بسم الله الرحمن الرحيم

General Biology for Medicine

MDCN1411 (2nd semester 2023/2024)

Handout collected and prepared by:

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Sources:

Lehninger Principles of Biochemistry 7th edition. Authors: David L. Nelson, Michael M. Cox. 2017.

Campbell Biology, 12th Edition. Authors: Lisa A. Urry, Micheal L. Cain, Steven A. asserman, Peter V. Minorsky, Rebecca B. Orr, Neil A. Campbell .2020.

Biology, 12th Edition.Authors Peter H. Raven, George B. Johnson, Kenneth A. Mason, Jonathan Losos, Tod Dunca, 2019.

Becker's World of the Cell 8th edition. Authors: Jeff Hardin, Gregory Paul Bertoni, Lewis J. Kleinsmith. 2018.

Concepts of Genetics 12th Edition. Authors: William S. Klug, Michael R. Cummings, Charlotte A. Spencer, Michael A. Palladino, Darrell Killian. 2019.

Course outline

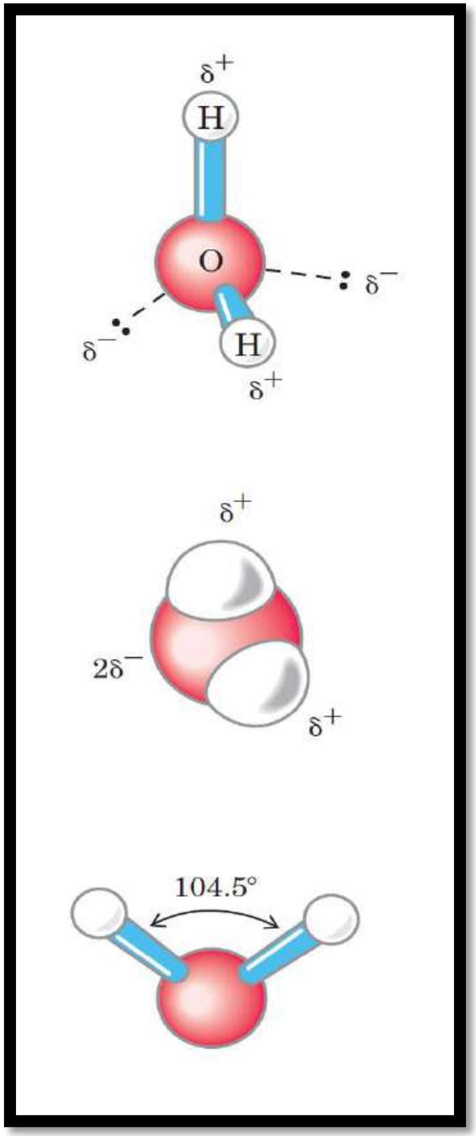
- **Water, pH, Weak Acids, Weak Bases, and buffers.**
- **Macromolecules, structure and function**
  - Amino acids and proteins, carbohydrates, Lipids, nucleic acids.
- **The cell: Prokaryotic and eukaryotic cells.**
- **Microscopy (principles of magnification and resolution).**
- **Eukaryotic cell compartmentalization, endomembrane system and organelles structure and function; Animal vs plant cell**
- **The cytoskeleton:** Microtubules, microfilaments , & intermediate filaments.
- **Extracellular components and connections between cells.**
  - Cell Walls of Plants (primary and secondary cell wall and the middle lamella)
  - The Extracellular Matrix (ECM) of Animal Cells
  - Cell Junctions Cells in animal (Tight Junctions, Desmosomes, and Gap Junctions in Animal Cells)and plant cells (Plasmodesmata in Plant Cells).
- **Biological Membranes and Transport**
  - Cell membrane structure and function (fluid mosaics model in details)
  - The Fluidity of Membranes
  - Membrane Proteins and Their Functions
  - Traffic across membranes including exocytosis and endocytosis
- **The cell cycle and cell divisions**
  - Mitosis and Meiosis (gametogenesis and nondisjunction) in details
- **DNA replication**

Water and life

- Water is the molecule that supports all of life
- Water is the **most abundant** substance in living systems, making up **70% or more** of the weight of most organisms.
- The **attractive forces (cohesion)** between water molecules and the **slight tendency of water to ionize** are of crucial importance to the structure and function of biomolecules and hence biological systems.

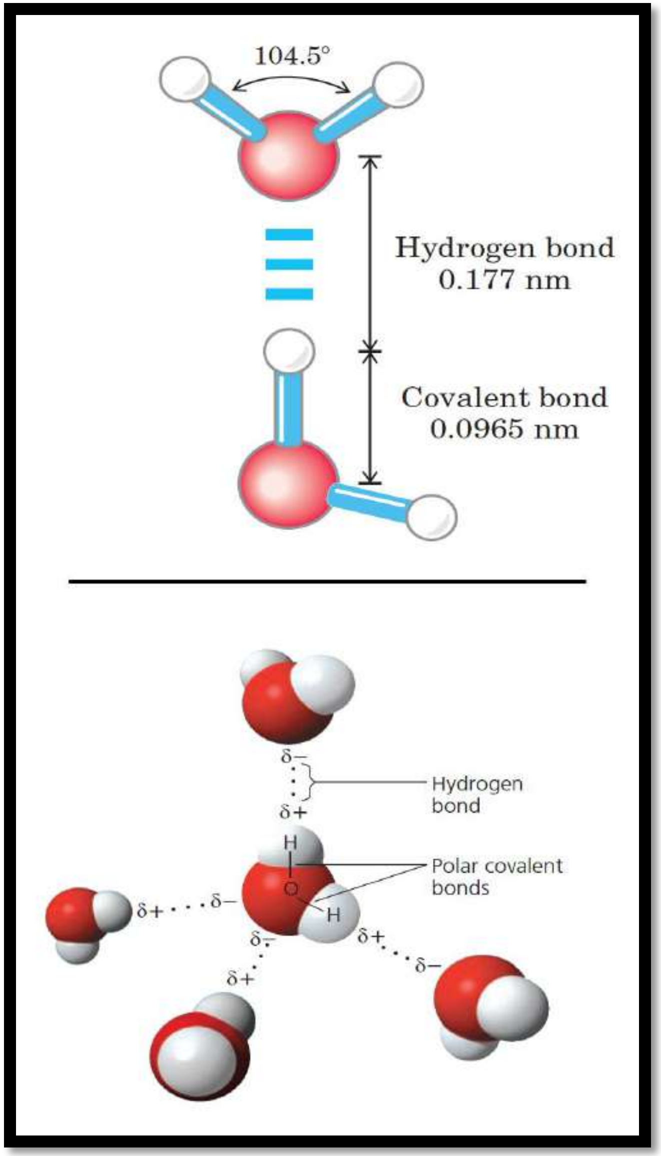
Structure of water molecule

- The water molecule is not as simple as its structure looks like.
- It is shaped like **a wide V**, with its two hydrogen atoms joined to the oxygen atom by single **covalent bonds**.
- Oxygen is **more electronegative** than hydrogen, so the electrons of the covalent bonds spend **more time closer (**unequal sharing) to oxygen than to hydrogen; these are **polar covalent bonds**.
- This **unequal sharing** of electrons and water's V-like shape make water a **polar molecule**.
- **Unequal sharing** of electrons results in the oxygen region of the water molecule has a **partial negative charge (δ-),** and each hydrogen has **a partial positive charge (δ+).**
- The H-O-H bond angle **is 104.5º,** slightly less than the 109.5º of a **typical tetrahedron** because of **crowding** by the unshared pairs of electrons of the oxygen atom



Hydrogen Bonds between water molecules

- As result of the partial negative charges **(δ-),** and the partial positive charges **(δ+),** of each water molecule , there is an **electrostatic attraction** between the **(δ-) of** oxygen atom of one water molecule and **(δ+) of** the hydrogen of another water molecule which is called a **hydrogen bond** (Hydrogen bonds are relatively weak bond).
- Hydrogen bonding is a special type of **dipole-dipole attraction** between molecules.
- Hydrogen bond **results** from the attractive force between a **hydrogen atom covalently** bonded to a very electronegative atom such as a N, O, or F atom and **another very electronegative atom.**
- Bond strength and bond length ?

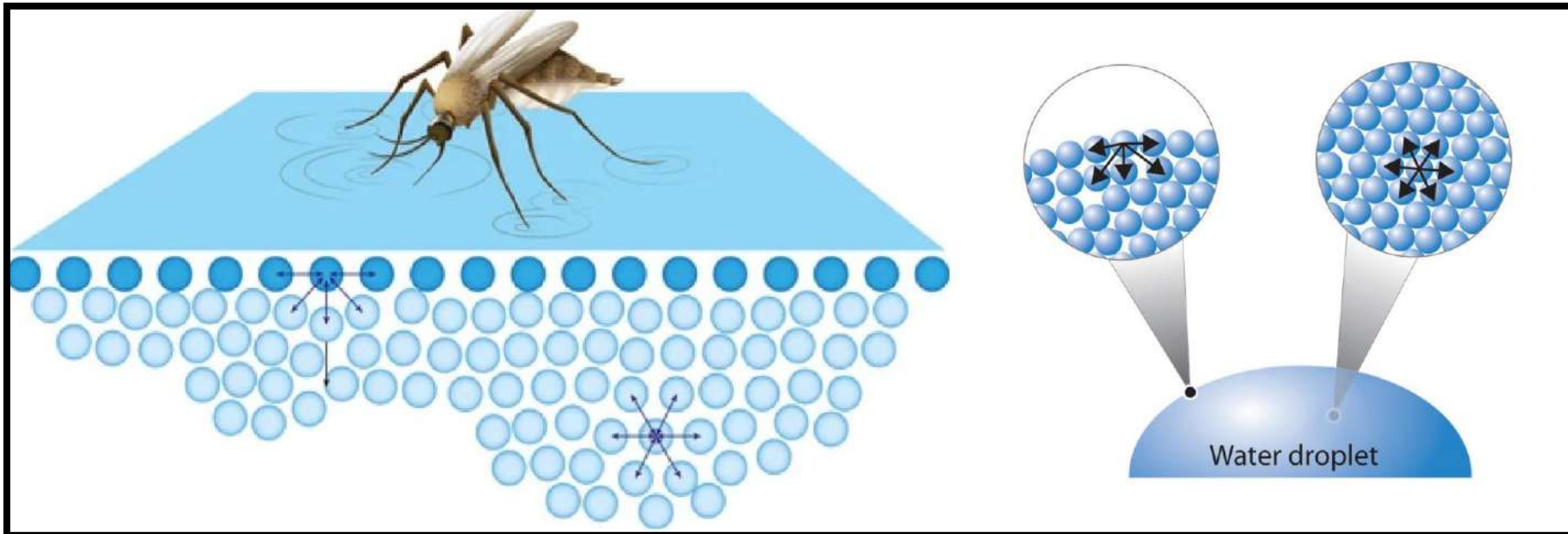


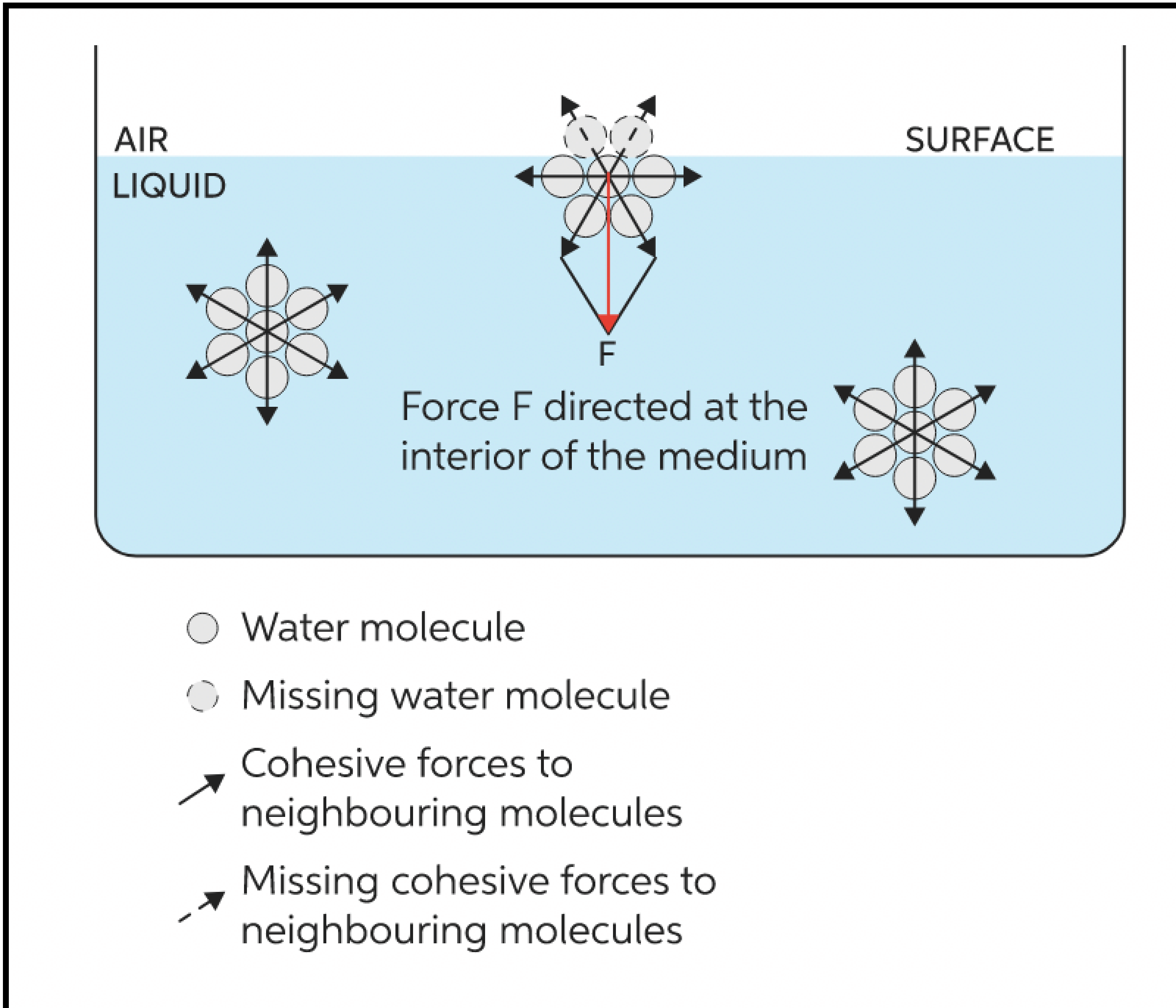
Cohesion of Water Molecules

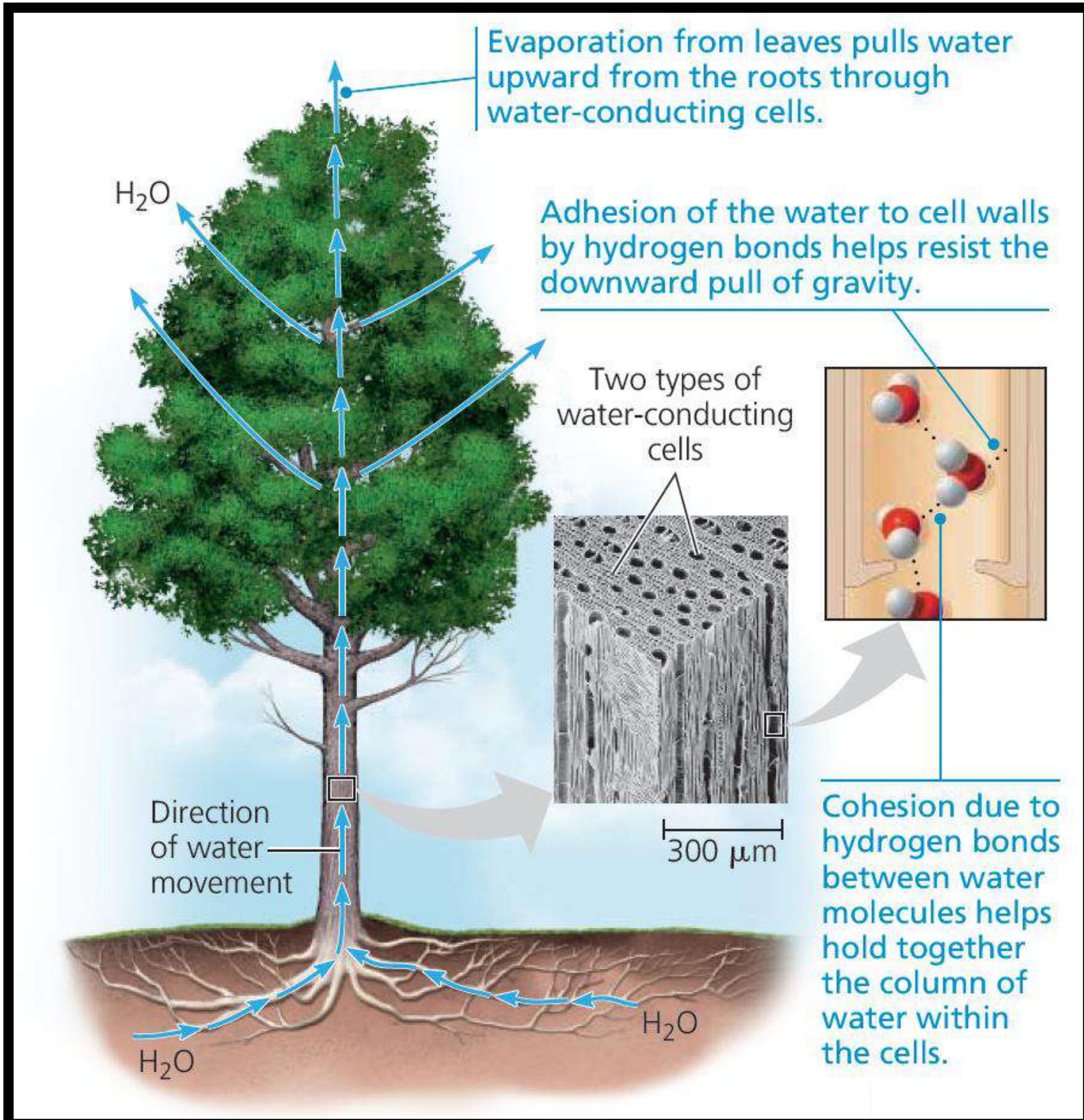
- Water molecules stay **close to each other** as a result of hydrogen bonding.
- **Hydrogen bonds** between water molecules provide the **cohesive forces** that make water a liquid at room temperature and that **favor the extreme orde**ring of molecules that is typical of crystalline water (**ice**).
- the arrangement of molecules in a sample of liquid water is constantly changing (**flickering clusters**), however at any given moment many of the molecules are **linked by multiple hydrogen bonds.** These linkages make water more structured than most other liquids .
- Collectively, the **hydrogen bonds hold the substance together** in a strong molecular interactions, a phenomenon **called cohesion**.

- **One result of cohesion of water** molecules due to hydrogen bonding is **high surface tension**, a measure of how difficult it is to stretch or break the surface of a liquid.
- At the air-water interface is an ordered arrangement of water molecules, hydrogen-bonded to one another and to the water below, but not to the air above, which gives water an unusually high surface tension, making it behave as though it were coated with an invisible film.

- **Cohesion** also contributes to the **transport of water** and dissolved nutrients against gravity in **plants**
- **Cohesion** attraction forces between molecules of the **same substance**
- **Adhesion** is attraction forces between molecules of **different substances**


Water droplet


AIR
SURFACE
LIQUID
F
Force F directed at the interior of the medium
Water molecule
Missing water molecule
Cohesive forces to neighbouring molecules
Missing cohesive forces to neighbouring molecules


Evaporation from leaves pulls water upward from the roots through water-conducting cells.
H_2O
Adhesion of the water to cell walls by hydrogen bonds helps resist the downward pull of gravity.
Two types of water-conducting cells
Direction of water movement
300 µm
Cohesion due to hydrogen bonds between water molecules helps hold together the column of water within the cells.
H_2O
H_2O

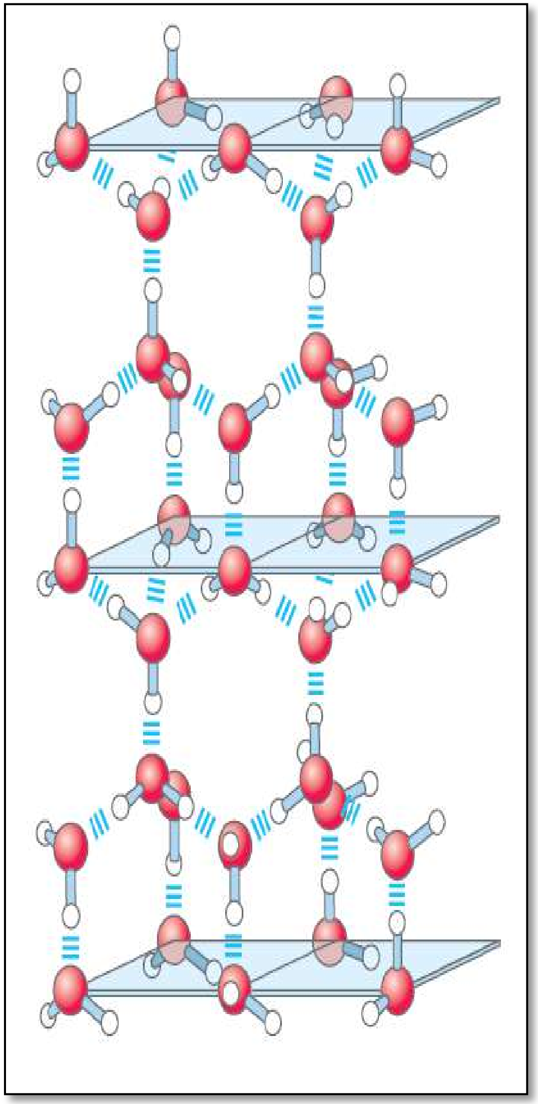
Hydrogen Bonding Gives Water Its Unusual Properties

Melting Point, Boiling Point, and Heat of Vaporization of Some Common Solvents

	Melting point (°C)	*Boiling point (°C)*	*Heat of vaporization (J/g)**
Water	0	100	2,260
Methanol (CH_3OH)	−98	65	1,100
Ethanol (CH_3CH_2OH)	−117	78	854
Propanol ($CH_3CH_2CH_2OH$)	−127	97	687
Butanol ($CH_3(CH_2)_2CH_2OH$)	−90	117	590
Acetone (CH_3COCH_3)	−95	56	523
Hexane ($CH_3(CH_2)_4CH_3$)	−98	69	423
Benzene (C_6H_6)	6	80	394
Butane ($CH_3(CH_2)_2CH_3$)	−135	−0.5	381
Chloroform ($CHCl_3$)	−63	61	247

- Water has a **higher melting point**, **boiling point**, and **heat of vaporization** than most other common solvents.
- These **unusual properties** are a consequence of attractions between adjacent water molecules that give liquid water great **internal cohesion**.
- **Hydrogen bonds are relatively weak**. Those in liquid water have a bond dissociation energy (the energy required to break a bond) of about **23 kJ/mol**, compared with **470 kJ/mol** for the covalent —OH bond in water or **348 kJ/mol** for a covalent C—C bond.
- *The heat energy required to convert 1.0 g of a liquid at its boiling point, at atmospheric pressure, into its gaseous state at the same temperature. It is a direct measure of the energy required to overcome attractive forces (cohesion) between molecules in the liquid phase.

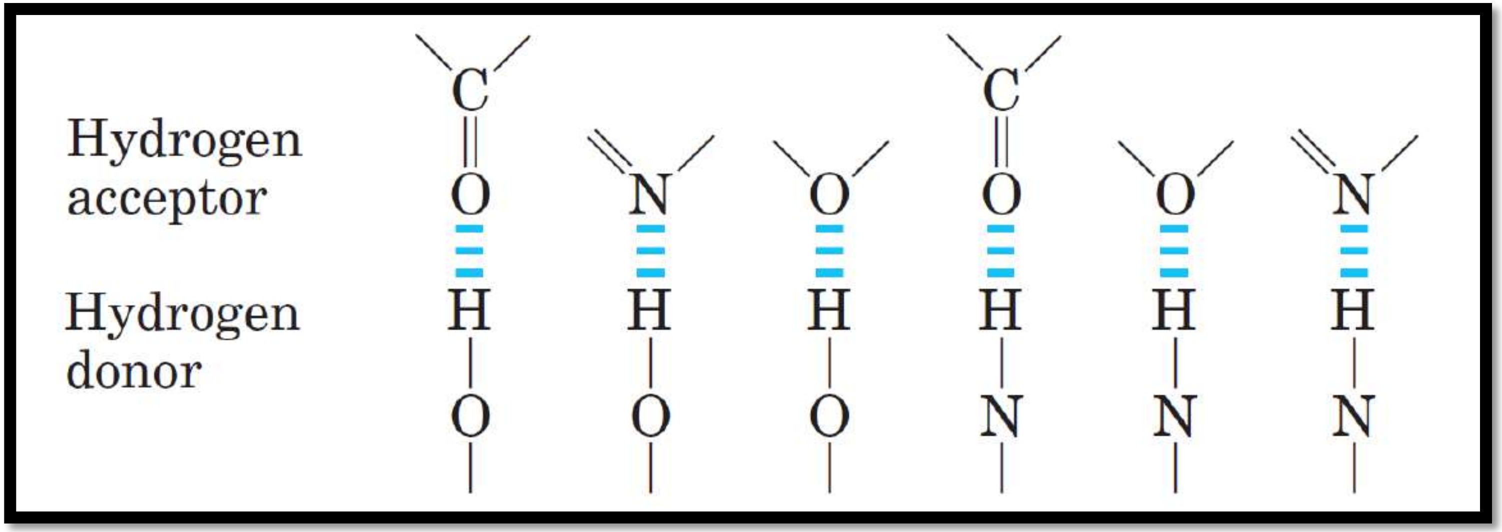
Liquid water, ice, and the flickering cluster



- **Hydrogen bonds** between water molecules provide the **cohesive forces** that make water a liquid at room temperature and that **favor the extreme ordering** of molecules that is typical of crystalline water (**ice**).
- In **ice**, each water molecule forms the maximum of four hydrogen bonds, creating a regular crystal lattice. This crystal lattice makes **ice less dense than liquid water**, and thus ice floats on liquid water
- However, **at any given time**, most of the molecules in liquid water are engaged in hydrogen bonding (an average of **3.4 with** other water molecules), but the **lifetime** of each hydrogen bond is just 1 to 20 **picoseconds** (1 ps 10^{-12} s)
- Upon breakage of one hydrogen bond, another hydrogen bond forms, with the same partner or a new one, **within ~ 0.1 ps**.
- The "**flickering clusters**" is the phrase that has been applied to the **short-lived groups of water molecules** interlinked by hydrogen bonds in liquid water.
- The sum of all the hydrogen bonds between H_2O molecules gives great internal cohesion on liquid water.

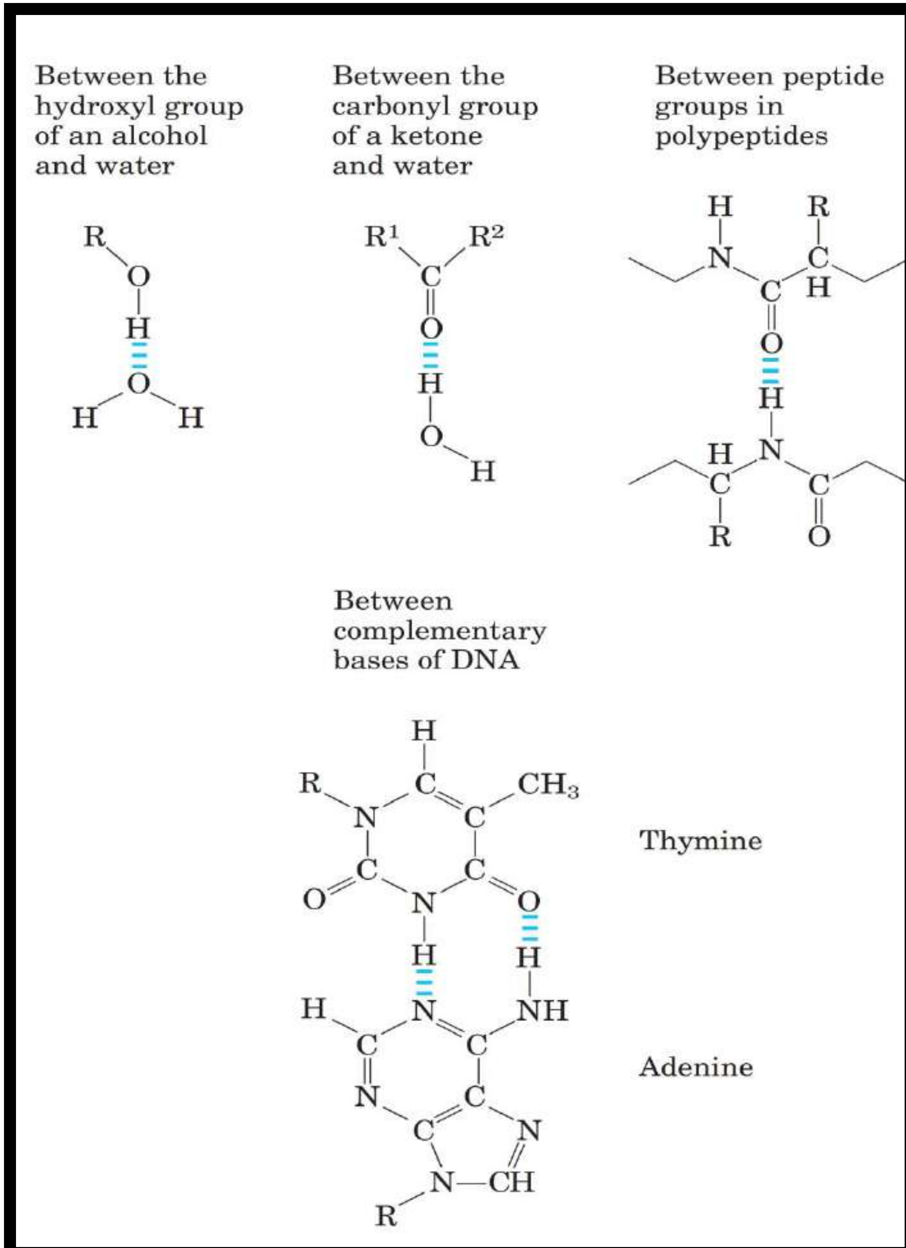
Water Forms Hydrogen Bonds with Polar Solutes

- Hydrogen bonds **are not exclusive** to water.
- Hydrogen bonds readily **form between** an electronegative atom (**the hydrogen acceptor**, usually oxygen or nitrogen with a lone pair of electrons) and a hydrogen atom covalently bonded to another electronegative atom (**the hydrogen donor**) in the same or another molecule
- Hydrogen atoms **covalently bonded to carbon atoms do not participate** in hydrogen bonding, because carbon is only slightly more electronegative than hydrogen and thus the C-H bond is only very weakly polar.
- Why butanol ($CH_3(CH_2)_2CH_2OH$) has a relatively high boiling point of 117 ^oC than butane ($CH_3(CH_2)_2CH_3$) which has a boiling point of only 0.5 ^oC.



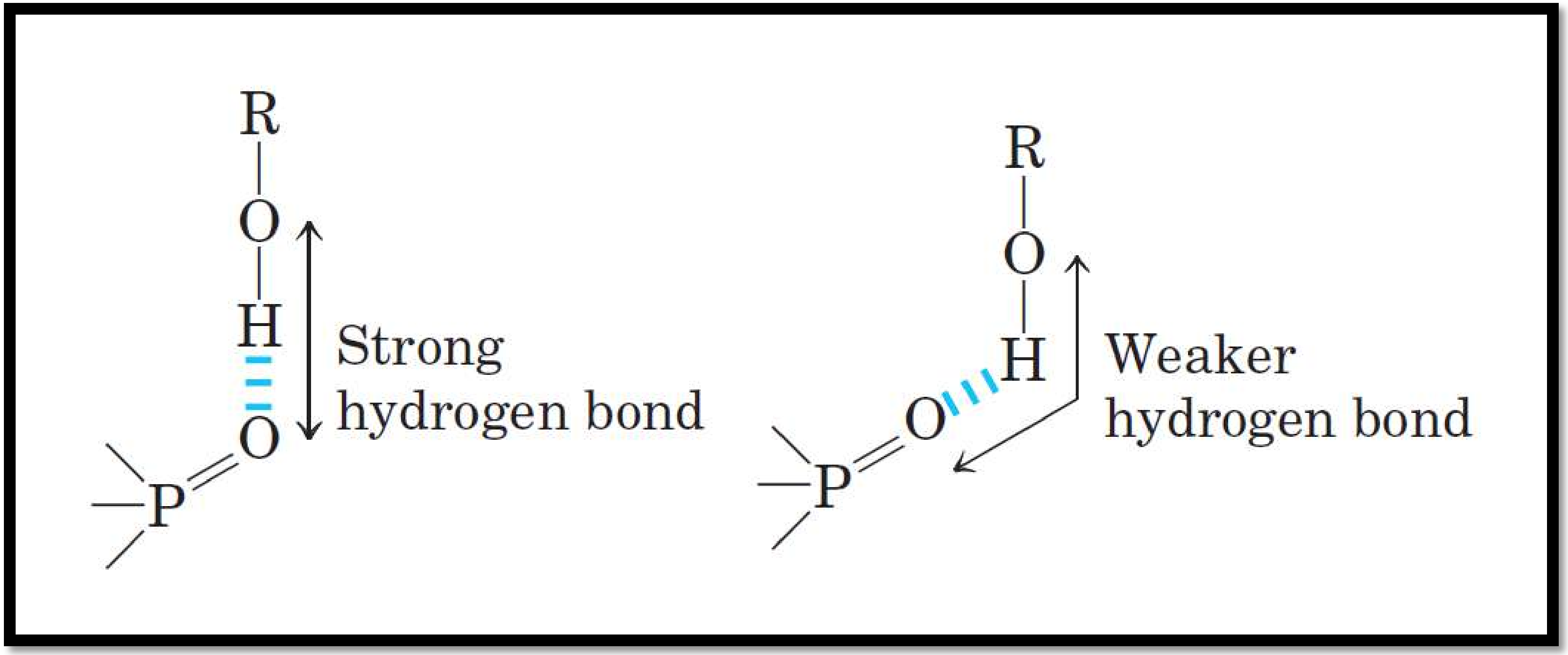
- **Polar biomolecules dissolve readily** in water because they can replace water-water interactions with **more energetically favorable water-solute** interactions.
- In contrast, **nonpolar biomolecules** interfere with water-water interactions but are unable to form water-solute interactions—consequently, nonpolar molecules are **poorly soluble in water**.

