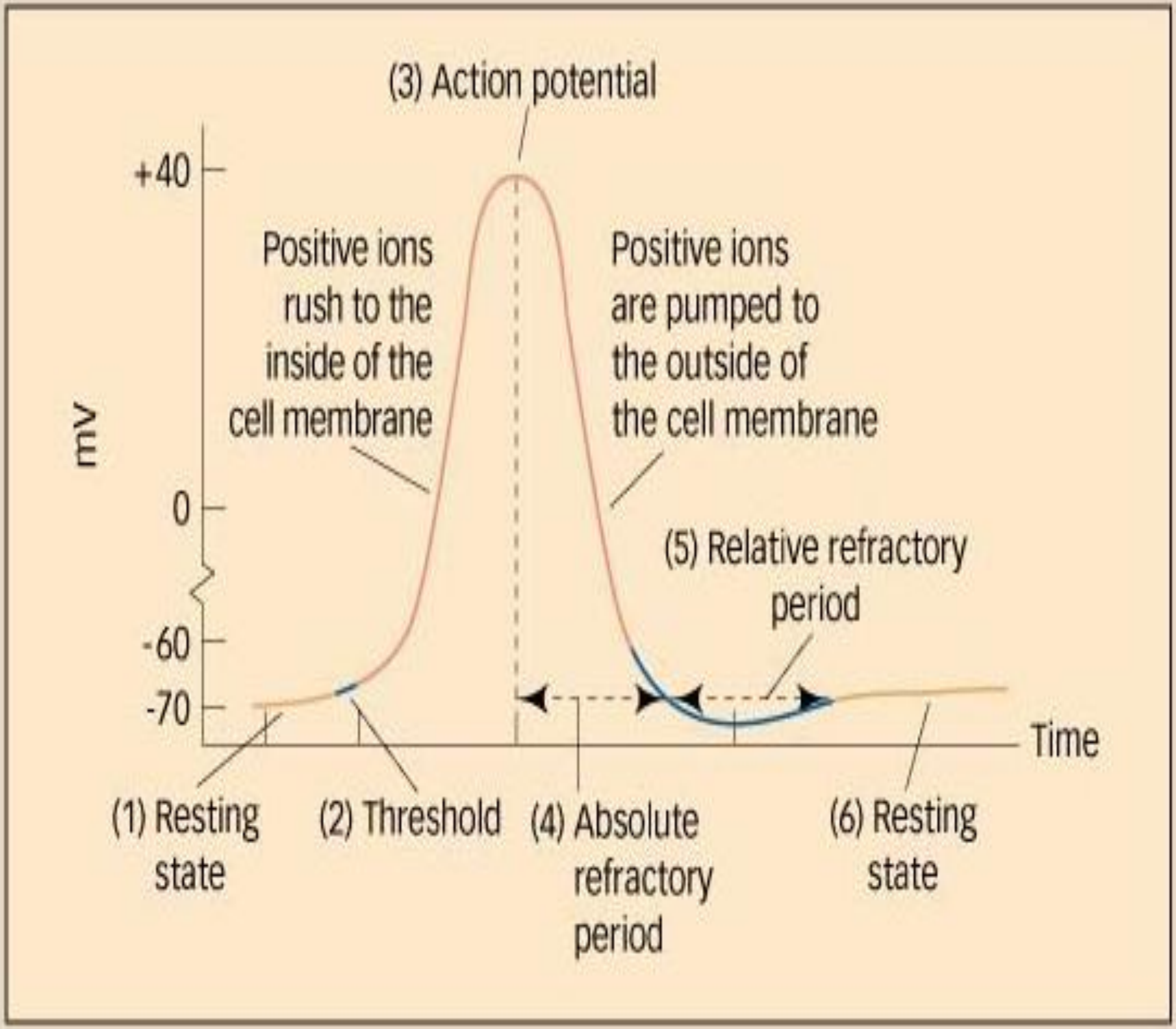
Inhibited (Hyperpolarization)

- Stimulation increases the polarization (e.g. from -70 to -80 mV). <u>**Less likely to fire.**</u>

