PHYSIOLOGY

FACULTY OF PHARMACEUTICAL SCIENCES

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LECTURE 4, PART (1)- SYMPATHETIC VERSUS PARASYMPATHETIC RESPONSES.

Objectives

1. Compare **the somatic and autonomic nervous systems.**

2. Discuss **ANS neurotransmitters and receptors**.

3. Distinguish **sympathetic versus parasympathetic responses.**

(Pages 524-540 of the reference).

General Overview

SOMATIC NERVOUS SYSTEM (SNS) (CONSCIOUSLY CONTROLLED)

1. **Sensory neurons** that convey information to CNS from somatic receptors in the head, body wall, and limbs and from receptors for the special senses of vision, hearing, taste, and smell.

2. **Motor neurons** that conduct impulses from the CNS to skeletal muscles only.

AUTONOMIC NERVOUS SYSTEM (ANS) (INVOLUNTARY)

1. **Sensory neurons** that convey information to CNS from autonomic sensory receptors, located primarily in blood vessels, muscles, the nervous system, and the visceral organs such as the stomach and lungs.

2. **Motor neurons** that conduct nerve impulses from the CNS to smooth muscle, cardiac muscle, and glands.

Note: The motor part of the ANS consists of two branches, the **sympathetic division and the parasympathetic division**.

AUTONOMIC NERVOUS SYSTEM (ANS) (INVOLUNTARY)

Unlike skeletal muscle, **tissues innervated by the ANS often function to some extent even if their nerve supply is damaged**.

For examples,

1- The heart continues to beat when it is removed for transplantation into another person.

2- Smooth muscle in the lining of the gastrointestinal tract contracts rhythmically on its own.

3- Glands produce some secretions in the absence of ANS control.

AUTONOMIC NERVOUS SYSTEM (ANS) (INVOLUNTARY)

- Myelinated somatic motor neuron extends from the central nervous system (CNS) all the way to the skeletal muscle fibers in its motor unit.

- **Unlike somatic output (motor), the output part of the ANS has two divisions: the sympathetic division and the parasympathetic division.**

AUTONOMIC NERVOUS SYSTEM (ANS) (INVOLUNTARY)

- **In some organs**, **nerve impulses from one division of the ANS stimulate the organ to increase its activity (excitation), and impulses from the other division decrease the organ's activity (inhibition).**

- For example, an **increased rate of nerve impulses from the sympathetic division increases heart rate**, and an **increased rate of nerve impulses from the parasympathetic division decreases heart rate.**

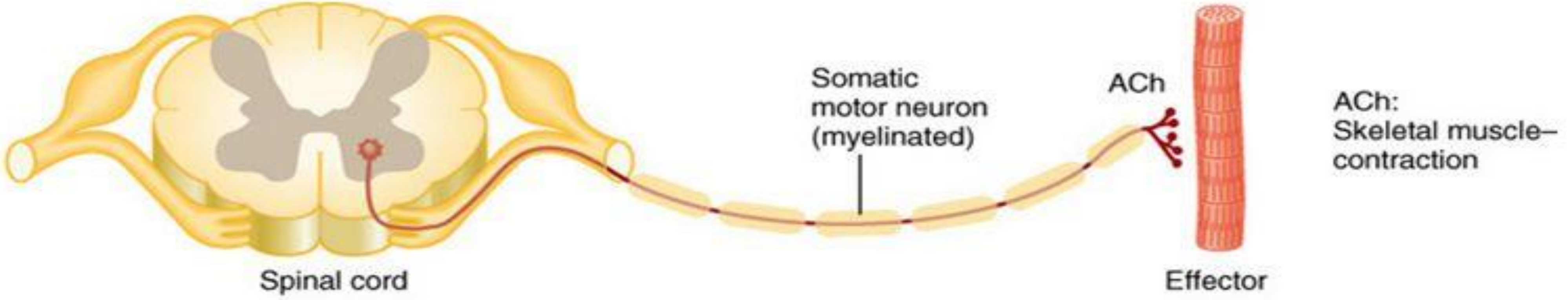
The first neuron **(preganglionic neuron)** has its cell body in the CNS; its myelinated axon extends from the CNS to an autonomic ganglion. (Recall that **a ganglion is a collection of neuronal cell bodies in the PNS**.)

The cell body of the second neuron **(post ganglionic neuron)** is also in that same autonomic ganglion; its unmyelinated axon extends directly from the ganglion to the effector (smooth muscle, cardiac muscle, or a gland).

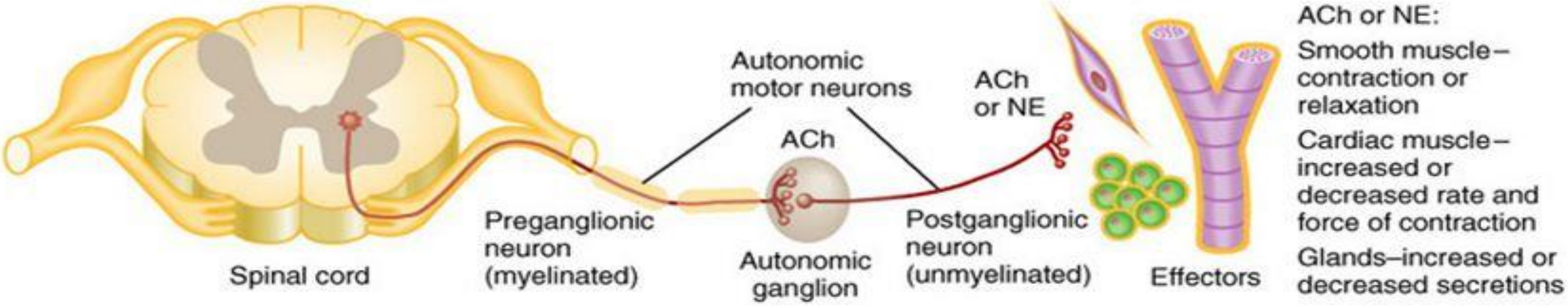
Alternatively, **in some autonomic pathways, the first motor neuron extends to specialized cells called chromaffin cells in the adrenal medullae** (inner portions of the adrenal glands) rather than an autonomic ganglion. **Chromaffin cells secrete the neurotransmitters epinephrine and norepinephrine (NE).**

All **somatic motor neurons** release only acetylcholine (ACh) as their neurotransmitter, but **autonomic motor neurons** release either ACh or norepinephrine (NE).