- Uncharged but polar biomolecules such as **sugars dissolve readily** in water because of the stabilizing effect of **hydrogen bonds between the hydroxyl groups or carbonyl oxygen** of the sugar and the polar water molecules.
- Alcohols, aldehydes, ketones, and compounds containing N-H bonds all form hydrogen bonds with water molecules and tend to be **soluble in water.**



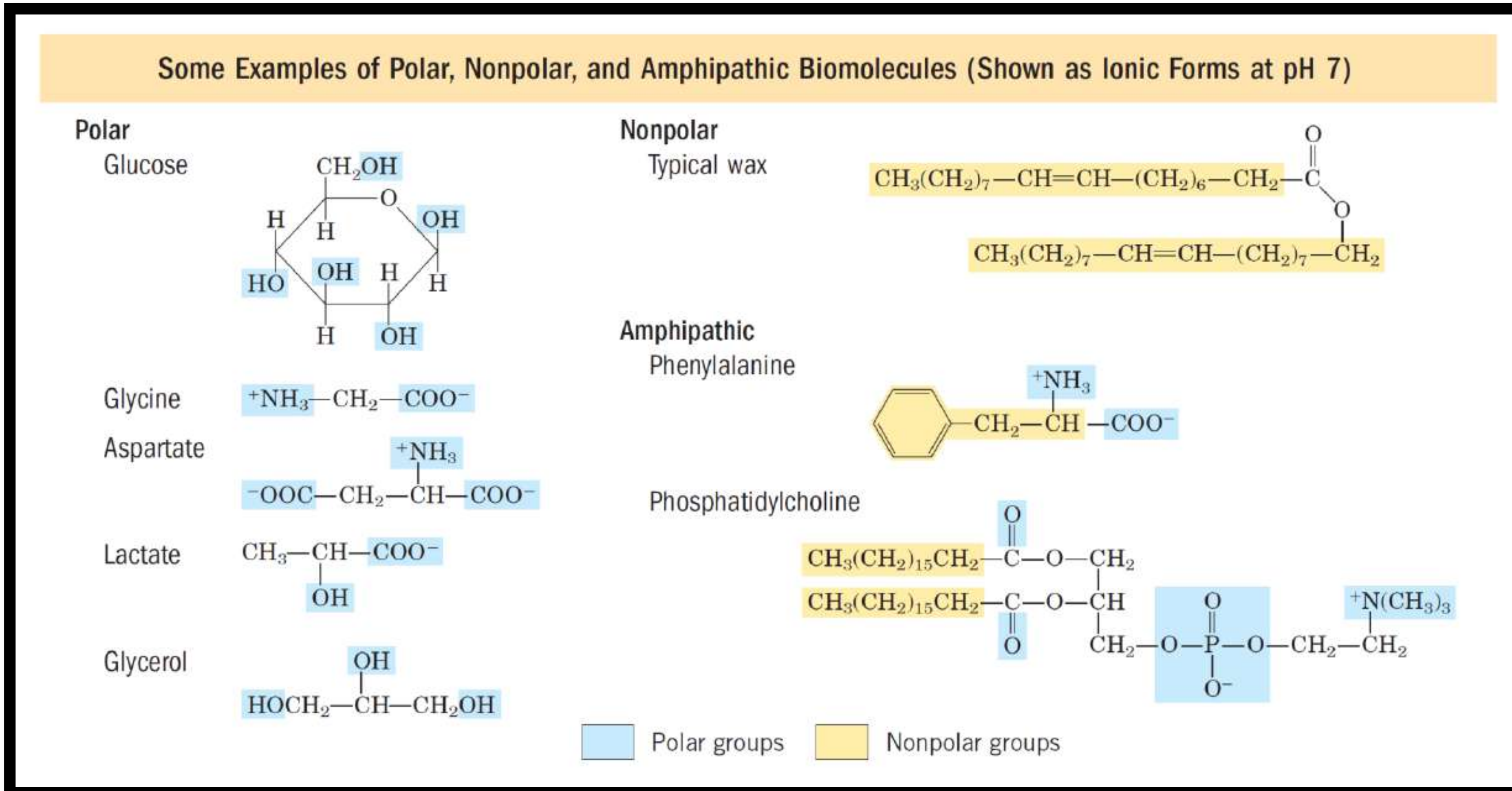
Relatively strong and weak Hydrogen bonds

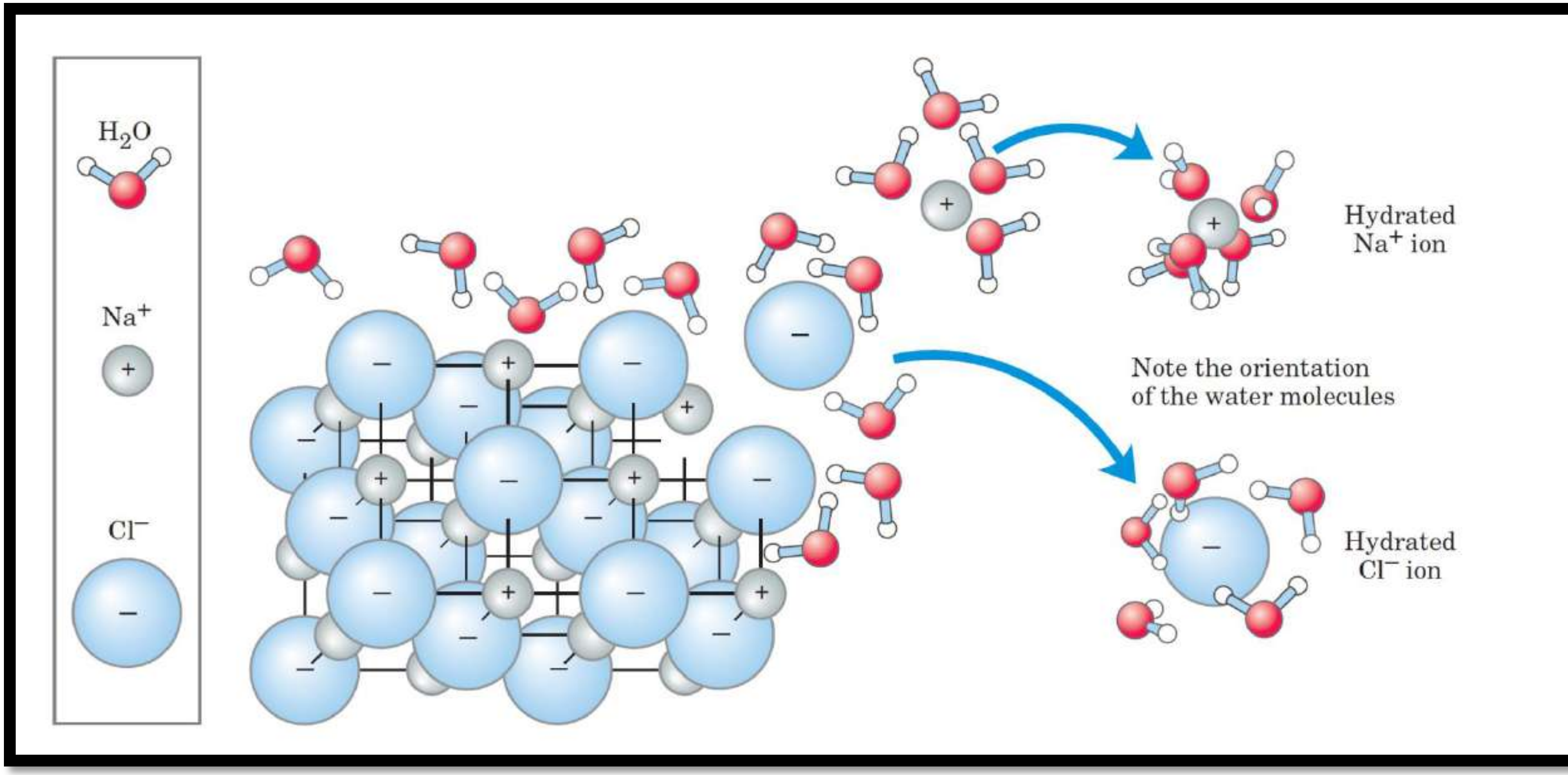
- Hydrogen bonds are **strongest when** the bonded molecules are oriented to **maximize electrostatic interaction** and **minimize charge repulsion** which occurs when the hydrogen atom and the two atoms that share it are **in a straight line**—that is, when the acceptor atom is in line with the covalent bond between the donor atom and H.
- **Hydrogen bonds are thus highly directional** and capable of holding two hydrogen-bonded molecules or groups in a specific geometric arrangement.



Water Interacts Electrostatically with Charged Solutes

- As a polar solvent, water readily dissolves most biomolecules, which are generally **charged or polar compounds**
- Compounds that dissolve easily in water are **hydrophilic** (Greek, “water-loving”).
- **Nonpolar** solvents such as chloroform and benzene **are poor solvents for polar** biomolecules but easily dissolve those that are **hydrophobic**—nonpolar molecules such as lipids and waxes.





Water dissolves salts such as NaCl by **hydrating and stabilizing** the Na+ and Cl- ions, weakening the electrostatic interactions between them and thus **counteracting their tendency to associate in a crystalline lattice**

The same factors apply to charged biomolecules, compounds with functional groups such as ionized carboxylic acids ($-COO^-$), protonated amines ($-NH_3^+$), and phosphate esters.

Water readily dissolves such compounds by **replacing solute-solute hydrogen bonds** with solute-water hydrogen bonds

Entropy increases as Crystalline Substances Dissolve

Entropy : It is a measure of randomness or disorder of the system: the greater is the randomness, the higher is the entropy.

As a salt such as **NaCl dissolves**, the Na+ and Cl- ions leaving the crystal lattice acquire far greater freedom of motion (**increase entr**opy).

The resulting increase in entropy (randomness) of the system is largely responsible for the ease of dissolving salts such as NaCl in water.

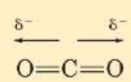
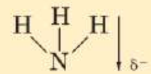
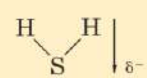
Melting of the ice is accompanied by an increase of entropy.

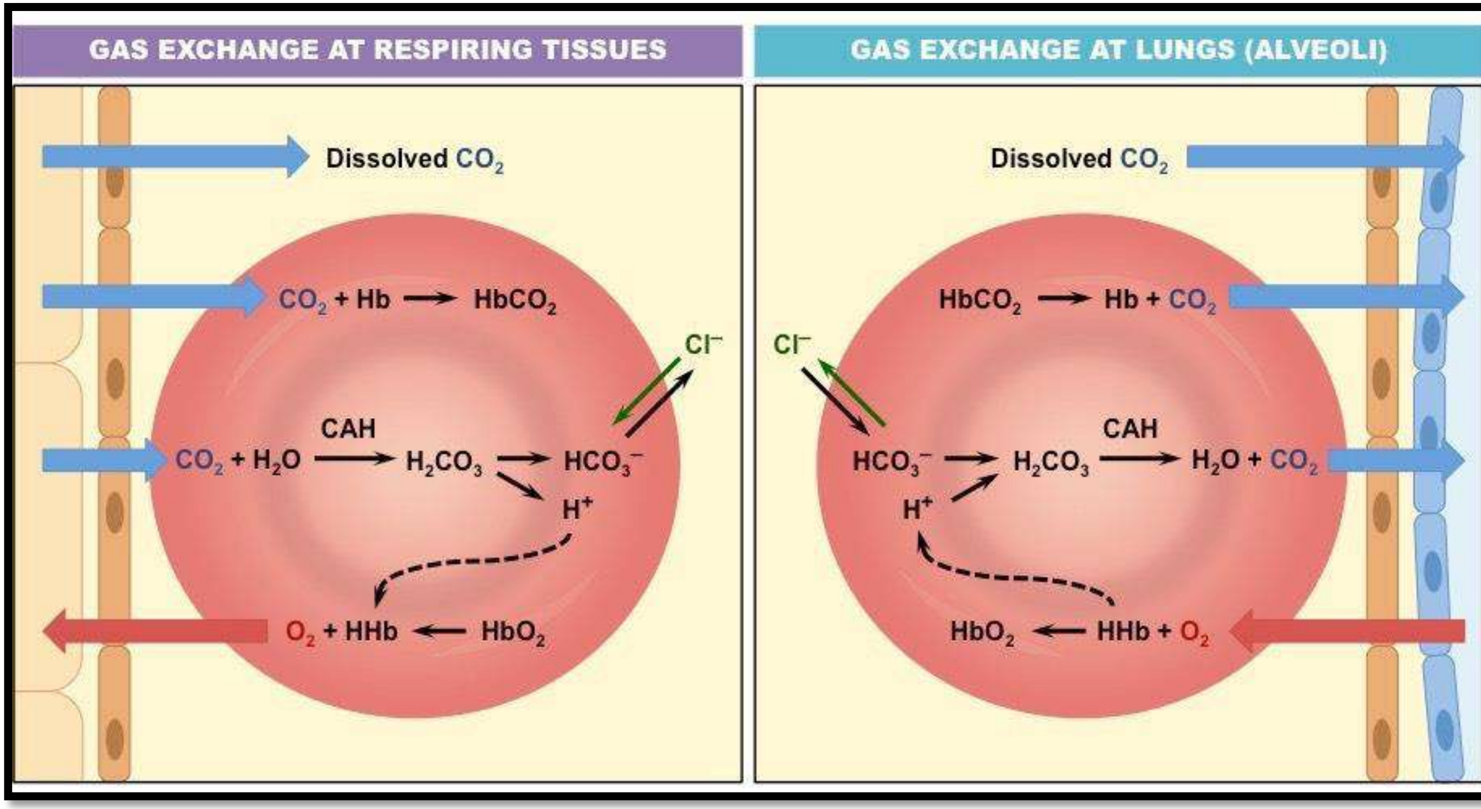
Molecules of H_2O in **ice have fixed position** but as soon as it changes into liquid , the molecules of H_2O began to move about freely i.e the randomness increases .

Nonpolar Gases Are Poorly Soluble in Water

- The molecules of the biologically important gases **CO_2, O_2, and N_2 are nonpolar**.
- In **O_2 and N_2**, electrons are shared equally by both atoms.
- In **CO_2, each C=O bond is polar**, but the two dipoles are **oppositely directed and cancel each other**.
- The movement of molecules from the disordered gas phase into aqueous solution constrains their motion and the motion of water molecules and therefore represents **a decrease in entropy**.
- **The nonpolar nature of these gases and the decrease in entropy** when they enter solution combine to make them **very poorly soluble in water** .
- **water-soluble carrier proteins** (**hemoglobin**) that facilitate the transport of O_2.
- **CO_2** forms carbonic acid (H_2CO_3) in aqueous solution and is transported as the HCO_3^- (bicarbonate) ion, either free—bicarbonate is very soluble in water (~100 g/L at 25 C)—or bound to hemoglobin.
- Two other gases, **NH_3 and H_2S**, also have biological roles in some organisms; these gases **are polar** and dissolve readily in water.

Solubilities of Some Gases in Water

Gas	*Structure**	*Polarity*	*Solubility in water (g/L)*†
Nitrogen	N≡N	Nonpolar	0.018 (40 °C)
Oxygen	O=O	Nonpolar	0.035 (50 °C)
Carbon dioxide		Nonpolar	0.97 (45 °C)
Ammonia		Polar	900 (10 °C)
Hydrogen sulfide		Polar	1,860 (40 °C)



Transport of CO2 as Carbonic Acid

- When CO2 enters the erythrocyte, it combines with water to form carbonic acid (reaction catalyzed by carbonic anhydrase CAH)
- The carbonic acid (H2CO3) then dissociates to form hydrogen ions (H+) and bicarbonate (HCO3–)
- Bicarbonate is pumped out of the cell in exchange with chloride ions (exchange ensures the erythrocyte remains uncharged)
- The bicarbonate in the blood plasma combines with sodium to form sodium bicarbonate (NaHCO3), which travels to the lungs
- The hydrogen ions within the erythrocyte make the environment less alkaline, causing hemoglobin to release its oxygen
- The hemoglobin absorbs the H+ ions and acts as a buffer to maintain the intracellular pH
- When the red blood cell reaches the lungs, bicarbonate is pumped back into the cell and the entire process is reversed.

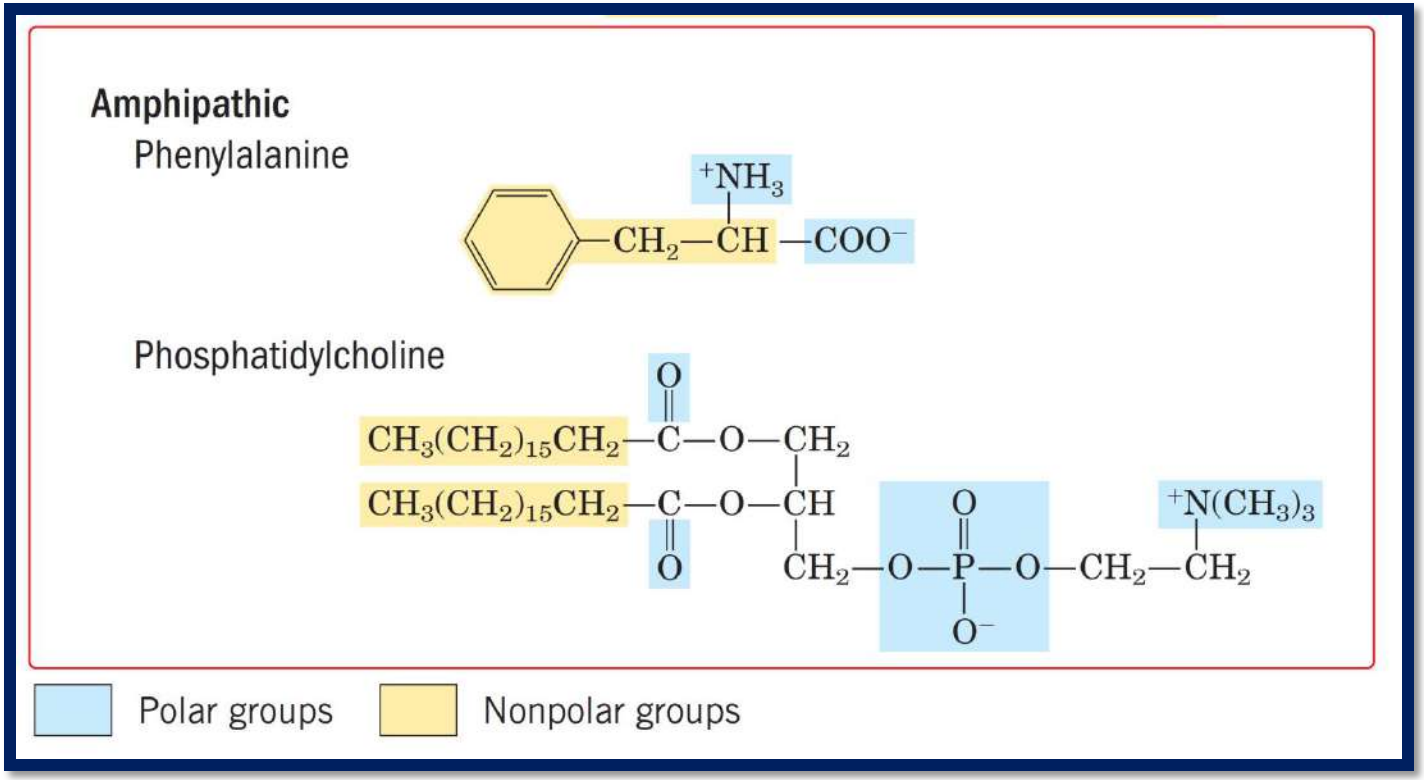
Nonpolar Compounds Force Energetically Unfavorable Changes in the Structure of Water

- When **water is mixed with benzene** or hexane, **two phases form**; neither liquid is soluble in the other.
- Nonpolar compounds such as **benzene and hexane** are **hydrophobic—they** are **unable** to undergo energetically favorable interactions with water molecules, and **they interfere with the hydrogen bonding** among water molecules.
- All molecules or ions in aqueous solution interfere with the hydrogen bonding of some water molecules in their immediate proximity or neighborhood.
- **polar or charged solutes** (such as NaCl) **compensate** for lost water-water hydrogen bonds by forming **new solute-water interactions**.
- **Hydrophobic solutes**, however, **offer no such compensation**, and their addition to water may therefore result in a measurable decrease in entropy.

- **Water molecules** in the immediate proximity or neighborhood of a nonpolar solute are constrained in their possible orientations as they form a highly ordered cage-like shell around each solute molecule.

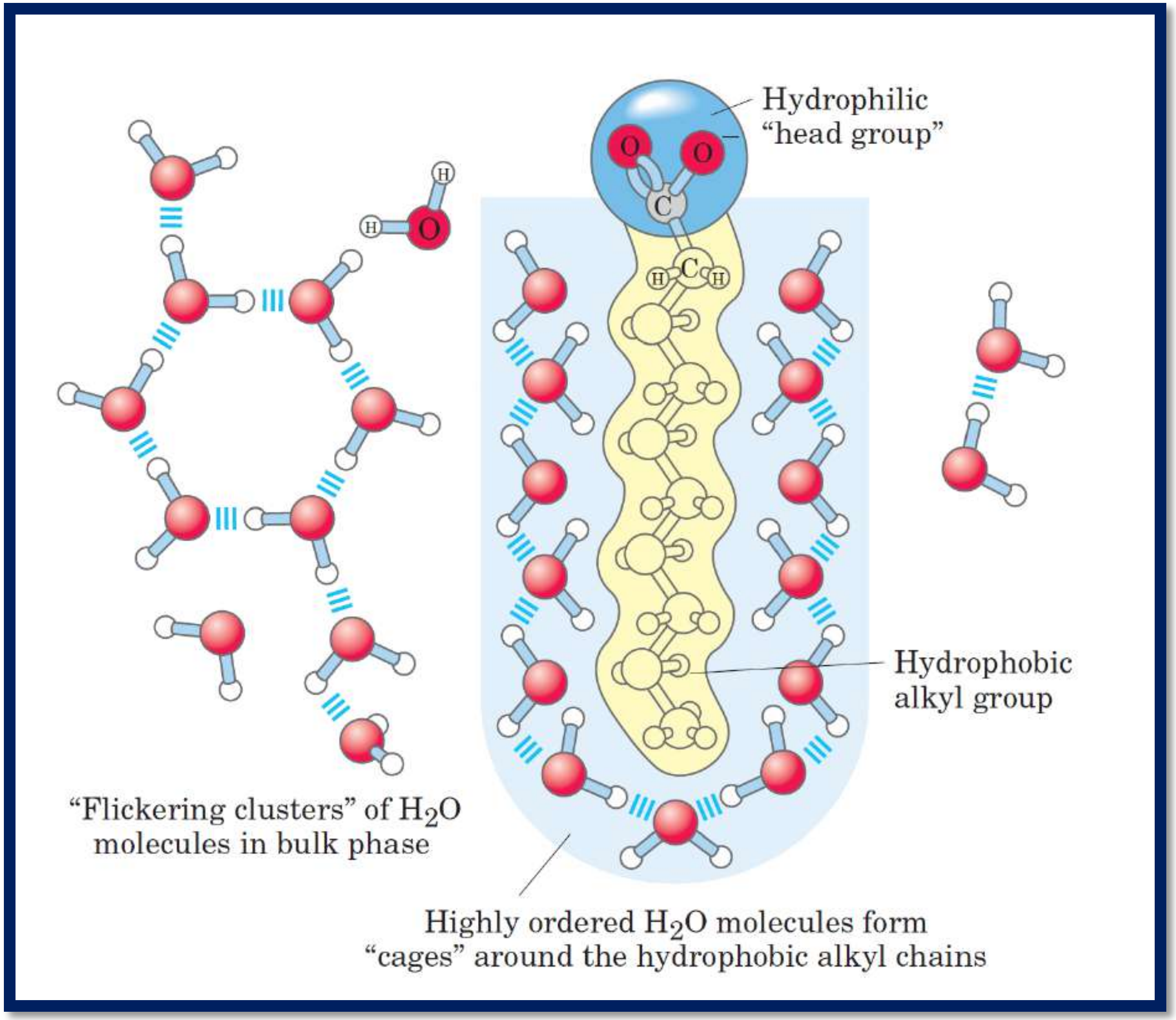
Amphipathic compounds

- **Amphipathic** compounds contain regions that are **polar (or charged) and regions that are nonpolar**.
- When an amphipathic compound is mixed with water, the polar, hydrophilic region interacts favorably with the solvent and tends to dissolve, but the nonpolar, hydrophobic region tends to avoid contact with the water

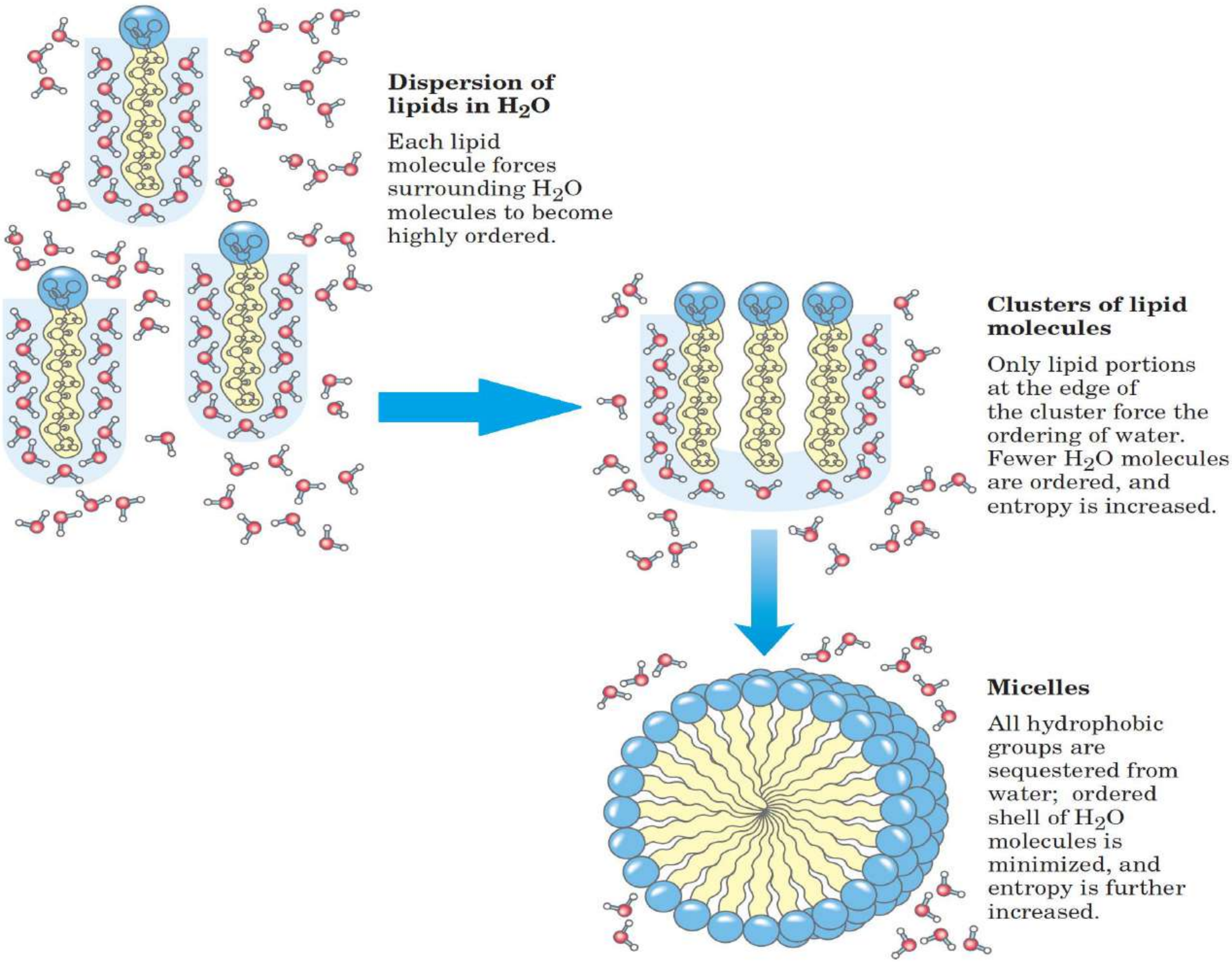


Amphipathic interaction with water

- The **nonpolar regions** of the amphipathic molecules **cluster together to present the smallest hydrophobic area** to the aqueous solvent, and the **polar regions are arranged to maximize their interaction with the polar solvent**, thus forming relatively stable structures of amphipathic compounds in water, called **micelles.**
- The **forces that hold the nonpolar regions** of the molecules together are called **hydrophobic interactions.**
- **The strength of hydrophobic interactions** is not due to any intrinsic attraction between nonpolar moieties. Rather, **it results from the system's achieving greatest thermodynamic** stability by **minimizing** the number of **ordered water** molecules required to surround hydrophobic portions of the solute molecules.
- **Many biomolecules are amphipathic**, e.g. proteins, pigments, certain vitamins, and the sterols and phospholipids of membranes all have polar and nonpolar surface regions.
- **Hydrophobic interactions** among lipids, and between lipids and proteins, are the most important determinants of **structure in biological membranes**. Hydrophobic interactions between nonpolar amino acids also stabilize the three-dimensional structures of proteins.

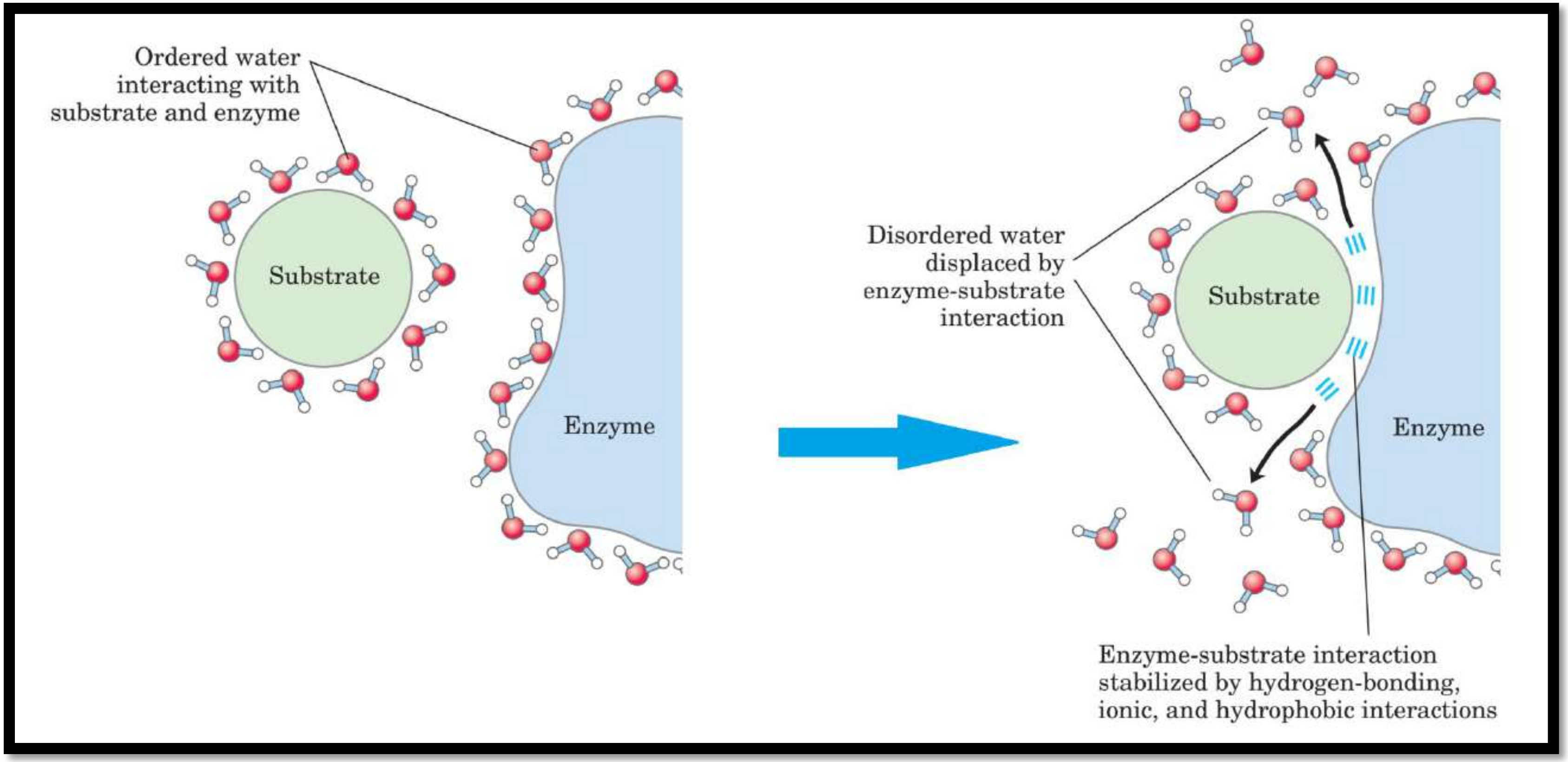


Long-chain fatty acids have very hydrophobic alkyl chains, each of which is surrounded by a layer of **highly ordered water molecules**.


Dispersion of lipids in H_2O
Each lipid molecule forces surrounding H_2O molecules to become highly ordered.
Clusters of lipid molecules
Only lipid portions at the edge of the cluster force the ordering of water. Fewer H_2O molecules are ordered, and entropy is increased.
Micelles
All hydrophobic groups are sequestered from water; ordered shell of H_2O molecules is minimized, and entropy is further increased.

Release of ordered water favors formation of an enzyme-substrate complex

- Hydrogen bonding between water and polar solutes also causes some ordering of water molecules, but the effect is less significant than with nonpolar solutes.
- Part of the driving force for binding of a polar substrate (reactant) to the complementary polar surface of an enzyme (both are separate entities) is the entropy increase as the enzyme displaces ordered water from the substrate.