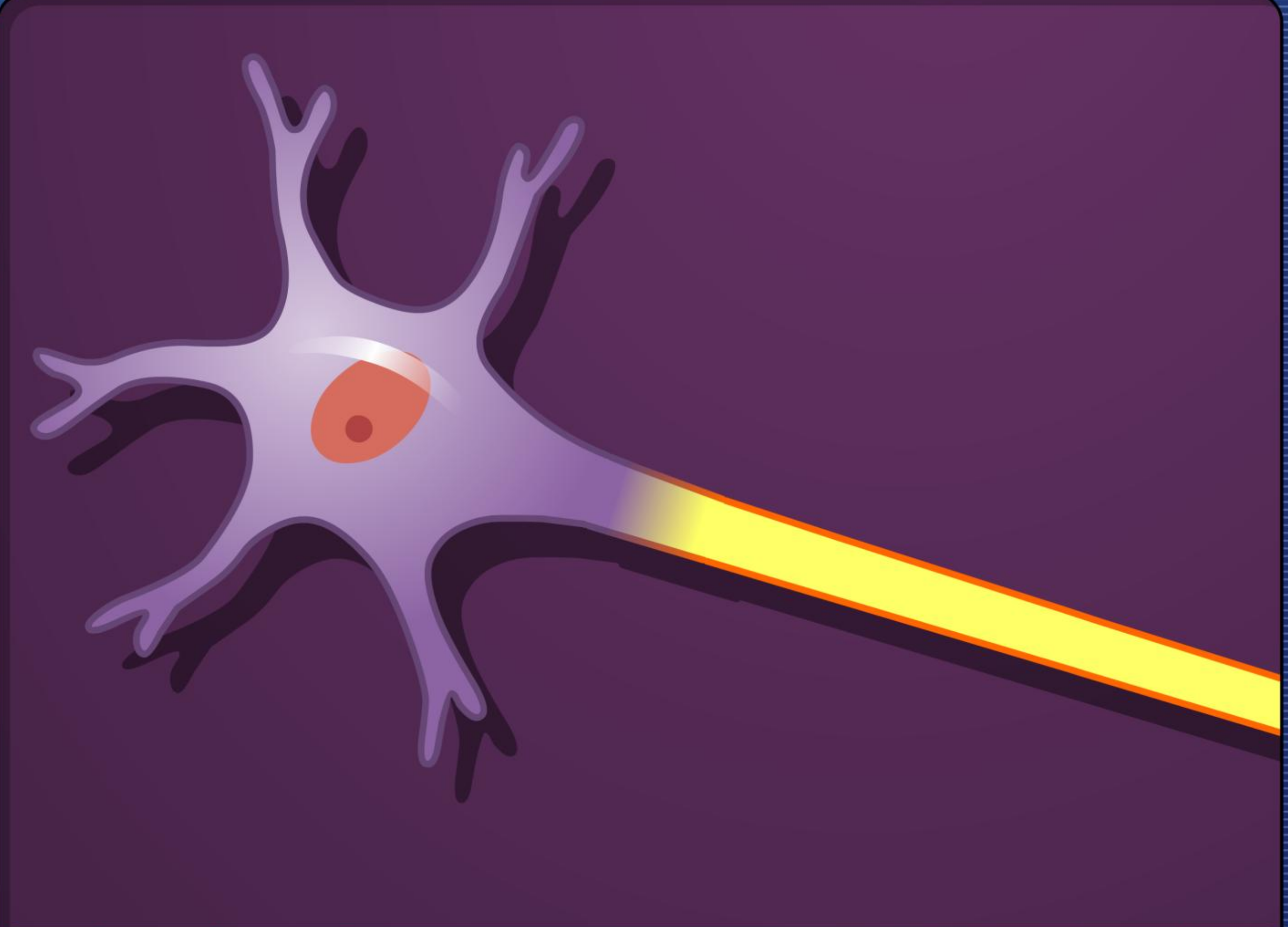
- Firing of postsynaptic neuron is an <u>**all-or-nothing event.**</u>
- If the message is strong enough, an <u>**action potential**</u> will occur.

Action Potential: Sequence of Events

- Initially the cell is resting at around -70 mV.
- The cell becomes excited.
- Channels open and the membrane permeability to sodium is suddenly increased greatly.
- Na^+ rushes into the cell (depolarization) creating AP.
- Voltage-activated Potassium channels open.
- Permeability to K^+ increases slowly (Leaves) (Repolarization).
- Positive charges accumulate within the cell.
- The membrane potential approaches the equilibrium potential for Sodium (E Na).
- Na^+ channels close
- K+ continues to leave the cell undershoot (Hyperpolarization)


(3) Action potential
+40
0
-60
-70
mV
Positive ions rush to the inside of the cell membrane
Positive ions are pumped to the outside of the cell membrane
(5) Relative refractory period
Time
(1) Resting state
(2) Threshold
(4) Absolute refractory period
(6) Resting state