Comparison of Somatic and Autonomic Nervous Systems

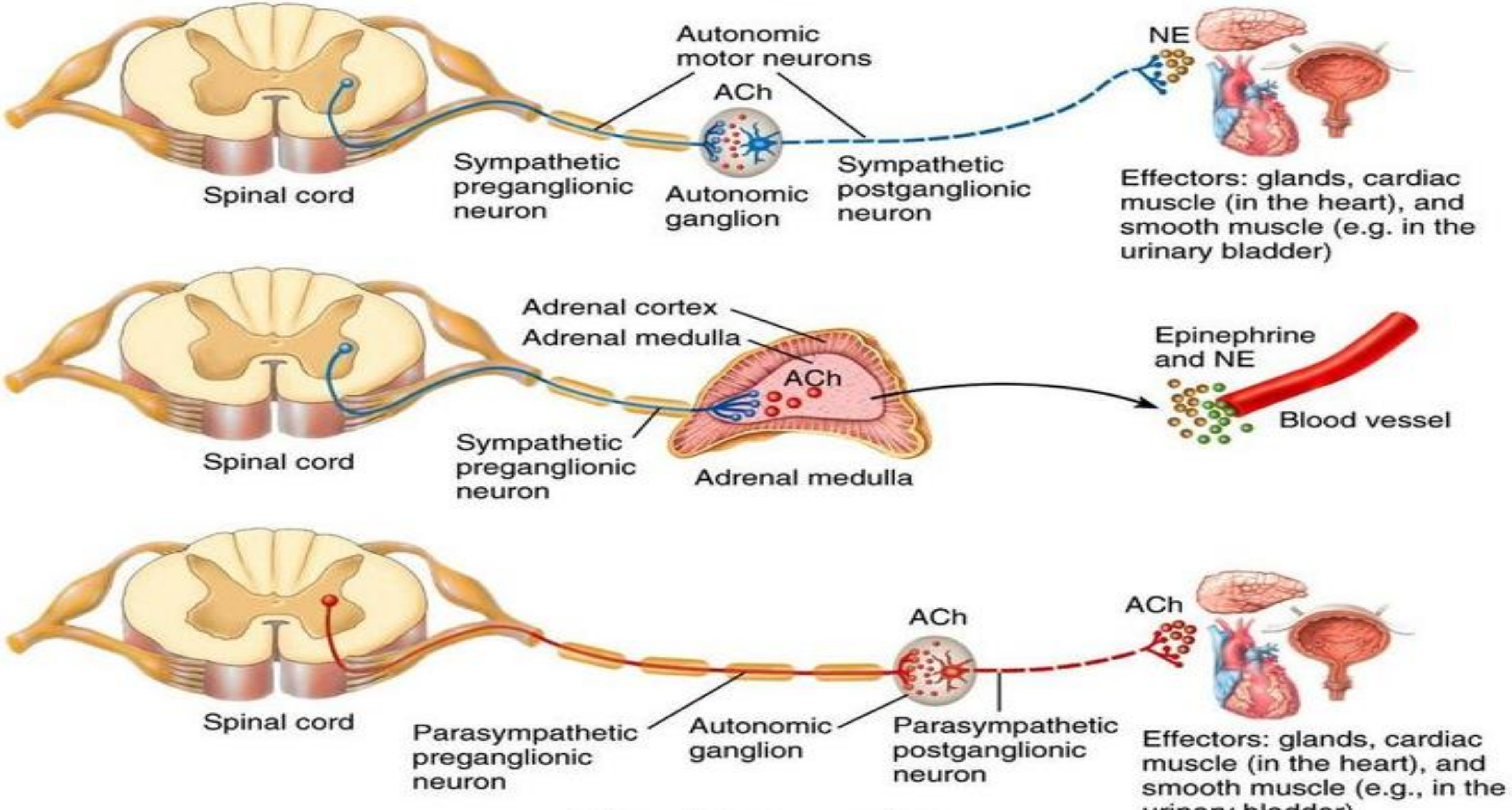


(a) Somatic nervous system



(b) Autonomic nervous system

ANS Motor Pathways



Autonomic nervous system

SYMPATHETIC DIVISION

- Is often called the **fight-or-flight division**.
- Result in increased alertness and metabolic activities in order to prepare the body for an emergency situation (i.e. rapid heart rate, faster breathing rate, dilation of the pupils).

PARASYMPATHETIC DIVISION

- Is often referred to as the **rest-and-digest division** because its activities conserve and restore body energy during times of rest or digesting a meal.
- Conserves energy and replenishes nutrient stores.

- **Although both the sympathetic and parasympathetic divisions are concerned with maintaining homeostasis, they do so in dramatically different ways.**

ANS NEUROTRANSMITTERS AND RECEPTORS

Based on the neurotransmitter they produce and release, **autonomic neurons** are classified as either **cholinergic or adrenergic**.

The **receptors for the neurotransmitters** are **integral membrane proteins** located in the plasma membrane of the postsynaptic neuron or effector cell.