Solutes Affect the Colligative Properties of Aqueous

- **Solutes** of all kinds **alter certain physical properties** of the solvent, water: its
    - **vapor pressure**
    - **boiling point**
    - **freezing point**
    - **osmotic pressure**.
- These are called **colligative** ("tied together") **properties,** because the effect of solutes on all four properties has the same basis: the concentration of **water is lower in solutions** than in pure water.
- The effect of solute concentration on the colligative properties of water **is independent of the chemical properties** of the solute; it depends only on the **number** of solute particles (molecules, ions) in a given amount of water.
- A compound such as **NaCl,** which dissociates in solution**, has twice the effect** as does an equal number of moles of a **nondissociating solute such as glucose**.
- E.g the tendency of water molecules to move from the aqueous phase to the surface of a forming ice crystal is reduced when some of the molecules that collide with the crystal are solute, not water. In that case, the solution will freeze more slowly than pure water and at a lower temperature.

- **For a 1.00 M aqueous solution** of an ideal, nonvolatile, and nondissociating solute, the freezing point is 1.86 ^{o}C lower (- 1.86) and the boiling point is 0.543 ^{o}C (100.543) higher than for pure water.
- **For a 0.100 M solution** of the same solute, the changes are **one-tenth as large**

Pure Water Is Slightly Ionized

- Water molecules have **a slight tendency** to undergo reversible ionization to yield a hydrogen ion (a proton) and a hydroxide ion, giving the equilibrium
-

$$H_2O \rightleftharpoons H^+ + OH^-$$

The position of equilibrium of any chemical reaction is given by its **equilibrium constant, *K*eq** (sometimes expressed simply as ***K***).

$$A + B \rightleftharpoons C + D$$

$$K_{eq} = \frac{[C][D]}{[A][B]}$$

$$K_{eq} = \frac{[H^+][OH^-]}{[H_2O]}$$

The Ionization of Water Is Expressed by an equilibrium Constant

$$K_{\mathrm{eq}} = \frac{[\mathrm{H}^+][\mathrm{OH}^-]}{[\mathrm{H_2O}]}$$

$$K_{\mathrm{eq}} = \frac{[\mathrm{H}^+][\mathrm{OH}^-]}{55.5\ \mathrm{M}}$$

$$(55.5\ \mathrm{M})(K_{\mathrm{eq}}) = [\mathrm{H}^+][\mathrm{OH}^-] = K_{\mathrm{w}}$$

$$\begin{aligned} K_{\mathrm{w}} = [\mathrm{H}^+][\mathrm{OH}^-] &= (55.5\ \mathrm{M})(1.8 \times 10^{-16}\ \mathrm{M}) \\ &= 1.0 \times 10^{-14}\ \mathrm{M}^2 \end{aligned}$$

$$K_{\mathrm{w}} = [\mathrm{H}^+][\mathrm{OH}^-] = [\mathrm{H}^+]^2$$

$$[\mathrm{H}^+] = \sqrt{K_{\mathrm{w}}} = \sqrt{1 \times 10^{-14}\ \mathrm{M}^2}$$

$$[\mathrm{H}^+] = [\mathrm{OH}^-] = 10^{-7}\ \mathrm{M}$$

The **concentration of pure water** at 25 °C is **55.5 M** (grams of H_2O in 1 L divided by its gram molecular weight: (1,000 g/L)/(18.0 g/mol)).

Kw = the ion product of water at 25 °C.

The value for *K_{eq}*, determined by electrical-conductivity measurements of pure water,

$K_{eq} = 1.8 \times 10^{-16}$ M at 25 °C .

pH

- What does pH mean?

- power of hydrogen → Denmark
- potenz (also meaning power) → German
- puissance → French
- pondus hydrogenii (meaning quantity of hydrogen) → Romans
- potentia hydrogenii (capacity of hydrogen) → Romans
- potential hydrogen → British
- p = -log "mathematicians"

- The **initials pH stand for "power of hydrogen**" or "**Potential of Hydrogen**" The pH of a solution is nothing more than that, the potential of Hydrogen
- pH= - log $[H^+]$ → for pure water pH =-log $[10^{-7}]$ = 7

- pOH = - log $[OH^-]$
- $[H^+]$ $[OH^-]$= 10^{-14}

- **pH + pOH= 14**

The pH Scale

$[H^+]$ (M)	pH	$[OH^-]$ (M)	pOH*
10^{0} (1)	0	10^{-14}	14
10^{-1}	1	10^{-13}	13
10^{-2}	2	10^{-12}	12
10^{-3}	3	10^{-11}	11
10^{-4}	4	10^{-10}	10
10^{-5}	5	10^{-9}	9
10^{-6}	6	10^{-8}	8
10^{-7}	7	10^{-7}	7
10^{-8}	8	10^{-6}	6
10^{-9}	9	10^{-5}	5
10^{-10}	10	10^{-4}	4
10^{-11}	11	10^{-3}	3
10^{-12}	12	10^{-2}	2
10^{-13}	13	10^{-1}	1
10^{-14}	14	10^{0} (1)	0

pH	Examples of solutions
0	Battery acid, strong hydrofluoric acid
1	Hydrochloric acid secreted by stomach lining
2	Lemon juice, gastric acid, vinegar
3	Grapefruit juice, orange juice, soda
4	Tomato juice, acid rain
5	Soft drinking water, black coffee
6	Urine, saliva
7	"Pure" water
8	Sea water
9	Baking soda
10	Great Salt Lake, milk of magnesia
11	Ammonia solution
12	Soapy water
13	Bleach, oven cleaner
14	Liquid drain cleaner

Strong and weak acids and bases

- **Strong acids** such as: Hydrochloric (HCl), sulfuric (H_2SO_4), and nitric acids (HNO_3), **are completely ionized** in aqueous solutions

  HCH $\longrightarrow$ H+ + Cl-

- **Strong bases** NaOH and KOH are also completely ionized.

  NaOH $\longrightarrow$ Na+ + OH-

- However, **weak acids and bases** are not completely ionized when dissolved in water, they **partially ionized** .Therefore, their behavior in aqueous solution is characterized by an equilibrium reaction, and **equilibrium constant, K_{eq}**
- According to Brønsted-Lowry definition, acids are proton donors and bases are proton acceptors

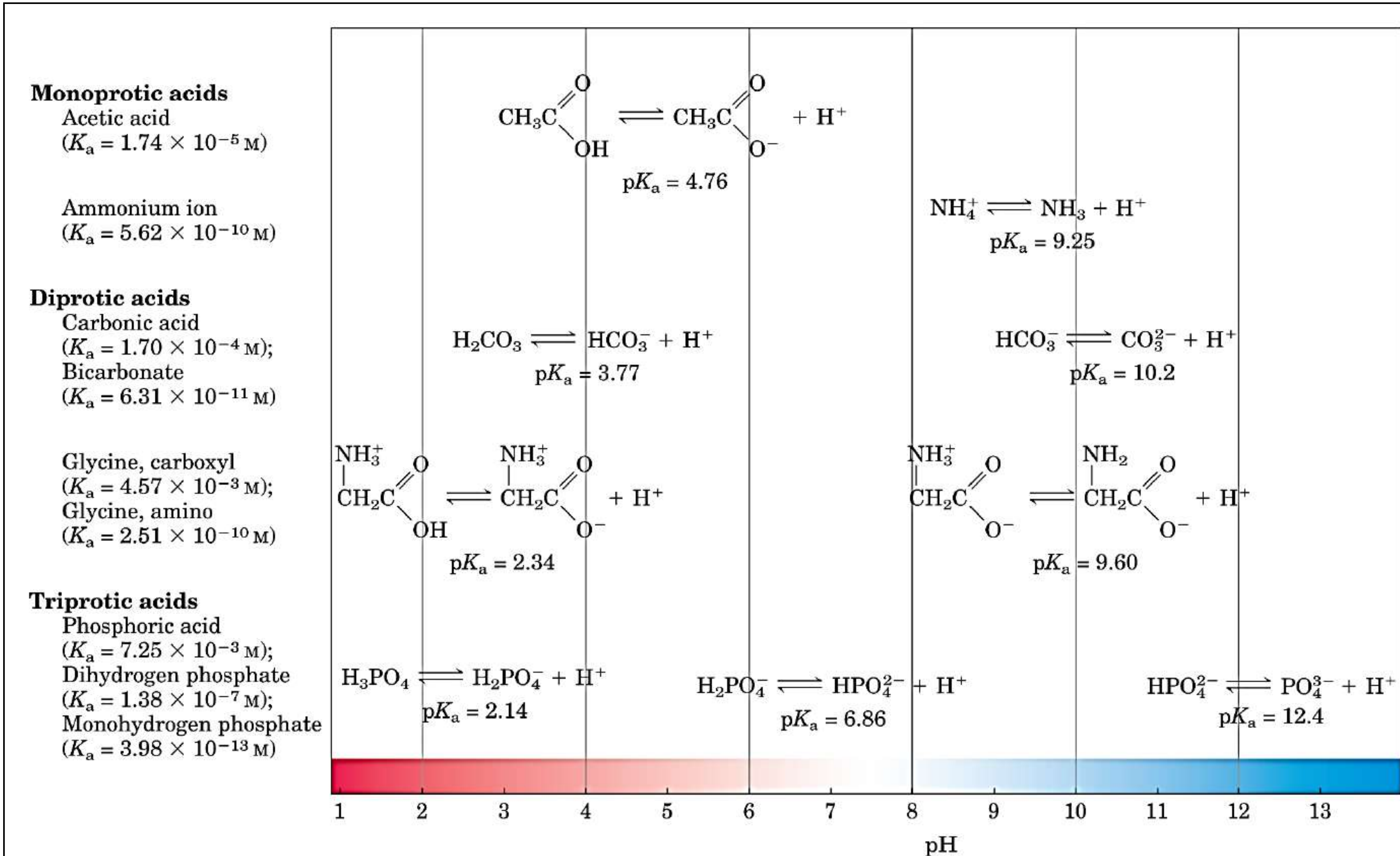
$$\mathrm{HA} \rightleftharpoons \mathrm{H}^+ + \mathrm{A}^-$$

$$K_{\mathrm{eq}} = \frac{[\mathrm{H}^+][\mathrm{A}^-]}{[\mathrm{HA}]} = K_{\mathrm{a}}$$

$$\mathrm{CH_3COOH} \rightleftharpoons \mathrm{H}^+ + \mathrm{CH_3COO}^-$$

- **Equilibrium constants K_{eq} for ionization** reactions are usually called ionization or dissociation constants, often **designated K_a**

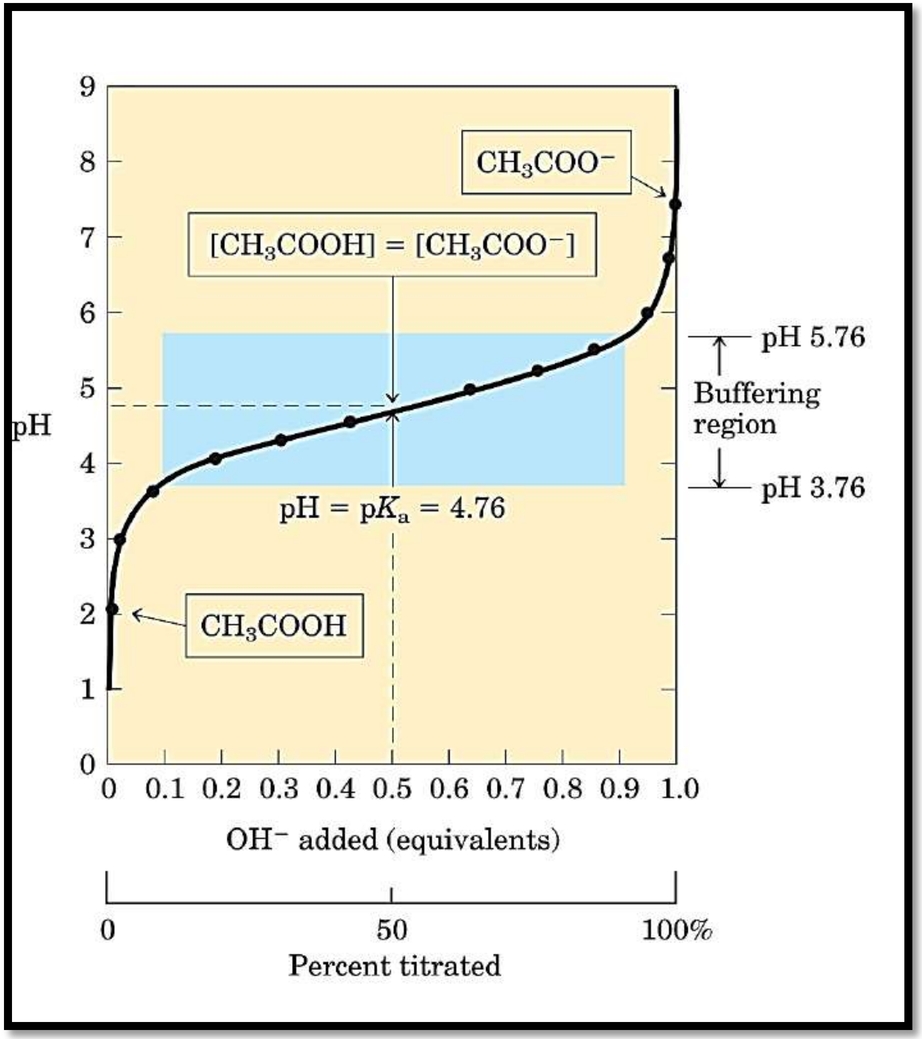
The dissociation constants of some acids: monoprotic, diprotic, polyprotic



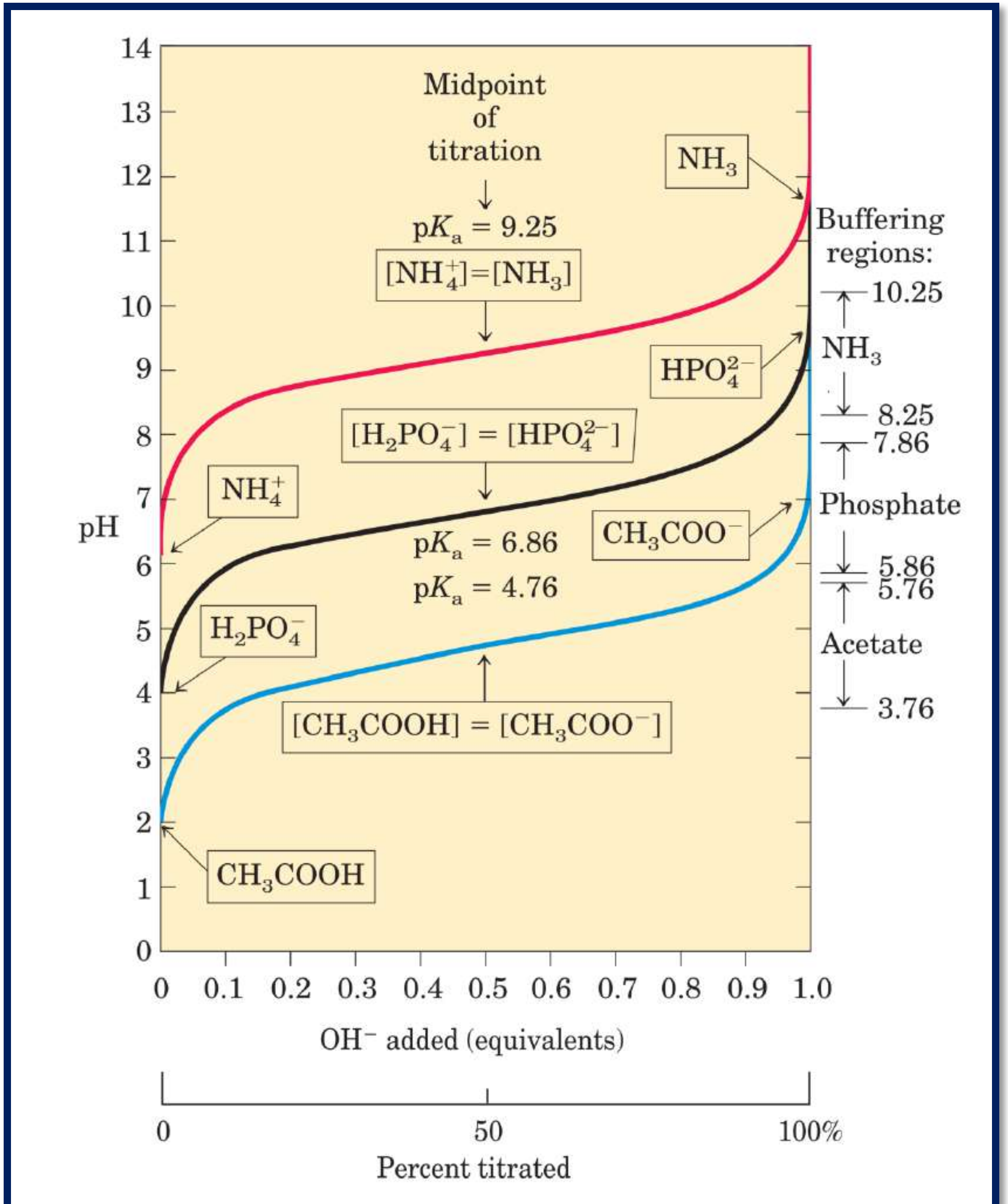
p*K*a = - log *K*a; The stronger the tendency to dissociate a proton, the stronger is the acid and the lower its p*K*a.

Weak Acids have Characteristic titration curves

- **Titration** is used to determine the **amount of an acid** in a given solution.
- During titration, a **measured volume of the acid is titrated** with a solution of **a strong base**, usually sodium hydroxide (NaOH), of known concentration.
- The NaOH is added in small increments until the acid is consumed (neutralized), The concentration of the acid in the original solution can be calculated from the volume and concentration of NaOH added.
- A plot of pH against the amount of NaOH added (a **titration curve**) reveals the p*K*a of the weak acid



The titration curve of acetic acid

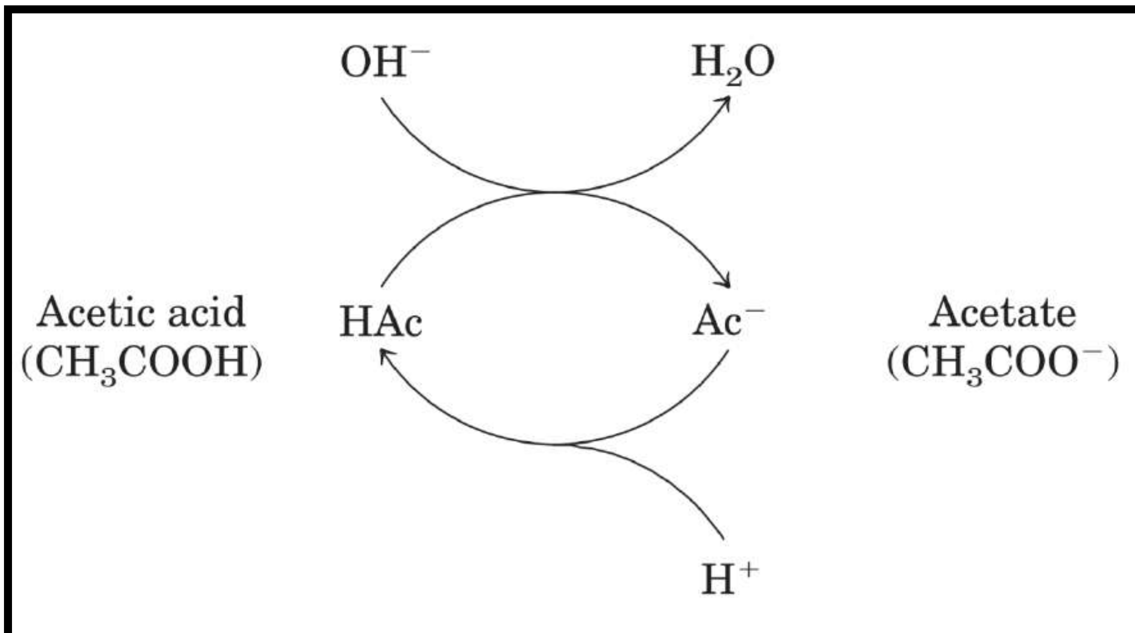


14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
pH
Midpoint
of
titration
$pK_a = 9.25$
$[NH_4^+]=[NH_3]$
NH_3
Buffering
regions:
10.25
NH_3
8.25
7.86
Phosphate
5.86
5.76
Acetate
3.76
HPO_4^{2-}
$[H_2PO_4^-] = [HPO_4^{2-}]$
NH_4^+
$pK_a = 6.86$
$pK_a = 4.76$
CH_3COO^-
$H_2PO_4^-$
$[CH_3COOH] = [CH_3COO^-]$
CH_3COOH
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0
OH^- added (equivalents)
0
50
100%
Percent titrated

Buffers Are Mixtures of Weak Acids and Their Conjugate Bases

- Almost every biological process **is pH dependent**; a small change in pH produces a large change (**unfavorable**) in the rate of the process.
- Cells and organisms **maintain** a specific and constant cytosolic pH, keeping biomolecules in their optimal ionic state, usually near pH 7.
- In multicellular organisms, the **pH of extracellular** fluids is also tightly regulated. **Constancy of pH is achieved primarily by biological buffers**.

- **Buffers are aqueous systems** that tend to **resist changes** in pH when small amounts of acid (H+) or base (OH-) are added. **A buffer system consists of** a weak acid (the proton donor) and its conjugate base (the proton acceptor).



Henderson-Hasselbalch equation relates pH, p*K*a, and Buffer Concentration

$$HA \rightleftharpoons H^+ + A^-$$

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

First solve for $[H^+]$: $\longrightarrow$ $[H^+] = K_a \frac{[HA]}{[A^-]}$

Then take the negative logarithm of both sides:

$$-\log [H^+] = -\log K_a - \log \frac{[HA]}{[A^-]}$$

Substitute pH for $-\log [H^+]$ and pK_a for $-\log K_a$:

$$pH = pK_a - \log \frac{[HA]}{[A^-]}$$

Now invert $-\log [HA]/[A^-]$

$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$

Stated more generally,

$$pH = pK_a + \log \frac{[\text{proton acceptor}]}{[\text{proton donor}]}$$

Biological Buffers protect Cells and Tissues against pH Changes

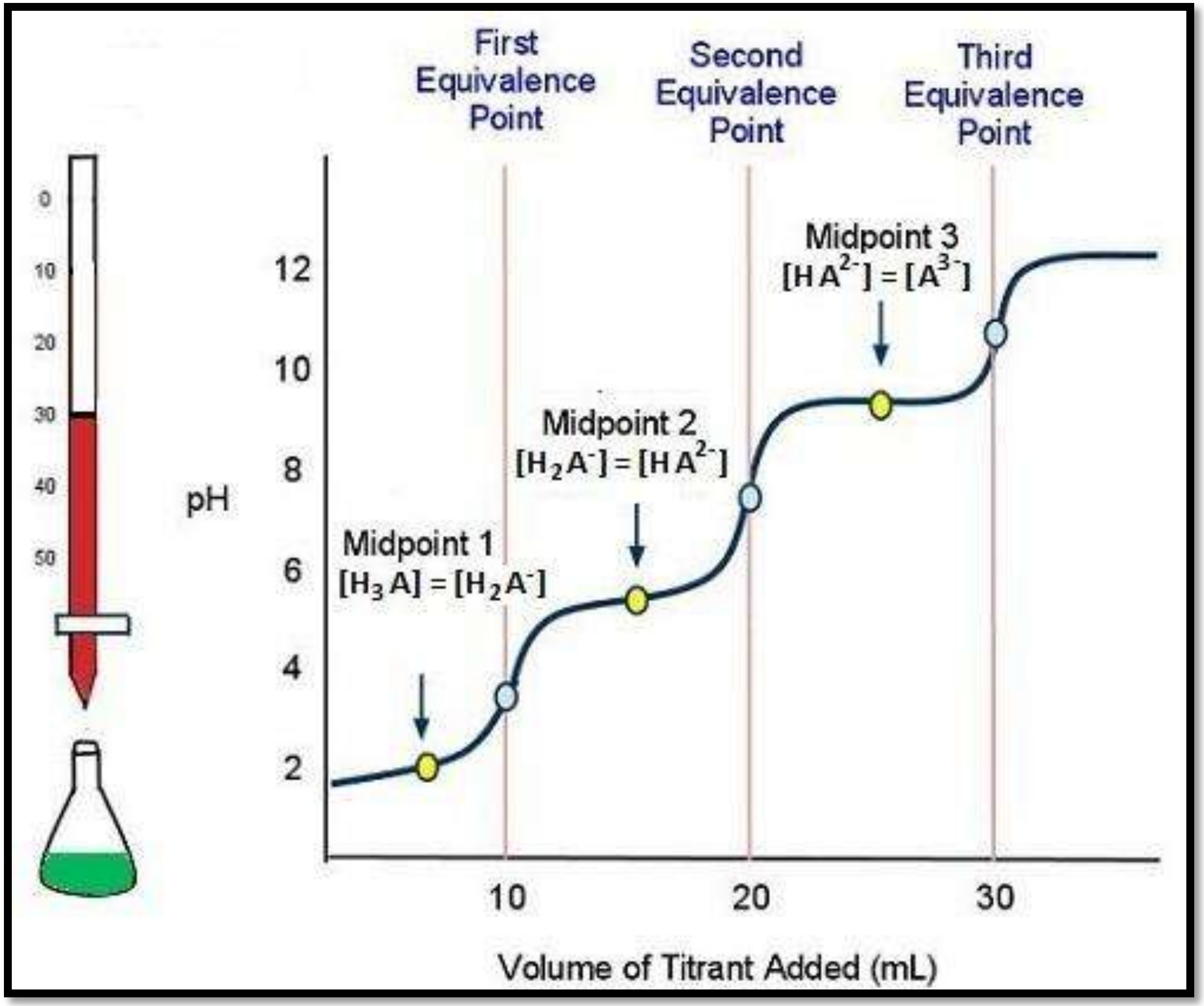
- The intracellular and extracellular fluids of multicellular organisms have a **characteristic and nearly constant pH**.
- The organism's **first line of defense** against changes in internal pH is provided by **buffer systems**.
- The cytoplasm of most cells contains high concentrations of **proteins**, which contain **many amino acids** with functional groups that are **weak acids or weak bases**.
- **Weak acids and its conjugate** base provide best **buffering power** around (±1) the pKa.
- Two especially important biological buffers are the **phosphate and bicarbonate** systems.
- The phosphate buffer system, which acts in the cytoplasm of all cells, consists of **$H_2PO^-_4$ as proton donor and HPO_4^{-2}** as proton acceptor
- The phosphate buffer system is maximally effective at a pH close to its pKa of 6.86 and thus tends to resist pH changes in the range between about 5.9 and 7.9.

$$H_2PO_4^- \rightleftharpoons H^+ + HPO_4^{2-}$$

- Blood plasma is buffered in part by the bicarbonate system, consisting of carbonic acid (H_2CO_3) as proton donor and bicarbonate (HCO_3^-) as proton acceptor:

$$H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

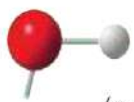
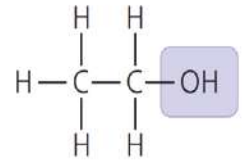
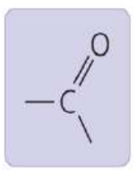
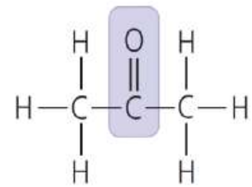
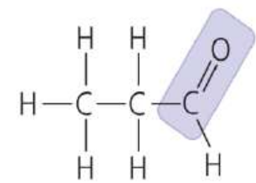
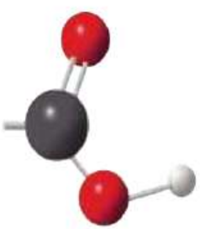
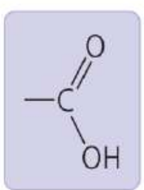
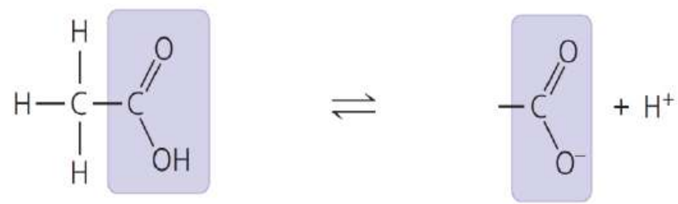
Titrantion curve of polyprotic (triprotic) acid

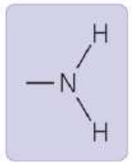
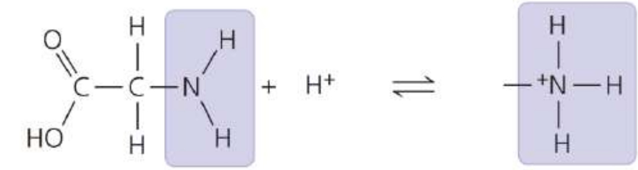
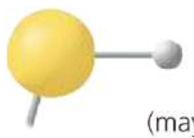
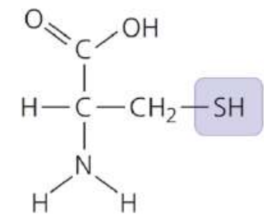
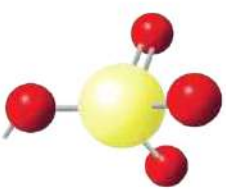
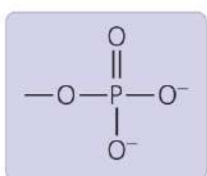
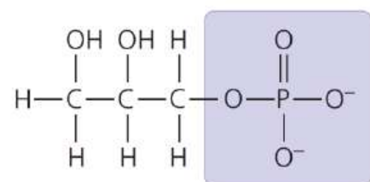
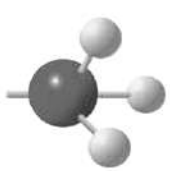
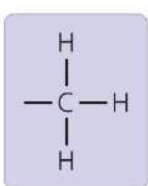
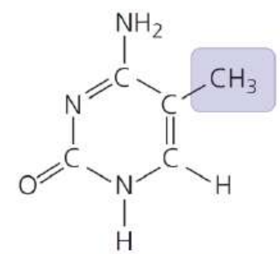


Macromolecules: The Chemical Building Blocks of Life

- The frameworks of **biological molecules** consist predominantly of **carbon** atoms bonded to **other carbon atoms or to atoms of oxygen, nitrogen, sulfur or hydrogen.**
- Because carbon atoms possess four valence electrons and so can form four covalent bonds, **molecules containing carbon** can form straight chains, branches, or even rings, generating **a wide range of molecular structures** and shapes.
- Organic molecules consisting only of carbon and hydrogen are called **hydrocarbons.** Covalent bonds between carbon and hydrogen **are energy-rich** making hydrocarbons as good fuels.
- Carbon and hydrogen atoms both have **very similar electronegativities**, so electrons in C—C and C—H bonds are evenly distributed, and there are no significant differences in charge over the molecular surface. For this reason, **hydrocarbons are nonpolar**.
- **Most organic molecules** (biological molecules) that are produced by cells contain **C—H core to which specific groups** of atoms called functional groups are attached. These atoms that often have **different electronegativities** giving biological molecules their **polar characteristics**

Functional Groups

Chemical Group	Group Properties and Compound Name	Examples
Hydroxyl group (—OH)  —OH (may be written HO—)	Is polar due to electronegative oxygen. Forms hydrogen bonds with water, helping dissolve compounds such as sugars. Compound name: **Alcohol** (specific name usually ends in *-ol*)	 **Ethanol**, the alcohol present in alcoholic beverages
Carbonyl group (⟩C=O)  	Sugars with ketone groups are called ketoses; those with aldehydes are called aldoses. Compound name: **Ketone** (carbonyl group is within a carbon skeleton) or **aldehyde** (carbonyl group is at the end of a carbon skeleton)	 **Acetone**, the simplest ketone  **Propanal**, an aldehyde
Carboxyl group (—COOH)  	Acts as an acid (can donate H^+) because the covalent bond between oxygen and hydrogen is so polar. Compound name: **Carboxylic acid**, or **organic acid**	 **Acetic acid**, which gives vinegar its sour taste; Ionized form of —COOH (carboxylate ion), found in cells

Chemical Group	Group Properties and Compound Name	Examples
Amino group (—NH_2)  	Acts as a base; can pick up an H^+ from the surrounding solution (water, in living organisms). Compound name: **Amine**	 **Glycine**, an amino acid (note its carboxyl group) Ionized form of —NH_2, found in cells
Sulfhydryl group (—SH)  —SH (may be written HS —)	Two —SH groups can react, forming a "cross-link" that helps stabilize protein structure. Hair protein cross-links maintain the straightness or curliness of hair; in hair salons, "permanent" treatments break cross-links, then re-form them while the hair is in the desired shape. Compound name: **Thiol**	 **Cysteine**, a sulfur-containing amino acid
Phosphate group (—OPO_3^{2-})  	Contributes negative charge (1– when positioned inside a chain of phosphates; 2– when at the end). When attached, confers on a molecule the ability to react with water, releasing energy. Compound name: **Organic phosphate**	 **Glycerol phosphate**, which takes part in many important chemical reactions in cells
Methyl group (—CH_3)  	Affects the expression of genes when bonded to DNA or to proteins that bind to DNA. Affects the shape and function of male and female sex hormones. Compound name: **Methylated compound**	 **5-Methylcytosine**: Cytosine, a component of DNA, has been modified by addition of a methyl group.

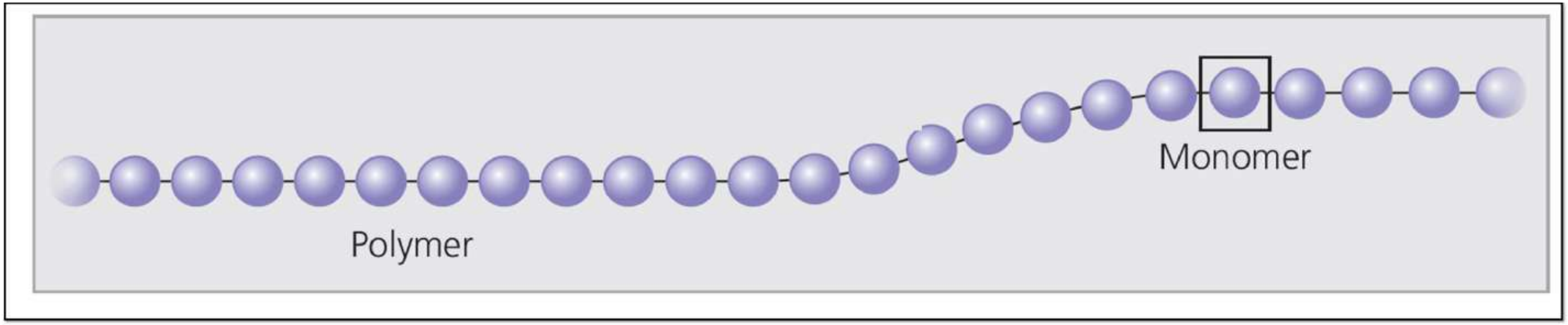
Biological Macromolecules

- Some organic molecules in organisms are small and simple, containing only one or a few functional groups. Others are large complex assemblies called **macromolecules.**

- In many cases, these **macromolecules are usually polymers**, molecules consisting of **many similar or identical building** blocks (called **monomers**) linked by covalent bonds.