Action Potential Propagation in an Unmyelinated Axon



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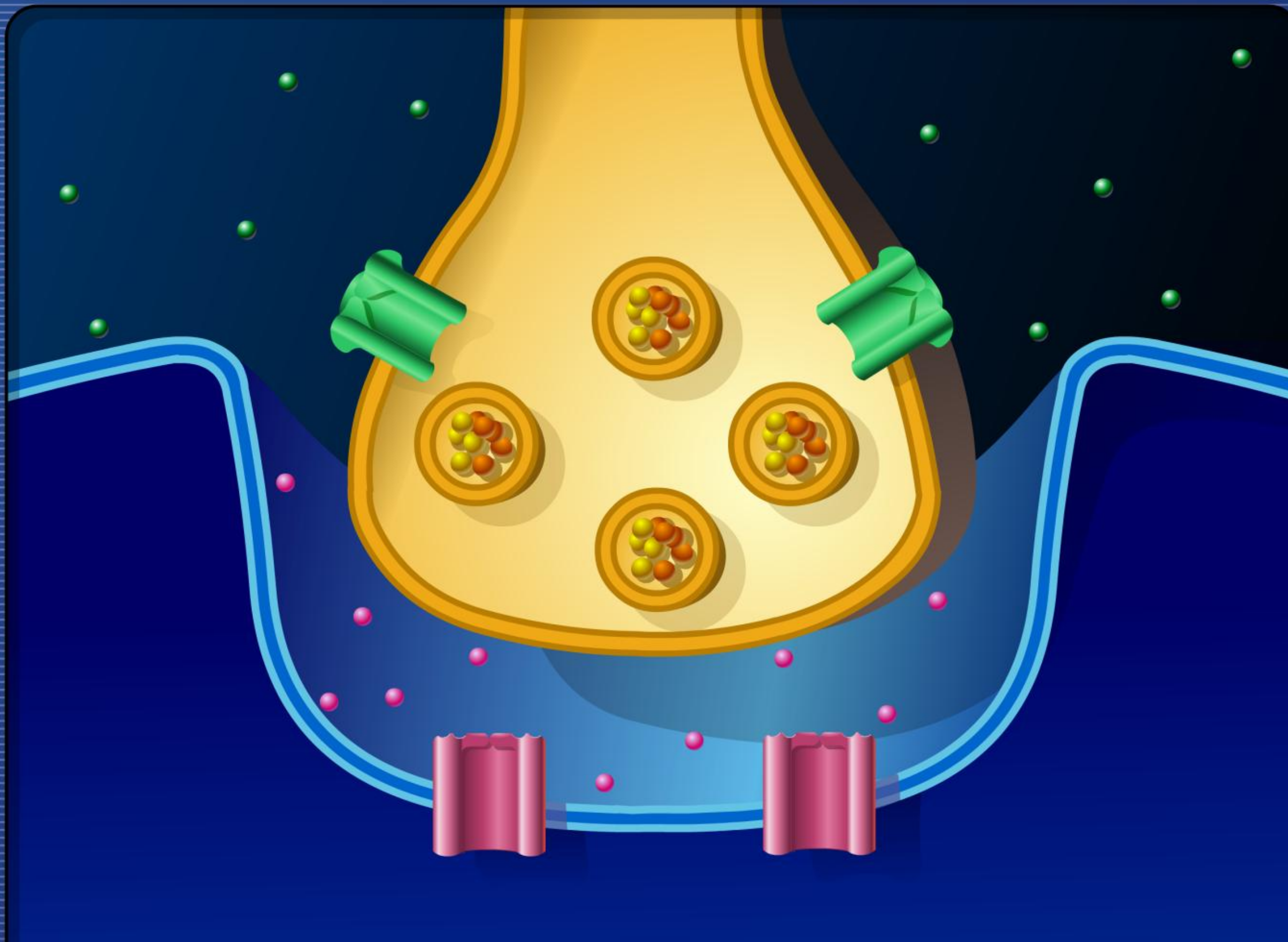
An action potential, depicted as a red band, is propagated in one direction along the axon.

Neurotransmission (1)

- Most neurons communicate at the synapse through a process that involves the conversion of the **electrical** charge to a **chemical** message.
- When this "message" is released, it alters the electrical charge of the next neuron.
- The "message" is a few thousand molecules of a chemical called **neurotransmitter.**
- Neurotransmitters-chemicals that transmit information from one cell to another.

Chemical Synapse



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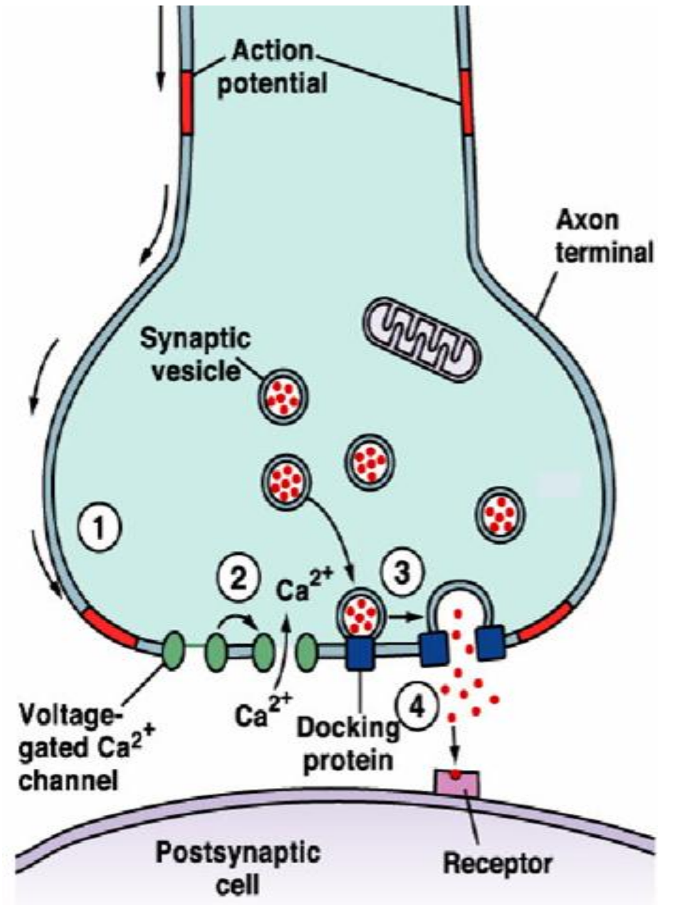
Action potentials arriving at the presynaptic terminal cause voltage-gated calcium ion channels to open.