CHOLINERGIC NEURONS AND RECEPTORS

- **Cholinergic neurons** release the **neurotransmitter acetylcholine (ACh).**

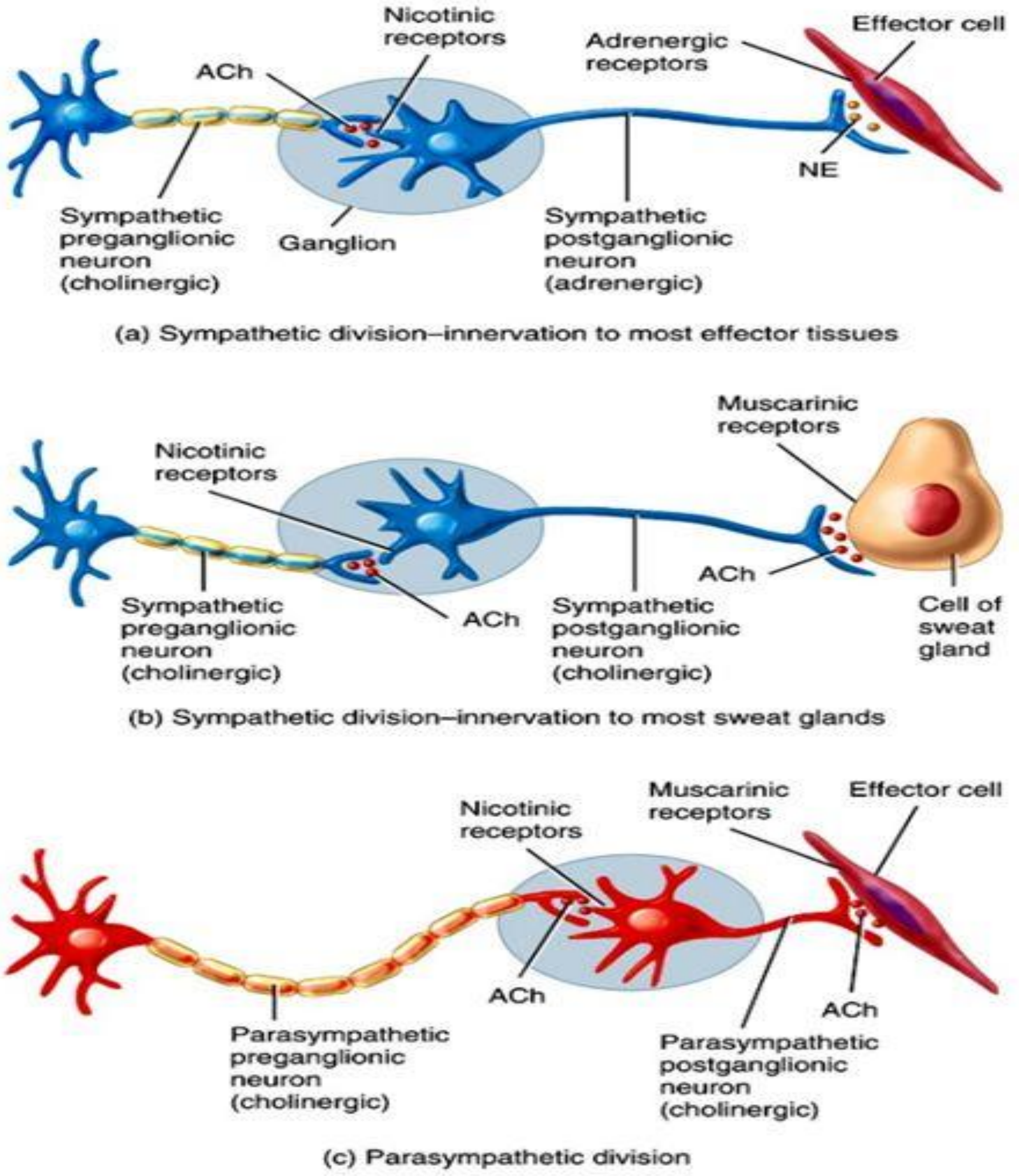
- In the ANS, the cholinergic neurons include (1) all **sympathetic and parasympathetic preganglionic neurons,** (2) **sympathetic postganglionic neurons that innervate most sweat glands,** and (3) all **parasympathetic postganglionic neurons.**

CHOLINERGIC NEURONS AND RECEPTORS

- **ACh is stored in synaptic vesicles** and **binds with specific cholinergic receptors**, integral membrane proteins in the postsynaptic plasma membrane.
- The two types of cholinergic receptors, both of which bind ACh, are **nicotinic receptors and muscarinic receptors.**

Cholinergic neurons release acetylcholine; adrenergic neurons release norepinephrine. Cholinergic receptors (nicotinic or muscarinic) and adrenergic receptors are integral membrane proteins located in the plasma membrane of a postsynaptic neuron or an effector cell.

Cholinergic and Adrenergic Neurons in the Autonomic Nervous System



CHOLINERGIC NEURONS AND RECEPTORS

Activation of nicotinic receptors by ACh causes **depolarization** and thus excitation of the postsynaptic cell, which can be a postganglionic neuron, an autonomic effector, or a skeletal muscle fiber.

CHOLINERGIC NEURONS AND RECEPTORS

- *Activation of muscarinic receptors by ACh* sometimes causes **depolarization** **(excitation)** and sometimes causes **hyperpolarization (inhibition)**, depending on which particular cell bears the muscarinic receptors.

CHOLINERGIC NEURONS AND RECEPTORS

Because **acetylcholine is quickly inactivated** by the enzyme acetylcholinesterase (AChE), **effects triggered by cholinergic neurons are brief**.

ADRENERGIC NEURONS AND RECEPTORS

- **Adrenergic neurons** release **norepinephrine (NE), also known as noradrenalin.**
- **Most sympathetic postganglionic neurons are adrenergic.**
- **Like ACh, NE is stored in synaptic vesicles and released by exocytosis.**
- **Molecules of NE diffuse across the synaptic cleft and bind to specific adrenergic receptors on the postsynaptic membrane, causing either excitation or inhibition of the effector cell.**

ADRENERGIC NEURONS AND RECEPTORS

- **Adrenergic receptors bind both norepinephrine and epinephrine.**

- **The two main types of adrenergic receptors are alpha (α) receptors and beta (β) receptors, which are found on visceral effectors innervated by most sympathetic postganglionic axons.**

ADRENERGIC NEURONS AND RECEPTORS

- These receptors are further classified into subtypes—**α1, α2, β1, β2, and β3**— based on the specific responses they elicit and by their selective binding of drugs that activate or block them. Although there are some exceptions, activation of α1 and β1 receptors generally produces excitation, and activation of and α2 and β2 receptors causes inhibition of effector tissues.

ADRENERGIC NEURONS AND RECEPTORS

- **Norepinephrine stimulates alpha receptors more strongly than beta receptors; epinephrine is a potent stimulator of both alpha and beta receptors.**

- **Compared to ACh**, norepinephrine lingers in the synaptic cleft for a longer time. Thus, effects triggered by adrenergic neurons typically are longer lasting than those triggered by cholinergic neurons.

RECEPTOR AGONISTS AND ANTAGONISTS

- A large variety of drugs and natural products can selectively activate or block specific cholinergic or adrenergic receptors.

- An **agonist** is a substance that binds to and **activates a receptor**, in the process mimicking the effect of a natural neurotransmitter or hormone.

- An **antagonist** is a substance that binds to and blocks a receptor, thereby preventing a natural neurotransmitter or hormone from exerting its effect.

SYMPATHETIC RESPONSES

- **During physical or emotional stress and various emotions,** the sympathetic division dominates the parasympathetic division.

- High sympathetic tone favors body functions that can **support vigorous physical activity and rapid production of ATP**.

- At the same time, the sympathetic division **reduces body functions that favor the storage of energy**.

FIGHT-OR-FLIGHT RESPONSE (SOME EXAMPLES)

- The pupils of the eyes dilate.
- Heart rate, force of heart contraction, and blood pressure increase.
- The airways dilate, allowing faster movement of air into and out of the lungs.
- Blood vessels that supply organs involved in exercise or fighting off danger—skeletal muscles, cardiac muscle, liver, and adipose tissue—dilate, allowing greater blood flow through these tissues.
- Release of glucose by the liver increases blood glucose level.