- In addition to forming polymers, **some monomers have functions of their own**. For example, complex carbohydrates like starch are polymers of simple ring-shaped sugars, proteins are polymers of amino acids, and nucleic acids (DNA and RNA) are polymers of nucleotides.
- Biological macromolecules are traditionally grouped into **four major categories**:

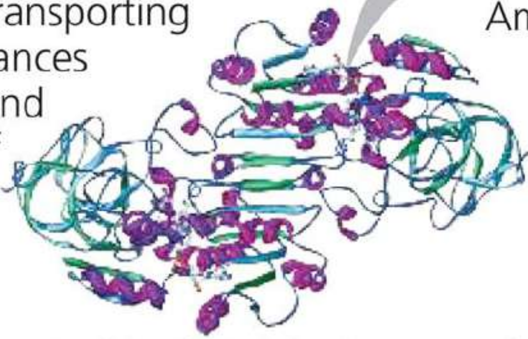
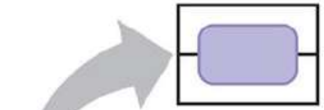
Proteins **Nucleic acids** **Lipids** **Carbohydrates**



Carbohydrates are a source of energy and provide structural support.

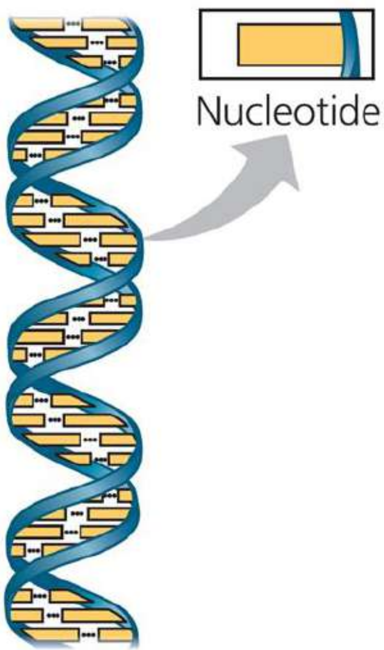
Carbohydrate (starch)

Proteins have a wide range of functions, such as catalyzing reactions and transporting substances into and out of cells.

Protein (alcohol dehydrogenase)

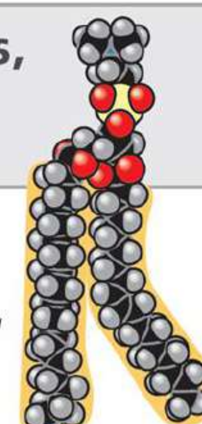
Nucleic acids store genetic information and function in gene expression.



Nucleic acid (DNA)

The fourth class, lipids, are not polymers

Lipids are a group of diverse molecules that do not mix well with water. Key functions include providing energy, making up cell membranes, and acting as hormones.



Lipid (phospholipid)

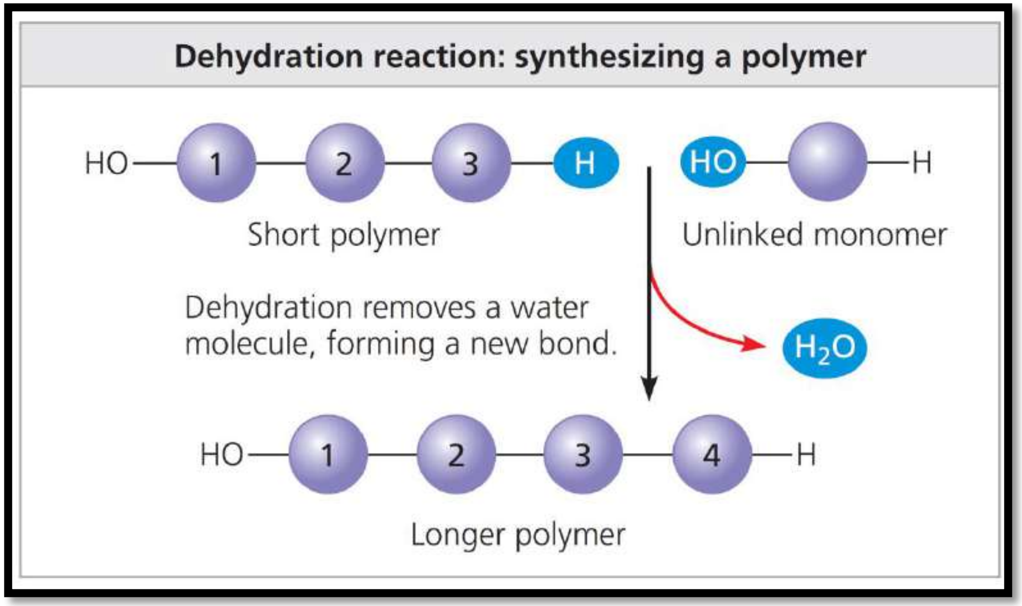
Macromolecules

Macromolecule	Subunit	Function	Example
CARBOHYDRATES			
Starch, glycogen	Glucose	Energy storage	Potatoes
Cellulose	Glucose	Structural support in plant cell walls	Paper; strings of celery
Chitin	Modified glucose	Structural support	Crab shells
NUCLEIC ACIDS			
DNA	Nucleotides	Encodes genes	Chromosomes
RNA	Nucleotides	Needed for gene expression	Messenger RNA
PROTEINS			
Functional	Amino acids	Catalysis; transport	Hemoglobin
Structural	Amino acids	Support	Hair; silk
LIPIDS			
Triglycerides (animal fat, oils)	Glycerol and three fatty acids	Energy storage	Butter; corn oil; soap
Phospholipids	Glycerol, two fatty acids, phosphate, and polar R groups	Cell membranes	Phosphatidylcholine
Prostaglandins	Five-carbon rings with two nonpolar tails	Chemical messengers	Prostaglandin E (PGE)
Steroids	Four fused carbon rings	Membranes; hormones	Cholesterol; estrogen
Terpenes	Long carbon chains	Pigments; structural support	Carotene; rubber

The Synthesis and Breakdown of Polymers

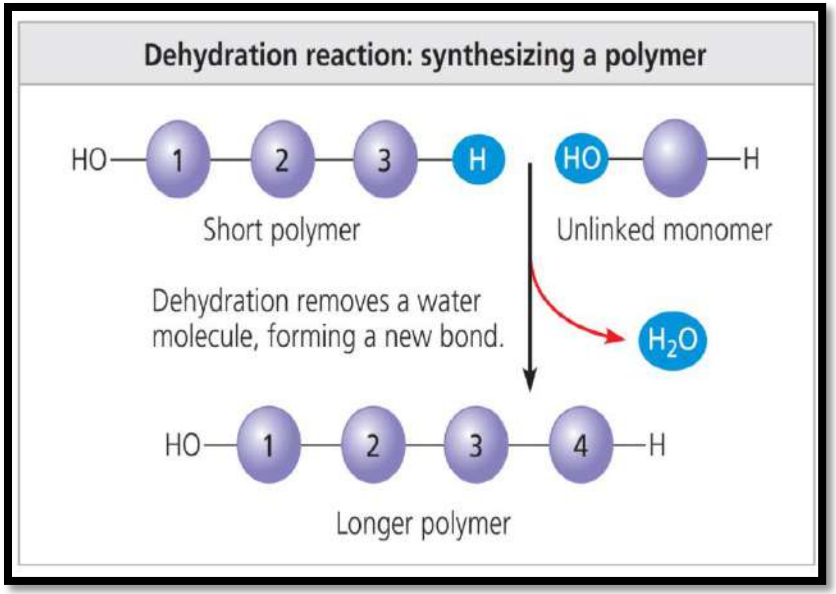
- Although **each class of polymer** is made up of a **different** type of monomer, the chemical mechanisms by which cells make polymers **(polymerization) and break them** down are **similar** for all classes of large biological molecules and, these processes are facilitated by **enzymes** that speed up (**catalysis**) chemical reactions.
- The reaction that connects a monomer to another monomer or a polymer is ***a condensation reaction***, a reaction in which two molecules are covalently bonded to each other with the **loss of a water** molecule so it is known as a **dehydration reaction**. For every subunit that is added to a macromolecule, **one water molecule is removed**. Energy is required to break the chemical bonds when water is extracted from the subunits, so cells **must supply energy** to assemble macromolecules.

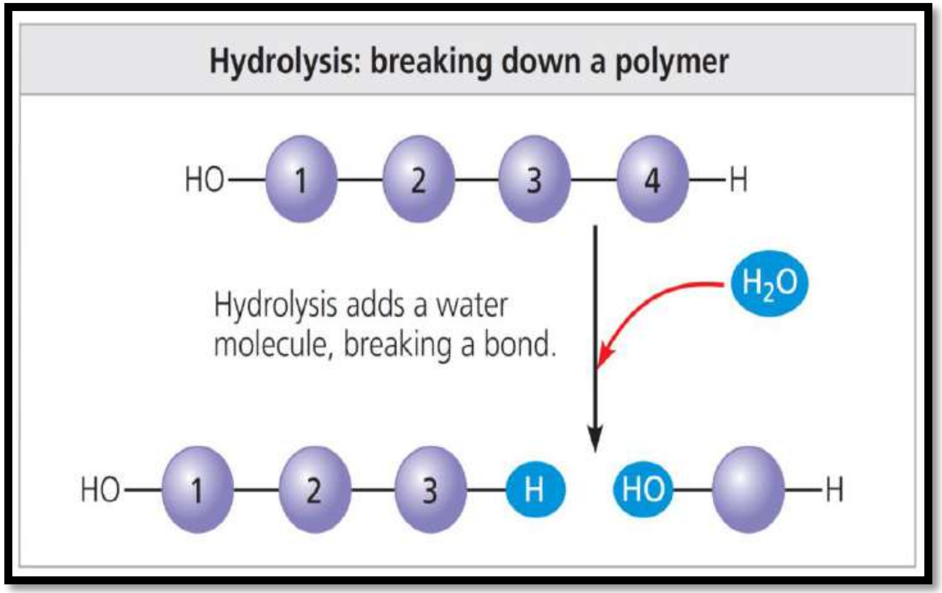
For example, carbohydrate and protein polymers are synthesized by **dehydration reactions**. Each reactant contributes part of the water molecule that is released during the reaction: **One provides a hydroxyl group (—OH), while the other provides a hydrogen (—H).**
This reaction is repeated as monomers are added to the chain one by one, lengthening the polymer



The Synthesis and Breakdown of Polymers

- Polymers are disassembled to monomers by **hydrolysis**, a process that is essentially the **reverse of the dehydration reaction** during which the bond between monomers is broken by the **addition of a water** molecule, with a hydrogen from water attaching to one monomer and the hydroxyl group attaching to the other.
- **Hydrolytic reactions release the energy** that was stored in the bonds that were broken.





Carbohydrates

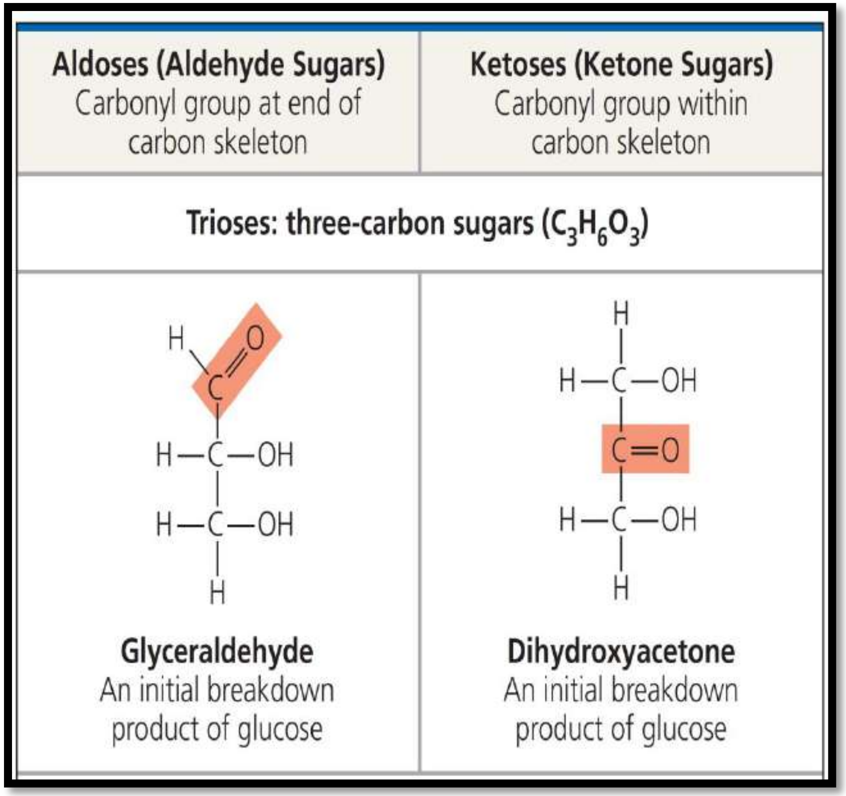
- Carbohydrates serve as **fuel** and **building material** and include sugars and polymers of sugars.
- Carbohydrates are polyhydroxy aldehydes or ketones, or substances that yield such compounds on hydrolysis.
- Many, but not all, carbohydrates have the **empirical formula (CH_2O)*n*;**
- There are three major size classes of carbohydrates:
  - **monosaccharides,**
  - **oligosaccharides,**
  - **polysaccharides**
- The simplest carbohydrates are the **monosaccharides, or simple sugars**; these are the monomers from which more complex carbohydrates are built.
- **Disaccharides** are double sugars, consisting of two monosaccharides joined by a covalent bond (**glycosidic bond**)
- **Polysaccharides** are carbohydrate **polymers** composed of many sugar building blocks.

Sugars

- **Monosaccharides** (from the Greek monos, single, and sacchar, sugar) generally have molecular formulas that are some multiple of the unit **CH_2O**.
- **Glucose ($C_6H_{12}O_6$)**, the most common monosaccharide, is of central importance in the chemistry of life

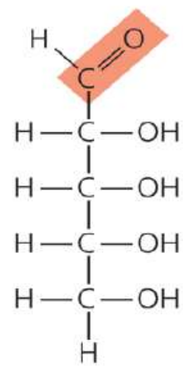
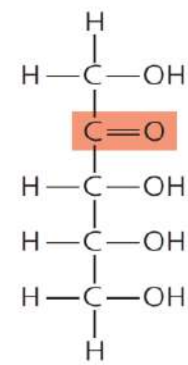
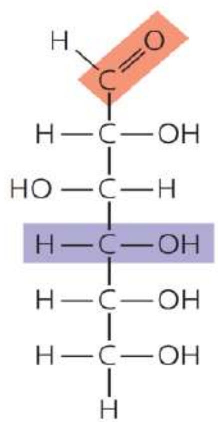
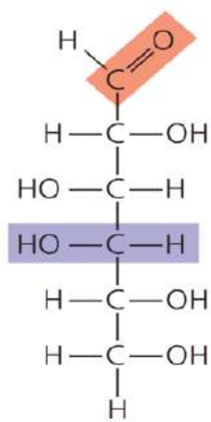
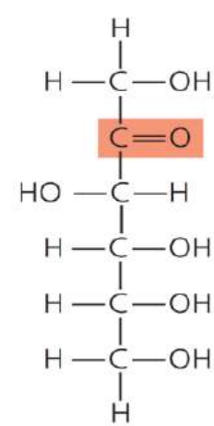
- Depending on the **location of the carbonyl group**, a monosaccharide is either an **aldose** (aldehyde sugar) or a **ketose** (ketone sugar).
- Glucose, for example, is an aldose; fructose, is a ketose.
- Another criterion for classifying monosaccharides is the **size of the carbon skeleton**, which ranges from **3 to 7 carbons** long.
- Glucose, fructose, and other sugars that have **six** carbons are called **hexoses**.

- **Trioses** (**three-carbon** sugars) and **pentoses** (five-carbon sugars) are also common.



The simplest monosaccharides are the two three-carbon trioses:

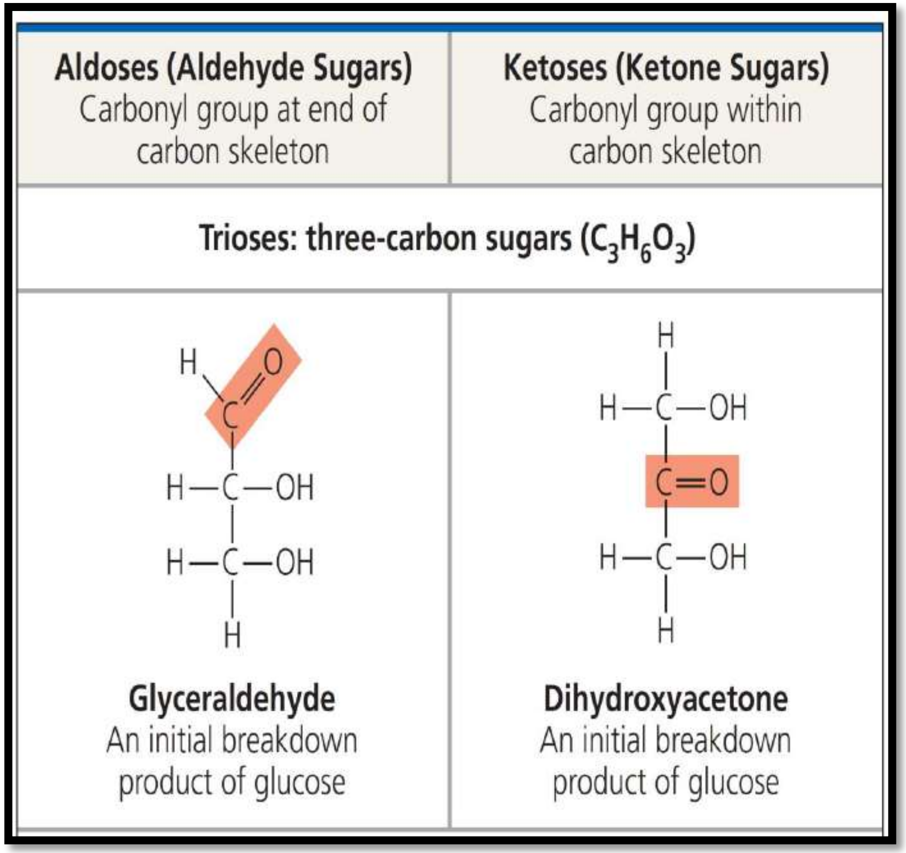
- **Glyceraldehyde, an aldotriose**
- **Dihydroxyacetone, a ketotriose**

Aldoses (Aldehyde Sugars) Carbonyl group at end of carbon skeleton	**Ketoses (Ketone Sugars)** Carbonyl group within carbon skeleton
Pentoses: five-carbon sugars ($C_5H_{10}O_5$)	
 **Ribose** A component of RNA	 **Ribulose** An intermediate in photosynthesis
Hexoses: six-carbon sugars ($C_6H_{12}O_6$)	
  **Glucose** **Galactose** Energy sources for organisms	 **Fructose** An energy source for organisms

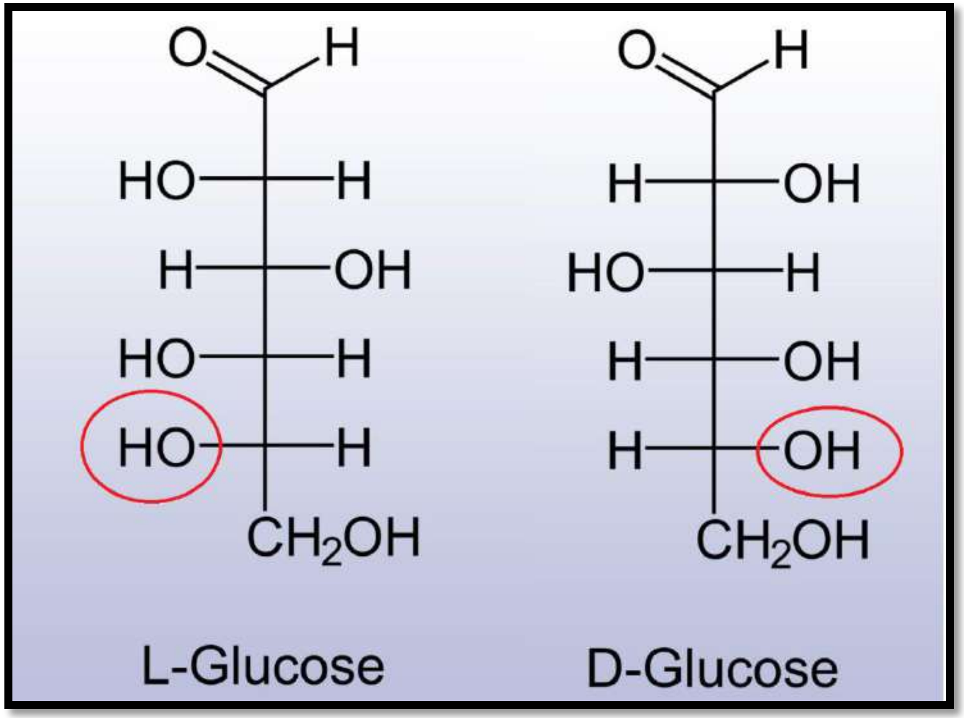
Monosaccharides Have Asymmetric Centers

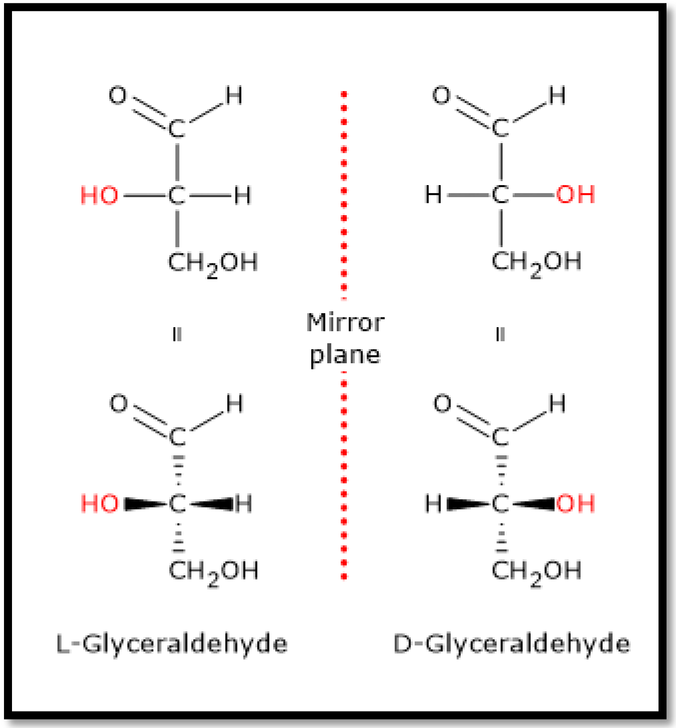
- All the monosaccharides **except dihydroxyacetone** contain one or more asymmetric (**chiral**) carbon atoms (carbon attached to four different atoms or groups of atoms and thus occur in optically active isomeric forms.
- All pure **chiral compounds** are **optically active**
- Many of the carbon atoms to which hydroxyl groups are attached are chiral centers, which give rise to the many sugar stereoisomers found in nature.

- The simplest aldose, **glyceraldehyde**, contains **one chiral center** (the middle carbon atom) and therefore has two different optical isomers, or enantiomers
- By convention, one of these two forms is designated the **D isomer, the other the L isomer.**

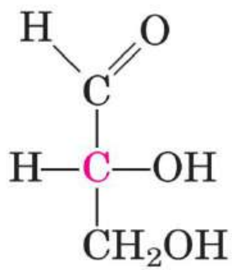


Stereoisomers of monosaccharides

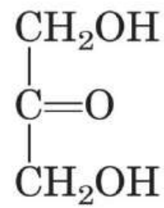




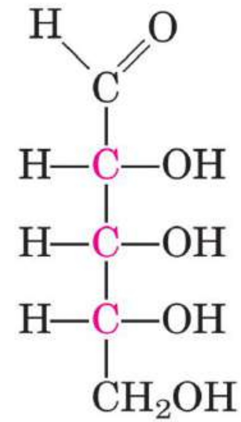
The stereoisomers of monosaccharides of each carbon-chain length can be divided into **D and L** as they differ in the configuration about the **chiral center** (asymmetric carbon atom) **most distant** from the carbonyl carbon



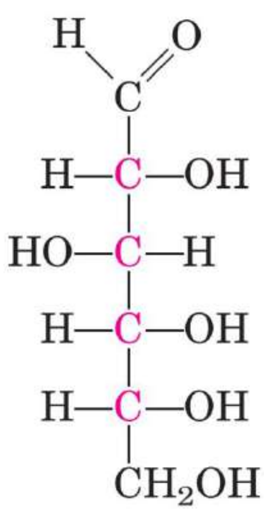
D-Glyceraldehyde



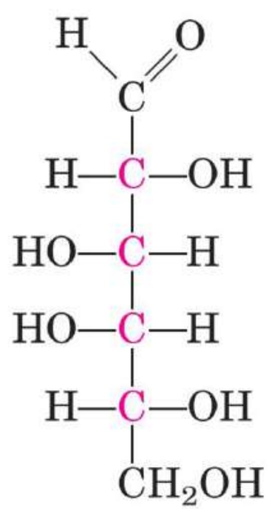
Dihydroxyacetone



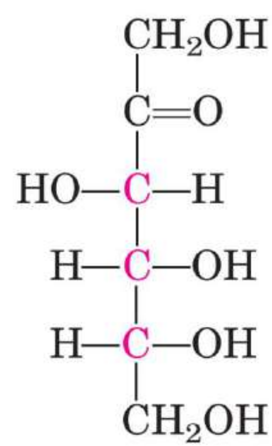
D-Ribose



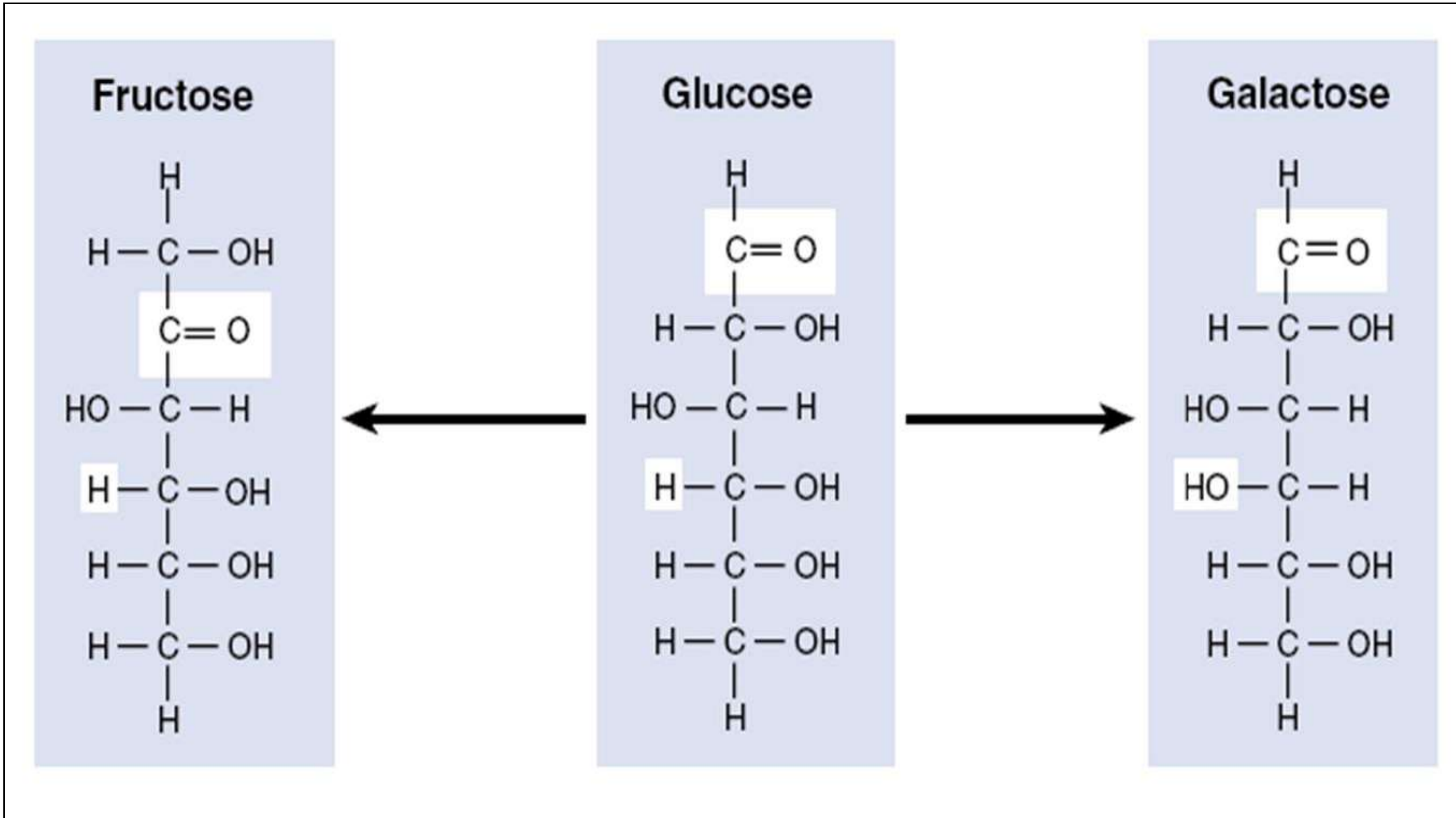
D-Glucose



D-Galactose

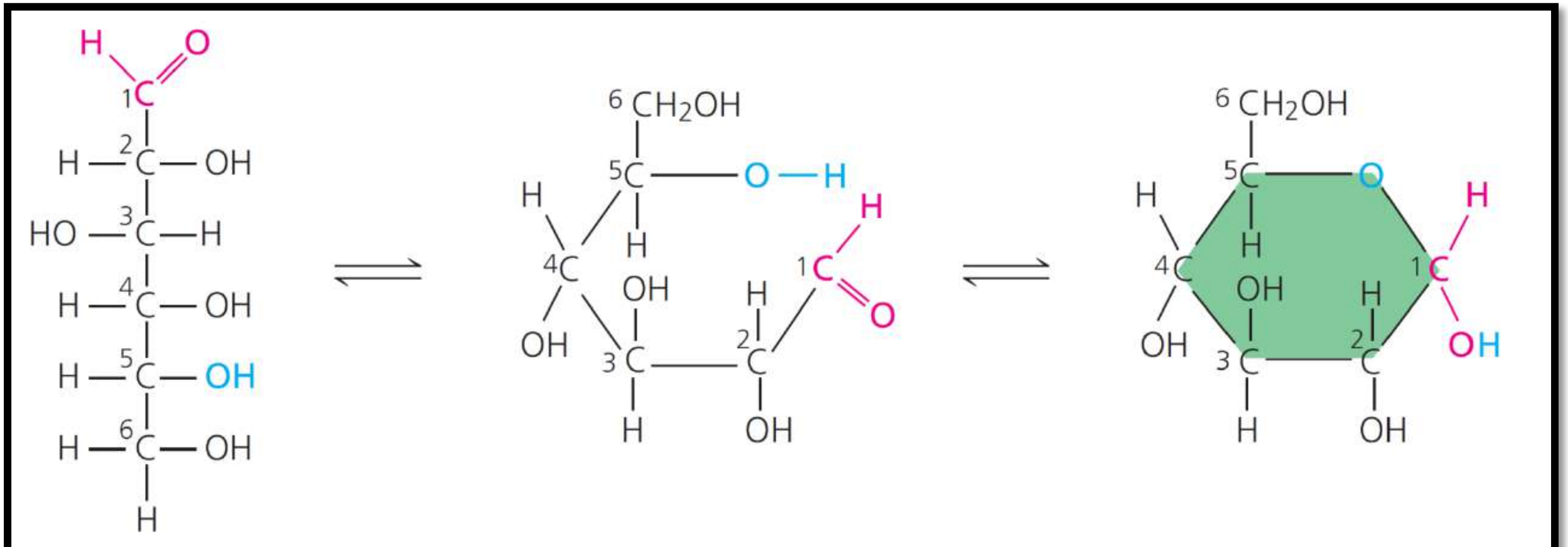


D-Fructose


Fructose
Glucose
Galactose

Linear and ring forms of monosaccharides

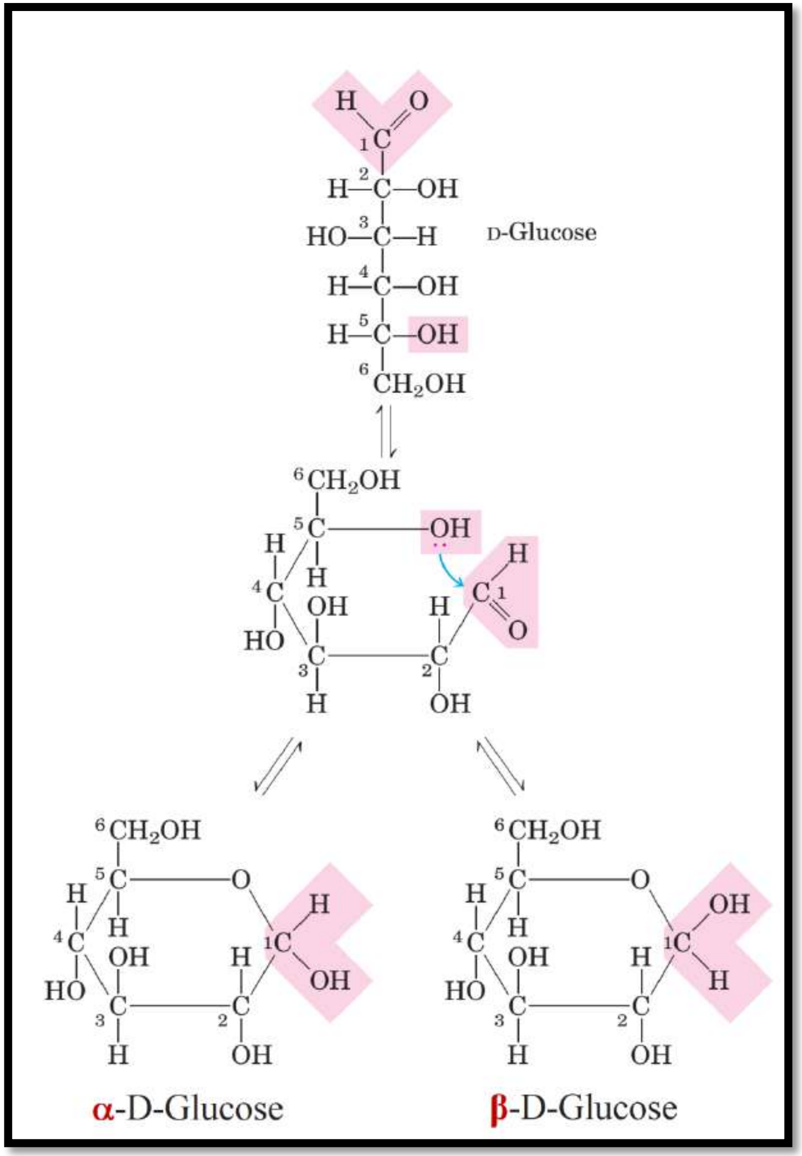
- In aqueous solutions, glucose molecules, as well as **most other five- and six-carbon** monosaccharides, **form rings**, because they are the **most stable form** of these sugars under physiological conditions.
- In these cyclic (ring) structures, the **carbonyl group** has formed a covalent bond with the **oxygen of a hydroxyl group** along the chain.
- The formation of these ring structures is the result of a general reaction between alcohols and aldehydes or ketones to form derivatives called **hemiacetals** or **hemiketals.**
- When an **alcohol adds to an aldehyde**, the result is called a hemiacetal; when an **alcohol adds to a ketone** the resulting product is a hemiketal.
- **Groups pointing to the right** in the Fisher (linear) straight chain form, they **point down in the ring form**, while those to the **left are point up** in the ring



α and β and anomers

- **Isomeric forms** of monosaccharides that differ only in **their configuration** about the hemiacetal or hemiketal carbon atom (anomeric carbon) are called **anomers**.

