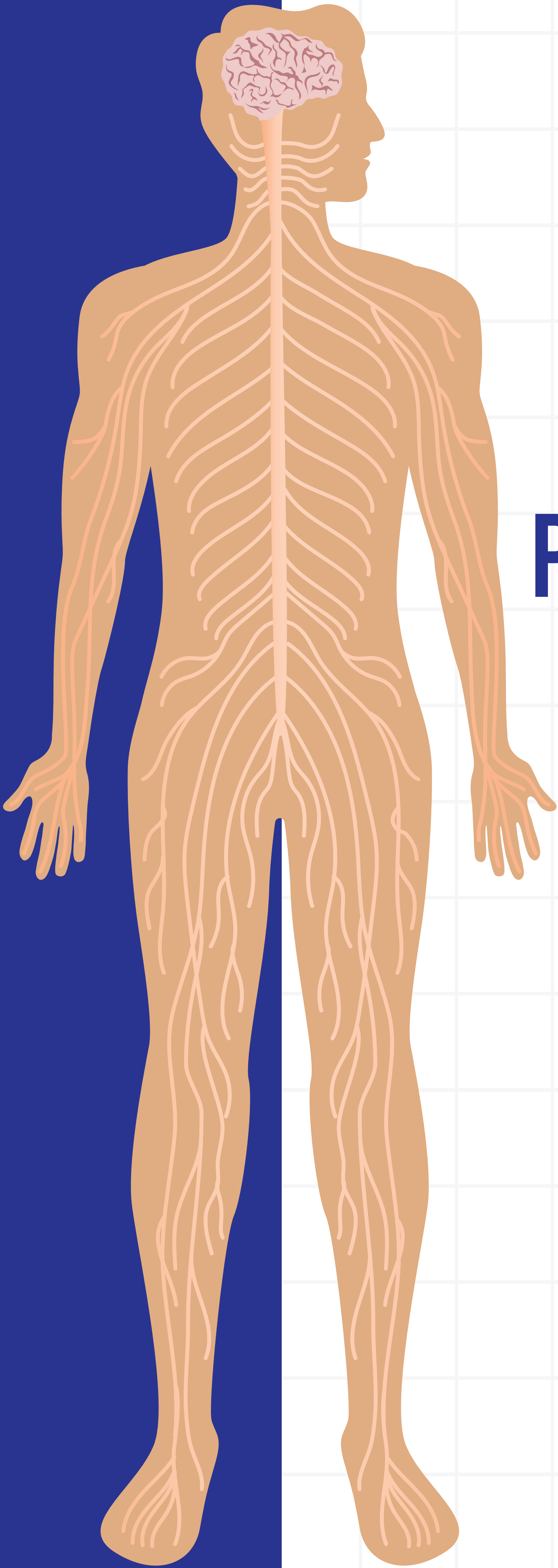
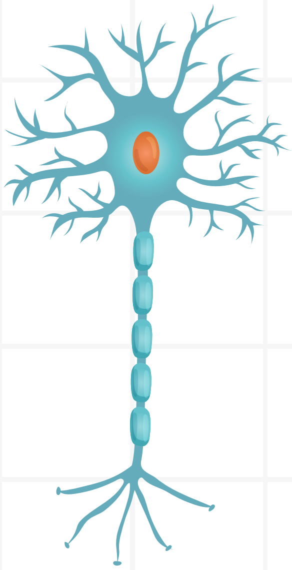


ARKAN
STUDY HOUSE

PHYSIOLOGY 2024

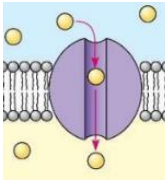


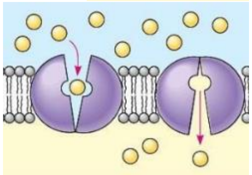
DR. AHMAD AL-QAWASMI

❖ Plasma membrane

- The membrane is a *selective permeable barrier* consisting of a lipid bilayer (phospholipids), many proteins (carriers, channels, receptors, enzyme) and carbohydrates (glycocalyx, glycoprotein)
    - *Fluid mosaic model:* The arrangement of molecules within the membrane resembles a sea of containing many types of proteins
    - The most common phospholipids are P-choline and P-ethanolamine which have a negative phosphate
    - Cholesterol decreaase the effect of temperature flucations on the membrane fluidity
    - The lipid bilayer is **permeable** to small hydrophobic molecules (O_2, CO_2, steroids) and water but **impermmeable** to large hydrophilic molecules (such as glucose, fructose, ions)

- Functions of the membrane proteins:
    - *Ion channels and transporters*
        - ✓ These proteins are selective and specific
        - ✓ Transporters undergo *conformational changes* during passing a specific molecule
        - ✓ Channels can be gated or leaky channels
        - ✓ ***Hyrophilic (water-soluble) molecules*** pass across the membrane by channels and transporters