The effects of sympathetic stimulation are longer lasting and more widespread than the effects of parasympathetic stimulation for three reasons:

1. **Sympathetic postganglionic axons diverge more extensively**; as a result, many tissues are activated simultaneously.
2. **Acetylcholinesterase quickly inactivates acetylcholine, but norepinephrine lingers in the synaptic cleft for a longer period.**

The effects of sympathetic stimulation are longer lasting and more widespread than the effects of parasympathetic stimulation for three reasons:

3. **Epinephrine and norepinephrine** secreted into the blood from the adrenal medullae **intensify and prolong the responses caused by NE liberated from sympathetic postganglionic axons**. These blood-borne hormones circulate throughout the body, affecting all tissues that have alpha and beta receptors. In time, blood-borne NE and epinephrine are destroyed by enzymes in the liver.

Sympathetic Response

- Increase HR
- Increase RR
- Increase metabolic rate
- Increase fat & glycogen breakdown
- Pupillary dilation
- Smooth muscle vasoconstriction
- Skeletal & cardiac muscle vasodilation
- Decrease GI activity
- Bronchial relaxation

PARASYMPATHETIC RESPONSES

- Parasympathetic responses support body functions that **conserve and restore body energy during times of rest and recovery.**
- **In the quiet intervals between periods of exercise**, parasympathetic impulses to the digestive glands and the smooth muscle of the gastrointestinal tract predominate over sympathetic impulses.
- This **allows energy-supplying food to be digested and absorbed**.

REST-AND-DIGEST (SOME EXAMPLES)

- **Increasing SLUDD responses**, which include: salivation (S), lacrimation (L), urination (U), digestion (D), and defecation (D).

- "**Three decreases**", which include: decreased heart rate, decreased diameter of airways (bronchoconstriction), and decreased diameter (constriction) of the pupils.

REST-AND-DIGEST (SOME EXAMPLES)

- **Increasing SLUDD responses**, which include: salivation (S), lacrimation (L), urination (U), digestion (D), and defecation (D).

- "**Three decreases**", which include: decreased heart rate, decreased diameter of airways (bronchoconstriction), and decreased diameter (constriction) of the pupils.

Table 8–5 FUNCTIONS OF THE AUTONOMIC NERVOUS SYSTEM

Organ	Sympathetic Response	Parasympathetic Response
Heart (cardiac muscle)	• Increase rate	• Decrease rate (to normal)
Bronchioles (smooth muscle)	• Dilate	• Constrict (to normal)
Iris (smooth muscle)	• Pupil dilates	• Pupil constricts (to normal)
Salivary glands	• Decrease secretion	• Increase secretion (to normal)
Stomach and intestines (smooth muscle)	• Decrease peristalsis	• Increase peristalsis for normal digestion
Stomach and intestines (glands)	• Decrease secretion	• Increase secretion for normal digestion
Internal anal sphincter	• Contracts to prevent defecation	• Relaxes to permit defecation
Urinary bladder (smooth muscle)	• Relaxes to prevent urination	• Contracts for normal urination
Internal urethral sphincter	• Contracts to prevent urination	• Relaxes to permit urination
Liver	• Changes glycogen to glucose	• None
Pancreas	• Secretes glucagon	• Secretes insulin and digestive enzymes
Sweat glands	• Increase secretion	• None
Blood vessels in skin and viscera (smooth muscle)	• Constrict	• None
Blood vessels in skeletal muscle (smooth muscle)	• Dilate	• None
Adrenal glands	• Increase secretion of epinephrine and norepinephrine	• None

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LECTURE 4, PART (2)- GENERATION AND CONDUCTION OF ACTION POTENTIAL.

Objectives

1. Discuss **myelination.**

2. Describe **electrical signals in neurons**.

(Pages 408-421 of the reference)

MYELINATION

- ***Axons surrounded by a multilayered lipid and protein covering, called the myelin sheath.***