- The **α and β** anomers of D-glucose interconvert in aqueous solution by a process called **mutarotation**.

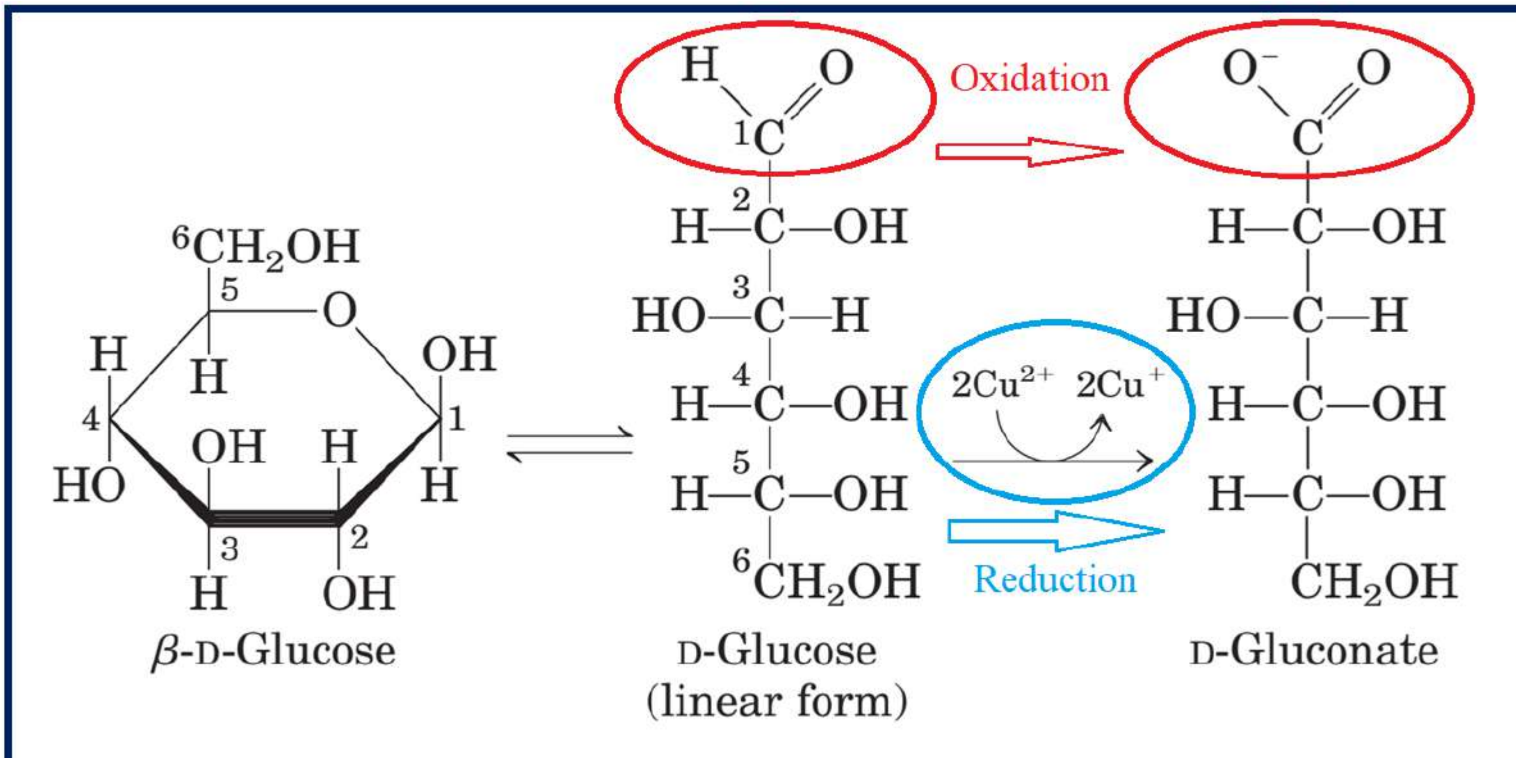


Classes of carbohydrates

- There are **three major size** classes of carbohydrates:
  - Monosaccharides
  - Oligosaccharides,
  - Polysaccharides
- **Monosaccharides**, or simple sugars, consist of a single polyhydroxy aldehyde or ketone unit. The **most abundant** monosaccharide in nature is the **six-carbon** sugar D-glucose, sometimes referred to as dextrose.
- **Oligosaccharides** consist of short chains of monosaccharide units, or residues, joined by characteristic linkages called glycosidic bonds. The **most abundant are the disaccharides**, with two monosaccharide units.
- In cells, **most oligosaccharides** consisting of **three or more units do not occur** as free entities but are joined to nonsugar molecules forming **glycoconjugates** (lipids: glycolipids or Proteins glycoproteins).
- The **polysaccharides** are sugar polymers containing more than **20 or so monosaccharide units**, and some have hundreds or thousands of units.
- Some polysaccharides, such as cellulose, are linear chains; others such as glycogen, are branched.

Monosaccharides are Reducing Agents

- Monosaccharides are Reducing Agents they can be oxidized by relatively mild oxidizing agents such as ferric (Fe^{3+}) or cupric (Cu^{2+}) ion.
- During this **reduction activity**, the carbonyl carbon (anomeric carbon) is oxidized to a carboxyl group.
- Sugars capable of reducing ferric or cupric ion are called **reducing sugars**.
- **Oxidation** is loss of electrons, loss of hydrogen or gain of oxygen
- **Reduction** is gain of electrons, gain of hydrogen, or loss of oxygen.



A disaccharide consists of two monosaccharides joined by a glycosidic linkage

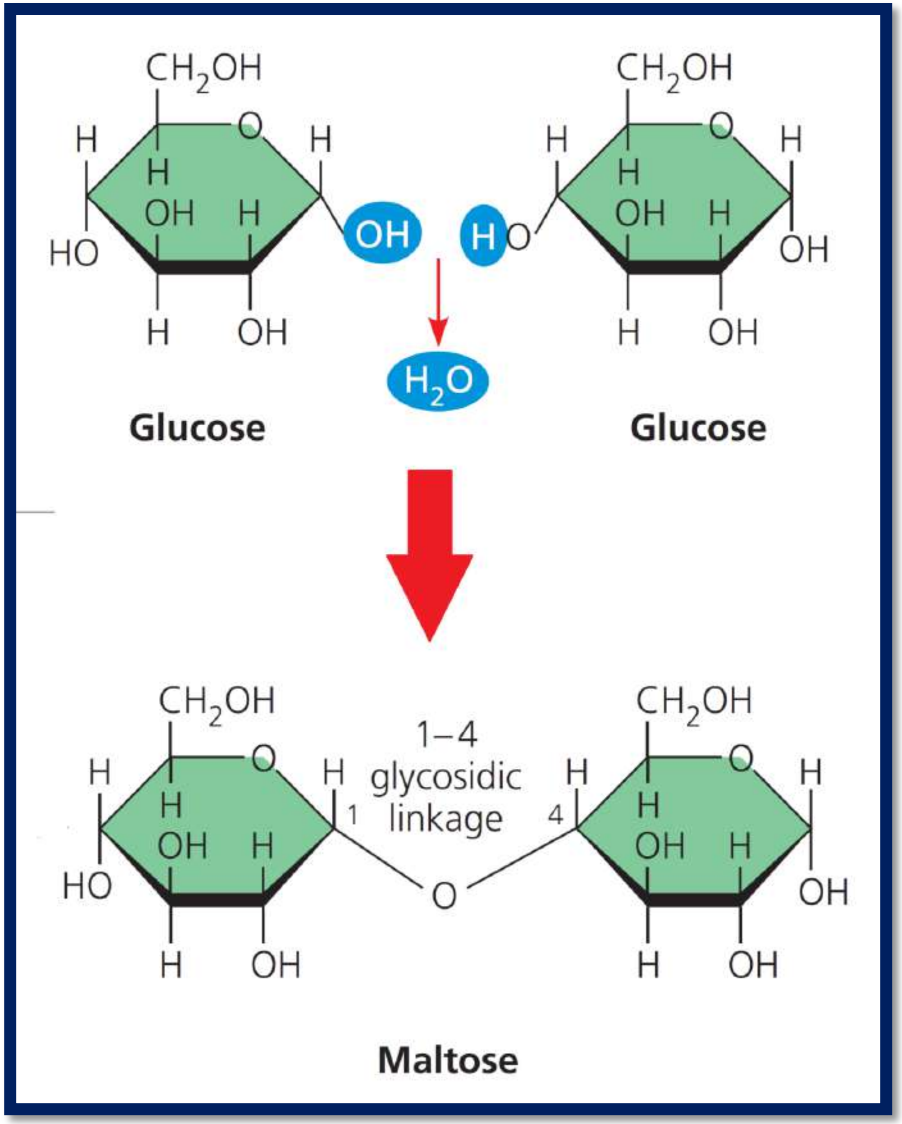
- A **disaccharide** consists of two monosaccharides joined by a **glycosidic linkage** (dehydration reaction), a covalent bond formed between two monosaccharides with a **hydroxyl group of one sugar and the anomeric** carbon of the other
- For example:
- **Maltose** is a disaccharide formed by the linking of **2 molecules of D-glucose**.
- **Sucrose**, the most prevalent disaccharide is formed by linking 2 different monomers: **D-glucose and D-fructose**
- **Lactose**, the sugar present in milk, is another disaccharide, in this case a **D-glucose joined to a D-galactose .**
- Disaccharides must be broken down into monosaccharides to be used for energy by organisms.

Dehydration reaction in the synthesis of maltose.

The bonding of two D-glucose units forms maltose.

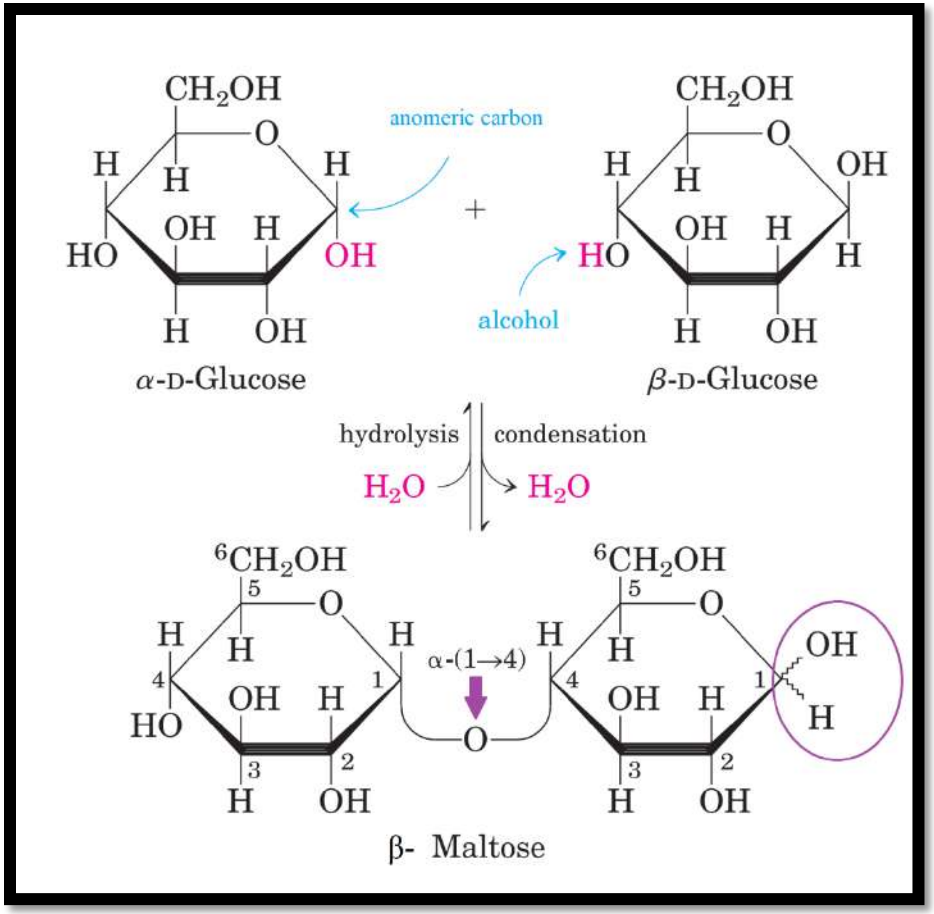
The **1→4 glycosidic linkage** joins the number 1 carbon of one D-glucose to the number 4 carbon of the second D-glucose.

Joining the glucose monomers in a **different way** would result in a different disaccharide.



The disaccharide maltose contains two **D-glucose residues** joined by a glycosidic linkage between C-1 (the anomeric carbon) of one glucose residue and C-4 of the other.

Because the disaccharide **maltose preserves a free anomeric** carbon C-1 of the glucose residue on the right, **maltose is a reducing sugar.**



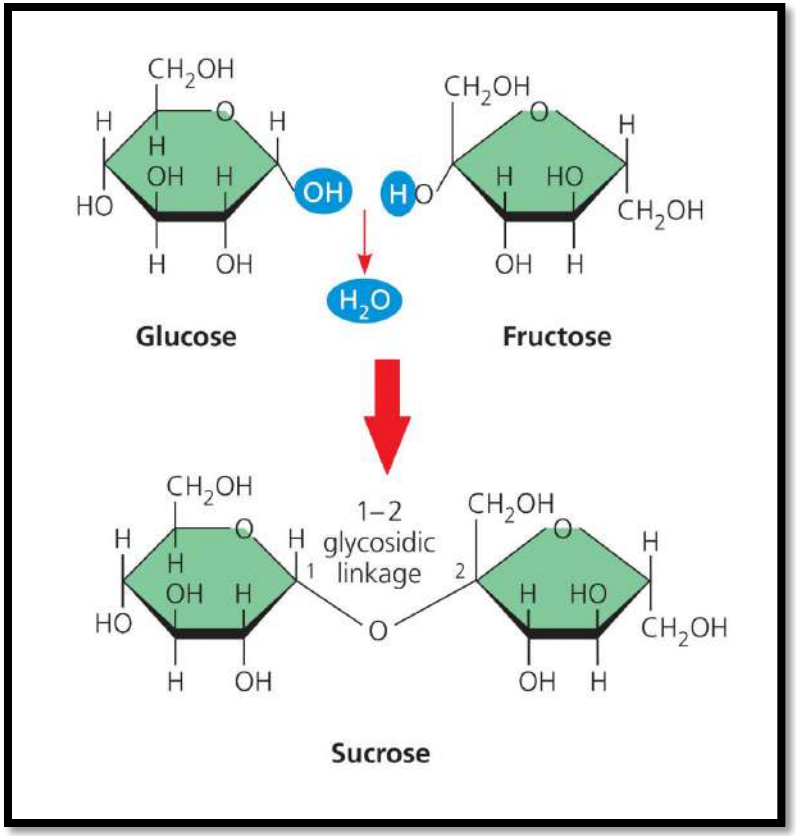
The **configuration** of the anomeric carbon atom in the **glycosidic linkage is α, so the linkage is α(1→4).**

The glucose residue with the **free anomeric** carbon is capable of existing in **α and β forms (anomers)**

Disaccharide Sucrose

- **Sucrose** is a disaccharide formed from **D-glucose and D-fructose.**
- Notice that fructose forms a five-sided ring, though it is a hexose like glucose.
- The **sucrose** molecule is **exceptional** among the common disaccharides in having an **α-1, β-2-glycosidic** (head-to-head) **α1↔ 2β** linkage.

- Because this **glycosidic linkage** is formed by the OH group on the anomeric carbon of α-D-glucose and the OH group on the **anomeric carbon of β-D-fructose,** it **ties up** the anomeric carbons of both glucose and fructose.
- In contrast to maltose and lactose, **sucrose** contains **no free anomeric carbon atom**; therefore, sucrose is **a non-reducing sugar**



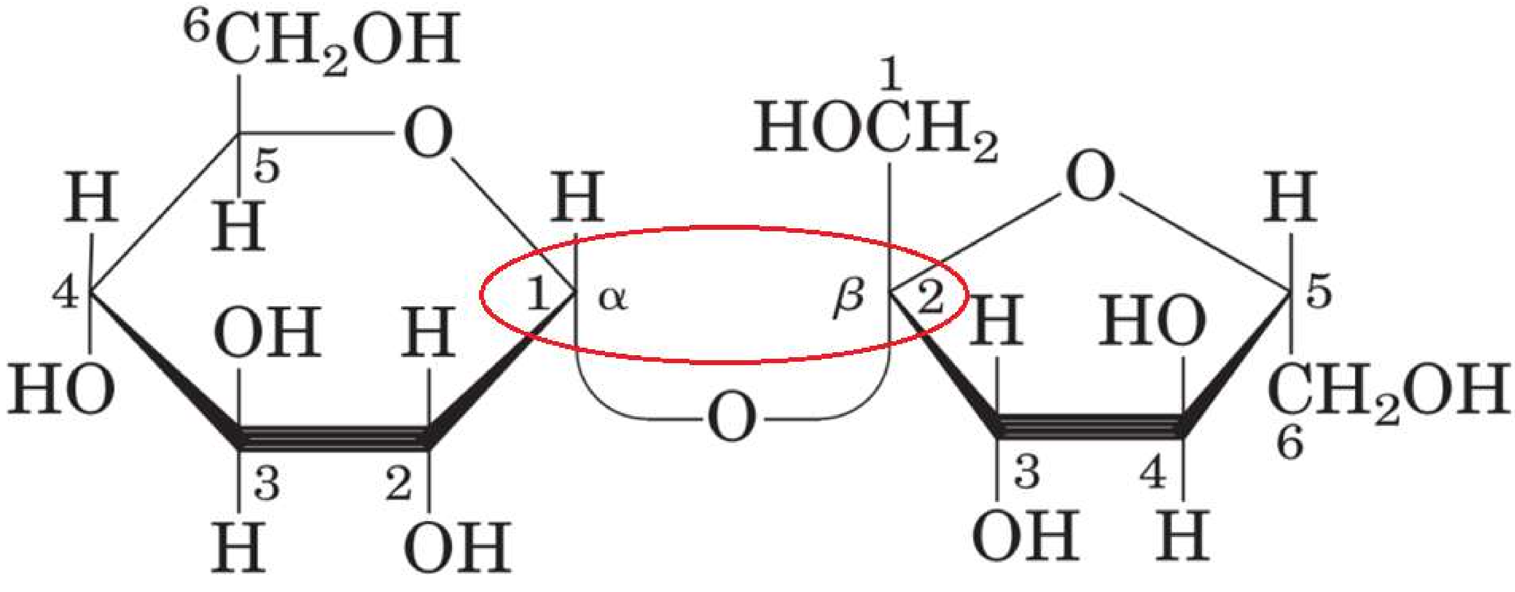
Nonreducing disaccharides are named as glycosides; in this case, the positions joined are the anomeric carbons.

In the abbreviated nomenclature, a **double-headed arrow connects** the symbols specifying the anomeric carbons and their configurations.

The abbreviated name of sucrose is either:

- Glc(α1 ↔ 2β)Fru
- Fru (β2 ↔ 1α)Glc

Disaccharide Sucrose



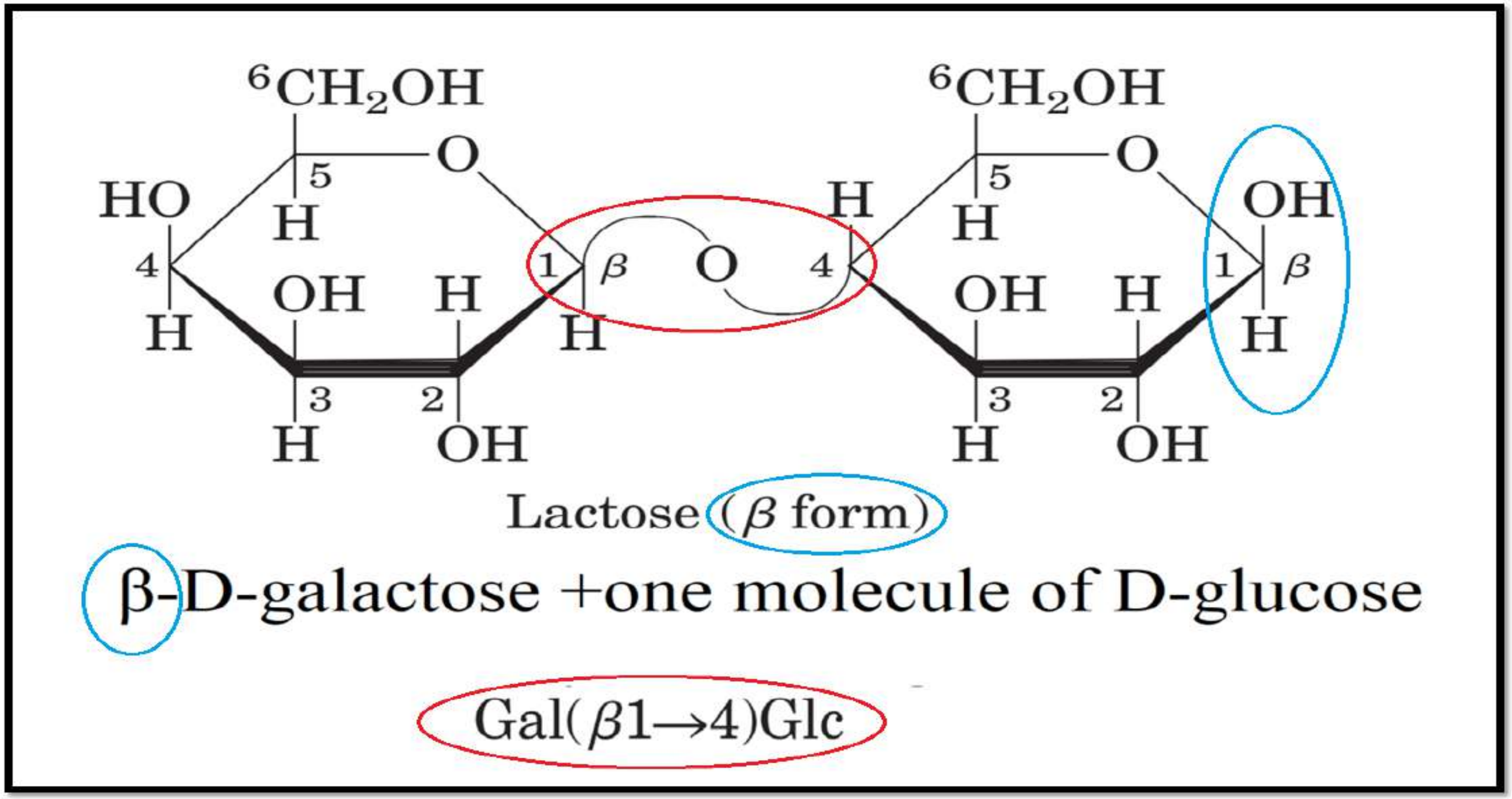
Sucrose

α-D-glucose + β-D-fructose

α1 ↔ 2β glycosidic linkage

(head-to-head)

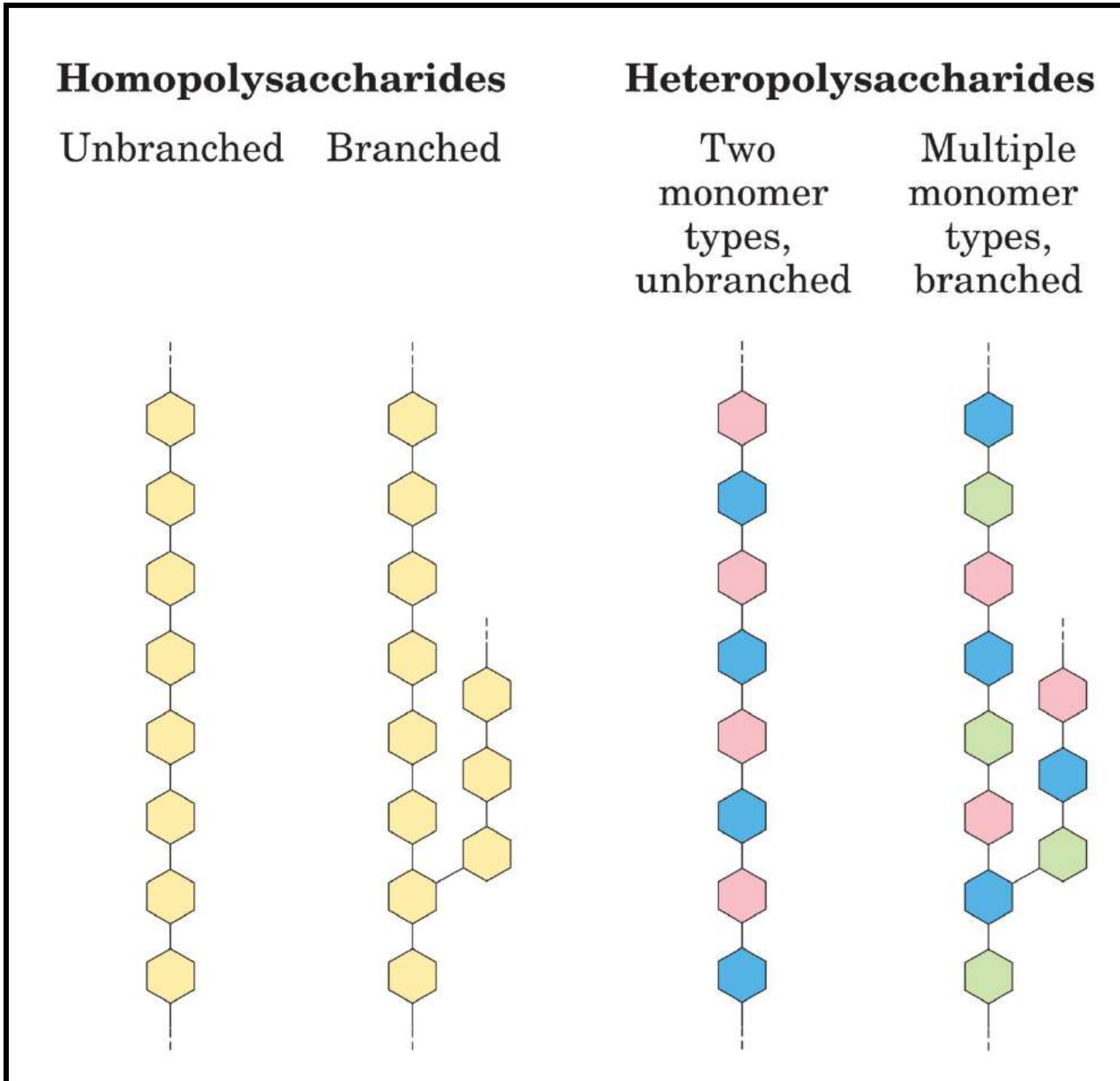
Disaccharide Lactose



- The disaccharide lactose, which yields **D-galactose and D-glucose** on hydrolysis, occurs naturally only in milk.
- The anomeric carbon of the D-glucose residue is available for oxidation, and thus **lactose is a reducing disaccharide**.
- Its abbreviated name is **Gal β(1→ 4)Glc**.

Polysaccharides

- **Most carbohydrates** found in nature occur as **polysaccharides**, polymers of medium to high molecular weight.
- Polysaccharides, also called **glycans,** differ from each other in:
  - ***The identity of their repeated monosaccharide units***
  - ***The length of their chains***
  - ***The types of bonds linking the units***
  - ***The degree of branching.***
- **Homopolysaccharides** contain only a single type of monomer.
- **Heteropolysaccharides** contain two or more different kinds.
- **Some** homopolysaccharides serve as storage forms of monosaccharides that are used as fuels; e.g. **starch and glycogen.**
- **Other** homopolysaccharides serve as structural elements in plant cell walls and animal exoskeletons; e.g. cellulose and chitin.
- **Heteropolysaccharides** provide **extracellular support** for organisms of all kingdoms. For example, the rigid layer of the bacterial cell envelope (the **peptidoglycan**) is composed in part of a heteropolysaccharide built from two alternating monosaccharide units.
- The **extracellular space of animal tissues** is occupied by several types of **heteropolysaccharides**, which form a matrix that holds individual cells together and provides protection, shape, and support to cells, tissues, and organs

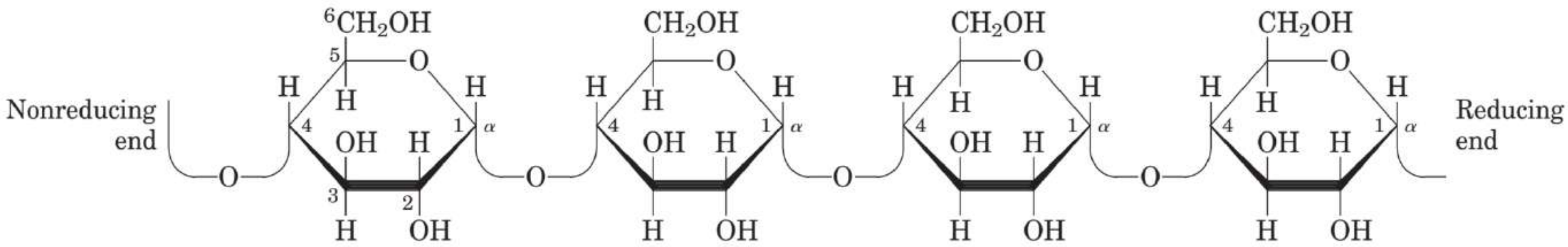

Homopolysaccharides
Heteropolysaccharides
Unbranched
Branched
Two monomer types, unbranched
Multiple monomer types, branched

Storage Polysaccharides

- The most important storage polysaccharides are **starch** in plant cells and **glycogen** in animal cells.
- **Organisms store the metabolic energy** contained in monosaccharides by converting them into disaccharides, such as *maltose*, which are then linked together into insoluble forms that are deposited in specific storage areas in their bodies. These **insoluble polysaccharides** are long **polymers** of monosaccharides formed by dehydration reaction.
- Both polysaccharides (**starch and glycogen**) occur intracellularly as large clusters or granules .
- Starch and glycogen molecules are **heavily hydrated**, because they have many exposed hydroxyl groups available to hydrogen-bond with water.
- **Plants store** starch as granules within **chloroplasts** and other organelles which provides a reservoir of energy available for future needs. Energy for cellular work can be retrieved by hydrolyzing the links that bind the glucose subunits together.
- Most plant cells have the ability to form **starch**, but it is especially abundant in **tubers, such as potatoes, and in seeds**.