    - *Receptors*
        - ✓ Signal transduction via binding to speicifc ligands (hormones) and producing second messengers iside the cell (intracellulary)
        - ✓ GPCR are receptors linked to G-proteins which can be G_s, G_i, G_q, …
        - ✓ G-proteins require **GTP** to be activated
        - ✓ G_s activates adenylyl cyclase and G_i inhibits adenylyl cyclase which forms cAMP
        - ✓ G_q activates phospholipase C-β (PLC-β) which cleaves PIP_2 into IP_3 and DAG
    - *Cell identity markers*
        - ✓ They are glycoproteins, where their carbohydrate part is the responsible for recognition
        - ✓ Also glycolipids contribute in the cell-cell recognition
        - ✓ Example: *MHC* molecules
    - *Enzymes* which catalyze chemical reactions
    - *Cell adhesion and communication*
        - ✓ It is done by some proteins, in the aid with carbohydrates
        - ✓ Examples: *CAM* (cell adhesion molecules) which include *cadherins*
    - *Linkers and junctions*, they include:
        - ✓ *Tight junctions (impermeable junction)*
            - Prevents the passing of foreign substances to the cells (separate 2 different compartments)
            - Present in the epithelial tissue such as the skin and epithilium of the GI system
        - ✓ *Gap junctions (communication junctions)*
            - Small tunnels between adjacent cells enable neighboring cell to communicate with each other
            - This tunnel is composed connexons protein which extend outward from the plasma membrane to join other connexon from the adjacent cell
            - Present in the heart (cardiac) and smooth muscle, enabling synchronyzation
        - ✓ *Desmosomes (adhering junctions)*
            - Consist of filaments that connect adjacent cells maintaining about 20 nm between them

- Integral proteins can be channels, transporters, receptors (signal transduction) and enzymes

- Transport across the membrane can be either:
  - ***Passive transport***
    - ✓ Does *not require* input of energy
    - ✓ Occurs *down* the concentration gradeint (downhill)
    - ✓ Includes *simple diffusion* (across the lipid bilayer) and *facilitated diffusion* (transporters, carriers)
  - ***Active transport***
    - ✓ *Requires energy* input
    - ✓ Occurs *against* concentration gradeint (uphill)
    - ✓ Include *primary* and *secondary* active transport

❖ Passive transport

Diffusion: is the continuous movement of particles in liquids and

1. *Simple Diffusion*

- Passive movement of particle across the membrane directly through ***lipid bilayer*** or channels proteins
- It is responsible for the passage of small lipid soluble (hydrophobic) molecules across the membrane
  - Examples: O_2, CO_2, steroids, monoglycerides, lipid-soluble vitamins …
- Diffusion depends on the following:

a. *Concentration gradeint (ΔC):* It is the difference in the concentration of a specific molecule between the 2 sides of the membrane
- ✓ It determines the direction of diffusion, where molecules difuse from the higher concentration to the lower concentration (downhill, down concentration gradeint)
- ✓ As the difference between the 2 sides increases, the rate of diffusion increases
- ✓ It is also called ***chemical gradeint*** (chemical potential)
- ✓ Also pressure and electrical gradeints affect the movement of substances across the membrane

b. *Permeability (P):* which depends on the lipids solubility of the transported molecule
- ✓ As the permeability of the molecule increases, the rate of diffusion increases

c. *Surface area*
- ✓ As the surface area increases, the rate of diffusion increases

d. *Molecular weight:* which represents the size of the molecule
- ✓ Smaller (lighter) molecules pass more easily and readily than larger (heavier) molecules

e. *Membrane thickness (distance of movement)*
- ✓ Greater the distance the slower the rate of diffusion

Fick's law

$J = P.\ \Delta C$

$P = D.A/\Delta X$

$J = D.A.\Delta C/\Delta X$

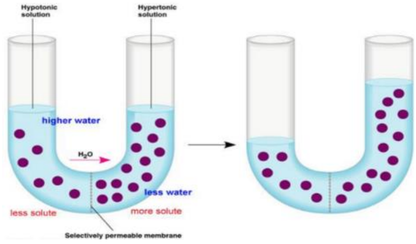
- All the factors the affect diffusion are explained in Fick's law of diffusion
  - **Directly** proportional factors: Concentration gradeint, Permeability, Surface area
  - **Inversely** proportional factors: Molecular Weight, Membrane Thickness

2. *Facilitated diffusion*

- Passive movement of particle using membrane proteins such as ***transporters (carriers)***
- Transportes ***larger and more hydrophilic*** substances
  - Example: glucose (by GLUT) in the basal surface of the enterocytes

- It is ***saturable***, which means that it has a maximum number of molecules to be transporter at the same time (limit) which is called Vmax
  - Vmax is due to the limited number of transporters in the membrane
- Diffusion throught ***channels*** can be considered as ***simple or facilitated diffusion***