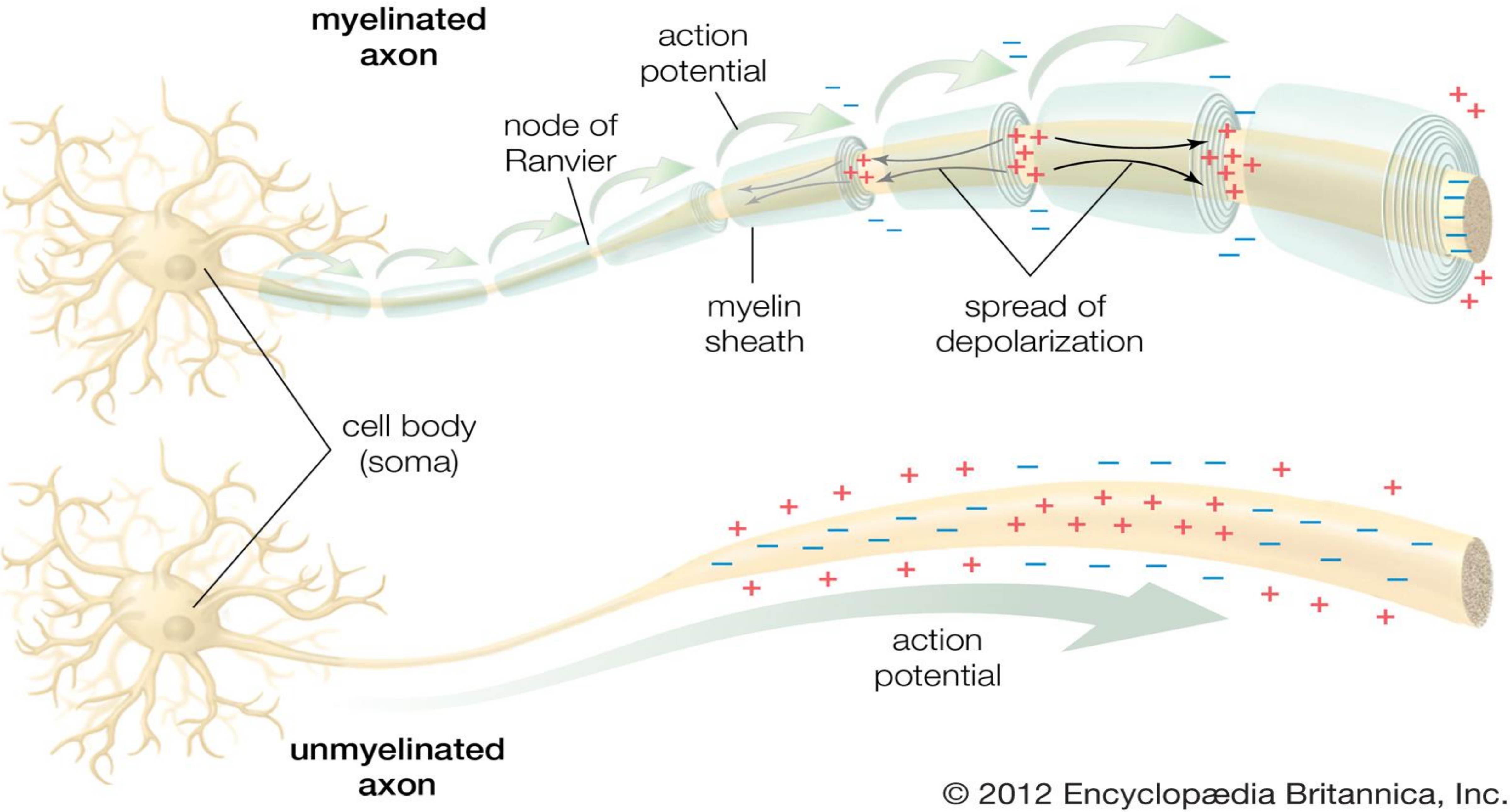
- The **myelin sheath:**

1. Insulates the axon of a neuron.

2. Increases the speed of nerve impulse conduction.

MYELINATION

- Two types of neuroglia produce myelin sheaths: Schwann cells (in the PNS) and oligodendrocytes (in the CNS).


myelinated axon
action potential
node of Ranvier
myelin sheath
spread of depolarization
cell body (soma)
action potential
unmyelinated axon

ELECTRICAL SIGNALS IN NEURONS

- **Neurons communicate** with one another using two types of electrical signals:

1. **Graded potentials** (for short- distance communication only).

2. **Action potentials** (for communication over long distances within the body).

- **Graded potentials and nerve and muscle action potentials** are involved in the relay of sensory stimuli, integrative functions such as perception, and motor activities.

Example (for writing)

1. As you touch the pen, a graded potential develops in a sensory receptor in the skin of the fingers.

2. The graded potential triggers the axon of the sensory neuron to form a nerve action potential, which travels along the axon into the CNS and ultimately causes the release of neurotransmitter at a synapse with an interneuron.

3. The neurotransmitter stimulates the interneuron to form a graded potential in its dendrites and cell body.

4. In response to the graded potential, the axon of the interneuron forms a nerve action potential. The nerve action potential travels along the axon, which results in neurotransmitter release at the next synapse with another interneuron.

5. This process of neurotransmitter release at a synapse followed by the formation of a graded potential and then a nerve action potential occurs over and over as interneurons in higher parts of the brain (such as the thalamus and cerebral cortex) are activated. Once interneurons in the cerebral cortex, the outer part of the brain, are activated, perception occurs and you are able to feel the smooth surface of the pen touch your fingers.

Note: Perception, the conscious awareness of a sensation, is primarily a function of the cerebral cortex.

6. A stimulus in the brain causes a graded potential to form in the dendrites and cell body of an upper motor neuron, a type of motor neuron that synapses with a lower motor neuron farther down in the CNS in order to contract a skeletal muscle. The graded potential subsequently causes a nerve action potential to occur in the axon of the upper motor neuron, followed by neurotransmitter release.

7. The neurotransmitter generates a graded potential in a lower motor neuron, a type of motor neuron that directly supplies skeletal muscle fibers. The graded potential triggers the formation of a nerve action potential and then release of the neurotransmitter at neuromuscular junctions formed with skeletal muscle fibers that control movements of the fingers.

8. The neurotransmitter stimulates the muscle fibers that control finger movements to form muscle action potentials. The muscle action potentials cause these muscle fibers to contract, which allows you to write with the pen.

THE PRODUCTION OF POTENTIALS

The production of graded potentials and action potentials depends on two basic features of the plasma membrane of excitable cells:

1. The existence of a resting membrane potential.
2. The presence of specific types of ion channels.

RESTING MEMBRANE POTENTIAL

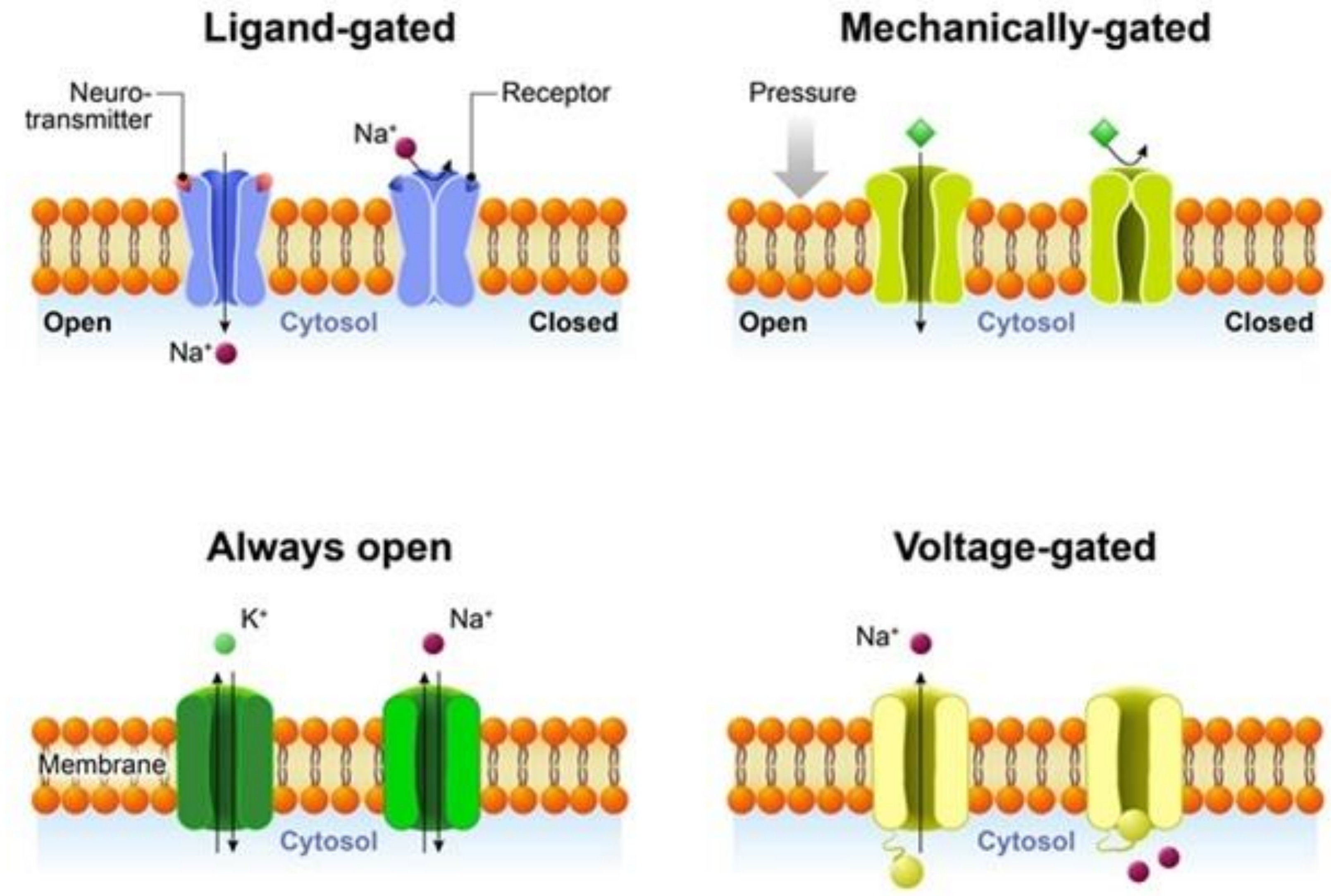
- The membrane potential, an electrical potential difference (voltage) across the membrane. This voltage is termed the resting membrane potential.