Major Neurotransmitters

- A chemical substance that is released by a transmitting neuron at the synapse and that alters the activity of a receiving neurons.
- Neurotransmitters only attach to specific receptors**- "lock and key"** principle.
- Serotonin
- Dopamine
- Acetylcholine (ACh)
- Norepinephrine
- Gamma amino butyric acid (GABA)
- Glutamate
- Endorphins

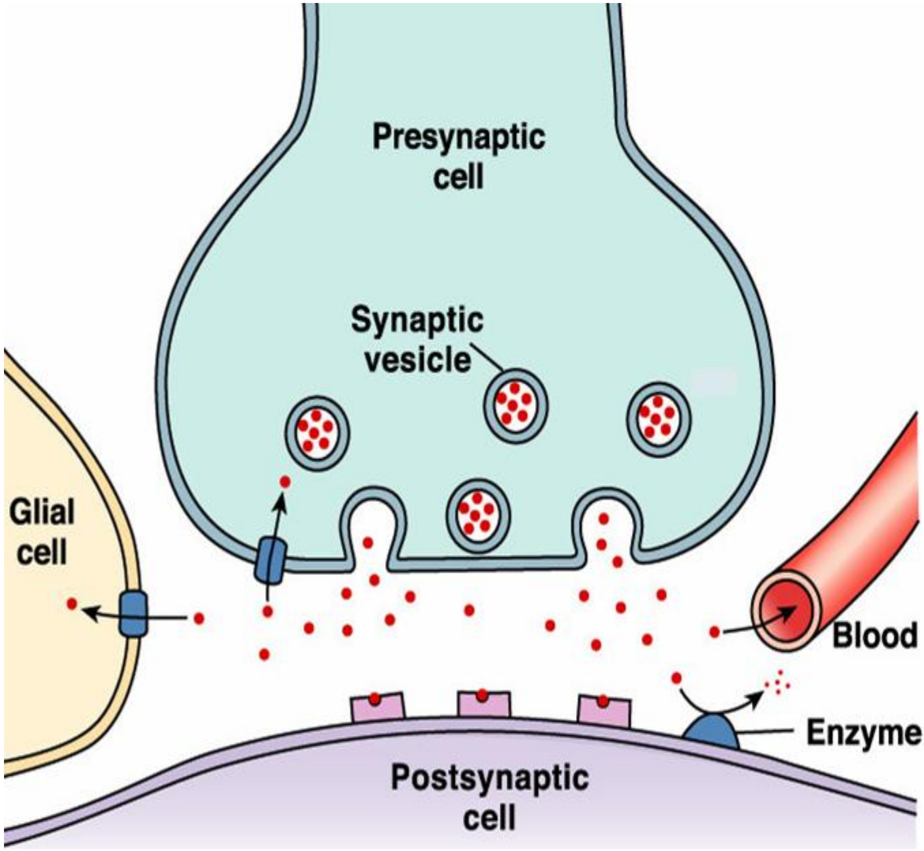
Neurotransmission (3)

•An AP reaches the axon terminal of the presynaptic cell and causes V-gated Ca^{2+} channels to open.
•Ca^{2+} rushes in, binds to regulatory proteins and initiates NT exocytosis.
•NTs diffuse across the synaptic cleft and then bind to receptors on the postsynaptic membrane and initiate some sort of response on the postsynaptic cell.



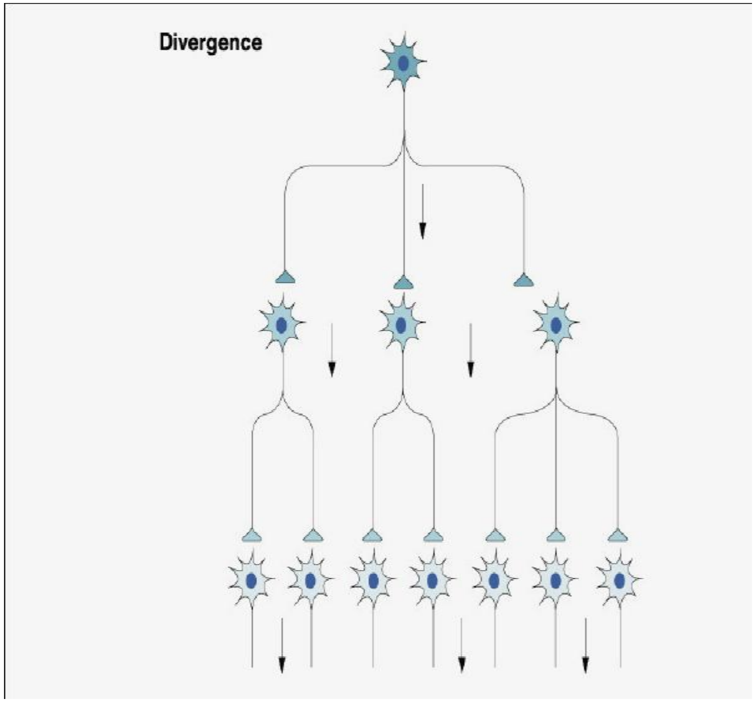
Neurotransmitter Removal (4)