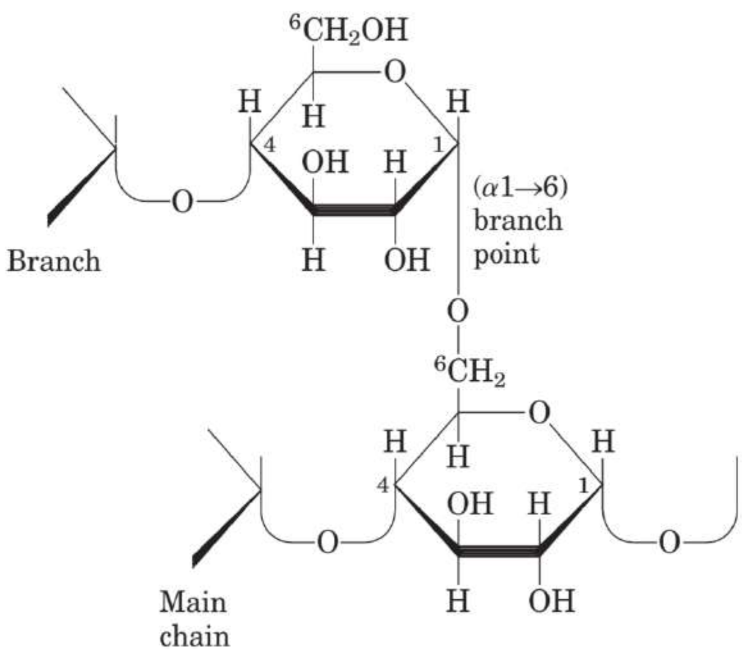
Storage Polysaccharides: Starch and Glycogen

- **Starch** contains two types of glucose polymer, **amylose and amylopectin**. The **amylose** consists of long, **unbranched chains of D-glucose** residues connected by **α (1→4) linkages**. Such chains vary in molecular weight from a few thousand to more than a million.
- **Amylopectin** also has a high molecular weight (up to 100 million) but unlike amylose is **highly branched**.
- The glycosidic linkages joining successive glucose residues in amylopectin chains are **(α 1→4)**; the branch points (**occurring every 24 to 30 residues**) are **(α 1→6) linkages**.
- **Glycogen** is the main storage polysaccharide of animal cells.
- Like amylopectin, glycogen is a polymer of (α 1→4) -linked subunits of glucose, with (α 1→6) –linked branches, but **glycogen is more extensively branched** (on average, **every 8 to 12 residues**) and more compact than starch.
- **Glycogen** is especially abundant in the **liver** where it may constitute as much as 7% of the wet weight; it is also present in **skeletal muscle.**

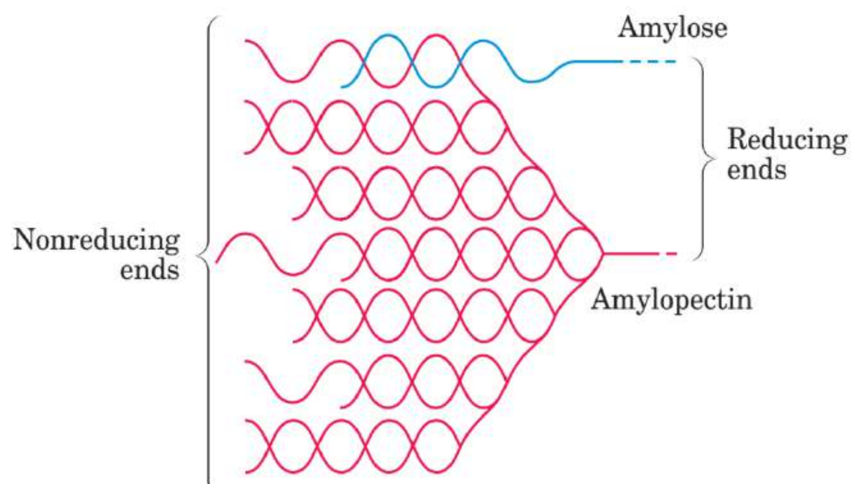


Nonreducing end
Reducing end
$^6CH_2OH$
CH_2OH
O
H
OH
α

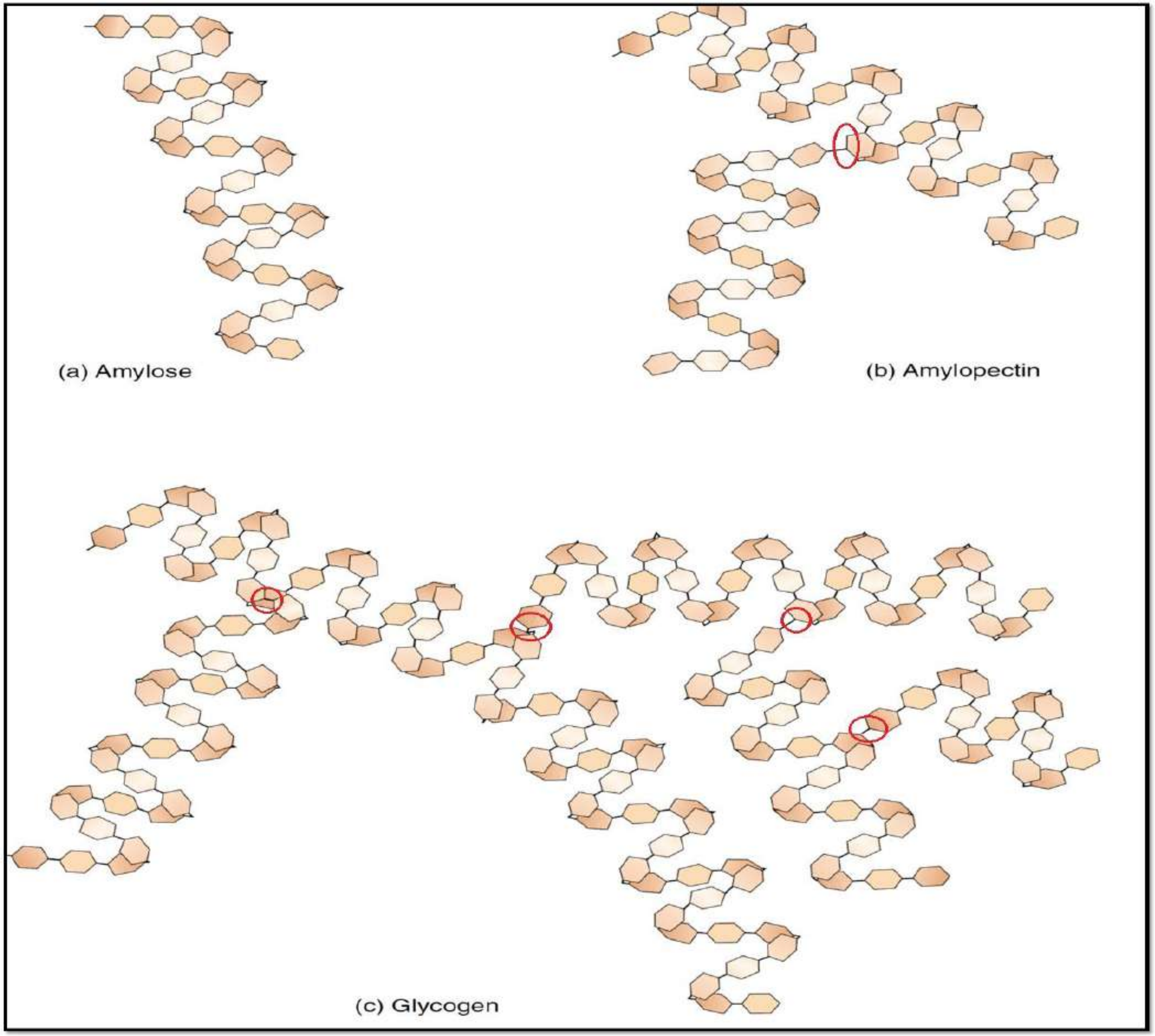
(a) amylose



$^6CH_2OH$
$^6CH_2$
O
H
OH
(α1→6) branch point
Branch
Main chain



Amylose
Reducing ends
Nonreducing ends
Amylopectin

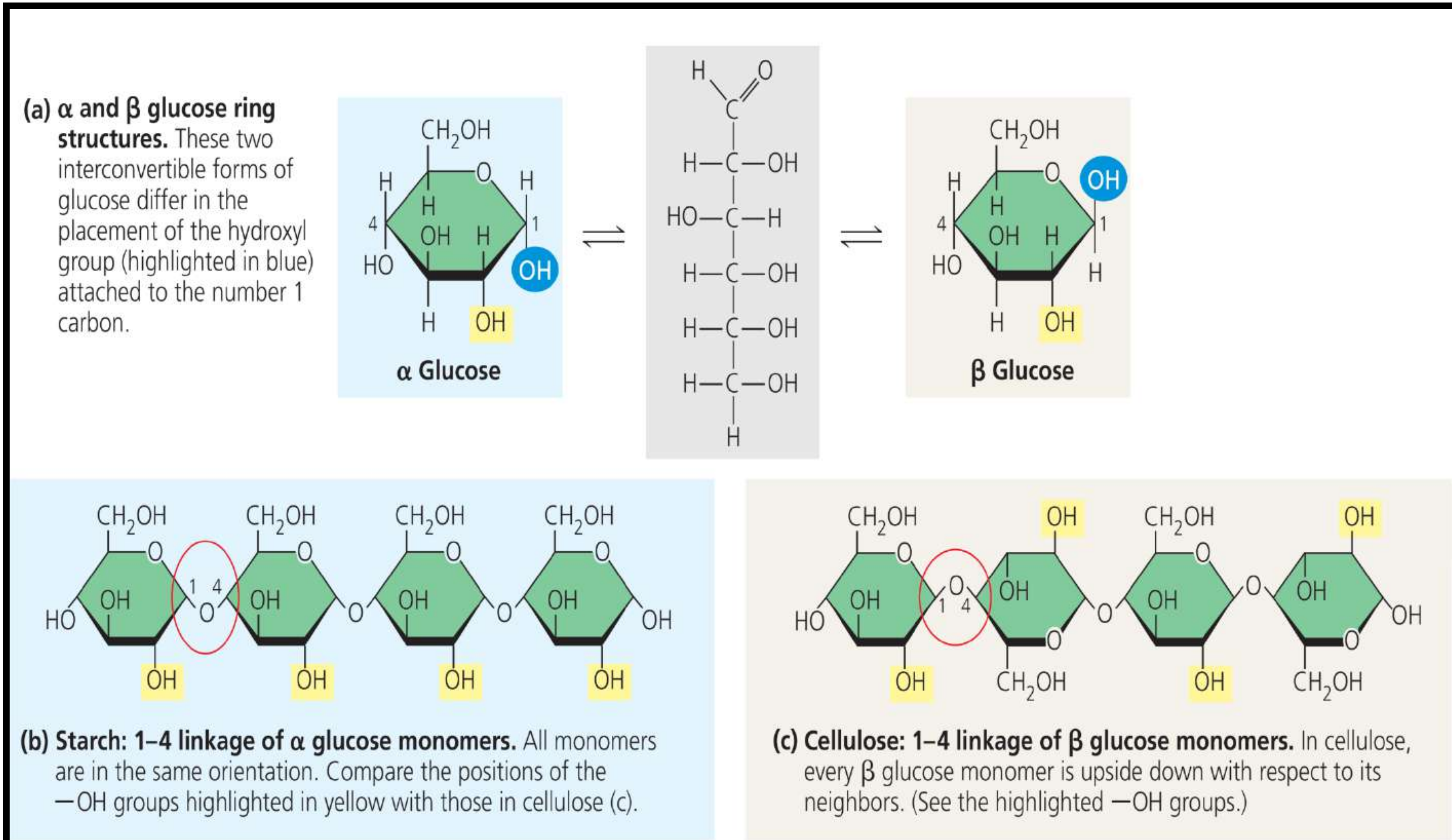

(a) Amylose
(b) Amylopectin
(c) Glycogen

Some Homopolysaccharides Serve Structural Roles

- **Cellulose**, a fibrous, tough, water-insoluble substance, is found in the **cell walls** of plants,
- Like amylose and the main chains of amylopectin and glycogen, the **cellulose** molecule is a **linear, unbranched homopolysaccharide**, consisting of 10,000 to 15,000 D-glucose units, but in the β configuration **(β 1→4)** glycosidic linkage).
- **Chitin** is a linear **homopolysaccharide** composed of **N-acetylglucosamine** residues in β linkage. The only chemical difference from cellulose is the replacement of the hydroxyl group at **C-2 with an acetylated amino group**.
- **Chitin** forms extended fibers similar to those of cellulose, and like cellulose **cannot be digested by vertebrates.**
- **Chitin** is the principal component of the **hard exoskeletons** of nearly a million species of **arthropods—insects**, lobsters, and crabs,— many fungi, and is probably the second most abundant polysaccharide, next to cellulose, in nature.

- **Dextrans** are bacterial and yeast polysaccharides made up **of (α 1→6)** -linked poly-D-glucose; all have **(α 1→3) branches**, and some also have (α 1→2) or (α 1→4) branches.

Starch and cellulose structures.



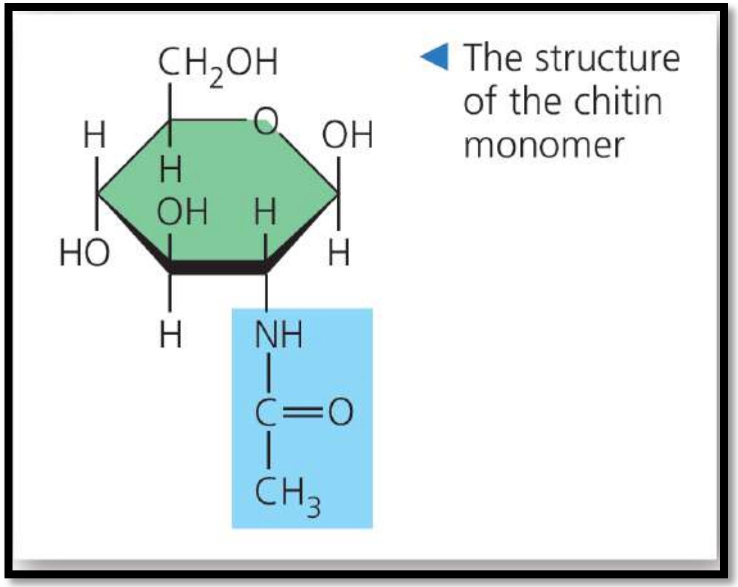
(a) α and β glucose ring structures. These two interconvertible forms of glucose differ in the placement of the hydroxyl group (highlighted in blue) attached to the number 1 carbon.

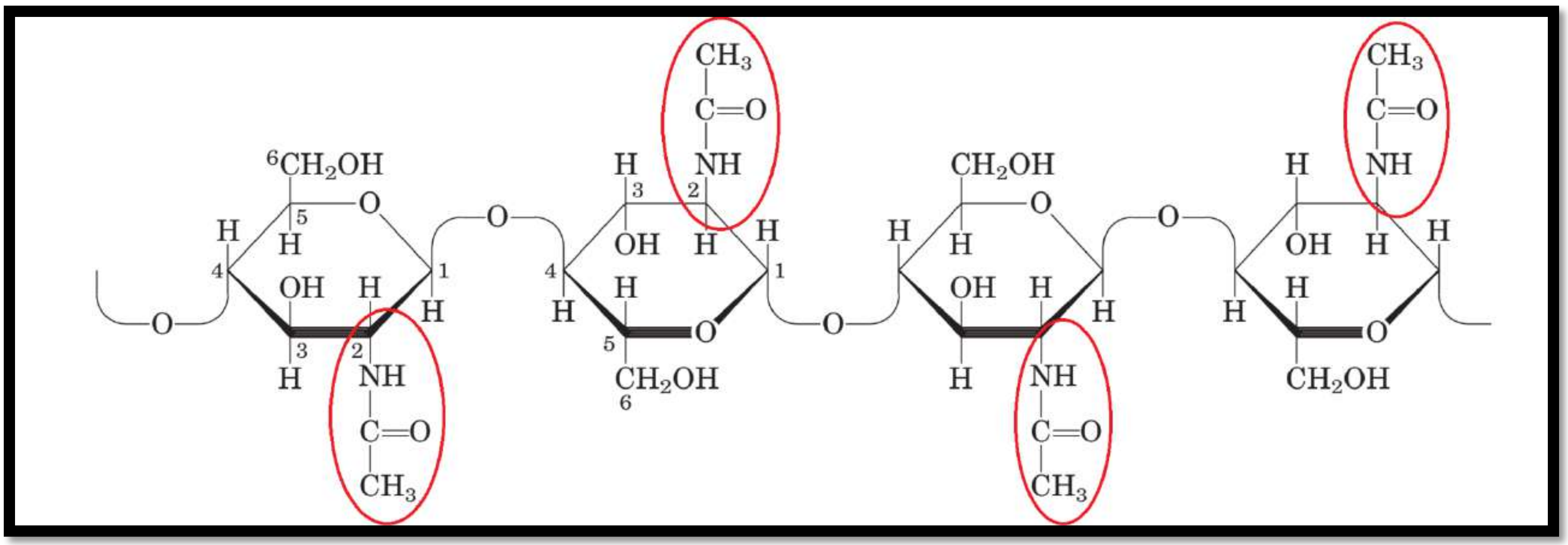
(b) Starch: 1–4 linkage of α glucose monomers. All monomers are in the same orientation. Compare the positions of the —OH groups highlighted in yellow with those in cellulose (c).

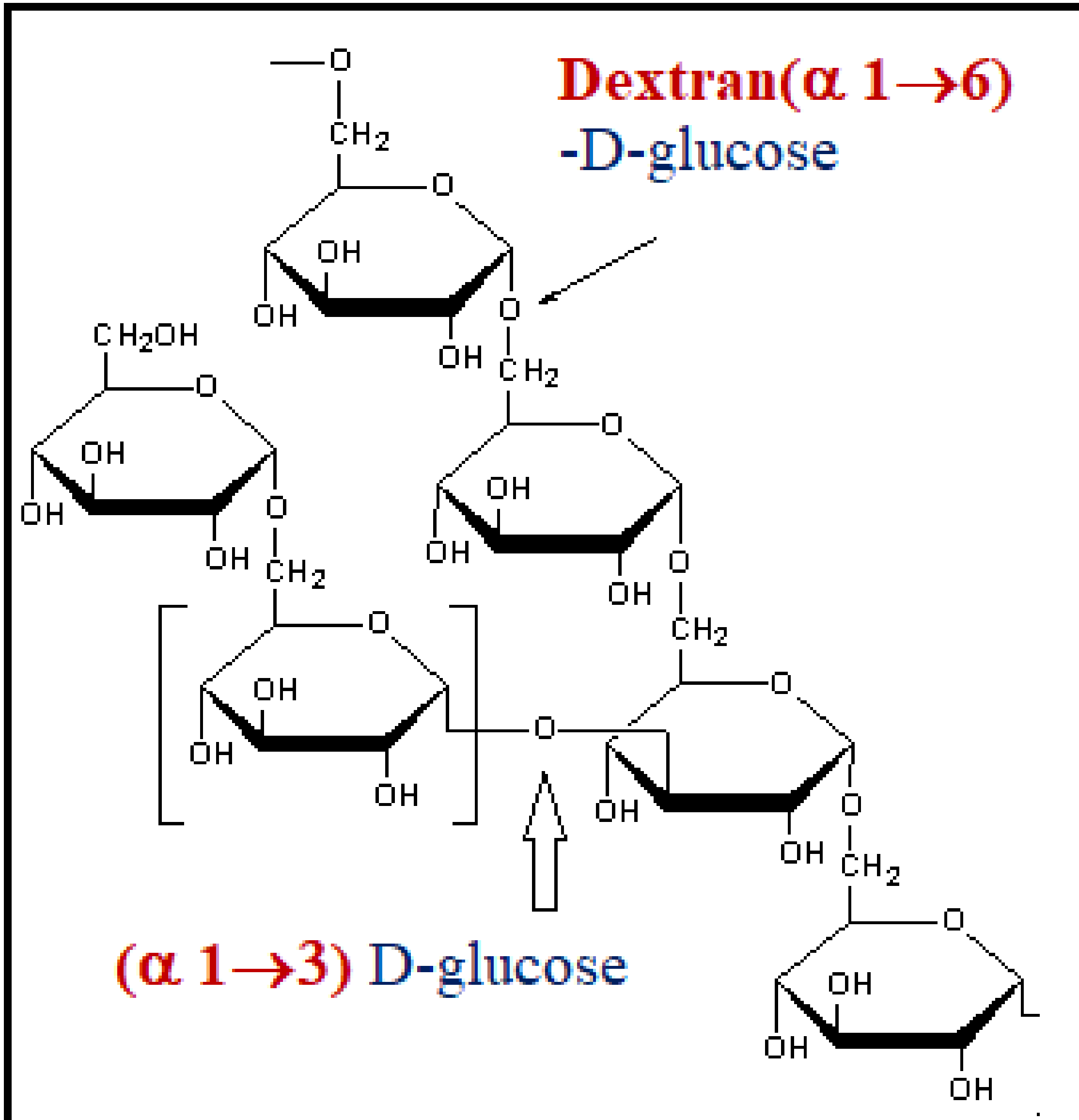
(c) Cellulose: 1–4 linkage of β glucose monomers. In cellulose, every β glucose monomer is upside down with respect to its neighbors. (See the highlighted —OH groups.)

Chitin is a linear homopolysaccharide composed of **N-acetylglucosamine** residues in β- linkage.

The only chemical difference from cellulose is the replacement of the hydroxyl group at **C-2 with an acetylated amino group**






Dextran(α 1→6)
-D-glucose
(α 1→3) D-glucose

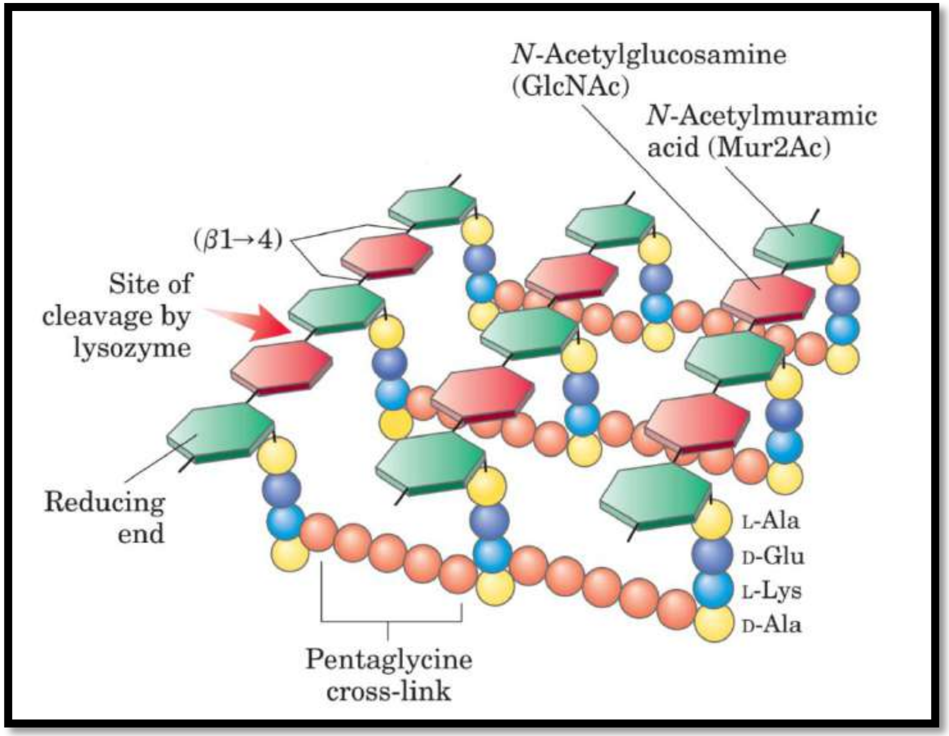
Structural Heteropolysaccharides: Bacterial Cell Wall (Peptidoglycan or murine)

- The rigid component of **bacterial cell walls** (known as peptidoglycan or murein) **is a heteropolymer** of alternating (β1→4)-linked:

  N-acetylglucosamine and

  N-acetylmuramic acid residues.

- The linear polymers lie side by side in the cell wall, **crosslinked by short peptides** that join or interfuse the polysaccharide chains (glycan) into a strong sheath that envelops the entire cell and prevents cellular swelling and lysis due to the osmotic entry of water.



The enzyme **lysozyme** (notably present in tears) kills bacteria by hydrolyzing the **(β1→4) glycosidic** bond between *N*-acetylglucosamine and *N*acetylmuramic acid

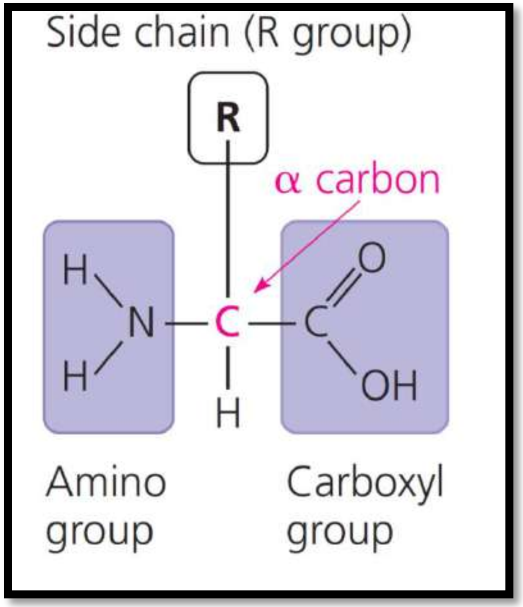
Structures and Roles of Some Polysaccharides

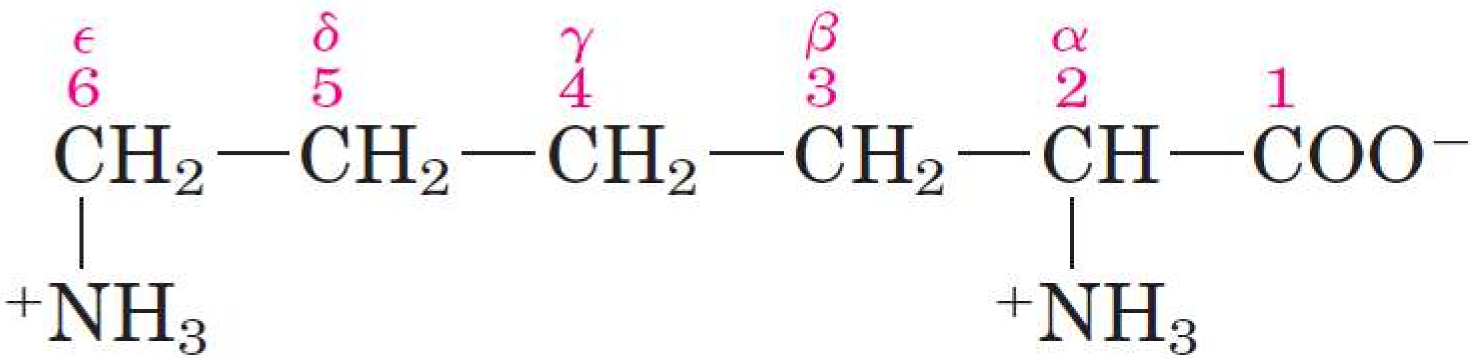
Polymer	*Type*	*Repeating unit*	*Roles/significance*
Starch			Energy storage: in plants
Amylose	Homo-	(α1$\rightarrow$4)Glc, linear	
Amylopectin	Homo-	(α1$\rightarrow$4)Glc, with (α1$\rightarrow$6)Glc branches every 24–30 residues	
Glycogen	Homo-	(α1$\rightarrow$4)Glc, with (α1$\rightarrow$6)Glc branches every 8–12 residues	Energy storage: in bacteria and animal cells
Cellulose	Homo-	(β1$\rightarrow$4)Glc	Structural: in plants, gives rigidity and strength to cell walls
Chitin	Homo-	(β1$\rightarrow$4)GlcNAc	Structural: in insects, spiders, crustaceans, gives rigidity and strength to exoskeletons
Dextran	Homo-	(α1$\rightarrow$6)Glc, with (α1$\rightarrow$3) branches	Structural: in bacteria, extracellular adhesive
Peptidoglycan	Hetero-; peptides attached	4)Mur2Ac(β1$\rightarrow$4) GlcNAc(β1	Structural: in bacteria, gives rigidity and strength to cell envelope
Agarose	Hetero-	3)D-Gal(β1$\rightarrow$4)3,6-anhydro-L-Gal(α1	Structural: in algae, cell wall material

Amino Acids Are the Building Blocks of Proteins

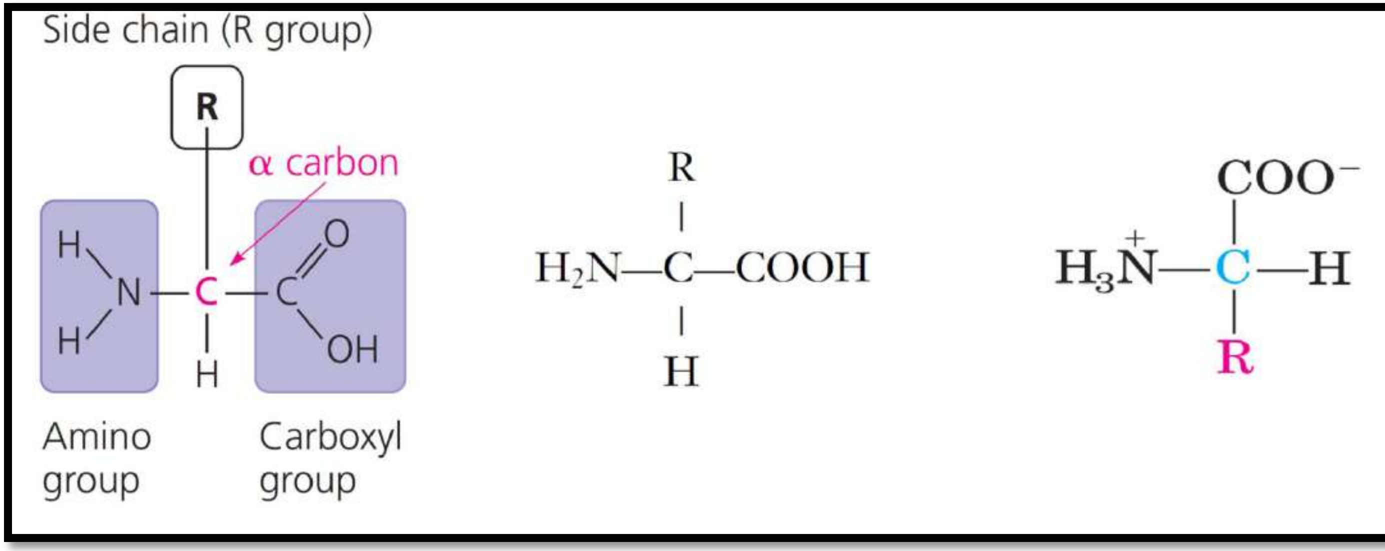
- Proteins are polymers of amino acids, with each **amino acid residue** joined to its neighbor by a specific type of covalent bond: **the peptide bond**
- Although **proteins** are complex and multipurpose molecules, they are **all polymers** of only 20 amino acids (α-amino acids) , in a specific order.
- An **amino acid** is a molecule containing an **amino group** (—NH2), a **carboxyl group** (—COOH), a hydrogen atom, and a variable group symbolized **by R**.
- All four components are bonded to a **central asymmetric carbon** atom called the **α carbon (C#2), except glycine .** The R group, also called the side chain, differs with each amino acid.

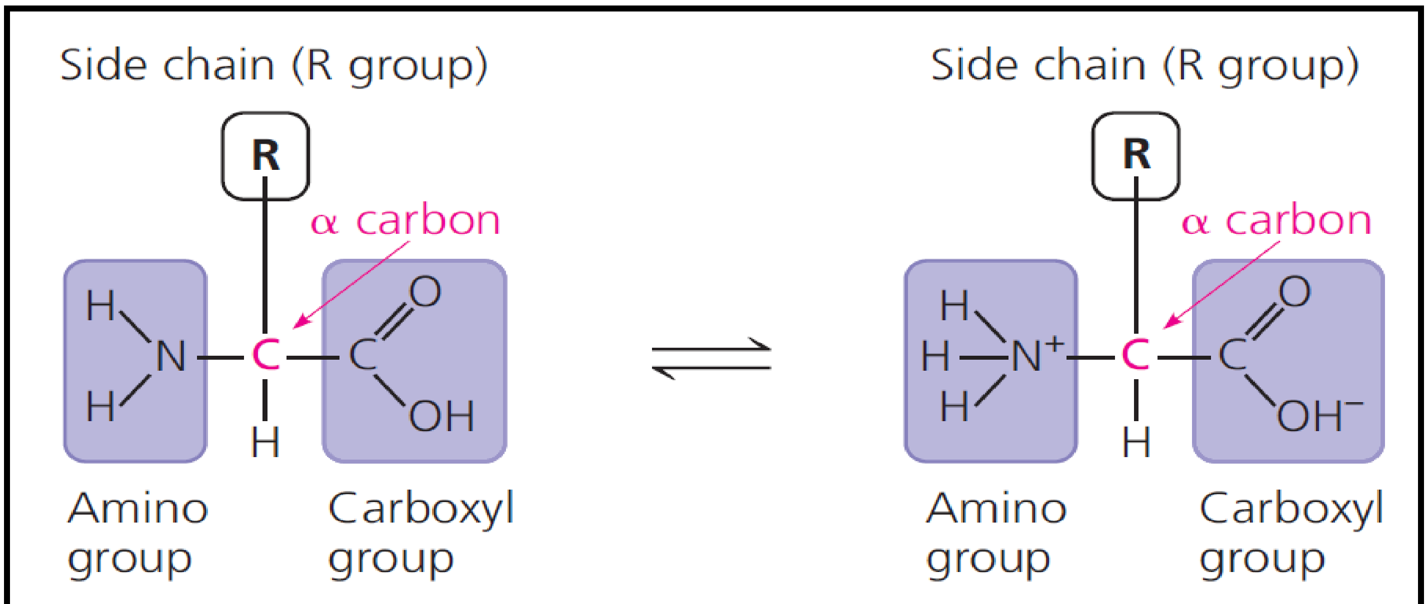
R groups may be simple as hydrogen atom, or it may be a carbon skeleton with various functional groups attached.
The physical and chemical properties of the side chain **determine** the unique characteristics of a particular amino acid, thus affecting its functional role in a polypeptide.





