HUMAN PHYSIOLOGY (normal)

LECTURE 1. Introduction. General Physiology of Excitable tissues.

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The Subject of Physiology

Physiology (from the Greek *physis* = nature; *logos* = study) is the study of biological **function** - of how the body works, from cell to tissue, tissue to organ, organ to system, and of how the organism as a whole

Divisions of Physiology

- **Cell physiology**: processes within and between cells
- **Special physiology**: functions of specific organs
- **Systemic physiology**: functions of an organ system
- **Pathological physiology**: effects of diseases

Homeostasis

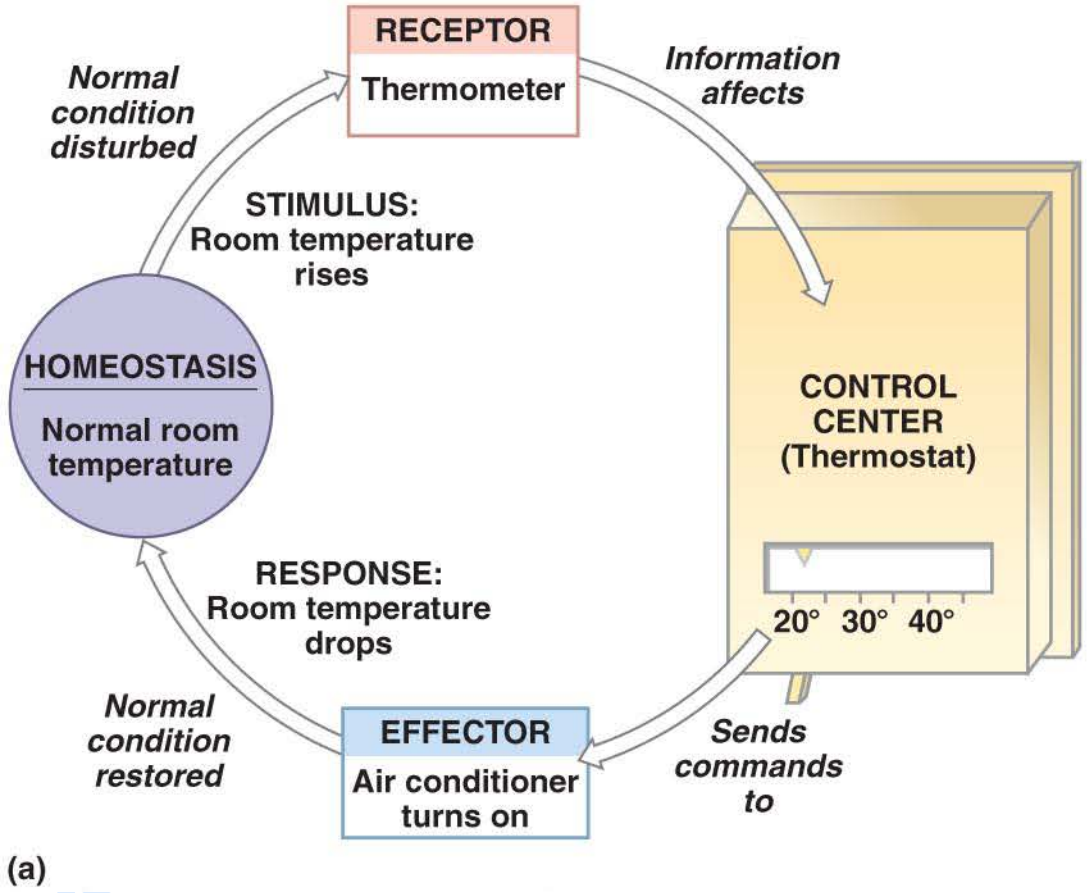
Homeostasis - maintenance of nearly constant conditions in the internal environment (state of **dynamic constancy,** in which conditions are stabilized above and below the **set point**)

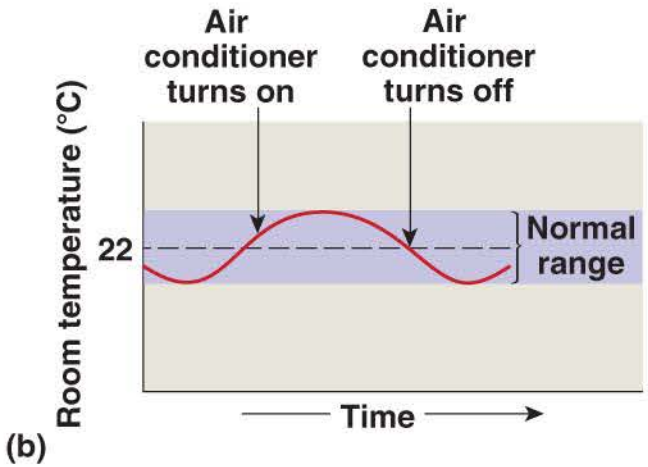
- Homeostasis is a **state of equilibrium** (opposing forces are in balance)
- Homeostasis is maintained due to the **systems respond** (regulation) to external and internal changes (to function within a **normal range**)
- The main **mechanisms of regulation**
  - **Autoregulation (intrinsic) -** response in a cell, tissue, or organ to changes
  - **Extrinsic regulation -** responses controlled by **nervous** and **endocrine systems**

Important Parameters of Homeostasis

Parameters of extracellular fluid	Normal Value	Normal Range	Unit
Oxygen	40	35–45	mm Hg
Sodium ion	142	138–146	mmol/L
Sodium ion	142	138–146	mmol/L
Glucose	85	75–95	mg/dl
Body temperature	37.0	37.0	C
Acid-base	7.4	7.3–7.5	pH

Mechanisms of Regulation





Negative and Positive Feedback

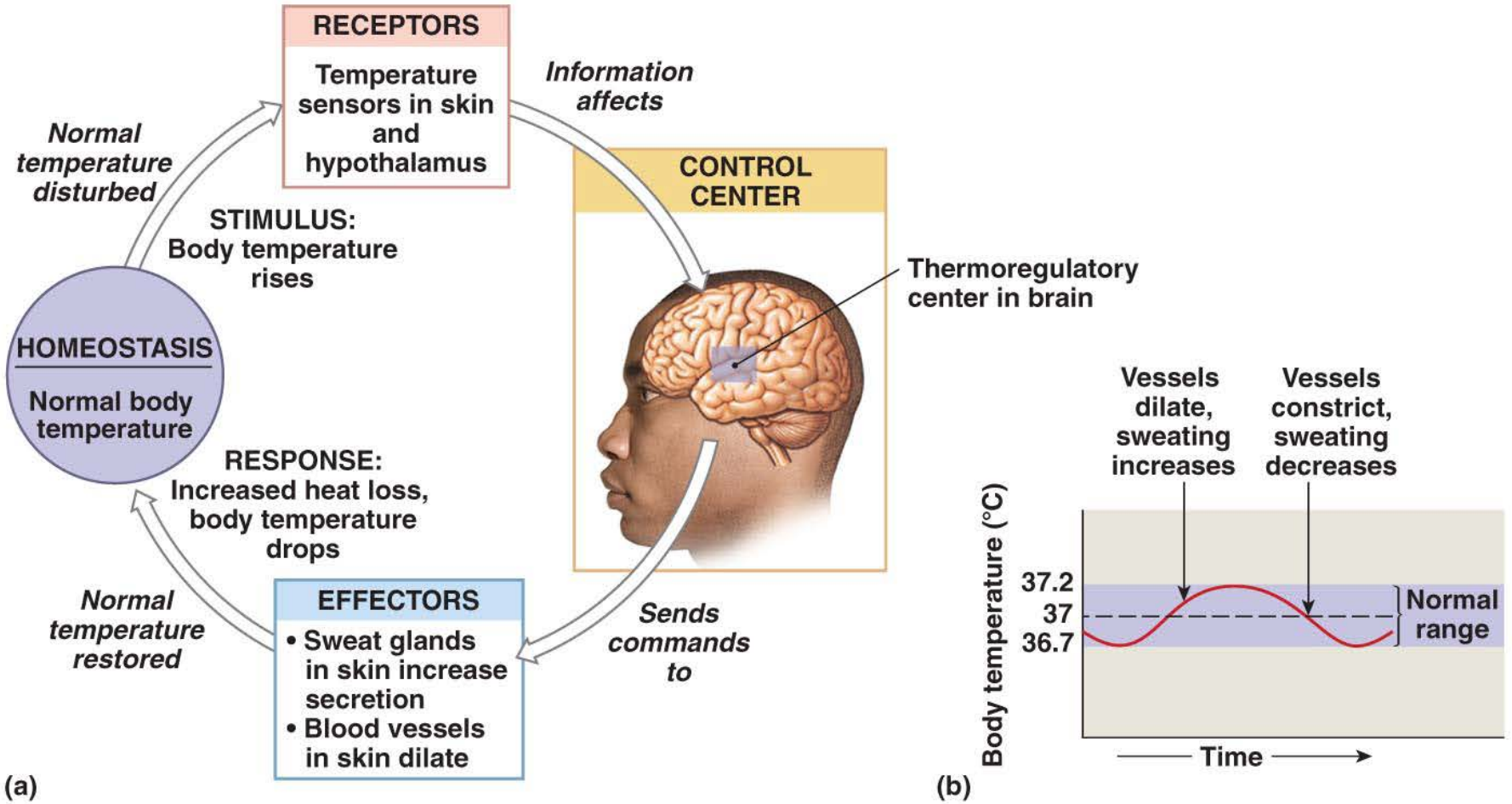
Negative Feedback

- The response of the **effector** negates the **stimulus**
- Body is brought back into homeostasis

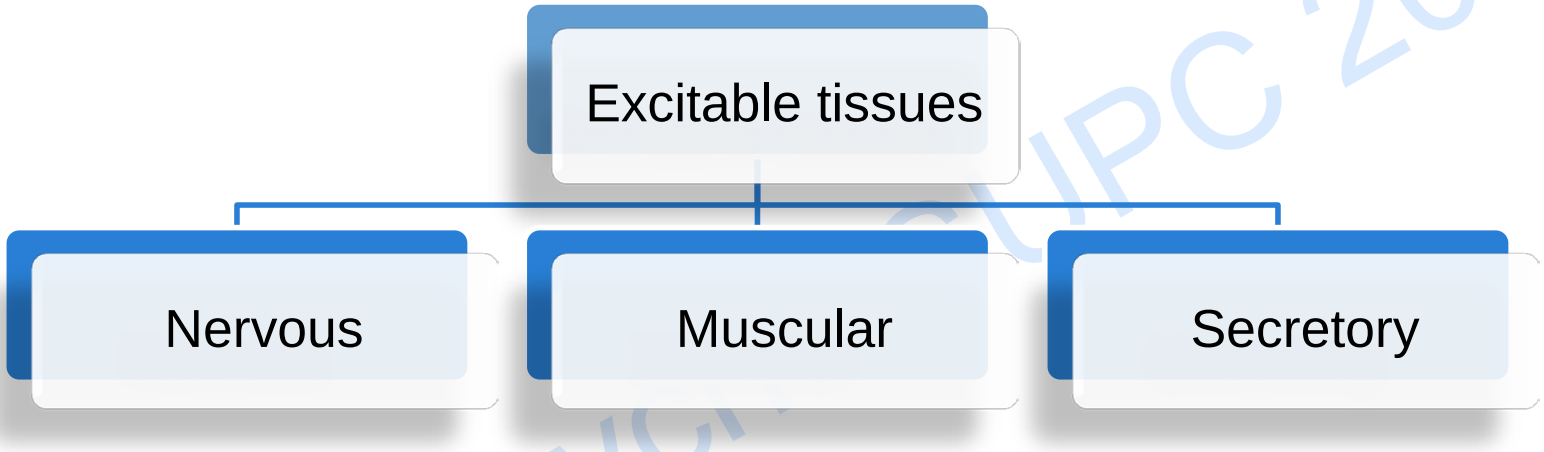
Positive Feedback

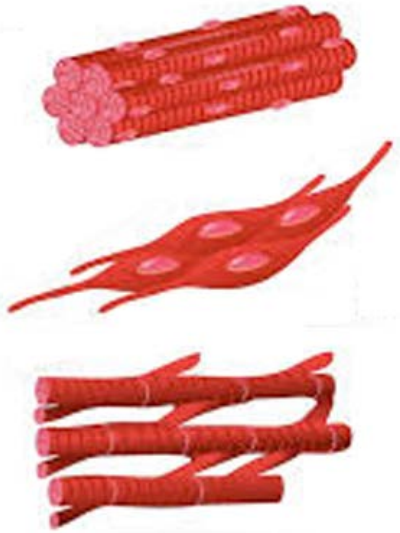
- The response of the effector increases change of the stimulus
- Body is moved away from homeostasis
- Normal range is lost
- Used to speed up processes