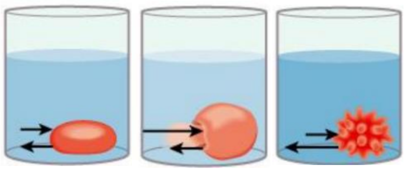
3. *Osmosis*



- It is the movement of ***water*** across a semipermeable membrane
- Water moves from the higher concentration of free water molecules (less solute) into the lower concentration of free water molecule (higher solute)
  - Water always goes *toward the region of higher solutes*
- ***Equilibrium:*** it is the condition where the *net movement equals zero*
  - It is reached when the hydrostatic pressure equals and opposes the osmotic pressure
  - *Hydrostatic pressur:* is the force done by the volume of water
  - *Osmotic pressure:* is the force that drives water to go toward soultes (ions, sugars, proteins, …)
  - When equilibrium is reached, if an external pressure is applied, that causes ***filtration***

- Concentration of particles is represented by
  - **Molarity:** Number of molecules per liter of water
  - **Osmolarity:** Number of active perticles per liter of water
  - **Osmolality:** Number of active perticles per Kg of water

Osmolarity of body fluids and blood is 300 mOsm



- **Isotonic solution:** A solution with osmolarity similar to body fluids
- **Hypertonic solution:** A solution with osmolarity higher than body fluids
- **Hypotonic solution:** A solution with osmolarity less than body fluids
- Van't Hoff's law (π = RTC) where C is the osmolarity

❖ Active transport

1. *Primary active transport*

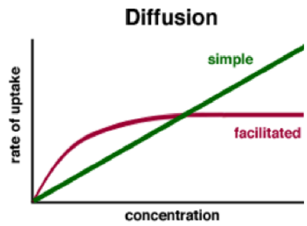
- Requires energy input by **direct** hydrolysis of ATP
- Requires transporter proteins called *pumps (ATPase)*, such as:
  - *Na^+-K^+ pump*
    - ✓ Pumps *3 Na^+ ions outward*, and *2 K^+ ions inward*
    - ✓ It maintains the gradeint of these ions across the membrane which ***regulates cell volume***
    - ✓ It changes its conformation by phosphorylation and dephosphorylation

  - *Ca^{++} pumps*
    - ✓ Maintain low Ca^{++} concentration in the cytosol
    - ✓ There are 2 types of Ca^{++} pumps:
      - In the *plasma membrane*, which expels Ca^{++} into the ECF
      - In the membranes of *internal organelles* (ER, mitochondria), which stores Ca^{++} into the lumen (reducing Ca^{++} in muscles causing muscle ***relaxation***)

  - *H^+ pumps (or H^+- K^+ pump)*
    - ✓ In the *pareital cells* of the gastric mucosa, which ***increases acidity*** (lowers pH) of the stomach
    - ✓ In the distal tubules and cortical collecting ducts in the *kidney*, which pumps H^+ into the urine and so ***controlling the amount of H^+*** in the body

2. *Secondary active transport*

- It requires energy input by **<u>indirect</u>** utilization of ATP, via utilizing the tendency of a specific particle (such as Na+) to move downhill to transport another molecule against its gradeint
  - Utilization of the *concentration gradeint* of a particle to transport another particle
  - Uses *sodium-dependent carriers*
  - *Co-transport:* Both substances are moved in the ***same*** direction
    - ✓ Co-transporters of *amino acids* or *glucose* in the apical surface of the enterocytes in the intestines (during absorption) which transport them with Na^+ into the cells
    - ✓ Also, Co-transporters of Fe^{++}, Cl^-, iodine and urate
  - *Counter-transport:* One substance passes in a direction and the other is pumped in ***opposite*** direction
    - ✓ *Na^+-Ca^{++}* counter transporter which is found in <u>most cells</u> such as cardiac muscles
    - ✓ *Na^+-H^+* counter transporter which is found in the proximal tubules of the nephron (<u>kidney</u>)



- Primary and secondary active transport are ***saturable*** (limited, V_{max})

❖ Vesicular transport

- Used for very large particles that can't pass through the membrane
  - They are transported via membranous vesicles
  - It requires energy (so it can be considered as an active transport mechanism)

1. *Endocytosis*

- The vesicle buds from the plasma membrane and carry the substances to ER, Golgi and other organelles
- It has many types including:
  - *Pinocytosis:* which is non-specific transport of solutions (***fluid***)
  - *Phagocytosis:* transport large multimolecular particles into the cell
  - *Receptor mediated endocytosis:* most specific type

2. *Exocytosis*

- Cellularly synthesized molceules (neurotransmitters, hormones, …) are transported out of the cell where the vesicle fuses with the plasma membrane and releases its contents into the ECF
  - It occurs in the *presence of Ca^{++}* ions
  - Vesicles are mostly synthesized in the ER

3. *Transcytosis*

- In involves endocytosis and exocytosis