Lysine

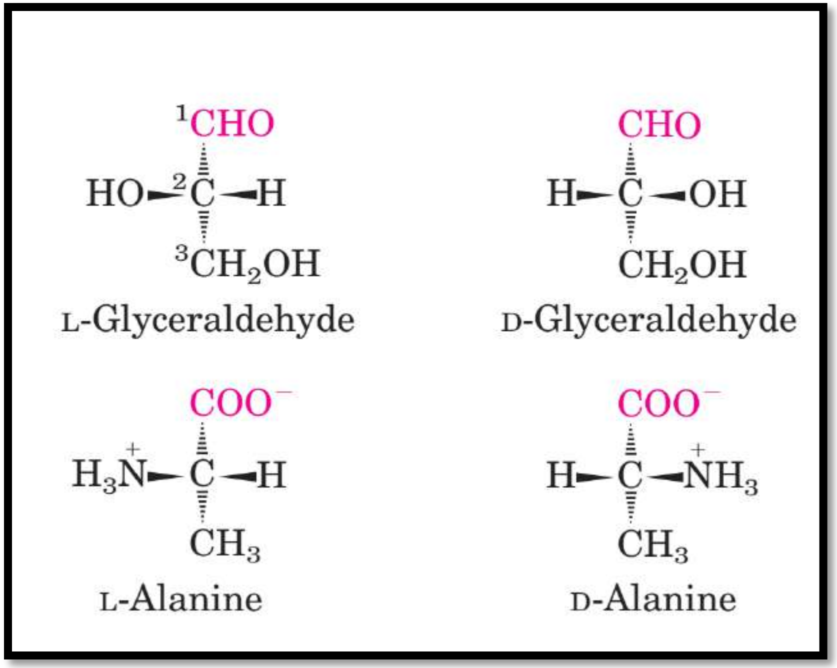




non-ionized amino acid **Ionized amino acid**

Stereoisomers of amino acids

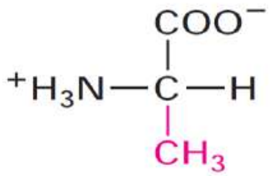
- For all the common amino acids **except glycine**, the α carbon is bonded to four different groups: a carboxyl group, an amino group, an R group, and a hydrogen atom.
- The α-carbon atom is thus a **chiral center** for all amino acids, **expect glycine**, and have two possible nonsuperimposable mirror images stereoisomers called **enantiomers**.
- **L-amino acids** are those with the α-amino group on the left,
- **D-amino acids** have the α-amino group on the right.
- The amino acids that make up the proteins in our bodies are **all L-amino acids.**



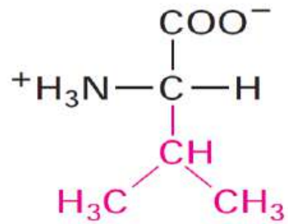
Classification of amino acids

- The 20 common amino acids are grouped into four chemical classes, based on their R side groups:
  - **Group I**: Hydrophobic (nonpolar) amino acids: alanine, valine, tyrosine, leucine, isoleucine, phenylalanine, methionine, and tryptophan.
  - **Group II:** Hydrophilic (polar uncharged) amino acids: are serine, threonine,, asparagine, and glutamine.
  - **Group III:** Hydrophilic (polar charged) amino acids (Ionizable amino acids: acidic –ve [aspartic acid and glutamic acid] and basic +ve [arginine, histidine, and lysine]).
  - **Group IV:** Special amino acids have distinctive individual properties: cysteine, glycine proline

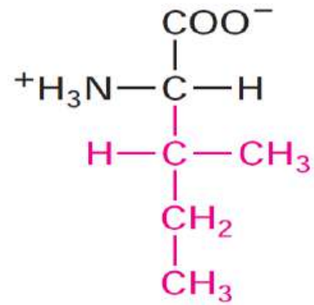
HYDROPHOBIC AMINO ACIDS



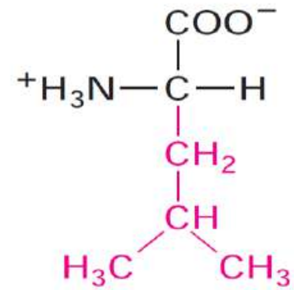
Alanine
(Ala or A)



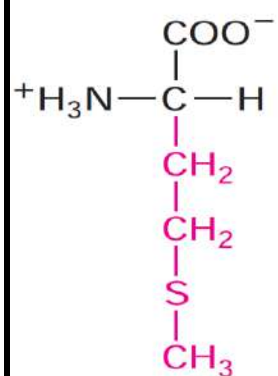
Valine
(Val or V)



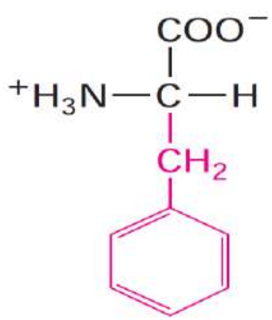
Isoleucine
(Ile or I)



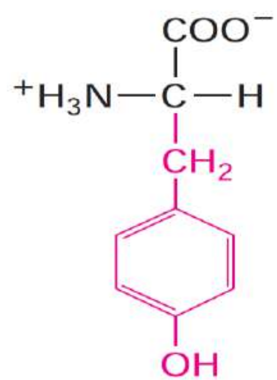
Leucine
(Leu or L)



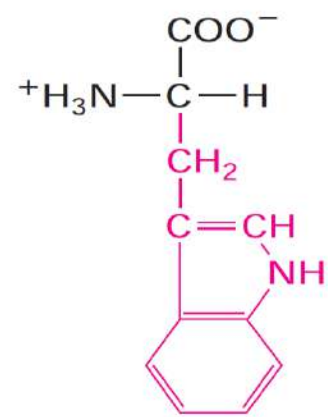
Methionine
(Met or M)



Phenylalanine
(Phe or F)

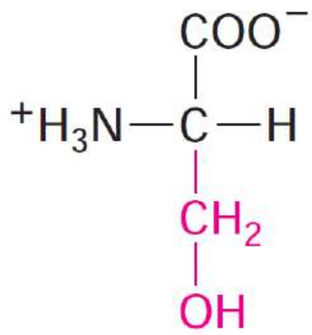


Tyrosine
(Tyr or Y)

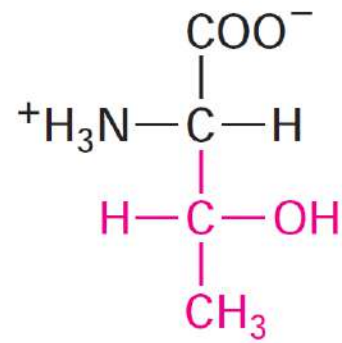


Tryptophan
(Trp or W)

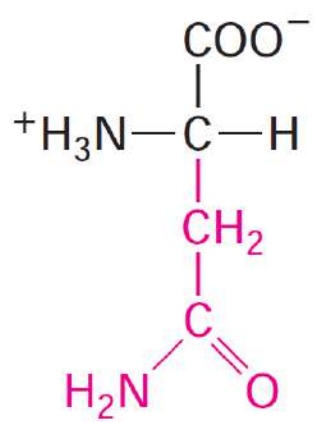
Polar amino acids with uncharged R groups



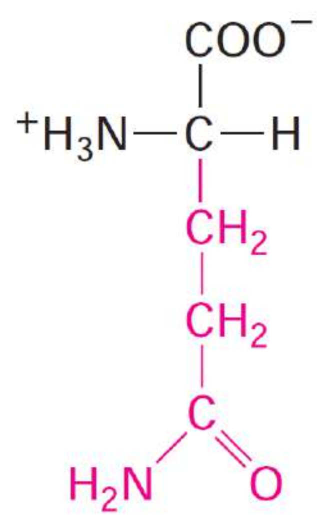
Serine
(Ser or S)



Threonine
(Thr or T)



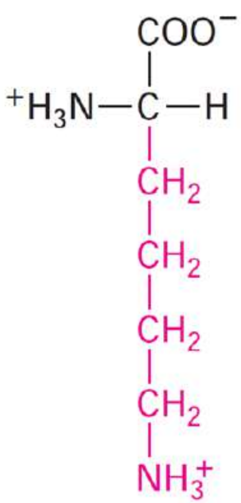
Asparagine
(Asn or N)



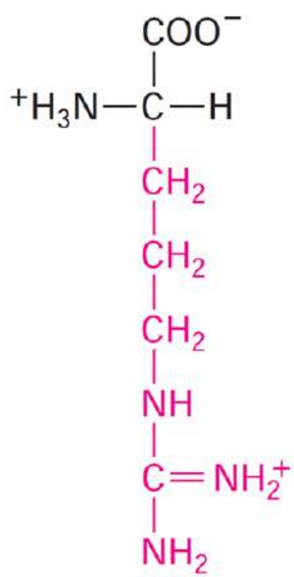
Glutamine
(Gln or Q)

Hydrophilic (polar) amino acids

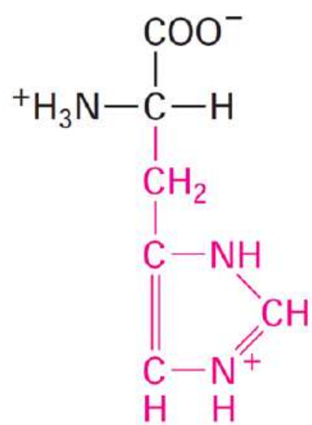
Basic amino acids



Lysine
(Lys or K)

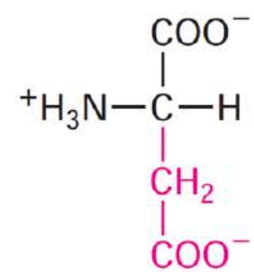


Arginine
(Arg or R)



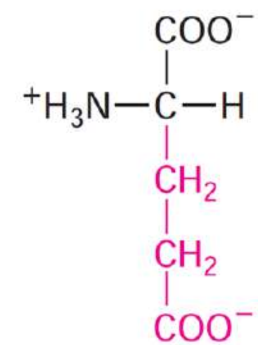
Histidine
(His or H)

Acidic amino acids



Aspartate
(Asp or D)

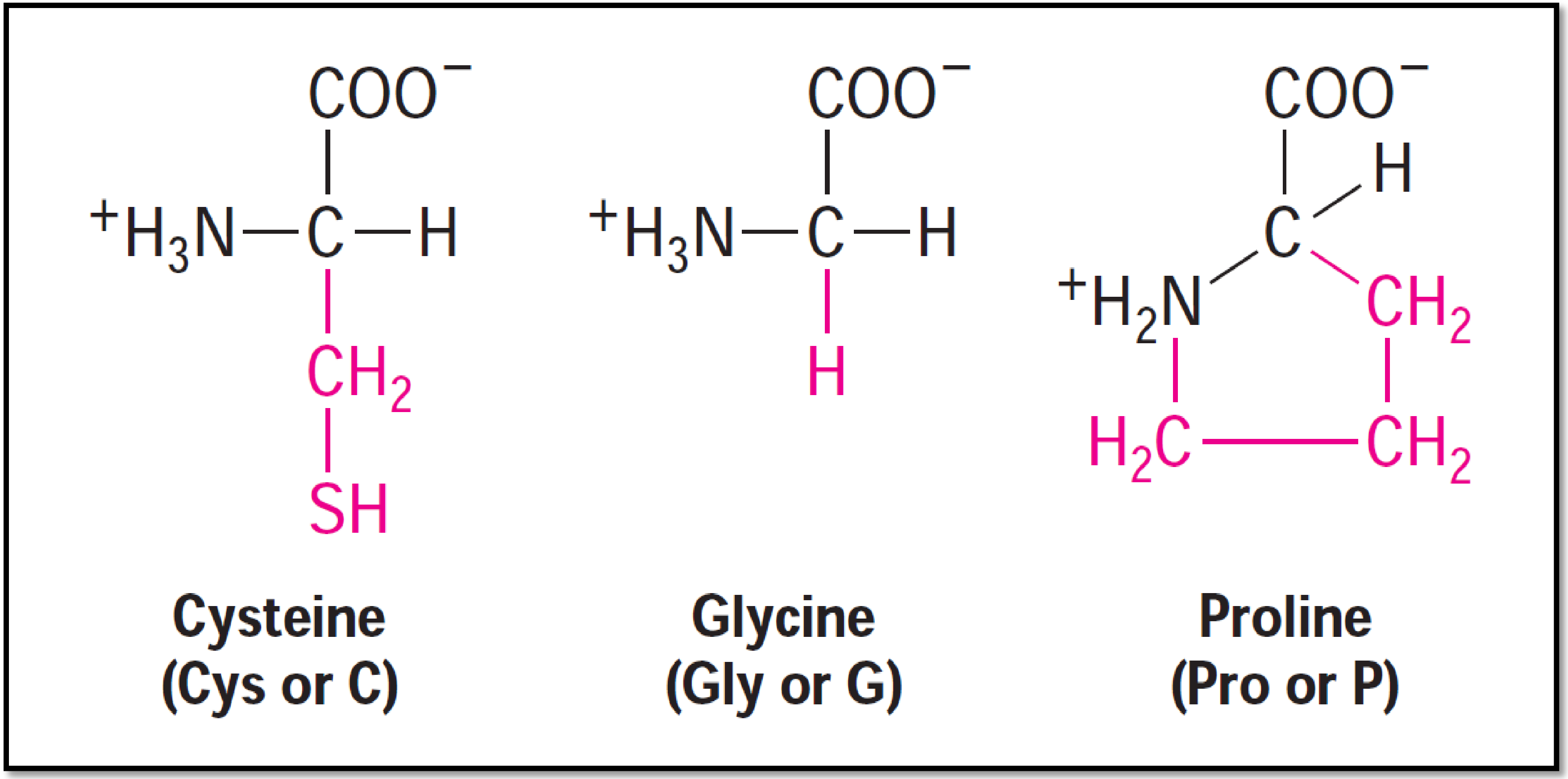
Aspartic acid

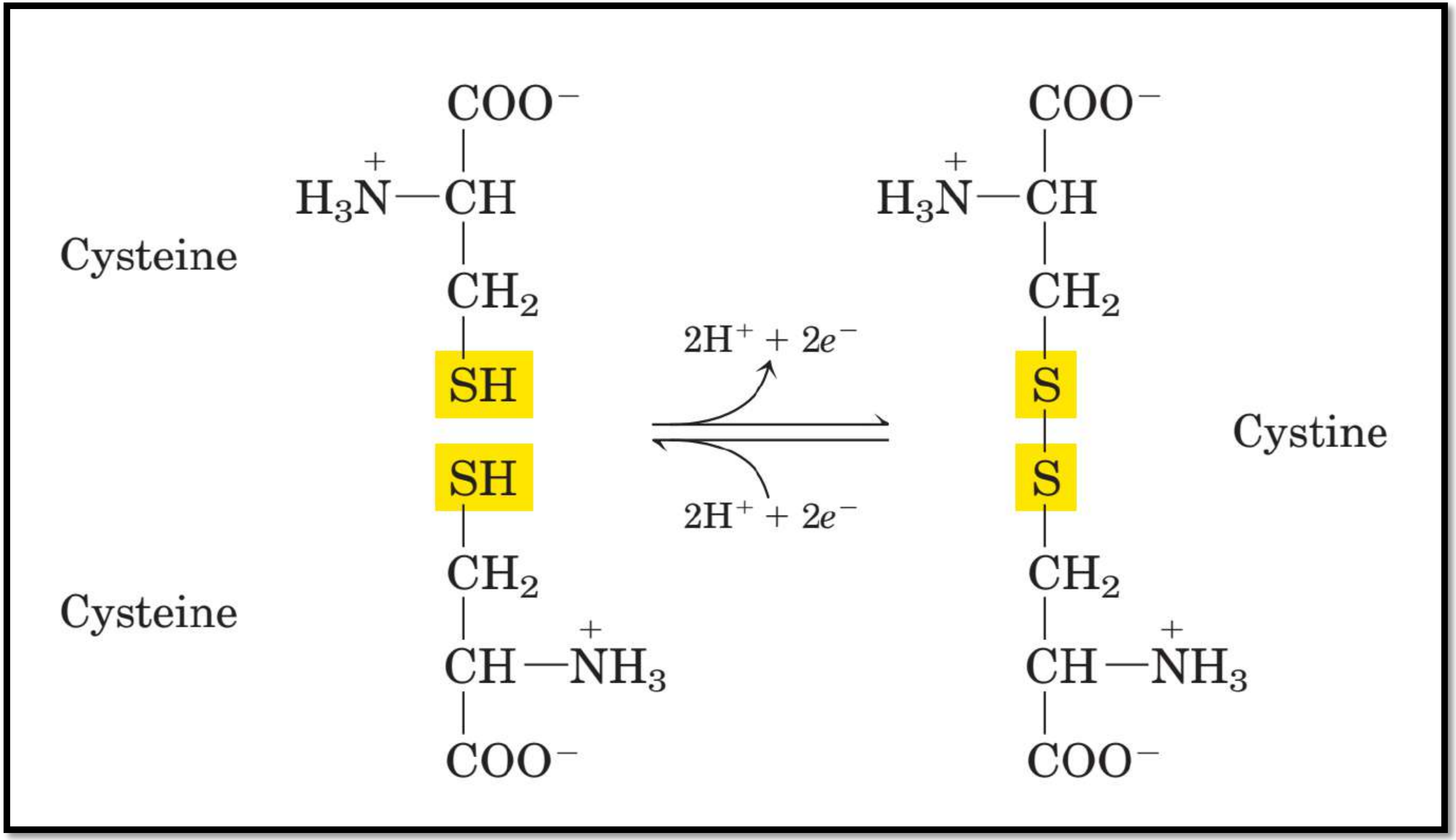


Glutamate
(Glu or E)

Glutamic acid

Special amino acids

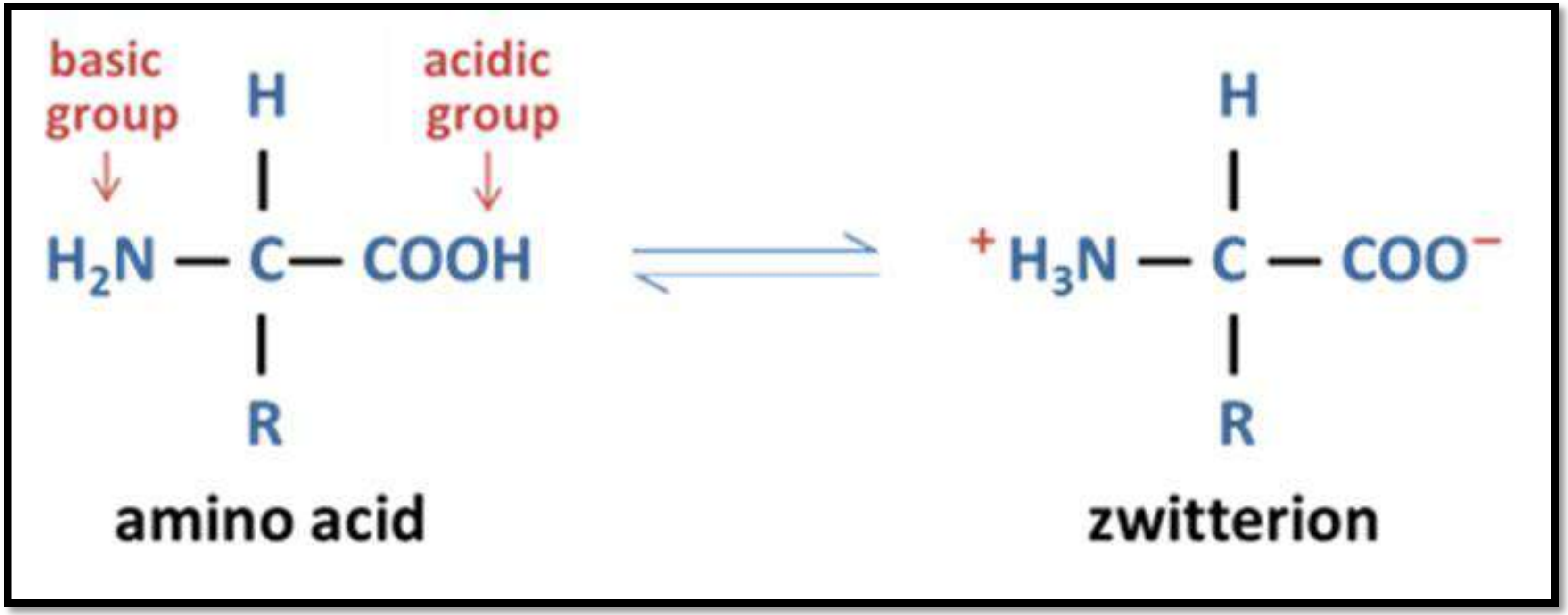




Reversible formation of a **disulfide (S-S)** bond by the oxidation of two molecules of cysteine.

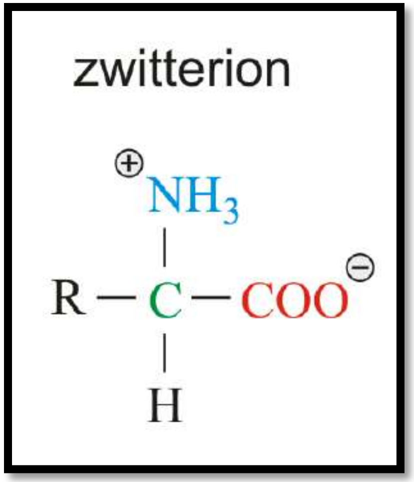
Disulfide bonds between Cys residues **stabilize** the structures of many proteins.

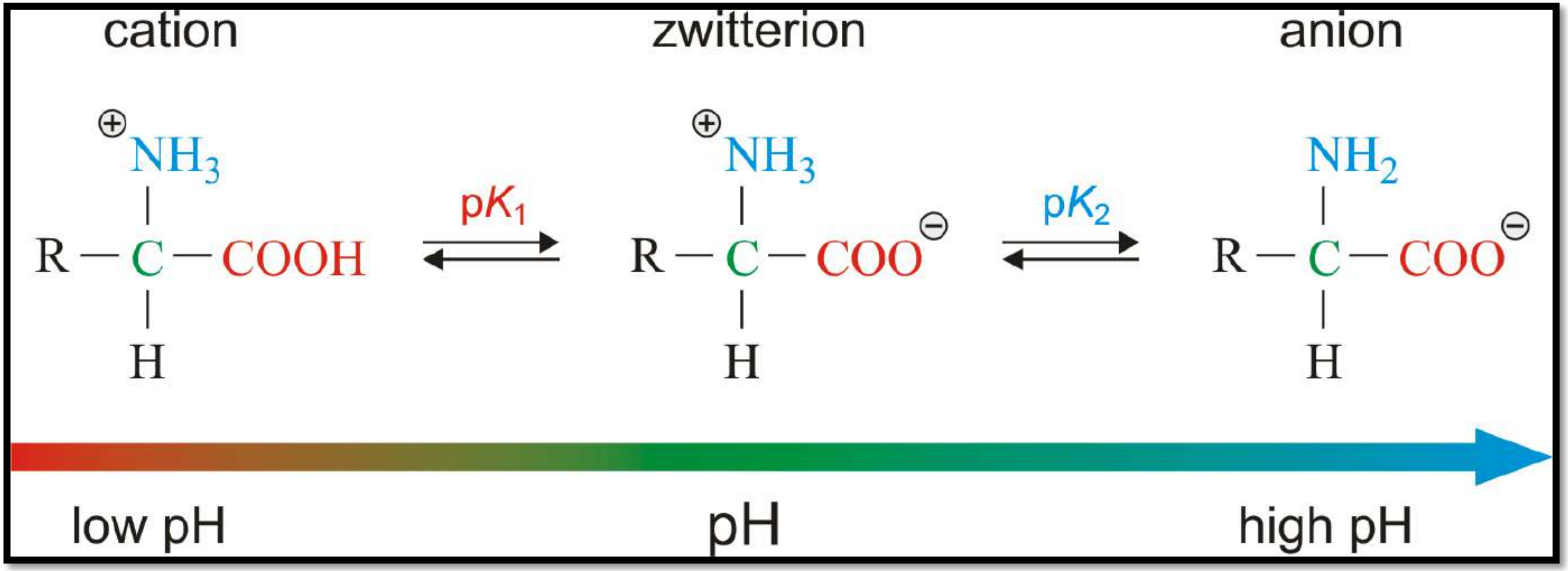
Amino Acids are Amphoteric act as Acid and Base



Amino Acids are Amphoteric act as Acid and Base

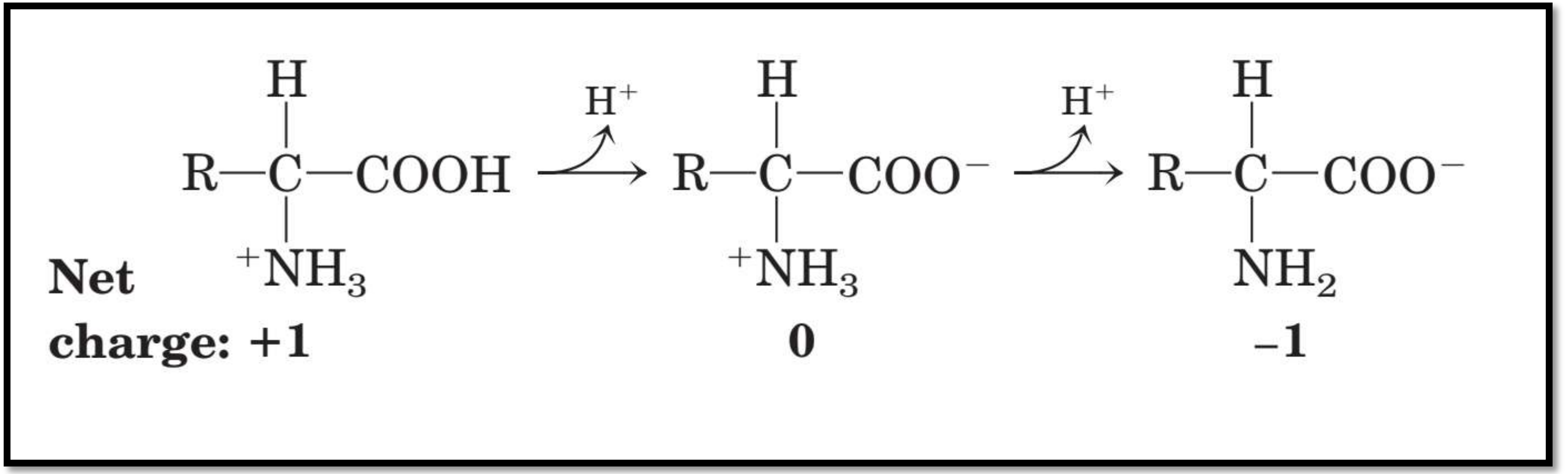
- When an amino acid is dissolved in water, it exists in solution as the dipolar ion, or **zwitterion** (German for "hybrid ion)
- A **zwitterion** can act as either an acid (**proton donor**) or a base (**proton acceptor**)





monoamino monocarboxylic α-amino acid

A simple monoamino monocarboxylic *α*- amino acid, such as alanine, is a **diprotic acid** when fully protonated—it has two groups, the COOH group and the NH_3^+ group, that can yield protons



البيتيدات هي سلاسل من الأحماض الأمينية

Peptides Are Chains of Amino Acids

- Two amino acid molecules can be covalently joined through a dehydration reaction resulting in a covalent bond termed a **peptide bond**, to yield a **dipeptide**.

يمكن أن ترتبط جزيئين من الأحماض الأمينية تساهميًا من خلال تفاعل إزالة الماء مما ينتج عنه رابطة تساهمية تسمى الرابطة الببتيدية، لإنتاج ثنائي الببتيد.

- Such a peptide bond is formed by **removal** of the elements of water (dehydration) from the **α-carboxyl group** of one amino acid and the **α-amino group** of another.

يتم تشكيل هذه الرابطة الببتيدية عن طريق إزالة عناصر الماء (الجفاف) من المجموعة الكربوكسيلية ألفا لحمض أميني واحد والمجموعة الأمينية ألفا لحمض أميني آخر.

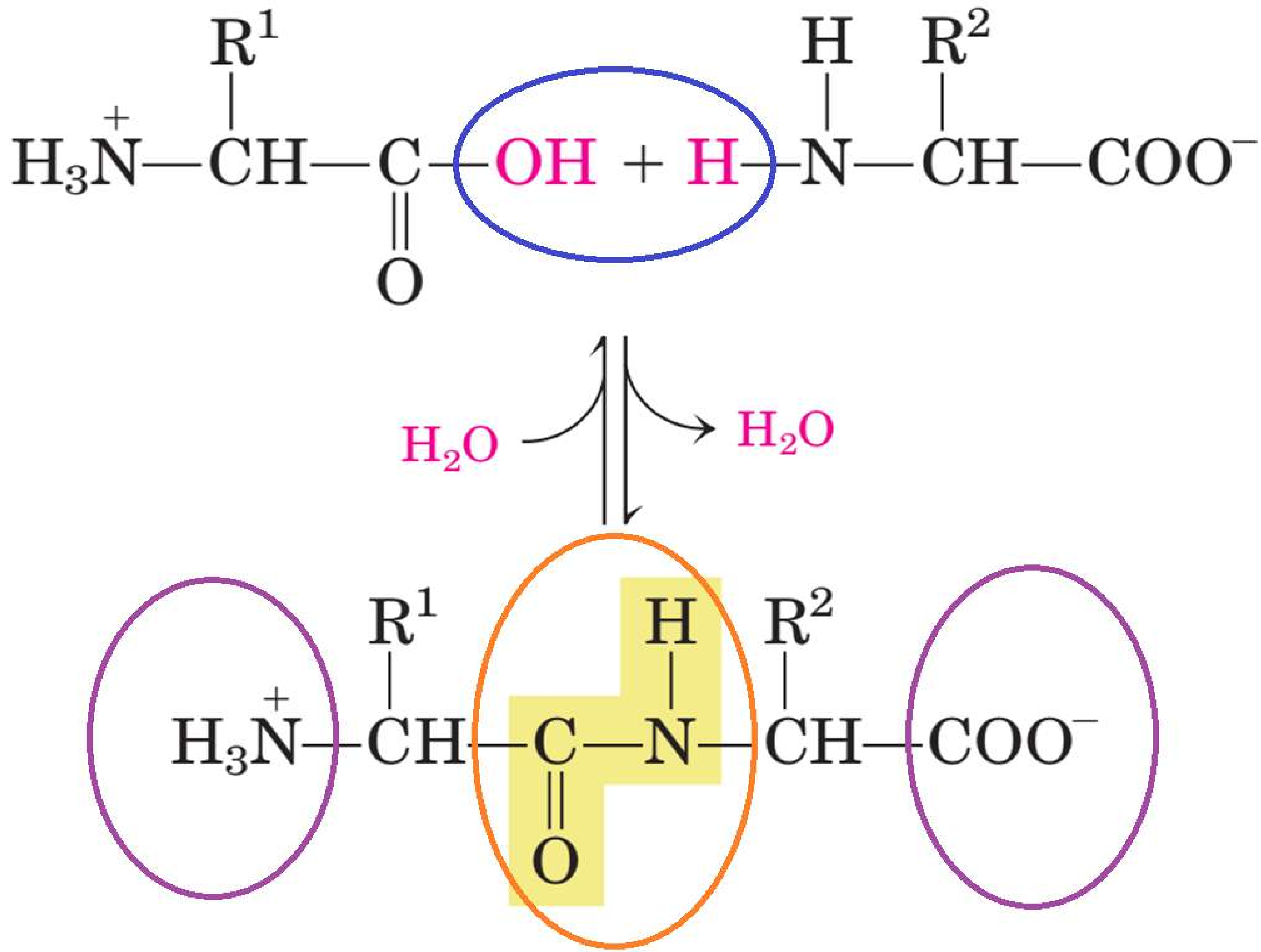
- **Three amino acids** can be joined by two peptide bonds to form a **tripeptide**; similarly, amino acids can be linked to form tetrapeptides, pentapeptides, and so forth.

يمكن ربط ثلاثة أحماض أمينية بواسطة رابطتين ببتيديتين لتكوين ثلاثي الببتيد؛ وبالمثل، يمكن ربط الأحماض الأمينية لتكوين رباعي الببتيدات، وخماسي الببتيدات، وما إلى ذلك.

- When a **few amino acids** are joined in this fashion, the structure is called an **oligopeptide**. عندما يتم ربط عدد قليل من الأحماض الأمينية بهذه الطريقة، يسمى الهيكل بالببتيد الأوليغوبي.

- When **many amino acids** are joined, the product is called a **polypeptide**. عندما يتم اتحاد العديد من الأحماض الأمينية معًا، يُطلق على المنتج اسم بولي ببتيد.
- Proteins may have thousands of amino acid residues

قد تحتوي البروتينات على آلاف بقايا الأحماض الأمينية



R1
H R2
H3N+ CH C OH + H N CH COO−
O
H2O
H2O
R1 H R2
H3N+ CH C N CH COO−
O

C و N محطات

N and C terminals

- In this oligopeptide (pentapeptide) the end with a free α-amino group is the **amino-terminal** (or N-terminal); while the other end, which has a free carboxyl group, is the **carboxyl-terminal** (*C*-terminal).

في هذا الببتيد الأوليجوببتيدي (خماسي الببتيد)، تكون النهاية التي تحتوي على مجموعة أمينية ألفا حرة هي الطرف الأميني (أو الطرف الأميني)؛ بينما الطرف الآخر، الذي يحتوي على مجموعة كربوكسيل حرة، هو الطرف الكربوكسيلي (الطرف الكربوكسيلي).

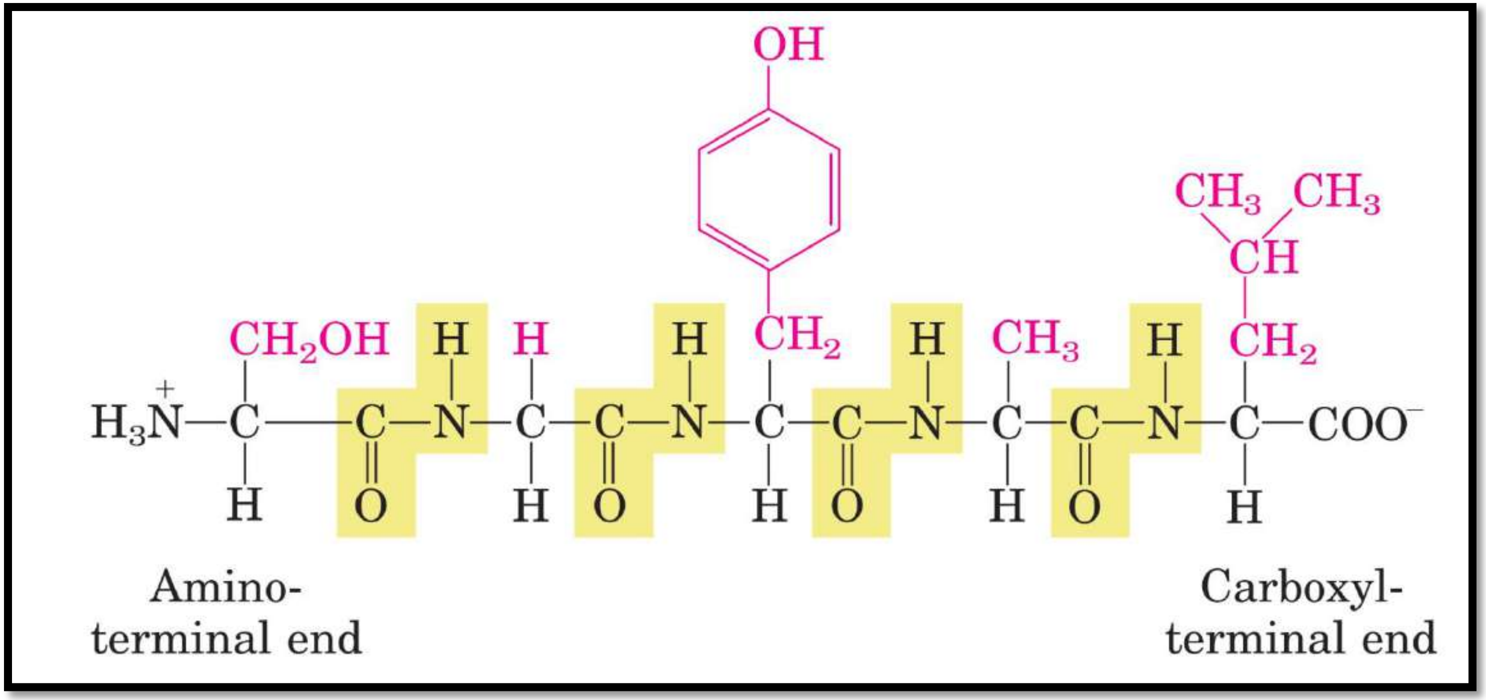
- This pentapeptide is :

serylglycyltyrosylalanylleucine, or Ser–Gly–Tyr–Ala–Leu.