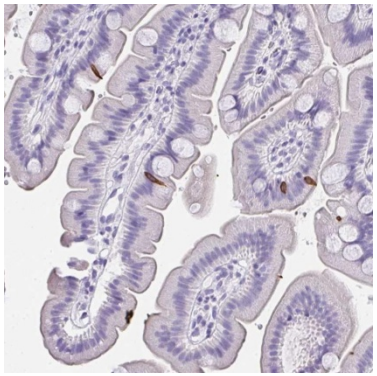
Negative Feedback



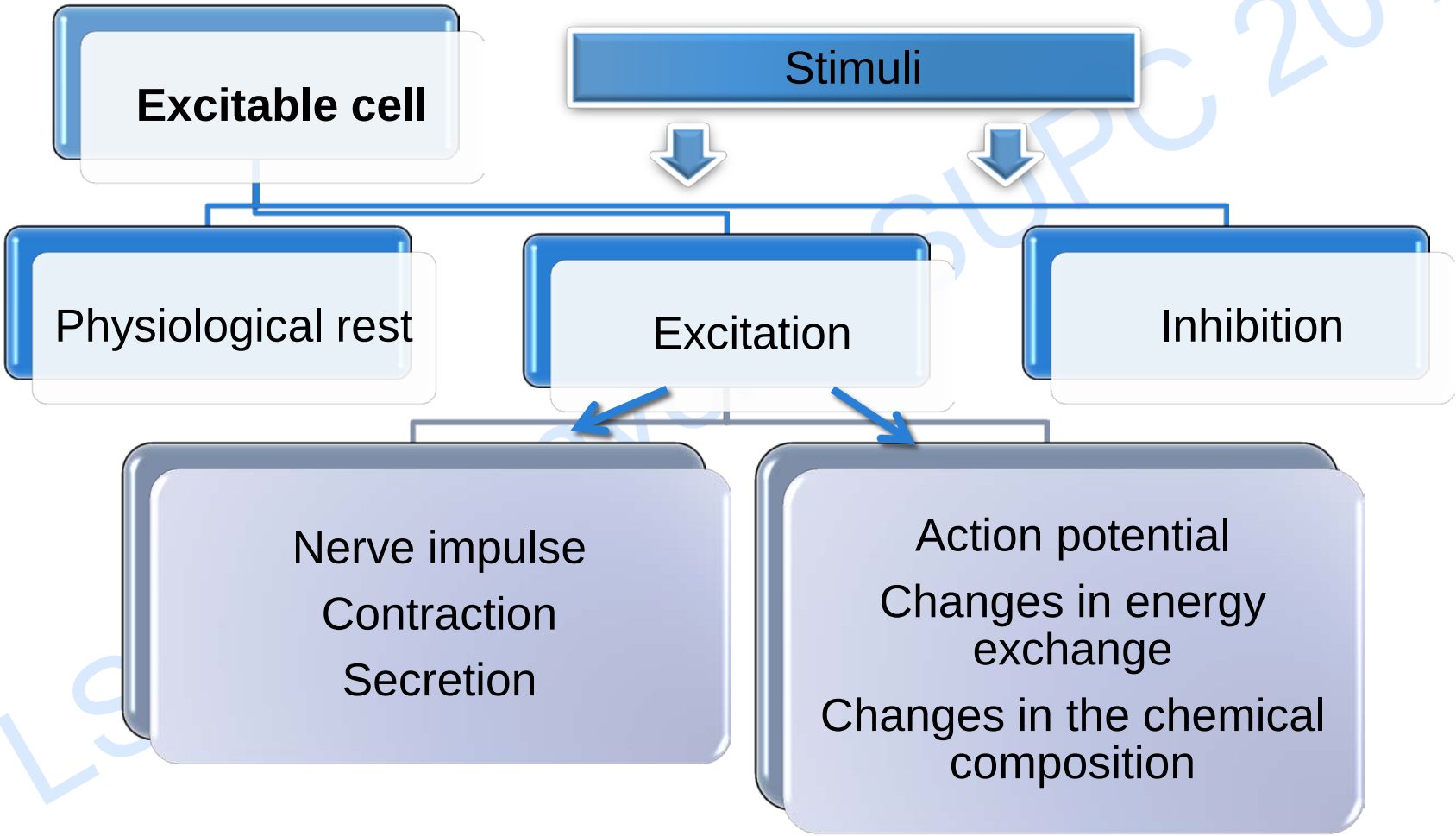
Excitable tissues



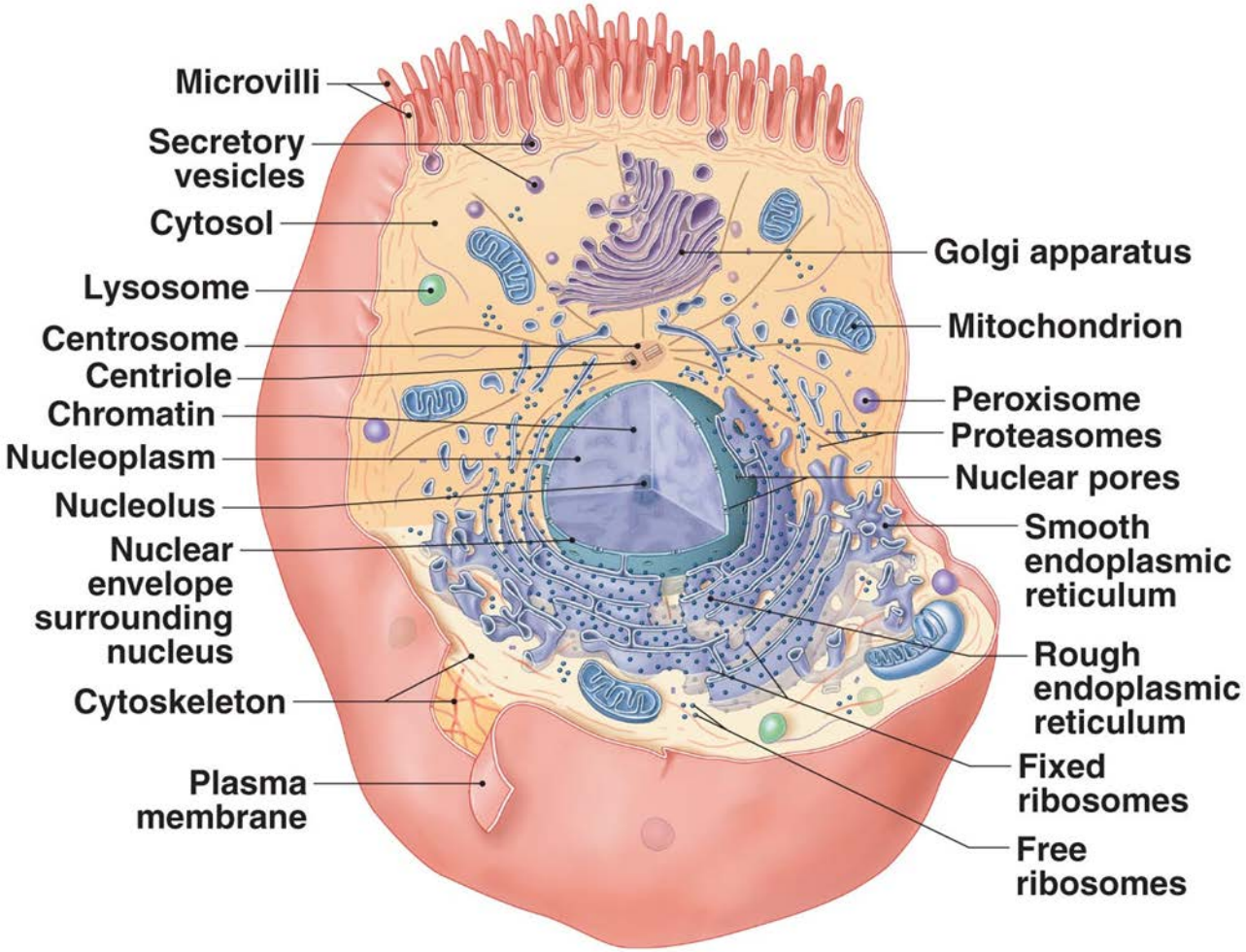




Excitable tissues



The Model Cell



Plasma Membrane

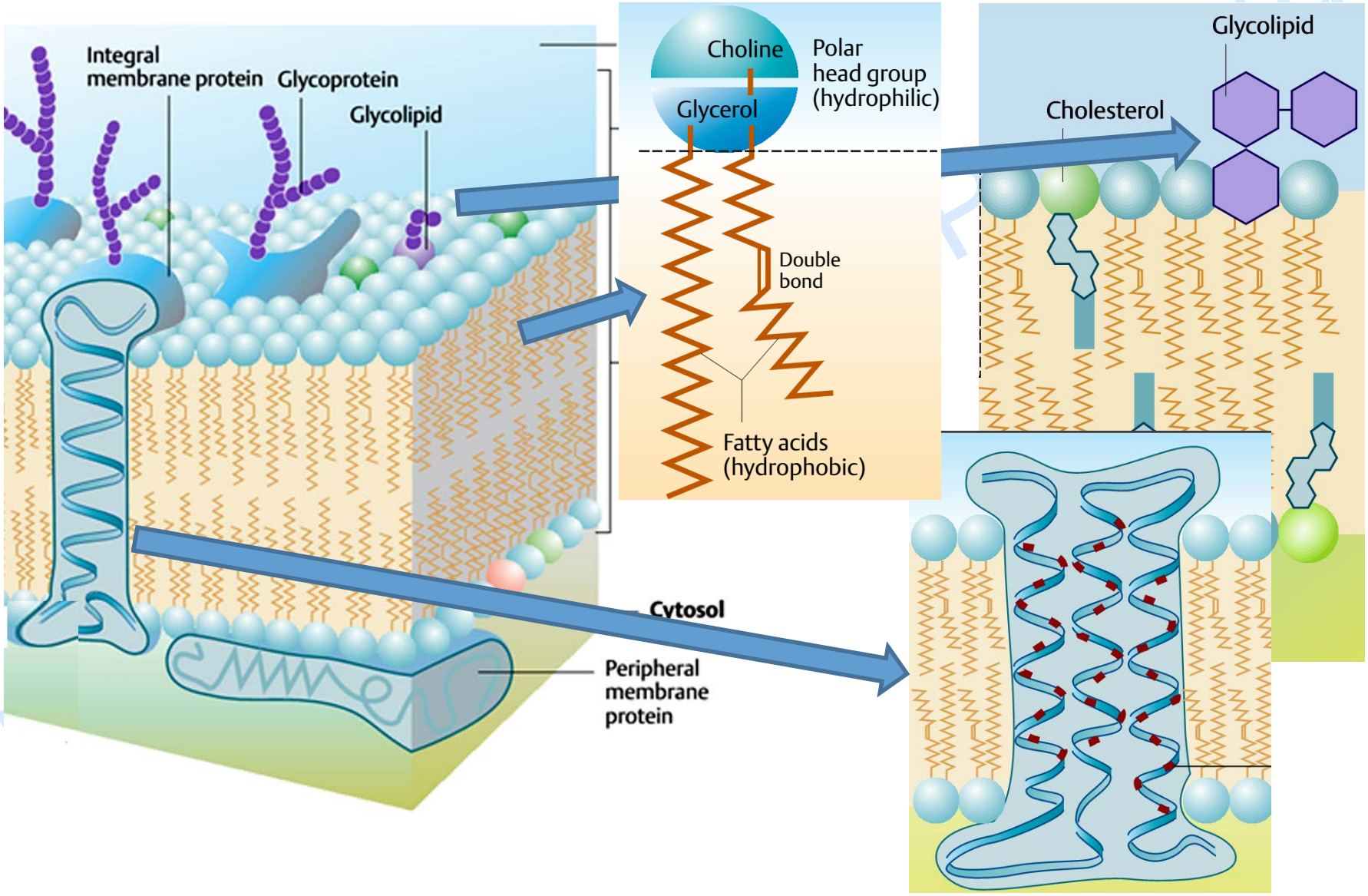
Functions of the Plasma Membrane

- **Physical isolation**
  - Barrier
- **Regulates exchange with environment**
  - Ions and nutrients enter
  - Wastes eliminated and cellular products released
- **Monitors the environment**
  - Extracellular fluid composition
  - Chemical signals
- **Structural support**
  - Anchors cells and tissues

Structure of the Plasma Membrane

- Double layer of **Phospholipid** molecules
- Membrane **Proteins**
  - Integral proteins (within the membrane)
  - Peripheral proteins (bound to inner or outer surface of the membrane)
- Membrane **Carbohydrates**

Structure of the Plasma Membrane



Function of the Membrane Proteins

- **Anchoring proteins (stabilizers)**
  Attach to inside or outside structures
- **Recognition proteins (identifiers)**
  Label cells as normal or abnormal
- **Enzymes**
  Catalyze reactions
- **Receptor proteins**
  Bind and respond to ligands (ions, hormones)