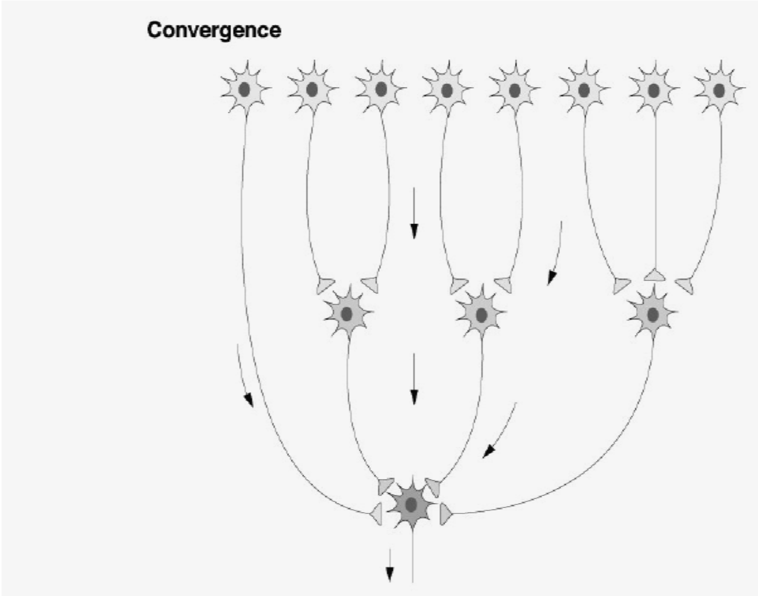
- Why did we want to remove Ach from the neuromuscular junction?
- How was Ach removed From the NMJ?
- NTs are removed from the synaptic cleft via:
  – Enzymatic degradation
  – Diffusion
  – Reuptake



Neurotransmission (5)

- Communication between neurons is not typically a one-to-one event.
- Sometimes a single neuron branches and its collaterals synapse on multiple target neurons. This is known as **Divergence.**
- A single postsynaptic neuron may have synapses with as many as 10,000 postsynaptic neurons. This is **Convergence.**
- Can you think of an advantage to have convergent and divergent circuit?





Neurotransmitters (6)

- Neurotransmitter can either increase or decrease neural firing-excitatory or inhibitory
- e.g. glutamate= excitatory, involved in learning, (MSG activates glutamate receptors)
- e.g. GABA = inhibitory (reduces anxiety – valium and alcohol increase this in the brain)
- **Neurotransmitters (NT) and Disorders**
- Deficiencies and dysfunction in neurotransmitters (NT) are involved in many psychological disorders and other medical conditions.

Neurotransmitters (7) and Disorders

- **Alzheimer's Disease (AD),** a number of NT have been implicated in AD
  - For example, in AD, many of the brain cells responsible for producing acetylcholine have been destroyed.
  - This deficit may account for memory loss.
- **Parkinson's Disease (PD)** is another dementia, and this disease has a gradual onset.
  - The degradation of brain cells that produce and use the NT **DOPAMINE** _appears to cause the symptoms of Parkinson's disease.
- **Schizophrenia,** develop due to imbalance in the NT **norepinephrine, dopamine and serotonin**
- Psychotic disorder characterized by delusion's, hallucinations, incoherent word associations, and inappropriate emotional reactions.

Neurotransmitters (8)
Acetylcholine

- Cholinergic synapses release acetylcholine
- Neuromuscular junction is an example of a cholinergic synapse
- Also found at all neuron-to-neuron synapses in the PNS

Neurotransmitters (8)
Norepinephrine

- Involved in:
  - Attention and consciousness
  - Control of body temperature
  - Regulation of pituitary gland secretions
- Widely distributed in the brain and autonomic nervous system
- Adrenergic synapses release norepinephrine
- Typically excitatory, depolarizing effect

Neurotransmitters (8)
Dopamine

- CNS neurotransmitter
- May have either excitatory or inhibitory effects
- Dopamine plays an important role in our precise control of movements by an inhibitory effect
- Dopamine's excitatory effects are exhibited in the use of cocaine
- Cocaine inhibits the removal of dopamine from synapses in specific areas of the brain
- This accumulation of dopamine at the synapses is responsible for the "high" experienced

Neurotransmitters (8)
Serotonin

- Neurotransmitter important in:
  - Emotional state
  - Mood
  - Body temperature
- Inadequate serotonin production can have widespread effects on a person's attention and emotional states
- May be responsible for chronic depression

Neurotransmitters (8)
GABA – (gamma aminobutyric acid)

- Generally has an inhibitory effect
- Not well understood
- It appears to reduce anxiety
- Some antianxiety drugs work by enhancing this effect
  - Valium
  - Xanax
  - Ativan

Factors that disrupt neural function

- Includes:
  - Changes in blood pH
  - Ionic composition
  - Body temperature

Effect of pH on neural function

- Normal extracellular pH averages 7.35 – 7.45
- If the pH rises, neurons are stimulated
- At a pH near 7.8, neurons generate action potentials spontaneously
  - This causes convulsions
- If the pH drops, neurons are inhibited
- At a pH around 7.0, the rate of generation of action potential is so low that the nervous system shuts down
  - The individual becomes unresponsive