- This looks like voltage stored in a battery; you connect the positive and negative terminals of a battery with a piece of wire, electrons will flow along the wire. This flow of charged particles is called current.

The types of ion channels:

1. Leak channels.
2. Ligand-gated channel.
3. Mechanically-gated channel.
4. Voltage-gated channel.

ION CHANNEL


Ligand-gated
Neuro-
transmitter
Receptor
Na+
Open
Cytosol
Closed
Na+
Mechanically-gated
Pressure
Open
Cytosol
Closed
Always open
K+
Na+
Membrane
Cytosol
Voltage-gated
Na+
Cytosol

Leak channels:

- Randomly alternate between open and closed positions.

- The plasma membranes have many more potassium ion leak channels than sodium ion leak channels.

- Leak channels are found in nearly all cells, including the dendrites, cell bodies, and axons of all types of neurons.

Ligand-gated channel:

- Opens and closes in response to the binding of a ligand (chemical) stimulus (a ligand can be including neurotransmitters (i.e. acetylcholine), hormones, and particular ions).

- Ligand-gated channels are located in the dendrites of some sensory neurons, such as pain receptors, and in dendrites and cell bodies of interneurons and motor neurons.

Mechanically-gated channel:

- It opens or closes in response to mechanical stimulation in the form of vibration (such as sound waves), touch, pressure, or tissue stretching.

- They are found in auditory receptors in the ears, in receptors that monitor stretching of internal organs, and in touch receptors and pressure receptors in the skin.

Voltage-gated channel:

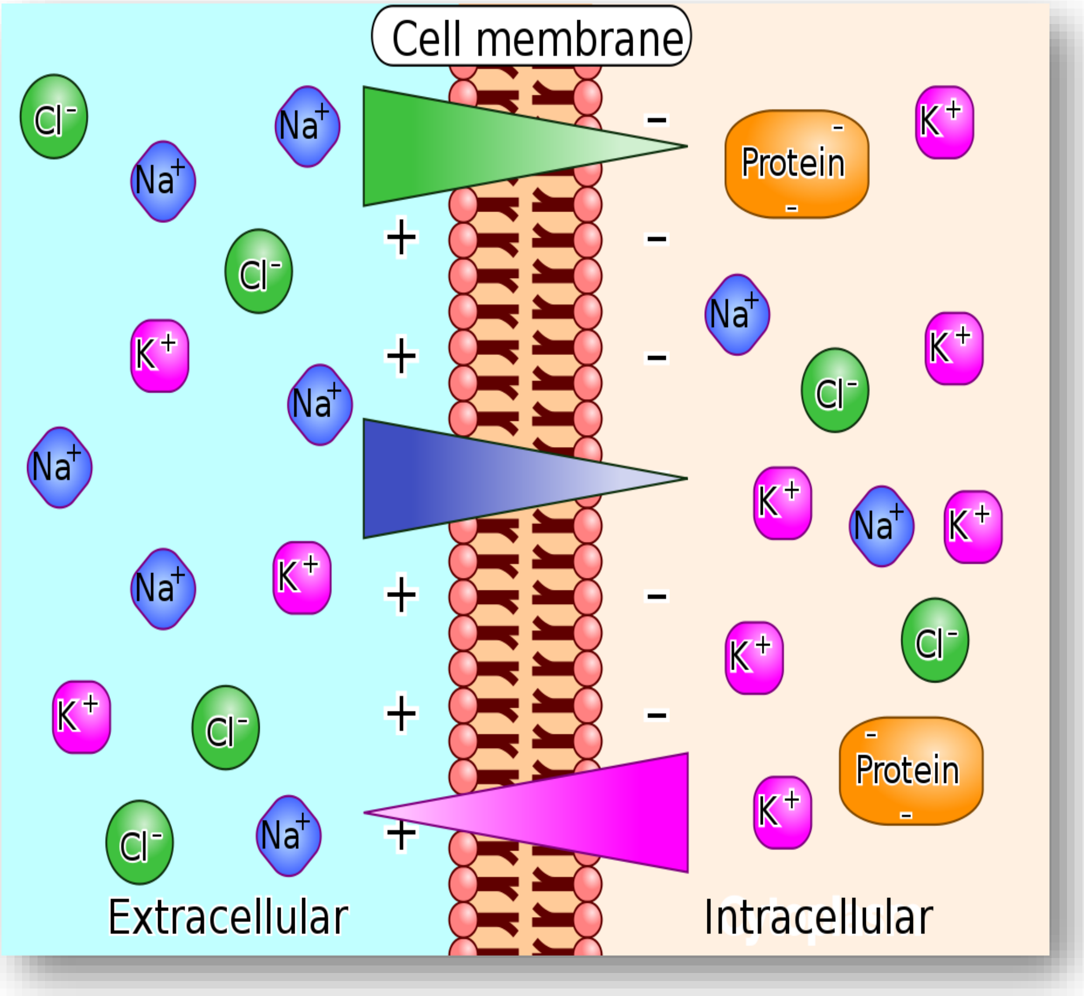
- It opens in response to a change in membrane potential (voltage).
- They participate in the generation and conduction of action potentials in the axons of all types of neurons.