- **Carrier proteins (pumps)**
  Transport specific solutes through membrane
- **Channels**
  Regulate water flow and solutes through membrane

Membrane Transport

The **plasma (cell) membrane** is a barrier, but

- **Nutrients** must get in
- **Products** and **wastes** must get out

Plasma membrane is **selectively permeable,** restricts some materials based on

- **Size**
- **Electrical charge**
- **Molecular shape**
- **Lipid solubility**

Membrane Transport

Transport	Passive (no energy required)	Active (requiring energy and ATP)
Without carriers	• **Diffusion** (simple) • **Osmosis**	---
Carrier-mediated	• Channel mediated **diffusion** • Facilitated **diffusion**	• Active transport by **pumps** • Secondary active transport by **exchangers** (cotransport or countertransport)

Diffusion

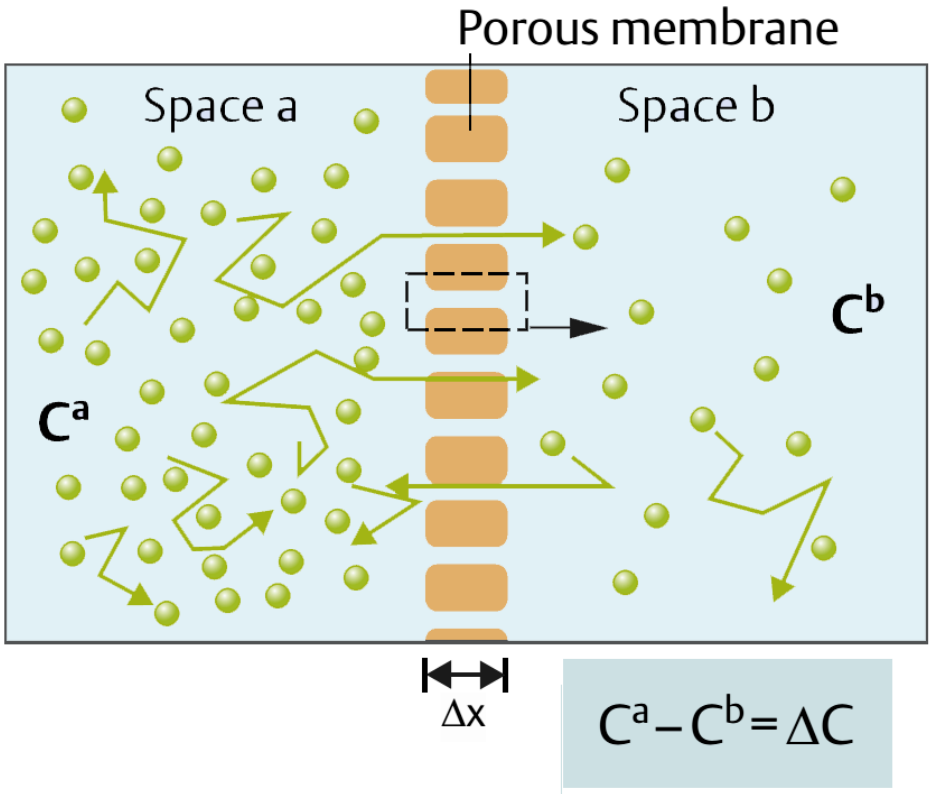
Simple diffusion

- lipid-soluble compounds (alcohols, fatty acids, steroids)
- dissolved gases (oxygen and carbon dioxide)

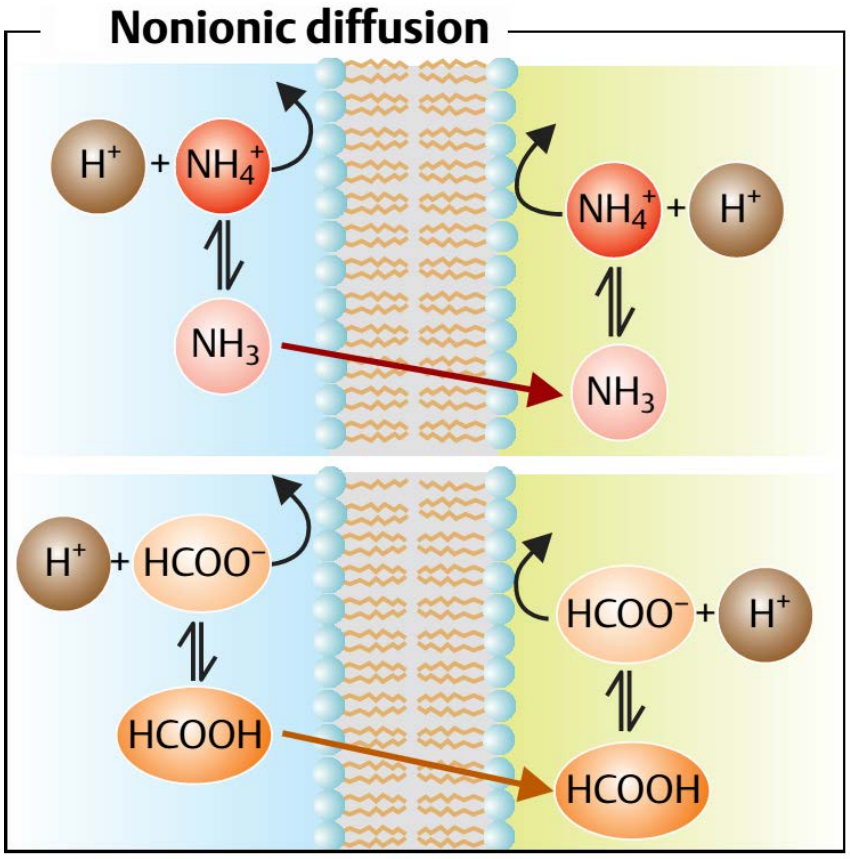
Through transmembrane proteins (channels)

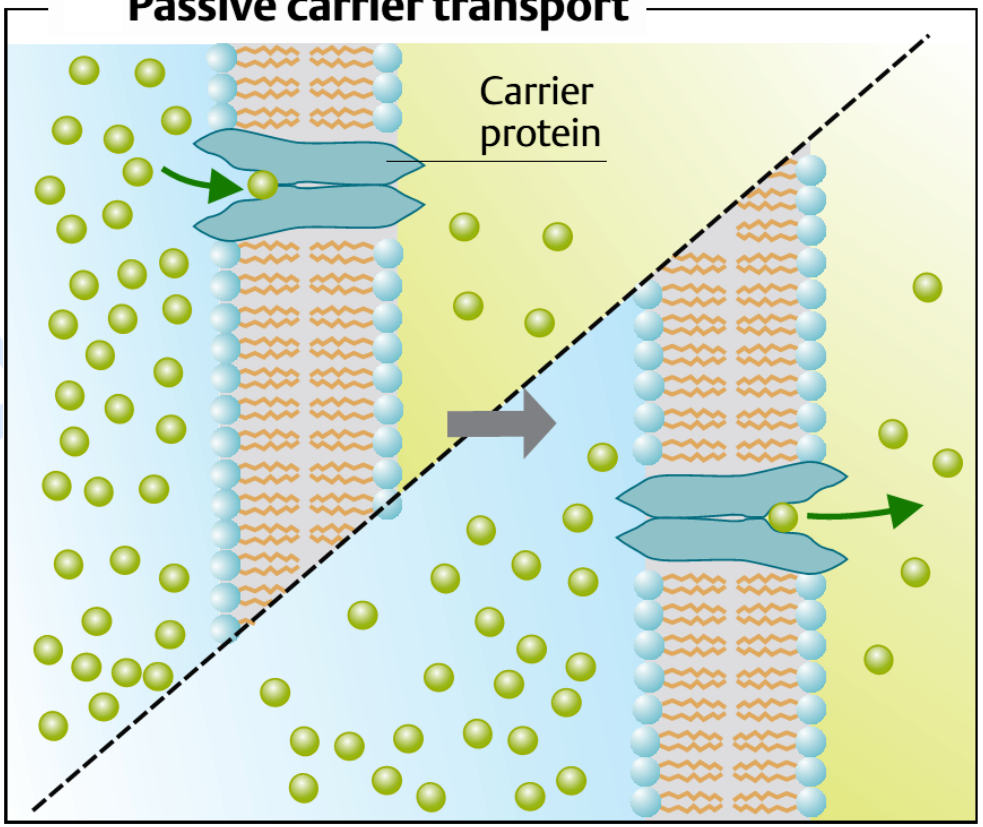
- water–soluble compounds
- ions

Osmosis (the diffusion of water across the cell membrane)