Effect of ionic composition on neural function

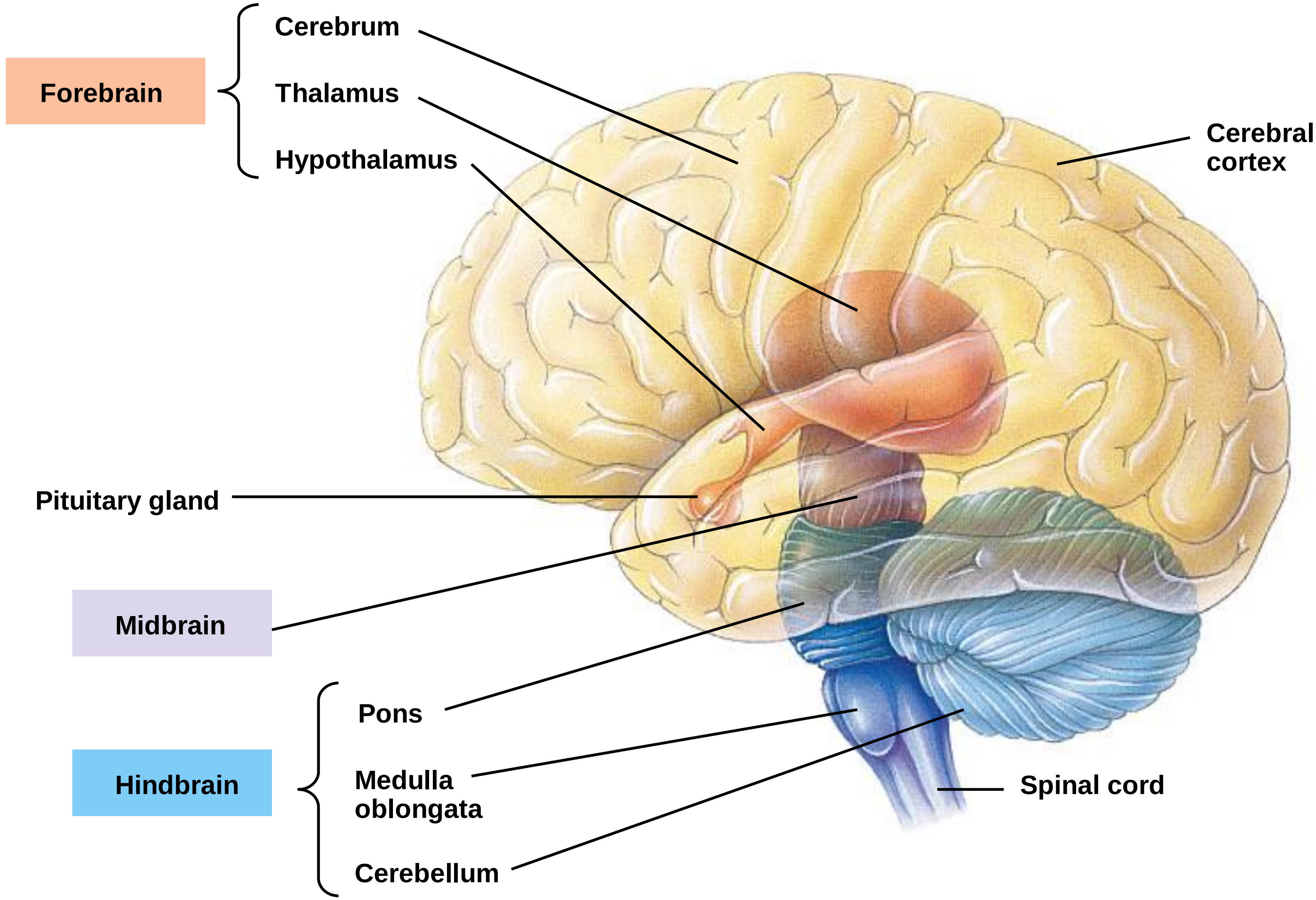
- Fluctuations in sodium or potassium concentrations may stimulate or inhibit neural activity by depolarizing or hyperpolarizing the cell membrane
  - Changes that would be likely to occur with kidney disease or dehydration
- For example, with hyperkalemia, (elevated extracellular potassium concentration)
  - Slight hyperkalemia causes stimulation
  - Extreme hyperkalemia interferes with repolarization and suppresses the generation of action potentials resulting in:
    - Paralysis of skeletal muscles
    - Death by cardiac muscles

Effect of body temperature on neural function

- Neurons become more excitable as body temperature increases
  - A person with a high fever may experience hallucinations or convulsions
- Neurons become inhibited as body temperature decreases
  - A person with a low body temperature will be lethargic and confused and may lose consciousness