Resting Membrane Potential

- A cell that exhibits a membrane potential is said to be polarized.

- **Three factors that contribute to the resting membrane potential:**

1. **<u>Unequal distribution of ions in the ECF and cytosol:</u>** as more and more positive potassium ions exit, the inside of the membrane becomes increasingly negative, and the outside of the membrane becomes increasingly positive.



Resting Membrane Potential

2. **Inability of most anions to leave the cell:** They cannot follow the potassium cations out of the cell because they are attached to nondiffusible molecules such as ATP and large proteins.

3. **Electrogenic nature of the Na–K ions ATPases**: The small inward Na ions leak, and outward K ions leak are offset by the Na–K ions ATPases (sodium–potassium pumps). However, they expel three Na ions each two K ions imported electrogenic, which means they contribute to the negativity of the resting membrane potential (it is very small: only -3 mV of the total -70 mV resting membrane potential in a typical neuron).

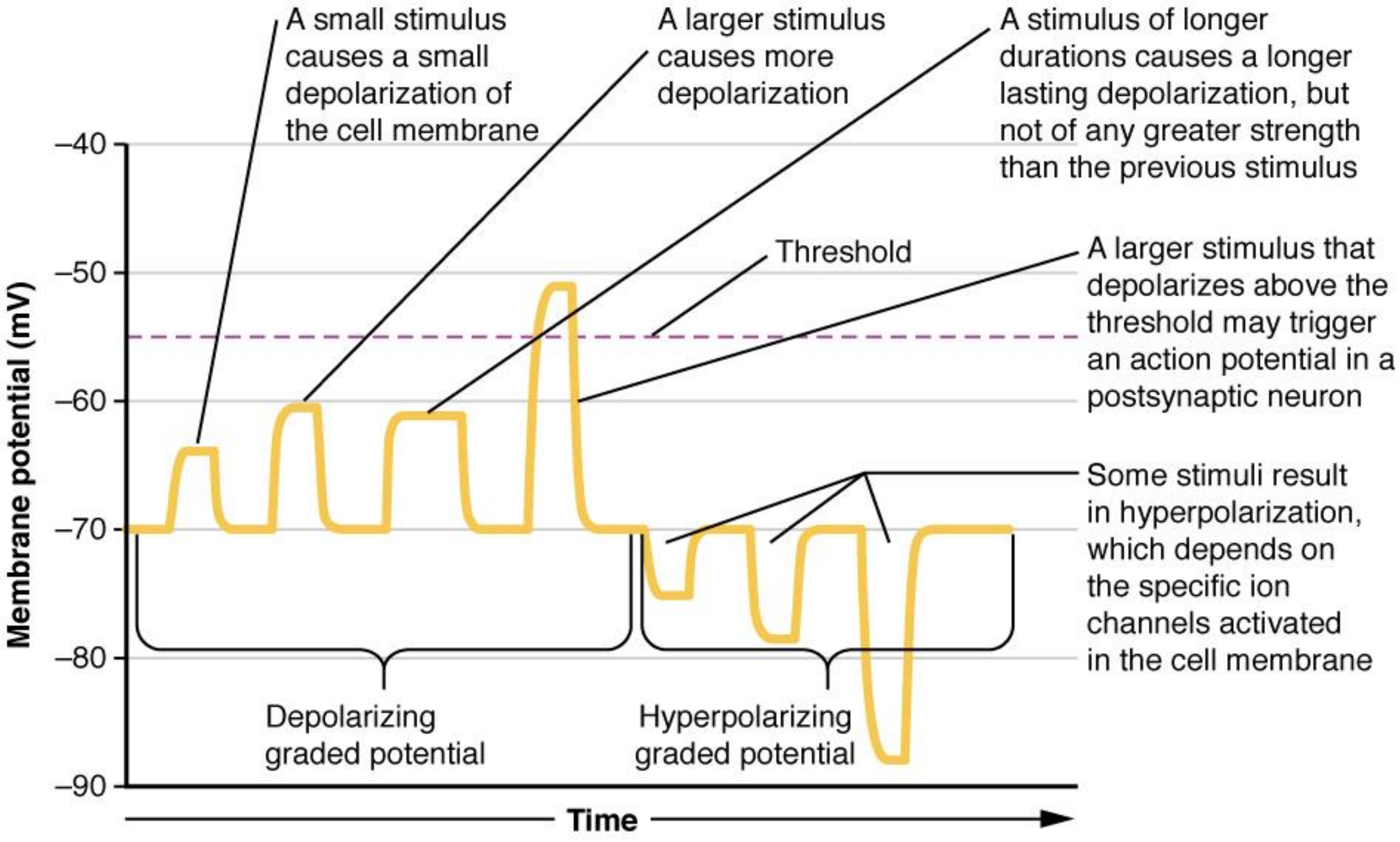
Comparison of Graded Potentials and Action Potentials

Graded Potential

1. Stimulus does not reach threshold level.
2. Stimulus causes local change in membrane potential e.g. -70 to -60mv
3. It dies down over short distance.
4. Can be summated.
5. Does not obey all or none law.

Action Potential

1. Stimulus reaches threshold level therefore causes AP.
2. Stimulus causes depolarization to threshold level.
3. It is propagated.
4. Can not be summated.
5. Obeys all or none law.


A small stimulus causes a small depolarization of the cell membrane
A larger stimulus causes more depolarization
A stimulus of longer durations causes a longer lasting depolarization, but not of any greater strength than the previous stimulus
Threshold
A larger stimulus that depolarizes above the threshold may trigger an action potential in a postsynaptic neuron
Some stimuli result in hyperpolarization, which depends on the specific ion channels activated in the cell membrane
–40
–50
–60
–70
–80
–90
Membrane potential (mV)
Depolarizing graded potential
Hyperpolarizing graded potential
Time

GRADED POTENTIALS

- **The graded potential** is a small deviation from the resting membrane potential that makes the membrane either more polarized (hyperpolarizing graded potential, inside more negative) or less polarized (depolarizing graded potential, inside less negative).

- The graded potential occurs when a stimulus causes mechanically- gated or ligand-gated channels to open or close in an excitable cell's plasma membrane.

GRADED POTENTIALS

- The graded potentials are useful for short-distance communication only (localized and dies after this distance). However, it can become stronger and last longer by summating with other graded potentials (summation is the process by which graded potentials add together).