Diffusion

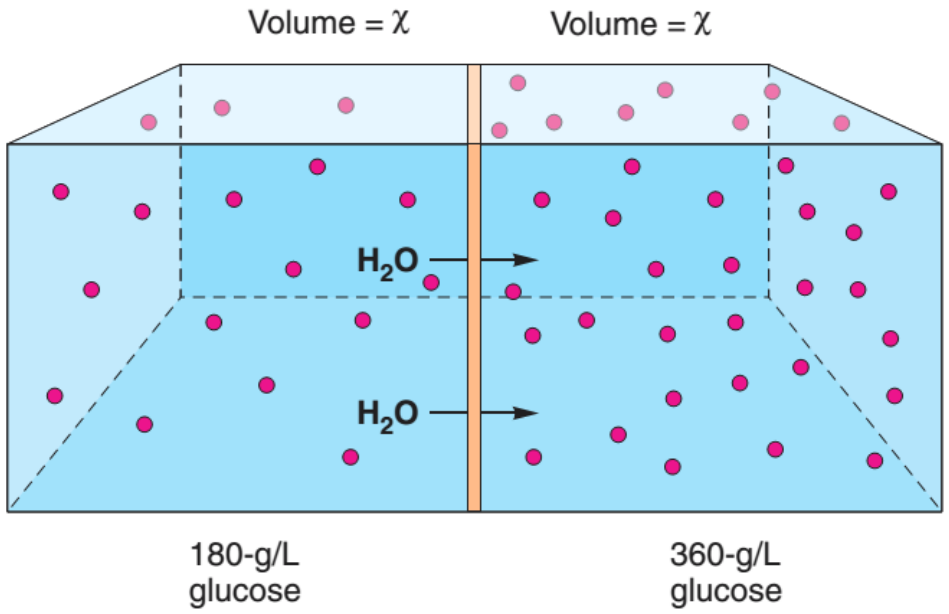

Nonionic diffusion
H+ + NH4+
NH3
NH4+ + H+
NH3
H+ + HCOO−
HCOOH
HCOO− + H+
HCOOH

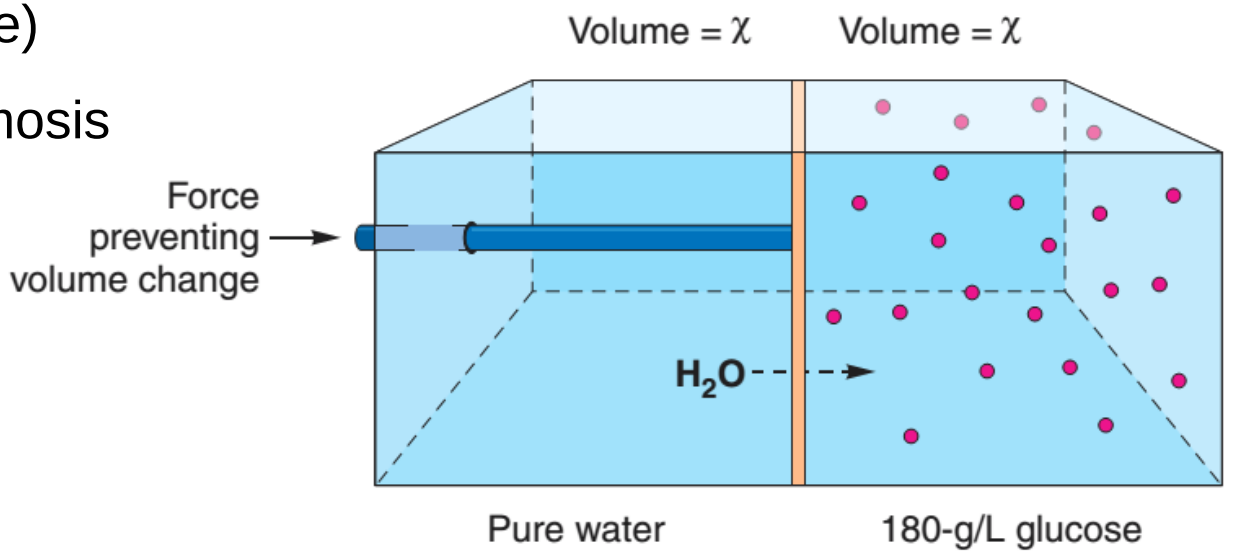

Passive carrier transport
Carrier protein

Osmosis

Osmotic Pressure

- Is the force of a concentration gradient of water
- Equals the force (hydrostatic pressure) needed to block osmosis





Osmosis and Tonicity

Solutions

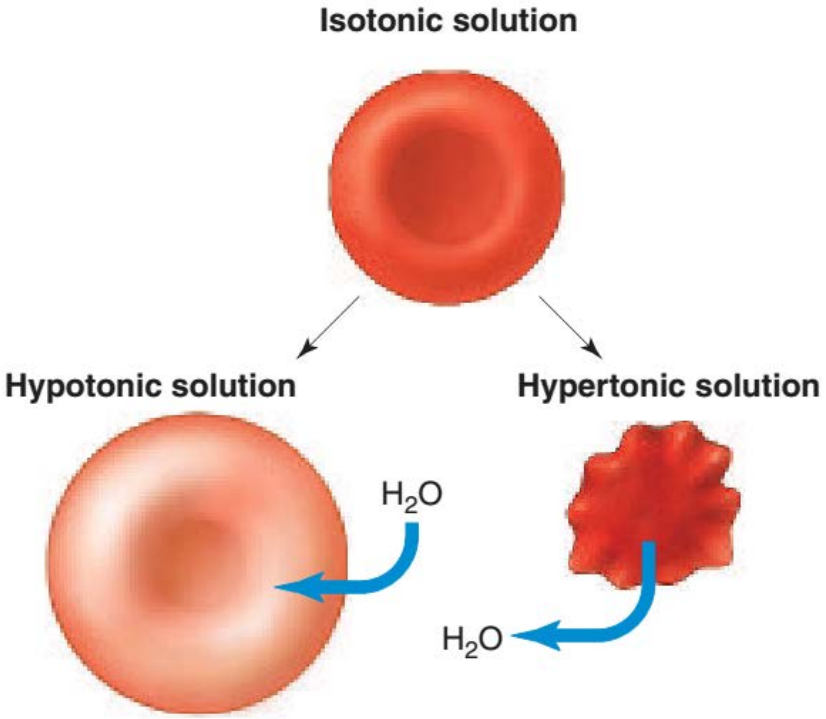
- **Isotonic** (iso- = same, tonos = tension) - a solution that does not cause osmotic flow of water in or out of a cell
- **Hypotonic** (hypo- = below) - less solutes and loses water through osmosis
- **Hypertonic** (hyper- = above) - more solutes and gains water by osmosis

A cell in a **hypotonic** solution:

- Gains water
- Ruptures (**hemolysis** of red blood cells)

A cell in a **hypertonic** solution:

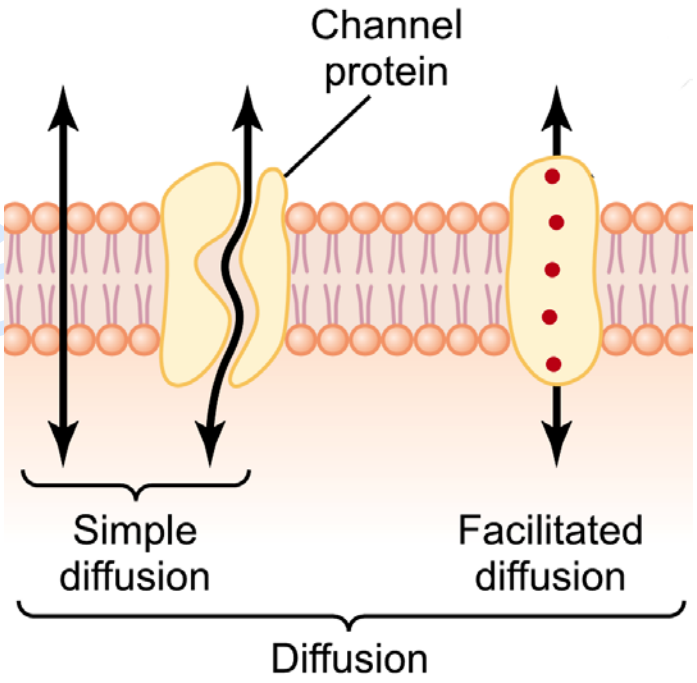
- Loses water
- Shrinks (**crenation** of red blood cells)



Carrier-mediated diffusion

Channel-mediated diffusion

Passage depends on: ion size, charge and interaction with the **channel**



Facilitated diffusion

Carrier proteins transport molecules too large to fit through channel proteins (glucose, amino acids):

- molecule binds to **receptor site** on carrier protein
- protein changes shape, molecules pass through
- receptor site is specific to certain molecules

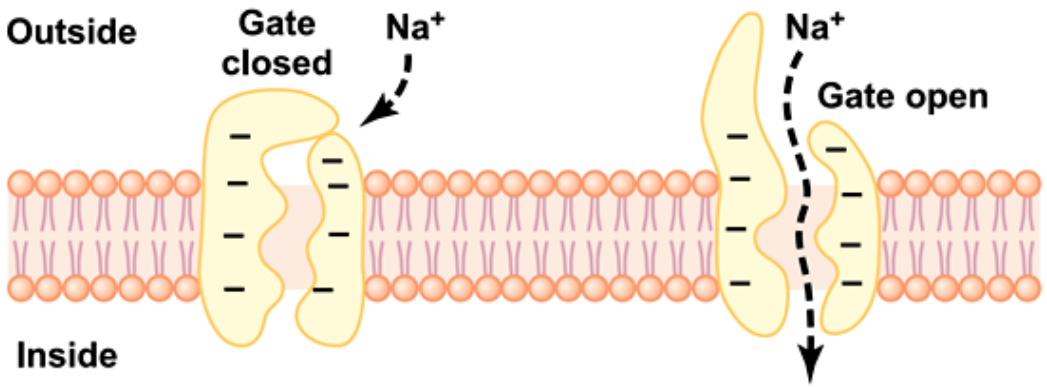
Types of channels

Passive channels (also called **leak channels**):