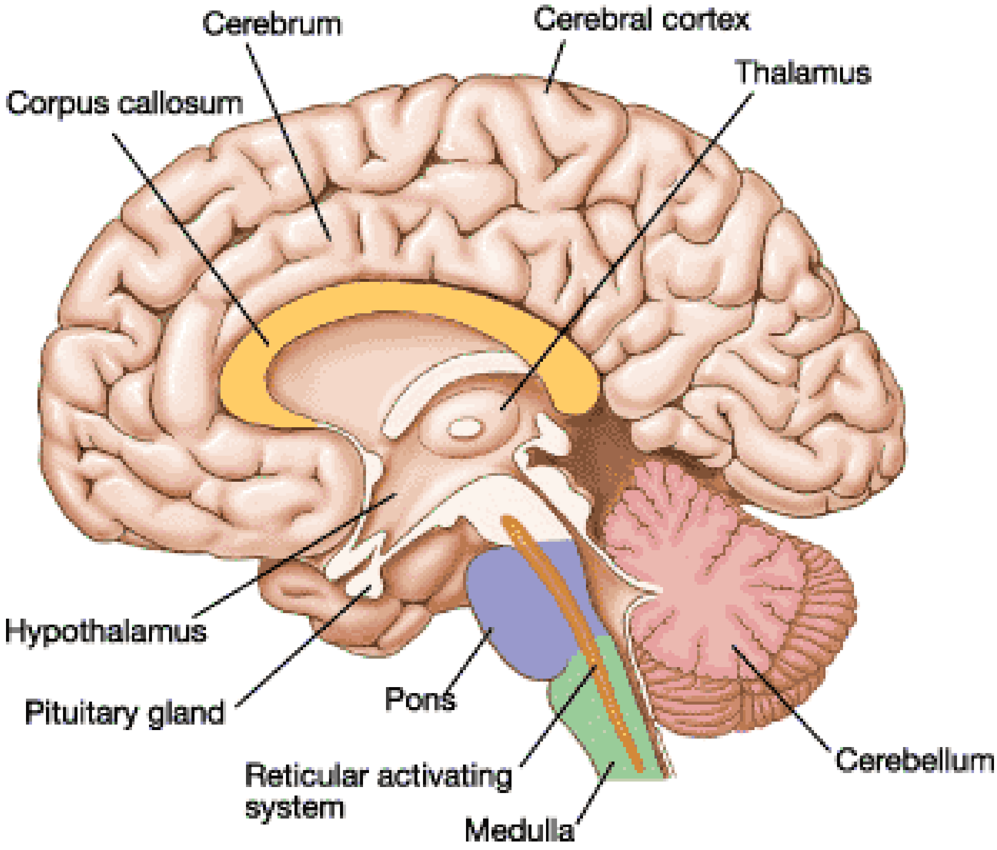
THE HUMAN BRAIN

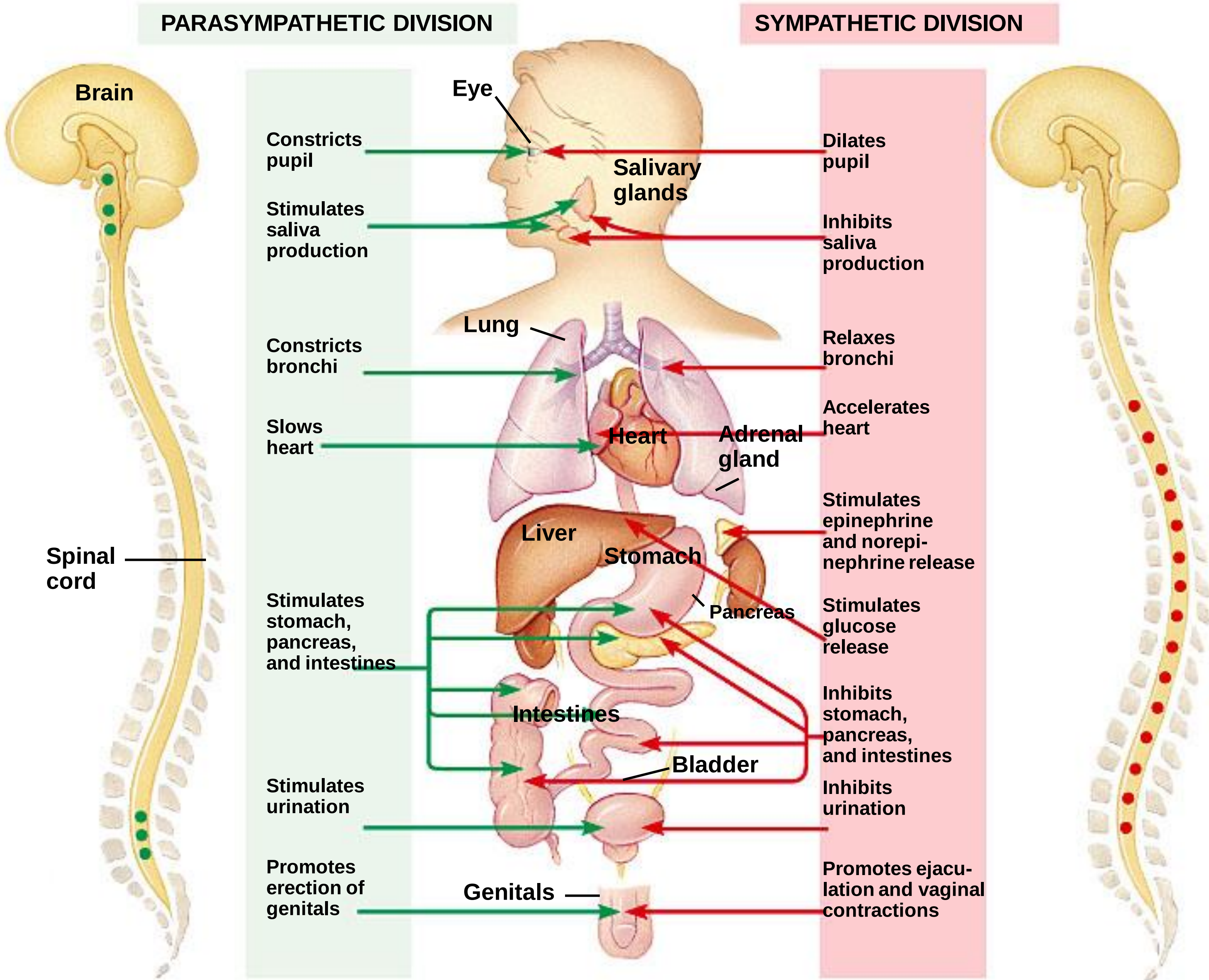
- The vertebrate brain evolved by the enlargement and subdivision of three anterior bulges of the neural tube
  - Forebrain
  - Midbrain
  - Hindbrain