- The graded potential occurs in the dendrites or cell body of a neuron in response to a neurotransmitter, it is called a postsynaptic potential.

- The graded potentials that occur in sensory receptors and sensory neurons are termed receptor potentials and generator potentials.

GENERATION OF ACTION POTENTIALS

- An action potential (AP) or impulse is a sequence of rapidly occurring events that decrease and reverse the membrane potential.

- An action potential has two main phases: a depolarizing phase and a repolarizing phase.

- During the depolarizing phase, the negative membrane potential becomes less negative, reaches zero, and then becomes positive. During the repolarizing phase, the membrane potential is restored to the resting state of -70 mV. Following the repolarizing phase there may be an after-hyperpolarizing phase, during which the membrane potential temporarily becomes more negative than the resting level.

ACTION POTENTIALS

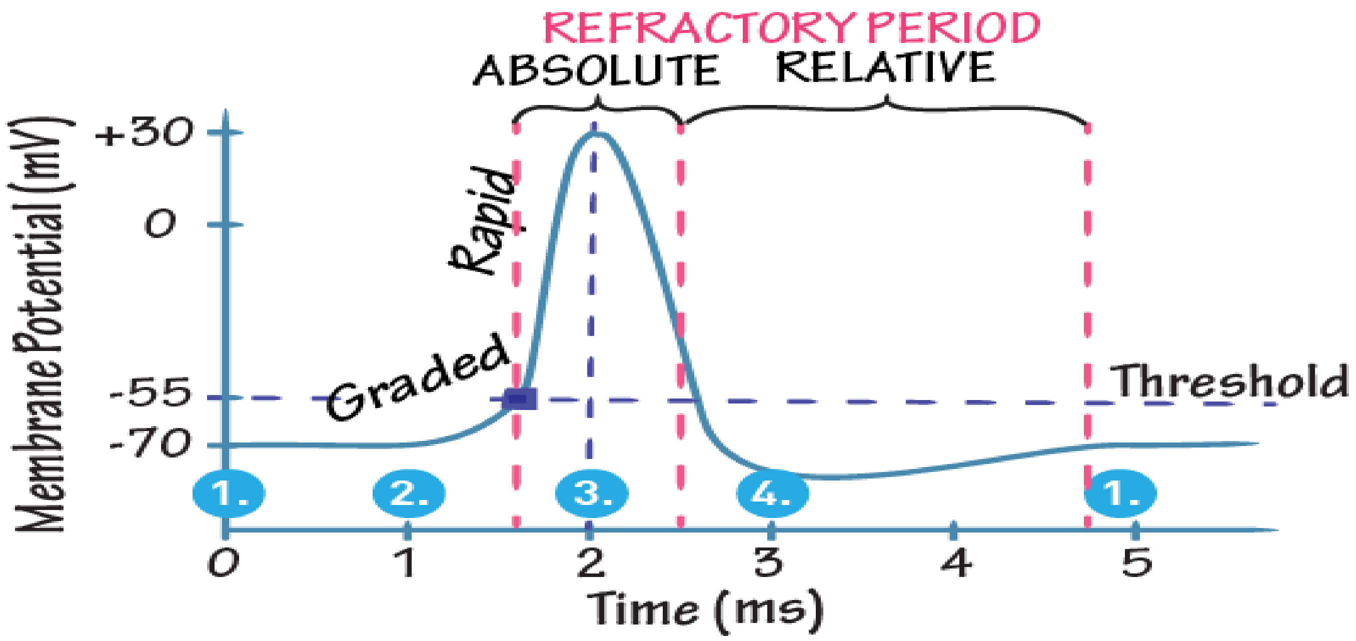
- An action potential occurs in the membrane of the axon of a neuron when depolarization reaches a certain level termed the **threshold**.

- An action potential will not occur in response to **a subthreshold stimulus**. However, an action potential will occur in response to a threshold stimulus, a stimulus that is just strong enough to depolarize the membrane to threshold. In other words, an action potential either occurs completely or it does not occur at all. This characteristic of an action potential is known as the **all-or-none principle**.

ACTION POTENTIALS

- Several action potentials will form in response to a **suprathreshold stimulus.** Each of the action potentials caused by a suprathreshold stimulus has the same amplitude (size) as an action potential caused by a threshold stimulus.

Action Potentials



1. Resting state - All gated ion channels closed
2. Depolarization - Na+ channels open, K+ channels closed
3. Repolarization - Na+ channels inactivated, K+ channels open
4. Hyperpolarization - Na+ channels reset and closed, K+ channels still open

DEPOLARIZING PHASE

- Inward movement of Na ions, the depolarizing phase of the action potential.

- This changes the membrane potential from -55 mV to +30 mV.

- Each voltage-gated Na ions channel has two separate gates, an activation gate and an inactivation gate.

DEPOLARIZING PHASE

- In the resting state of a voltage-gated Na ions channel, the inactivation gate is open, but the activation gate is closed (Na ions cannot move into the cell through these channels).

- At threshold, voltage-gated Na ions channels are activated, both the activation and inactivation gates in the channel are open and Na ions inflow begins (more channels open, Na ions inflow increases, the membrane depolarizes further).

- However, the concentration of Na ions hardly changes because of the millions of Na ions present in the extracellular fluid.

REPOLARIZING PHASE

- At threshold level, depolarization also opens voltage-gated K ions channels.

- Slower opening of voltage-gated K ions channels and closing of previously open voltage-gated Na ions channels produce the repolarizing phase of the action potential (Na ions inflow slows and accelerating K ions outflow, the membrane potential to change from +30 mV to -70 mV, inactivated Na ions channels to revert to the resting state).

AFTER-HYPERPOLARIZING PHASE

- During this phase, the voltage-gated K ions channels remain open and the membrane potential becomes even more negative (about -90 mV).

- As the voltage-gated K ions channels close, the membrane potential returns to the resting level of -70 mV.

REFRACTORY PERIOD

- The period of time after an action potential begins during which an excitable cell cannot generate another action potential in response to a normal threshold stimulus is called the refractory period.

- In contrast to action potentials, graded potentials do not exhibit a refractory period.

PROPAGATION OF ACTION POTENTIALS

- In contrast to the graded potential, an action potential is not decremental (it does not die out, action potentials function in communication over long distances.). Instead, an action potential keeps its strength as it spreads along the membrane. This mode of conduction is called propagation.

- The action potential regenerates over and over at adjacent regions of membrane from the trigger zone to the axon terminals. However, it cannot propagate back toward the cell body because any region of membrane that has just undergone an action potential is temporarily in the refractory period.

THANK YOU

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