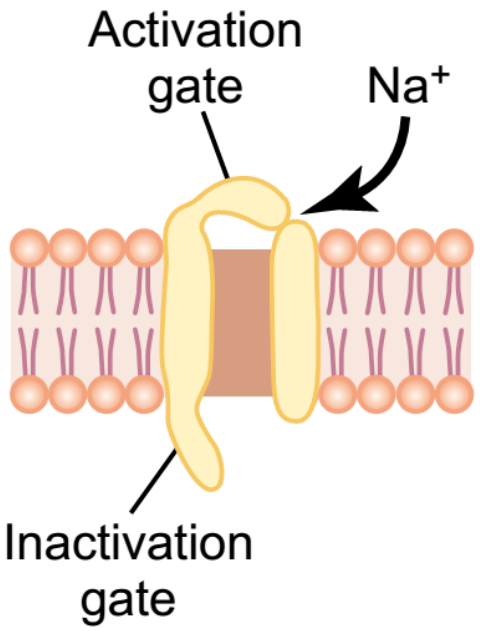
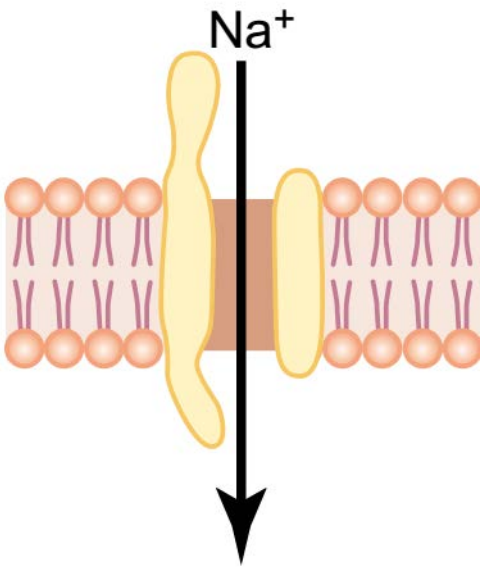
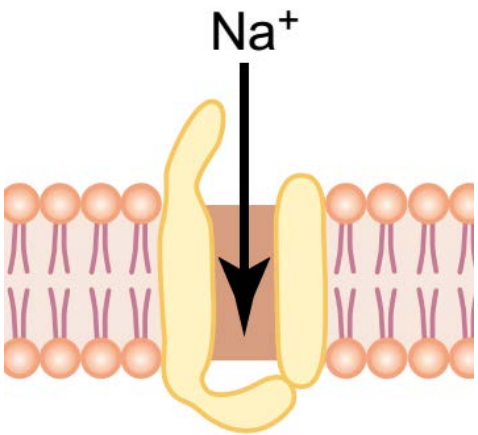
- are always open
- permeability changes with conditions

Active channels (also called **gated channels**):

- open and close in response to stimuli
- at resting potential, most gated channels are closed



Conditions of Gated Channels

Closed, but capable of opening	**Open (activated)**	**Closed,** not capable of opening **(inactivated)**
		

Classes of Gated Channels

- **Chemically gated channels**
  - Open in presence of specific chemicals (e.g., ACh) at a binding site
  - Found on neuron cell body and dendrites

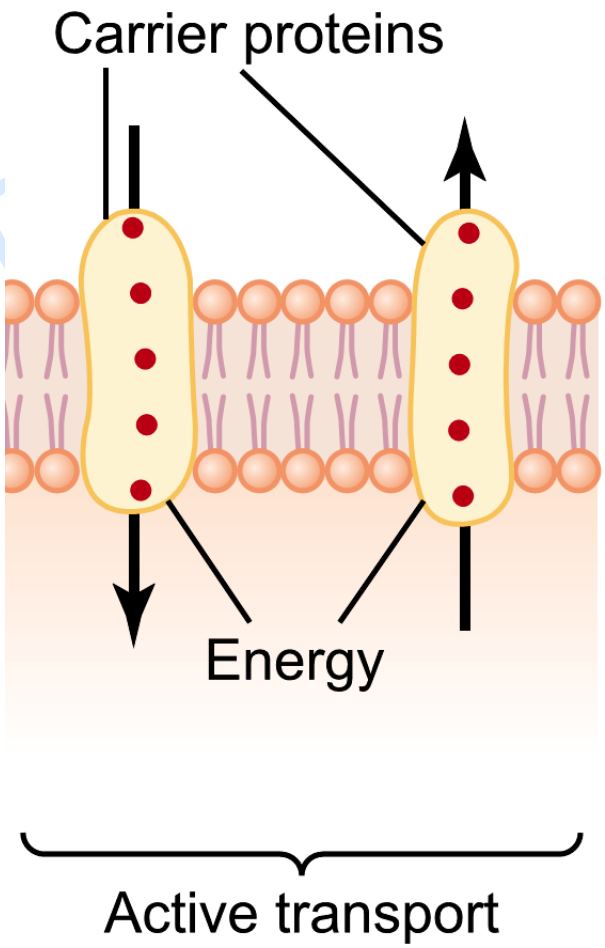
- **Voltage-gated channels**
  - Respond to changes in transmembrane potential
  - Have activation gates (opens) and inactivation gates (closes)
  - Characteristic of excitable membrane
  - Found in neural axons, skeletal muscle sarcolemma, cardiac muscle

- **Mechanically gated channels**
  - Respond to membrane distortion
  - Found in sensory receptors (touch, pressure, vibration)

Active transport

Active transport proteins (**pumps** or **exchangers**):

- move substrates ***against*** concentration gradient
- require energy, such as ATP (or ion gradient)
- ion pumps move ions (Na^+, K^+, Ca^{2+}, Mg^{2+})
- **exchangers** countertransports two ions at the same time



Transmembrane Potentials

Resting potential

- The transmembrane potential of resting cell

Graded (local) potential

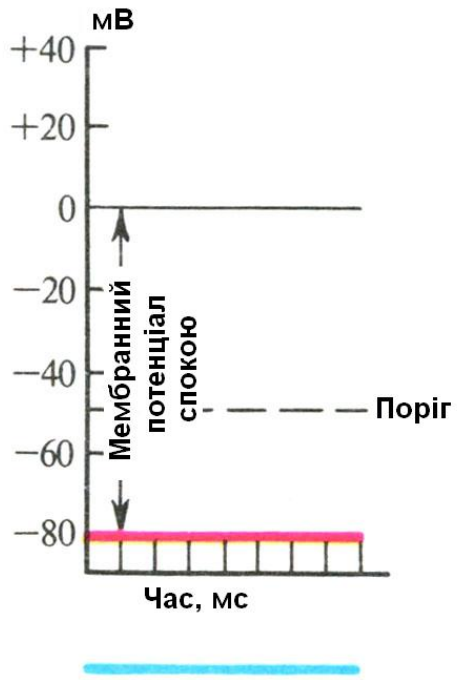
- Temporary, localized change in resting potential
- Caused by stimulus

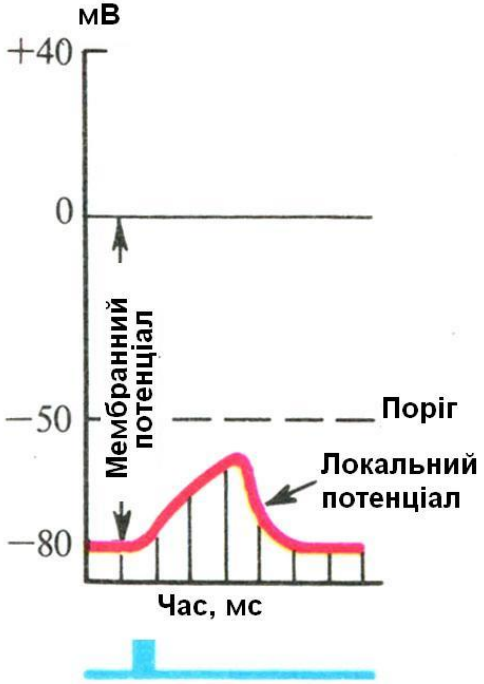
Action potential

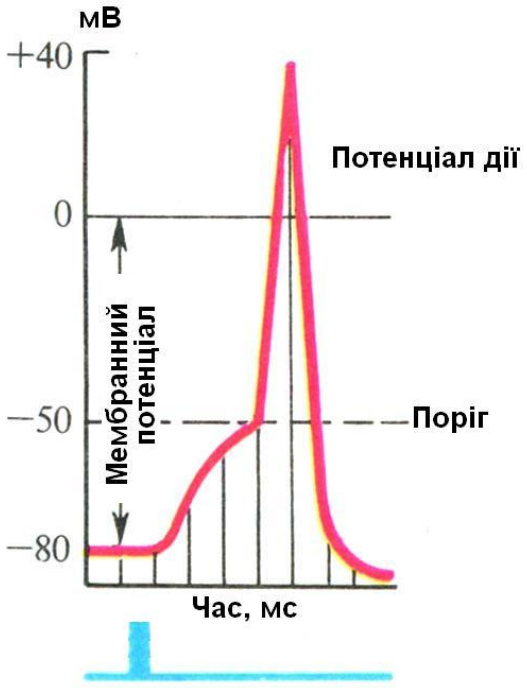
- Is an electrical impulse
- Produced by graded potential
- Propagates along surface of axon to synapse