Forebrain
Cerebrum
Thalamus
Hypothalamus
Cerebral cortex
Pituitary gland
Midbrain
Pons
Hindbrain
Medulla oblongata
Cerebellum
Spinal cord

The Human Brain

- The hindbrain
- The thalamus
- The hypothalamus and the pituitary gland
- The limbic system
- The basal ganglia
- The cerebrum and lobes of the cerebral cortex





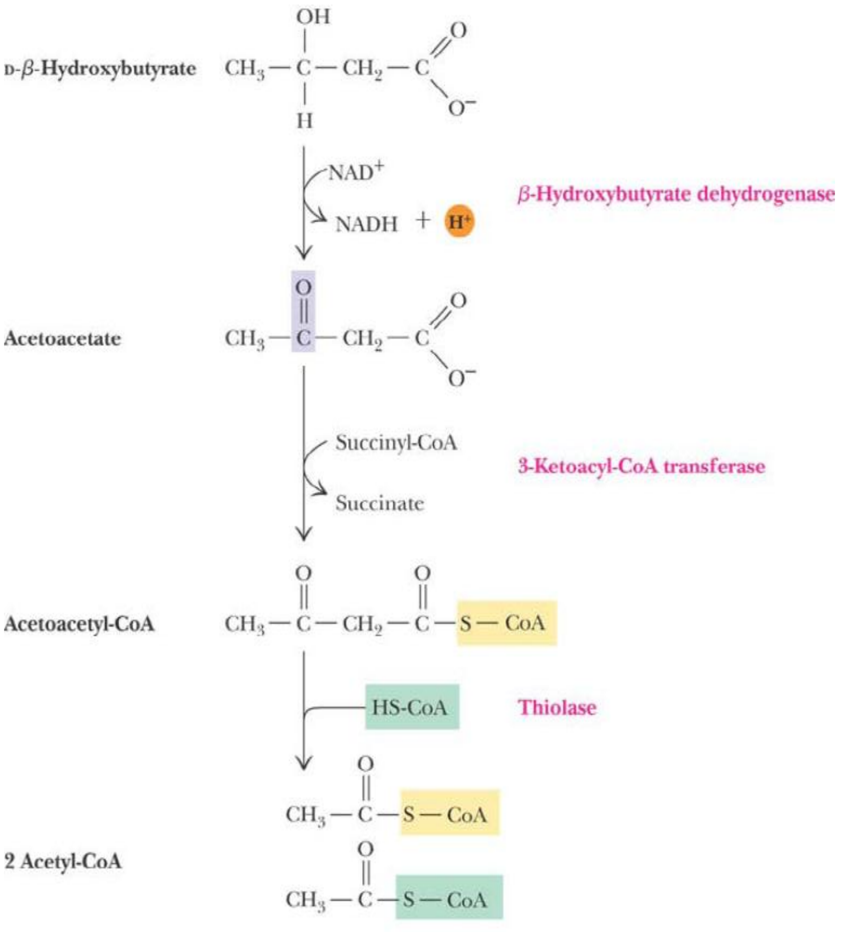
PARASYMPATHETIC DIVISION
SYMPATHETIC DIVISION
Brain
Spinal cord
Eye
Constricts pupil
Dilates pupil
Salivary glands
Stimulates saliva production
Inhibits saliva production
Lung
Constricts bronchi
Relaxes bronchi
Slows heart
Accelerates heart
Heart
Adrenal gland
Stimulates epinephrine and norepi-nephrine release
Liver
Stomach
Pancreas
Stimulates glucose release
Stimulates stomach, pancreas, and intestines
Inhibits stomach, pancreas, and intestines
Intestines
Bladder
Stimulates urination
Inhibits urination
Promotes erection of genitals
Genitals
Promotes ejacu-lation and vaginal contractions

The brain

- On cross section the embryonic neural tube develops into a central canal surrounded by:
- Gray matter
  - The cellular portion of the CNS
- White matter
  - The tract system of the CNS

Fueling the Brain

- Brain has very high metabolism but has no fuel reserves
- This means brain needs a constant supply of glucose
- Brain cannot use fatty acids directly
- In fasting conditions, brain can use β-hydroxybutyrate (from fatty acids), converting it to acetyl-CoA in TCA
- This allows brain to use fat as fuel indirectly!



Mechanism for Coupling Neuronal Activity to Glucose Utilization