Transmembrane Potentials

Resting potential	Graded (local) potential	Action potential

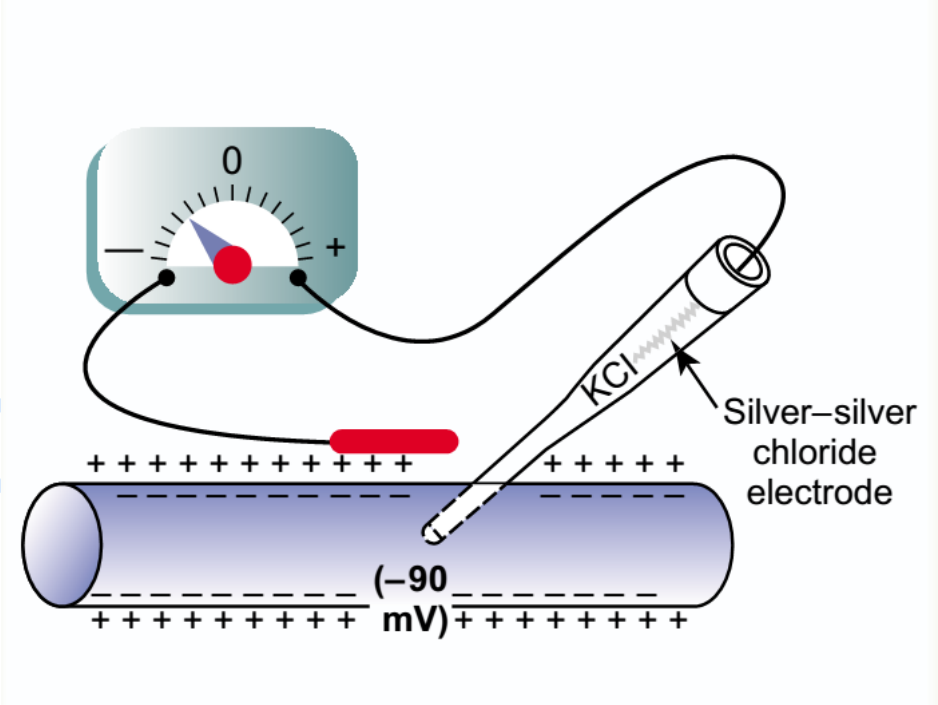






Resting potential

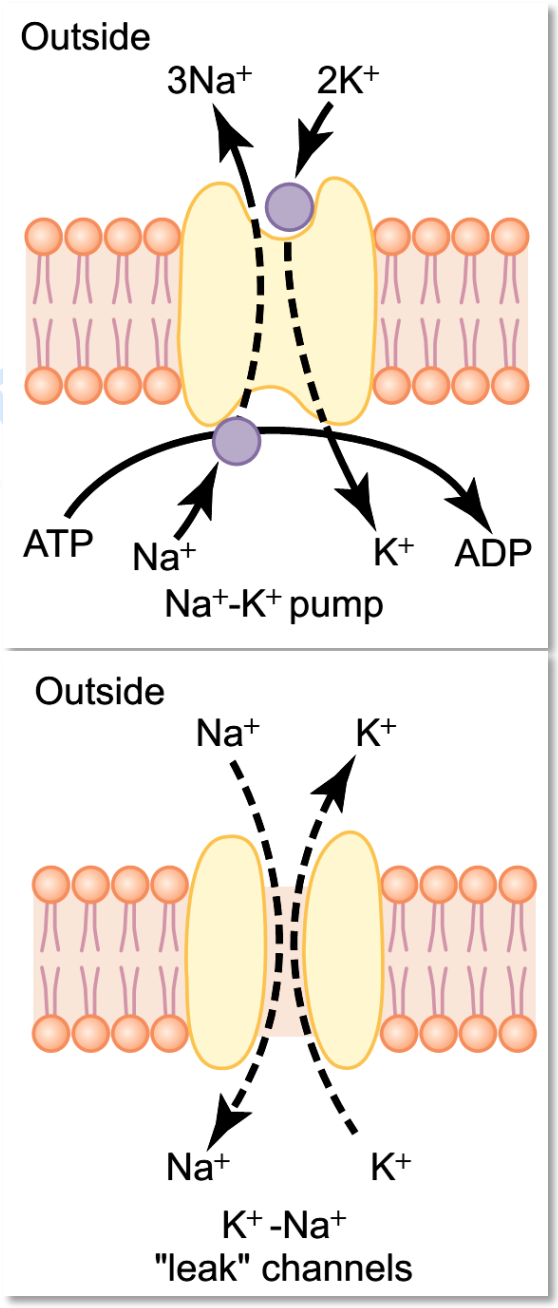
- The difference in electrical charges on either side of a cell membrane
- Positive charge outside and a negative charge inside (-70 - -90 mV)
- Remains constant in in the physiological rest state



Resting potential

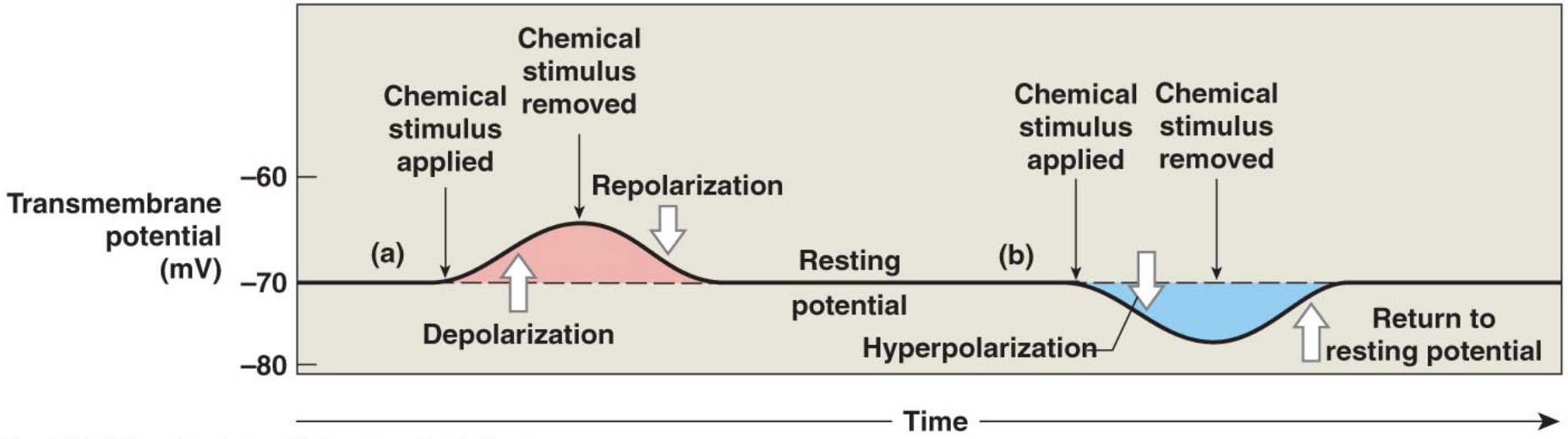
Mechanisms of generation:

- Active transport of sodium and potassium ions through the membrane by the **Sodium-Potassium (Na+-K+) Pump**
  - large *concentration gradients* for Na+ (20 times) and K+ (35 times) across the resting membrane
  - *electrogenic effect* because more positive charges are pumped to the outside than to the inside
- Leakage of potassium and sodium through the nerve membrane by **Potassium Sodium (K+-na+) "leak" Channel** *(*100 times more permeable to K+)



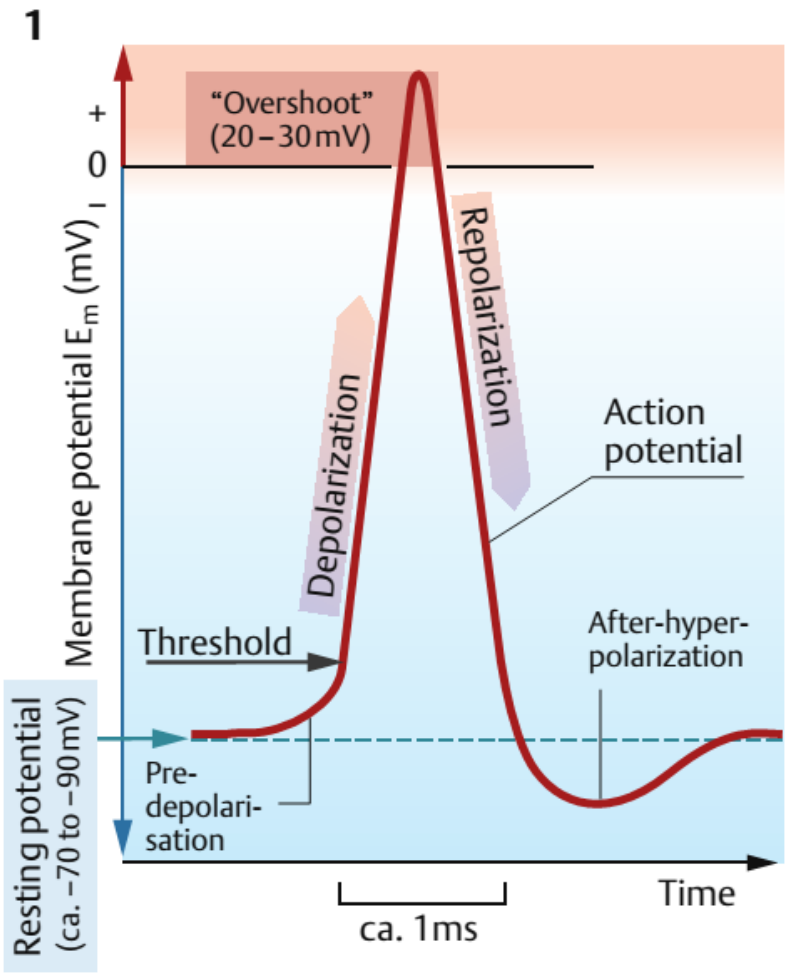
Graded (local) potential

- The **small changes** in electrical charges on the cell membrane
- Caused by small amplitude (**subthreshold**) stimuli
- The amplitude, direction (depolarization or hyperpolarization) and duration of the local potential is dependent on the amplitude, polarity and duration of applied stimulus
- Play an essential role in the mechanism of critical membrane depolarization and generation of action potential.



The Action Potential

- The **large amplitude**, **fast, all-or-none** changes in electrical charges on the cell membrane
- Is initiated by the **critical level depolarization** as the response to a **threshold** (and larger) stimulus
- Is caused by the **active changes** in membrane permeability to the ions
- The **amplitude is constant** regardless of the magnitude of the stimulus
- Consists of **two main stages**: **depolarization** followed by **repolarization**
- Can **spread** rapidly along the plasma membrane



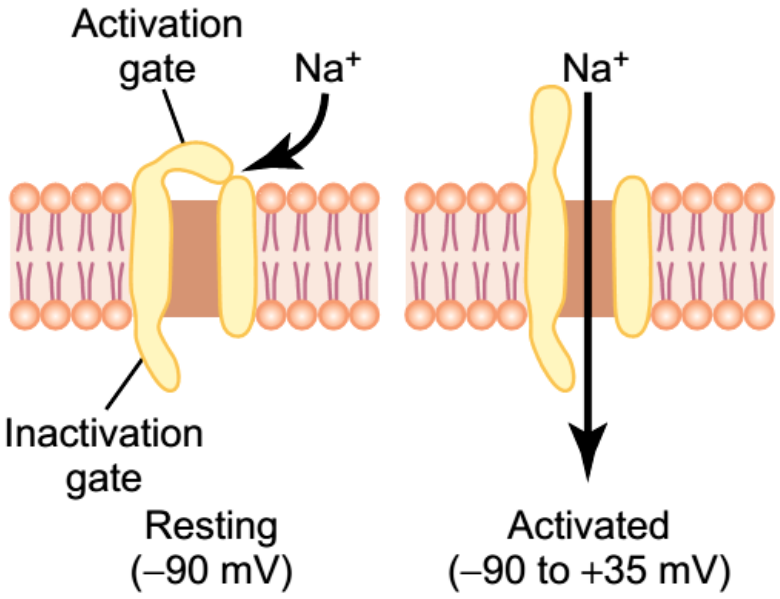
The Action Potential

Steps in the Generation of Action Potential

Step 1: Depolarization to threshold

Step 2: Activation of Na^+ channels

- Rapid depolarization
- Na^+ ions rush into cytoplasm
- Inner membrane changes from negative to positive

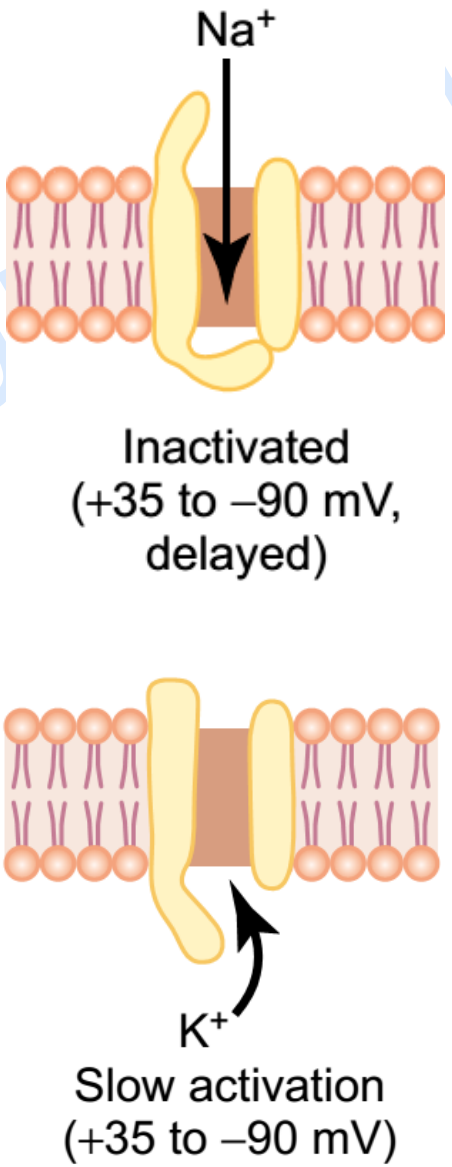


The Action Potential

Steps in the Generation of Action Potential

Step 3: Inactivation of Na^+ channels, activation of K^+ channels

- At +30 mV inactivation gates close (Na^+ channel inactivation)
- K^+ channels open
- Repolarization begins

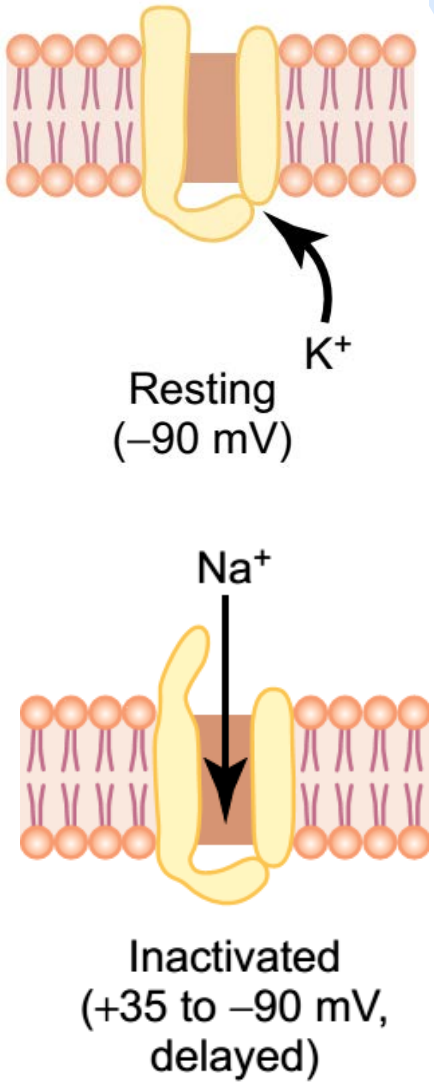


The Action Potential

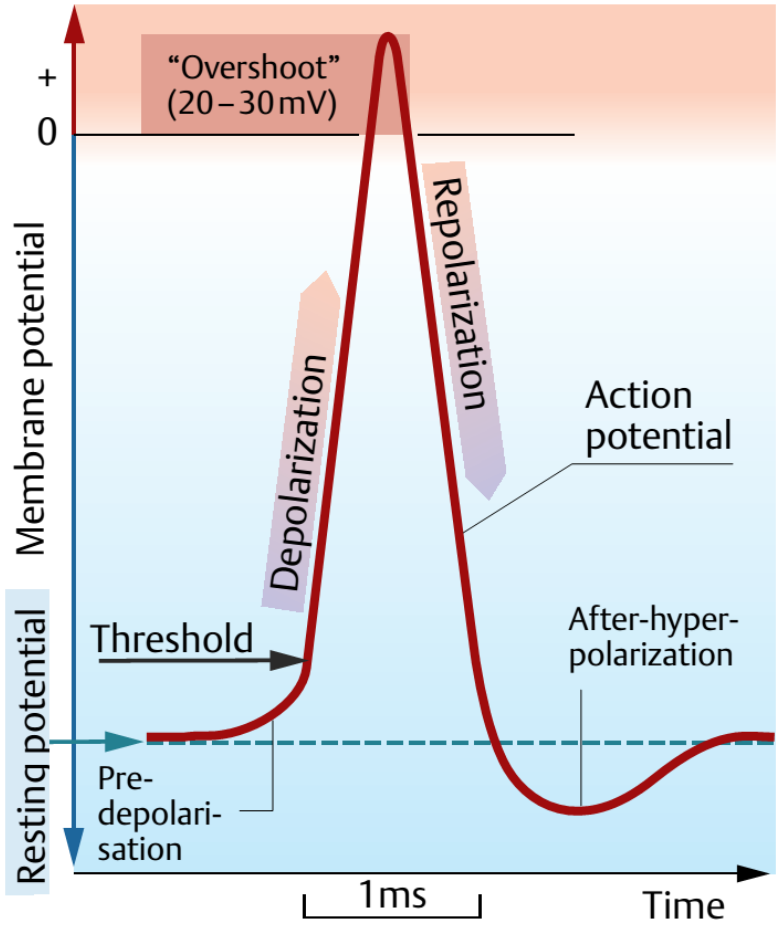
Steps in the Generation of Action Potentials

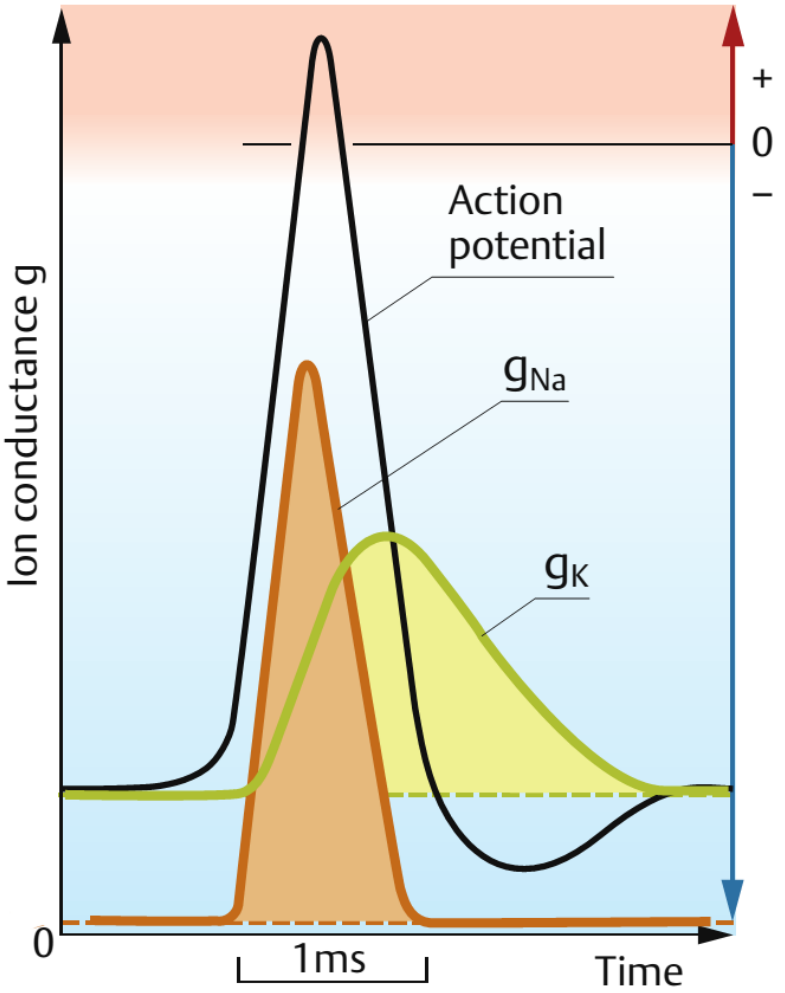
Step 4: Return to normal permeability

- K^+ channels begin to close when membrane reaches normal resting potential (–70 mV)
- K^+ channels finish closing membrane is hyperpolarized to -90 mV
- transmembrane potential returns to resting level
- action potential is over



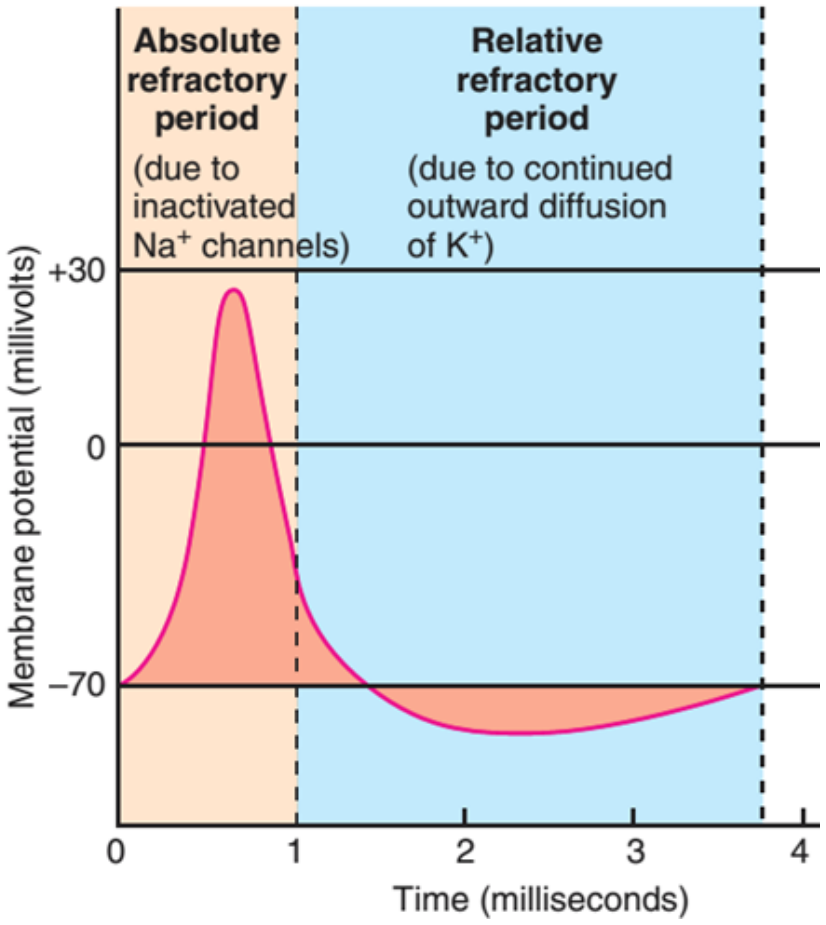
The Action Potential





The Refractory Period

- **The time period**
  - From beginning of action potential
  - To return to resting state
  - During which membrane will not respond normally to additional stimuli
- **Absolute refractory period**
  - Sodium channels open or inactivated
  - No action potential possible
- **Relative refractory period**
  - Membrane potential almost normal
  - Very large stimulus can initiate action potential



The Propagation of Action Potential

Propagation

- Moves action potentials *along the membrane*
- Action potential travels *in all directions* away from the stimulus
- The *all-or-nothing principle* - the depolarization process travels over the entire membrane if conditions are right, or it does not travel at all if conditions are not right.

Two methods of propagating action potentials

- *Continuous propagation*: unmyelinated axons
- *Saltatory propagation*: myelinated axons

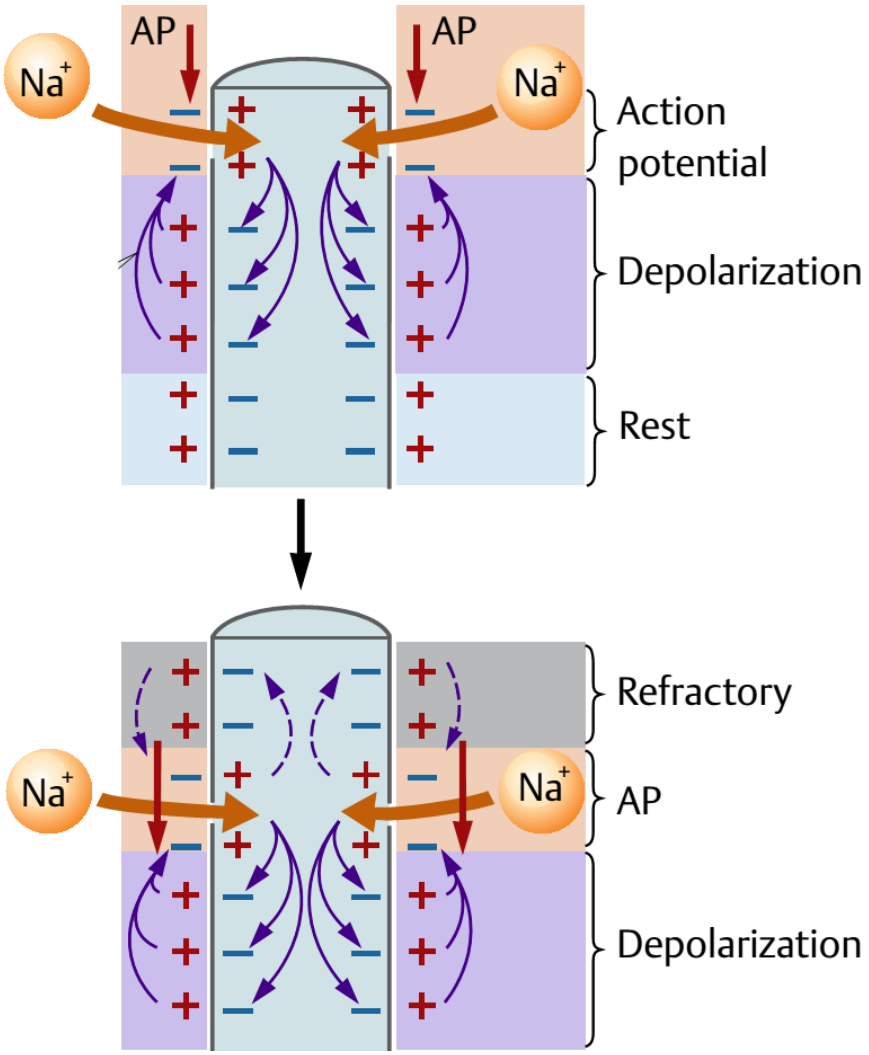
Continuous Propagation

Affects **one segment** of axon at a time

Action potential travels in one direction (**1 m/sec**)

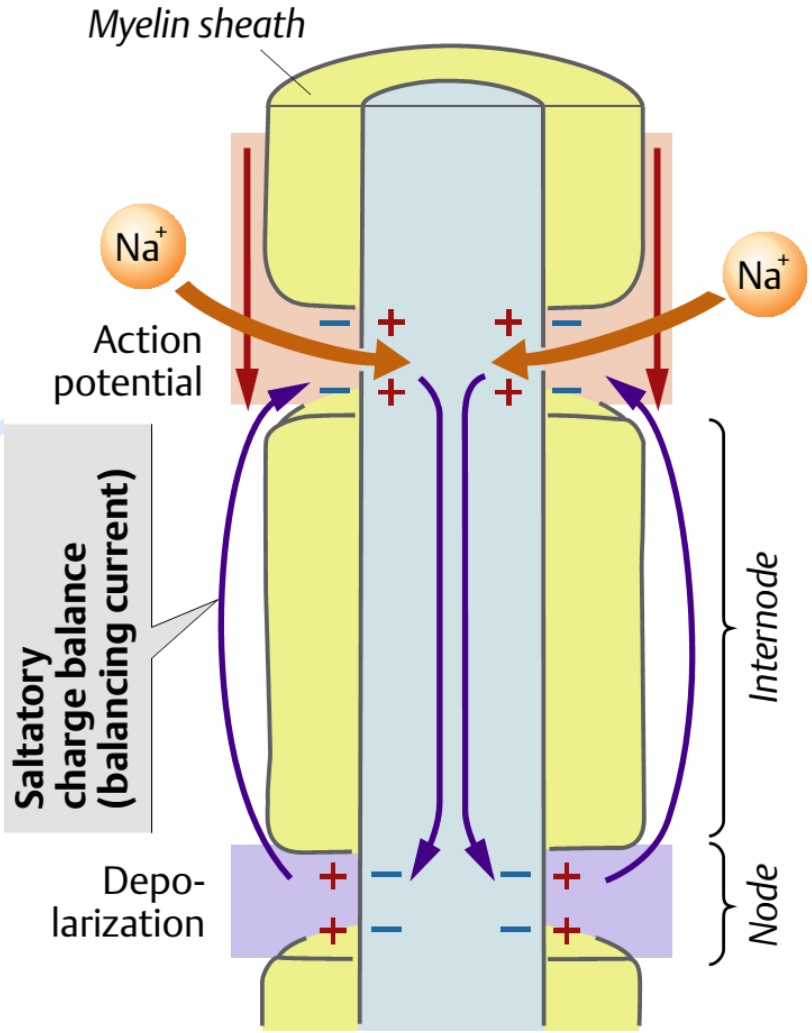
- **Step 1**: Action potential in segment 1 *depolarizes* membrane to +30 mV by **local current**
- **Step 2**: Depolarizes second segment to threshold, second segment *develops action potential*
- **Step 3**: First segment enters *refractory period*
- **Step 4**: Local current *depolarizes* next segment

Cycle repeats

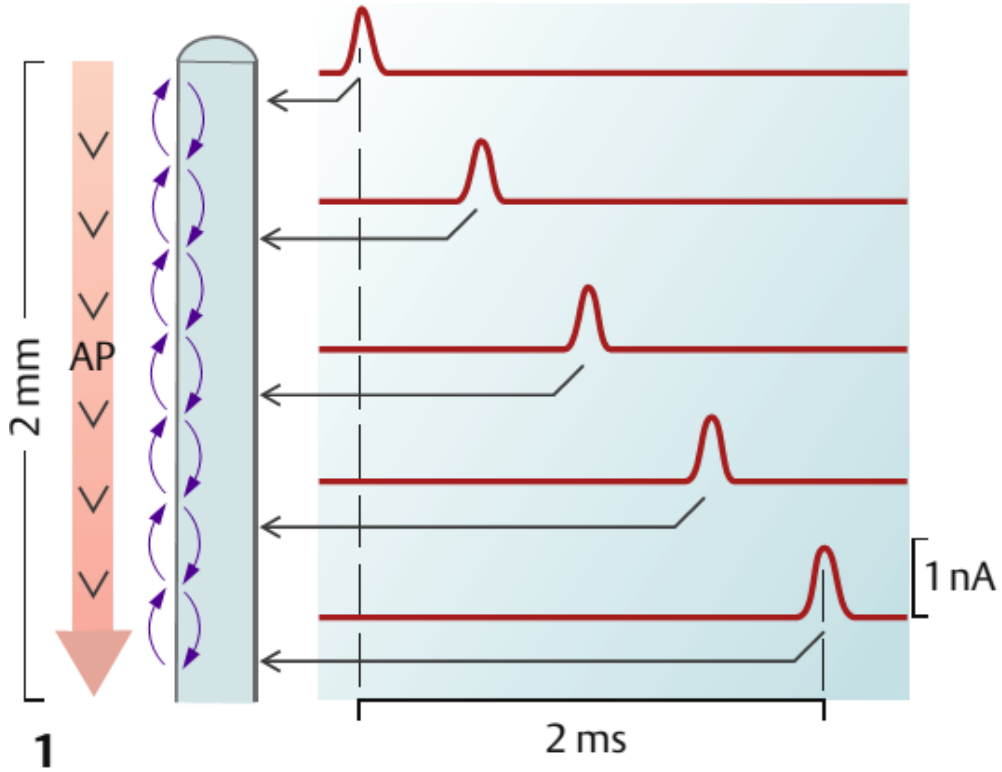


Saltatory Propagation

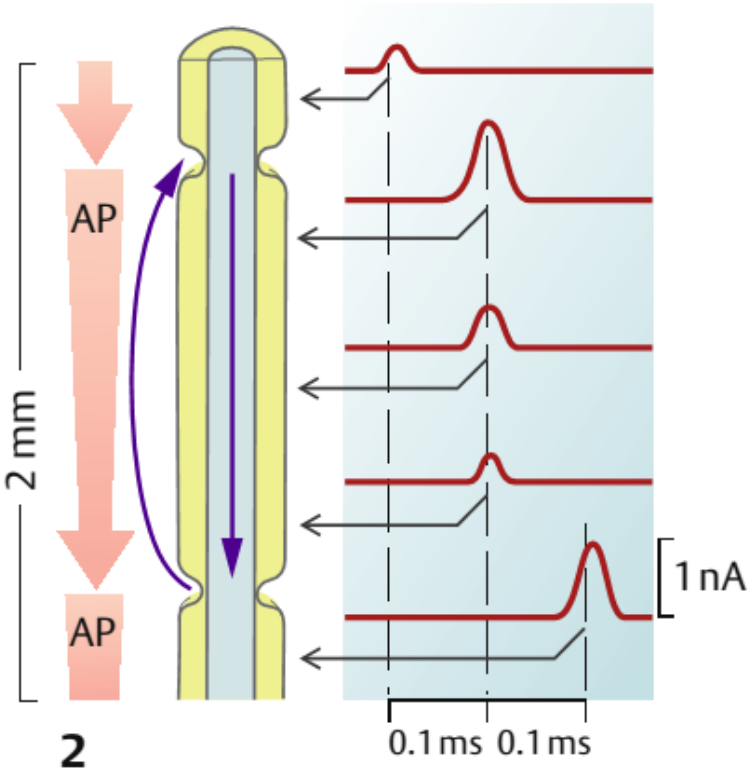
- Action potential spreads along *myelinated* axon
- *Faster* and uses *less energy* than continuous propagation
- Myelin prevents continuous propagation
- Local current **“jumps”** from node to node
- Depolarization occurs only at nodes



Continuous and Saltatory Propagation



Continuous Propagation



Saltatory Propagation

Classification of nerve fibers

- **Three Groups of Axons**
  - Type A fibers
  - Type B fibers
  - Type C fibers
- **These groups are classified by**
  - Diameter
  - Myelination
  - Speed of action potentials

Classification of nerve fibers

Type A	Type B	Type C
Myelinated	Myelinated	Unmyelinated
Large diameter	Medium diameter	Small diameter
High speed (140 m/sec)	Medium speed (18 m/sec)	Slow speed (1 m/sec)
Rapid information to/from CNS:	Intermediate signals:	Slower information
• position, • balance, • touch, • motor impulses	• sensory information, • to peripheral effectors	• to involuntary muscle, • gland controls

Classification of nerve fibers (in humans)

Fiber type	Function according to fiber type (Lloyd and Hunt types I–IV)	Diameter (μm)	Conduction rate (m/s)
Aα	Skeletal muscle efferent, afferents in muscle spindles (Ib) and tendon organs (Ib)	11–16	60 – 80
Aβ	Mechanoafferents of skin (II)	6–11	30 – 60
Aγ	Muscle spindle efferents	1 – 6	2 – 30
Aδ	Skin afferents (temperature and "fast" pain) (III)		
B	Sympathetic preganglionic; visceral afferents	3	3 – 15
C	Skin afferents ("slow" pain); sympathetic postganglionic afferents (IV)	0.5–1.5 (unmyelinated)	0.25 – 1.5

(After Erlanger and Gasser)

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