سيريل جليسيل تيروزيل الانيليوسين، أو سير-جليسيل تيروزيل ألانيليوسين.

- Peptides are **named** beginning with the **N-terminal**, which by convention is placed at the **left**

يتم تسمية الببتيدات بدءًا من الطرف الأميني، والذي يتم وضعه على اليسار حسب الاتفاقية



خصائص الرابطة الببتيدية: صلبة ومسطحة

Characteristic of peptide bond: Rigid and Planar

- **Planar:** The six atoms of the peptide group lie in a single plane, with the oxygen atom of the carbonyl group and the hydrogen atom of the amide nitrogen **trans to each other**.

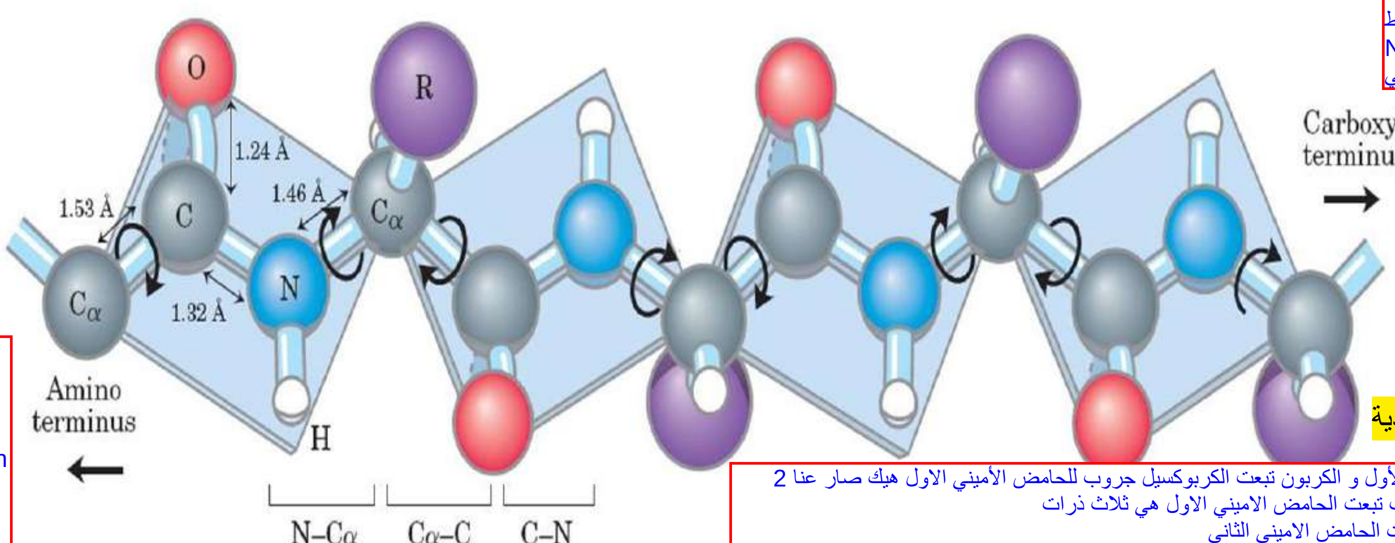
المستوى: تقع الذرات الستة للمجموعة الببتيدية في مستوى واحد، مع ارتباط ذرة الأكسجين في مجموعة الكاربونيل وذرة الهيدروجين في مجموعة النيتروجين الأميدية ببعضهما البعض.

- **Rigid, Unable to rotate around its axis.** The two amino acids linked by such a bond are **not free** to rotate around the N—C linkage because the peptide bond has a partial double-bond character, unlike the N—C and C—C bonds to the central carbon of the amino acid.

صلب، غير قادر على الدوران حول محوره. لا يستطيع الحمضان الأمينيان المرتبطان بمثل هذه الرابطة الدوران بحرية حول الرابطة N—C لأن الرابطة الببتيدية لها طابع الرابطة المزدوجة الجزئية، على عكس الروابط N—C وC—C مع الكربون المركزي للحمض الأميني.

- **Longer than double bond but shorter than a single bond**

• أطول من الرابطة المزدوجة ولكن أقصر من الرابطة المفردة



عندي 4 صفات
Planar
الاكسجين تبعت الكربونيل
الهيدروجين تبعت الامين
موجودين trans postion
انها الطول من الرابطة من المزدوجة واقصر من المفردة
رابع شغلة انها صلبة

شرح للذرات المشاركة في تكوين الرابطة الببتيدية

الالفا كربون تبعت الحامض الاميني الأول و الكربون تبعت الكربوكسيل جروب للحامض الأميني الاول هيك صار عنا 2
والاوكسجين تبعت الكربوكسيل جروب تبعت الحامض الاميني الاول هي ثلاث ذرات
والنيتروجين تبعت الامين جروب تبعت الحامض الاميني الثاني
والهيدروجين تبعت الامين جروب تبعت الحامض الاميني الثاني
والالفا كربون تبعت الحامض الاميني الثاني

تعتمد وظيفة البروتين على شكله

A Protein's Function Depends on the its Shape

- Proteins consist of long **amino acid chains folded** into complex shapes

تتكون البروتينات من سلاسل طويلة من الأحماض الأمينية مطوية في أشكال معقدة

- The **shape** of a protein is very important because it determines the **protein's function.** يعتبر شكل البروتين مهمًا جدًا لأنه يحدد وظيفة البروتين.
- a **general principle** about proteins structure and the folding of the polypeptide chain (s): essentially all the **internal amino acids are nonpolar ones**, amino acids such as leucine, valine, and phenylalanine. Water's tendency to hydrophobically exclude nonpolar molecules **pulls the nonpolar portions** of the amino acid chain **into the protein's interior**.
- This situation positions the **nonpolar amino acids in close contact** with one another, leaving little empty space inside.

يؤدي هذا الوضع إلى وضع الأحماض الأمينية غير القطبية في اتصال وثيق مع بعضها البعض، مما يترك مساحة فارغة صغيرة في الداخل.

- **Polar and charged amino** acids are restricted to **the surface of the protein** except for the few that play key functional roles.

تقتصر الأحماض الأمينية القطبية والمشحونة على سطح البروتين باستثناء القليل منها الذي يلعب أدوارًا وظيفية رئيسية.

- When a cell synthesizes a protein, polypeptides **folding is driven and reinforced** by the formation of **various bonds and forces** between parts of the chain, which in turn depends on the sequence of amino acids.
- Many proteins are roughly spherical (***globular proteins***), while others are shaped like long fibers (***fibrous proteins***).

العديد من البروتينات لها شكل كروي تقريبًا (بروتينات كروية)، في حين أن بعضها الآخر يكون على شكل ألياف طويلة (بروتينات ليفية).

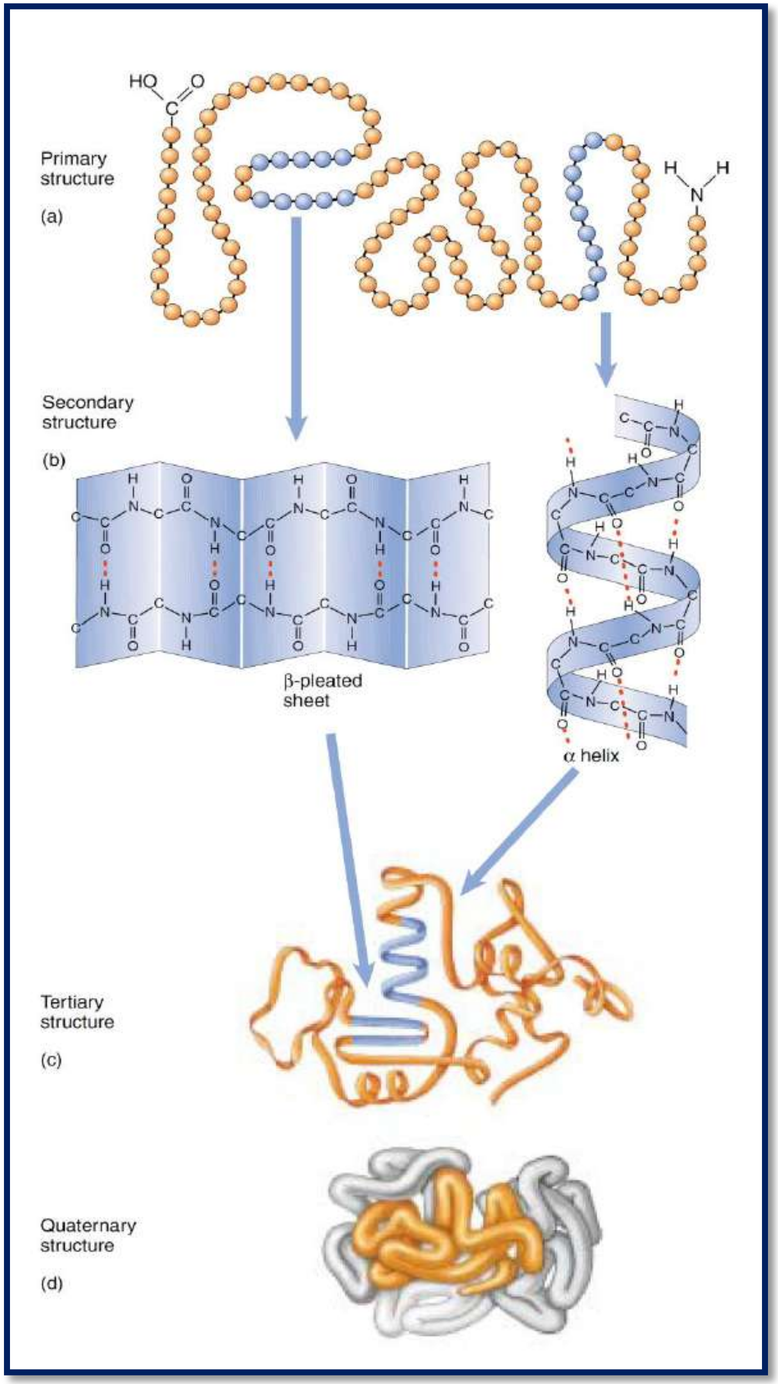
مستويات بنية البروتين

Levels of Protein Structure

- The structure of proteins is traditionally discussed in terms of four levels of structure:

تقليديا، تتم مناقشة بنية البروتينات من حيث أربعة مستويات من البنية:

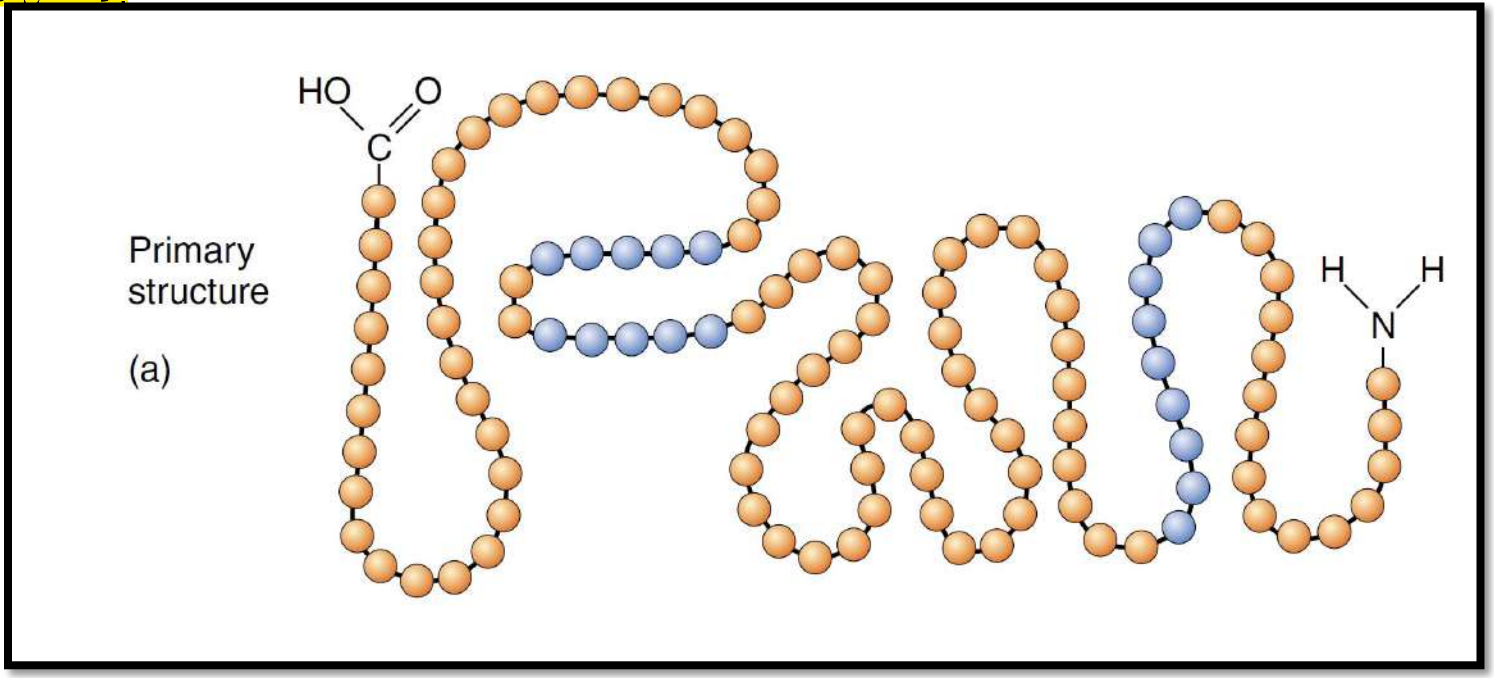
- *Primary,* اساسي
- *Secondary,* ثانوي
- *Tertiary,* ثالثي
- *Quaternary* رباعي



التركيب الأساسي للبروتين

Protein Primary Structure

- **Protein Primary Structure** refers to the specific amino acid sequence (type, number and order of amino acids) يشير الهيكل الأساسي للبروتين إلى تسلسل الأحماض الأمينية المحدد (النوع وعدد وترتيب الأحماض الأمينية)
- This sequence is determined by the nucleotide sequence of the gene (DNA) that encodes the protein. يتم تحديد هذا التسلسل من خلال تسلسل النوكليوتيدات في الجين (DNA) الذي يشفر البروتين.
- Because the R groups that distinguish the various amino acids play no role in the peptide backbone of proteins, a protein can consist of any sequence of amino acids. نظرًا لأن المجموعات R التي تميز الأحماض الأمينية المختلفة لا تلعب أي دور في العمود الفقري الببتيدي للبروتينات، يمكن أن يتكون البروتين من أي تسلسل من الأحماض الأمينية.



Protein Secondary Structure

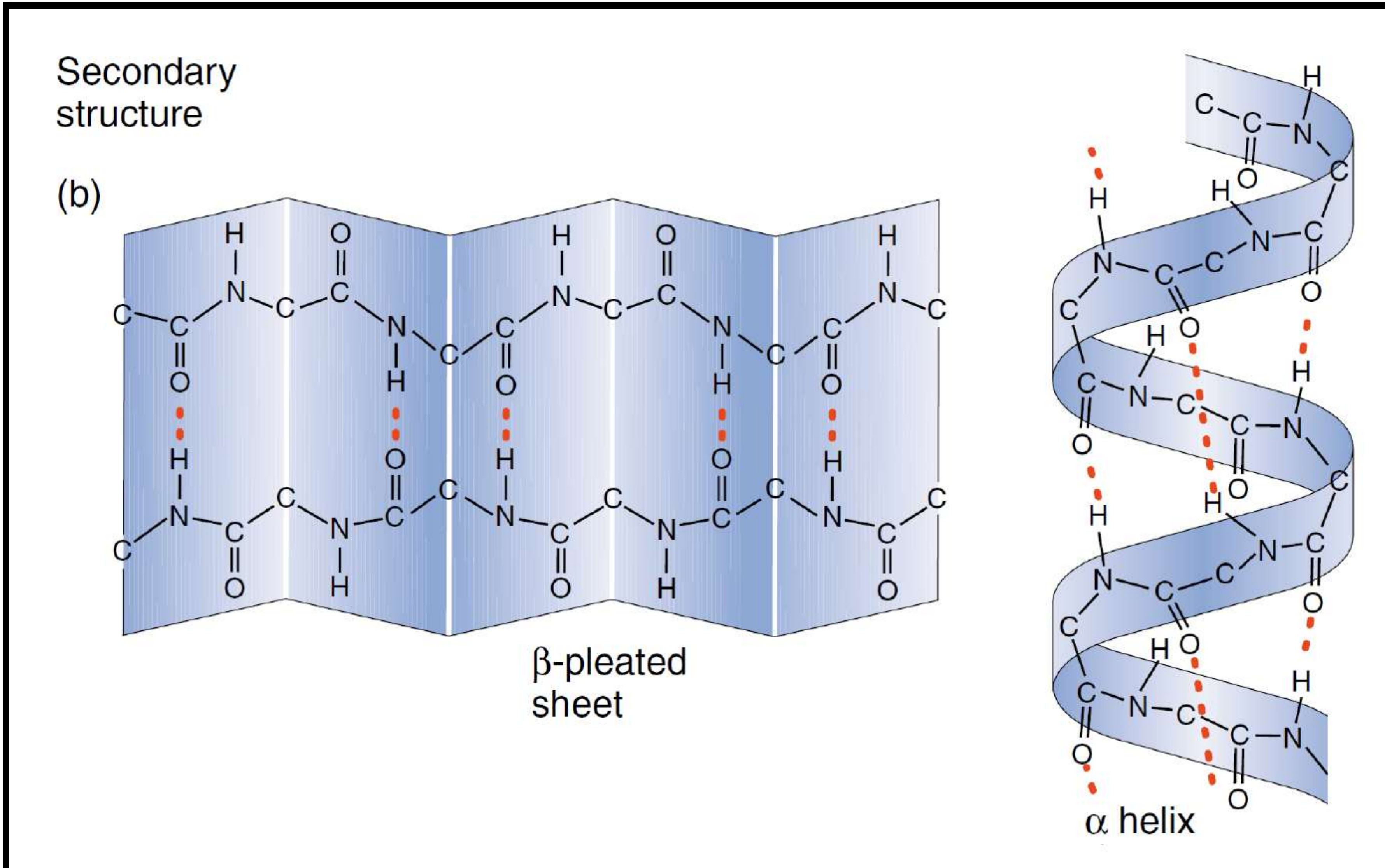
- **Secondary structure** is about the arrangement of the polypeptide chain in space
  تتعلق البنية الثانوية بترتيب سلسلة البولي ببتيد في الفضاء
- Most proteins have segments of their polypeptide chains repeatedly coiled or folded in patterns that contribute to the protein's overall shape.
  تحتوي معظم البروتينات على أجزاء من سلاسل البوليببتيد الخاصة بها ملتفة أو مطوية بشكل متكرر في أنماط تساهم في الشكل العام للبروتين.
- These **coils and folds (pleats),** collectively referred to as **secondary structure**, are the result of hydrogen bonds between the repeating constituents of the polypeptide backbone **(not the amino acid side (R) chains**).

هذه الملفات والثنيات (الثنيات)، والتي يشار إليها بشكل جماعي باسم البنية الثانوية، هي نتيجة الروابط الهيدروجينية بين المكونات المتكررة للعمود الفقري للبوليببتيد (وليس سلاسل الأحماض الأمينية الجانبية (R)).

- The folding of the amino acid chain by hydrogen bonding into these characteristic coils and pleats is called a protein's secondary structure. يُطلق على طي سلسلة الأحماض الأمينية عن طريق الروابط الهيدروجينية في هذه اللفات والتجاعيد المميزة اسم البنية الثانوية للبروتين.
- The α—COOH and α —NH_2 groups of the main chain form quite good hydrogen bonds. تشكل مجموعات α—COOH وα—NH_2 في السلسلة الرئيسية روابط هيدروجينية جيدة جدًا.
- Two patterns of H bonding occur: **α helix and β-pleated sheet** patterns.
- يحدث نمطان من الروابط الهيدروجينية: نمط حلزوني ونمط صفائحي مطوي β.
- In one, hydrogen bonds form along a single polypeptide chain (**intrachain**), linking one amino acid to another farther down the chain, and thus tends to pull the chain into a coil called an **α helix**.
  في الأولى، تتشكل الروابط الهيدروجينية على طول سلسلة بولي ببتيد واحدة (سلسلة داخلية)، وتربط حمض أميني بآخر أبعد في السلسلة، وبالتالي تميل إلى سحب السلسلة إلى ملف يسمى حلزون .
- In the other pattern, hydrogen bonds occur across two polypeptide chains (**interchain**), linking the amino acids in one chain to those in the other. Often, many parallel chains are linked, forming a pleated, sheet-like structure called **a β-pleated sheet**.

في النمط الآخر، تحدث الروابط الهيدروجينية عبر سلسلتين من البولي ببتيد (سلاسل متداخلة)، حيث تربط الأحماض الأمينية في سلسلة واحدة بتلك الموجودة في السلسلة الأخرى. غالبًا ما ترتبط العديد من السلاسل المتوازية، لتشكل بنية مطوية تشبه الصفائح تسمى صفائح مطوية بيتا.

α helix and β-pleated sheet

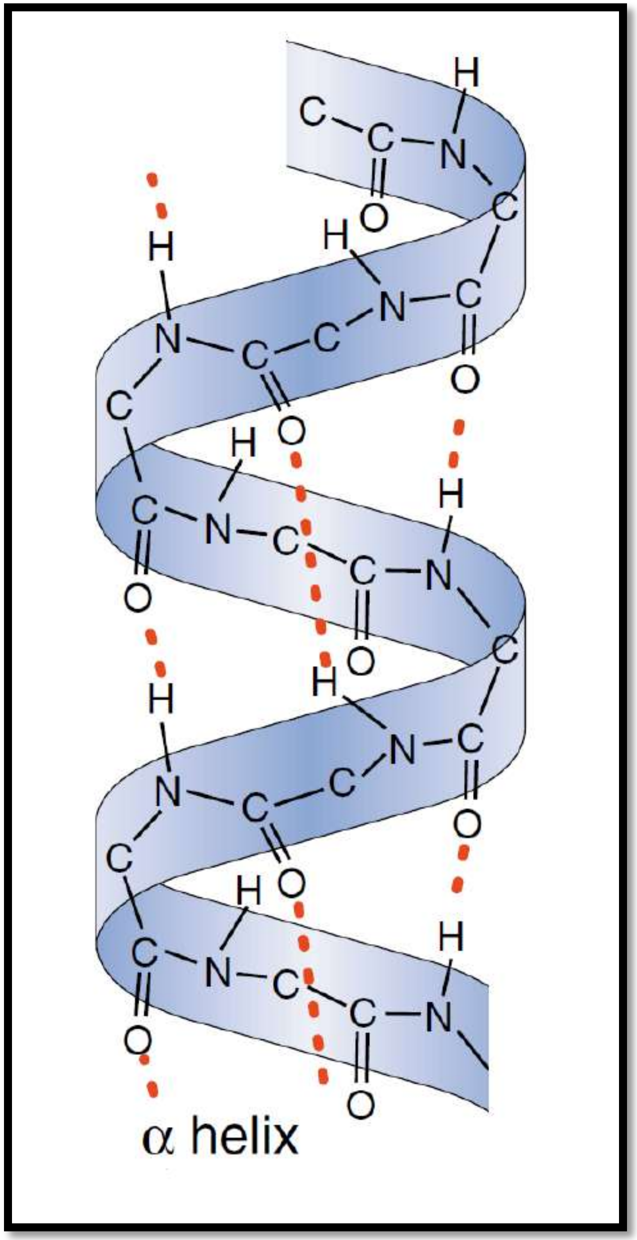


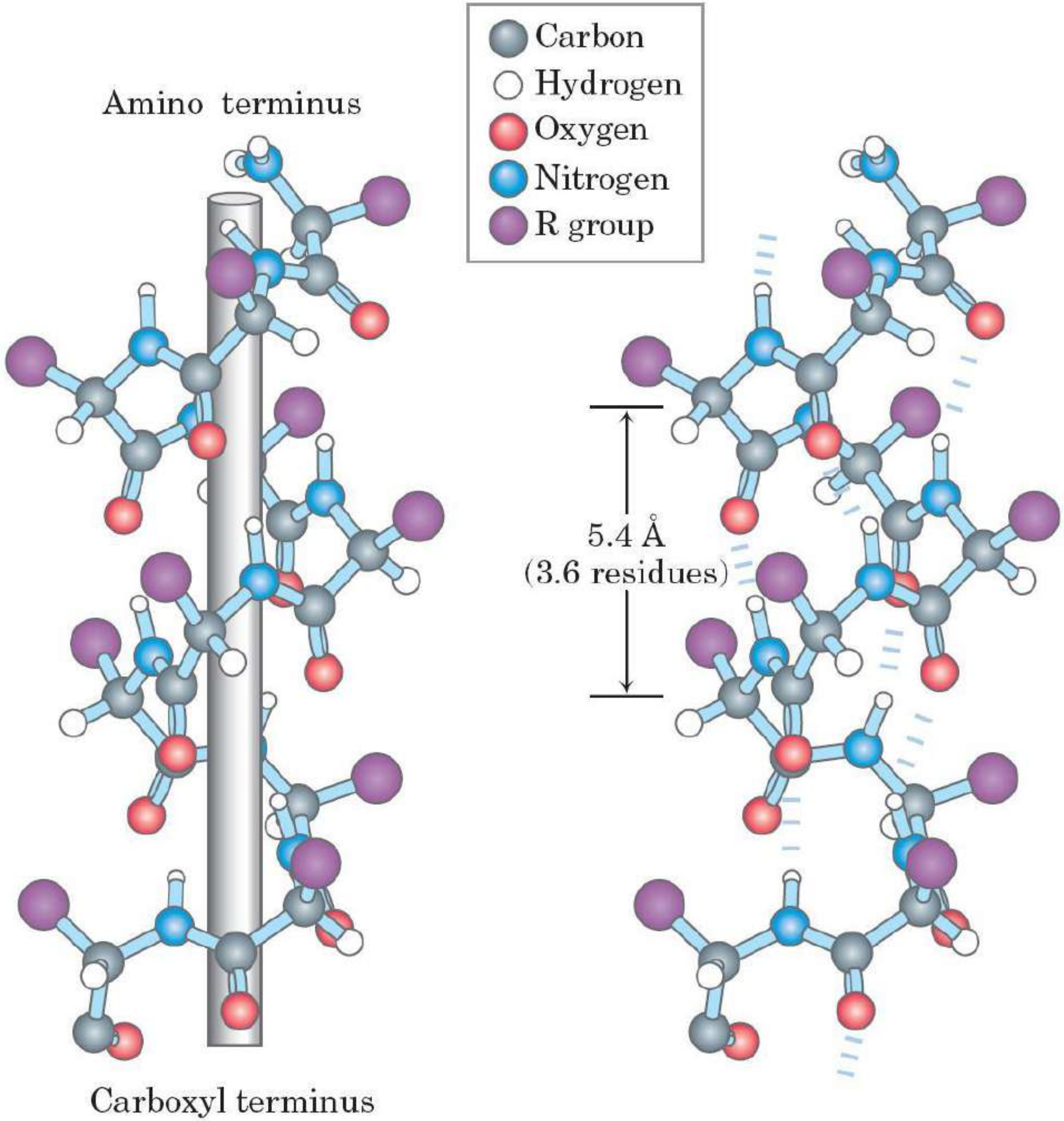
هو بنية ثانوية شائعة للبروتين الحلزون

The α Helix Is a Common Protein Secondary Structure

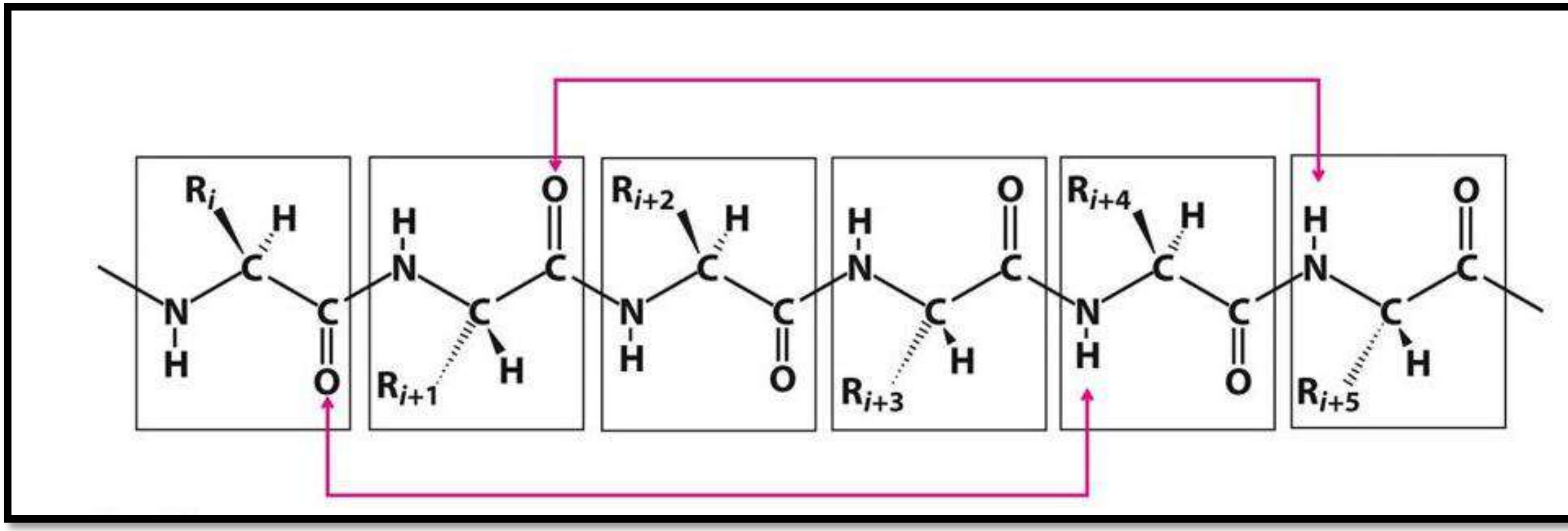
- The simplest arrangement the polypeptide chain could assume with its rigid peptide bonds (but other single bonds free to rotate) is a helical structure called the **α helix.**
- In **α helix** structure the polypeptide backbone is tightly coiled around an imaginary longitudinal axis, and the R groups of the amino acid residues protrude or extend outward from the helical backbone.
- A tightly coiled backbone forms the inner part of the rod and the side chains extend outward in a helical array
- The α helix is a coiled Structure stabilized by **intrachain hydrogen bonds**.
- The screw sense of a helix can be right-handed (clockwise) or left-handed (counterclockwise).
- However, right-handed helices are energetically more favorable because there is less steric clash between the side chains and the backbone.
- Essentially all α helices found in proteins are right-handed.

الموجودة في البروتينات هي حلزونات يمينية في الأساس، جميع حلزونات.




Carbon
Hydrogen
Oxygen
Nitrogen
R group
Amino terminus
Carboxyl terminus
5.4 Å
(3.6 residues)

Hydrogen-Bonding Scheme For an α helix.



In the a helix, the C=O group of residue *n* forms a hydrogen bond with the N-H group of residue *n*+ 4.

تتشكل رابطة هيدروجينية بين الامايد والكرونيل قبل او بعد 4

يؤثر تسلسل الأحماض الأمينية على استقرار الحلزون

Amino Acid Sequence Affects α Helix Stability

- Not all polypeptides can form a stable α helix. Interactions between amino acid side chains can **stabilize or destabilize** this structure.

لا يمكن لجميع البوليبيتيدات تكوين حلزون مستقر. يمكن للتفاعلات بين السلاسل الجانبية للأحماض الأمينية أن تعمل على تثبيت أو زعزعة استقرار هذا الهيكل

- If a polypeptide chain has a long block of **Glutamic acid** residues, this segment of the chain will not form an α helix at pH 7.0. The -ve carboxyl groups of adjacent Glutamic acid residues repel each other so strongly that they prevent formation of the helix. For the same reason, Lysine and/or Arginine residues (+ve).

إذا كانت سلسلة البولي ببتيد تحتوي على كتلة طويلة من بقايا حمض الجلوتاميك، فلن يشكل هذا الجزء من السلسلة حلزونًا عند درجة حموضة 7.0. تتنافر مجموعات الكربوكسيل السالبة لبقايا حمض الجلوتاميك المجاورة مع بعضها البعض بقوة لدرجة أنها تمنع تكوين الحلزون. لنفس السبب، فإن بقايا الليسين و/أو الأرجينين (موجبة).

- The bulk and shape of **Tyr, Trp, Phe, Met Ile, Val, Thr** residues can also **destabilize an α helix** if they are close together in the chain.

يمكن أيضًا أن يؤدي حجم وشكل بقايا Tyr وTrp وPhe وMet Ile وVal وTh إلى زعزعة استقرار الحلزون إذا كانت قريبة من بعضها البعض في السلسلة.

- **In Asp, Asn, Ser, H-bonding side chains compete** directly with backbone H-bonds.

في Asp و Asn و Ser، تتنافس السلاسل الجانبية الرابطة للهيدروجين بشكل مباشر مع الروابط الهيدروجينية الأساسية.

- A **constraint** on the formation of the α helix is the presence of **Pro or Gly** residues.

•إن أحد القيود التي تمنع تكوين الحلزون هو وجود بقايا البرو أو الجلايسين.

- In proline, the nitrogen atom is part of a rigid ring, so **free rotation is not** possible. Thus, a Pro residue introduces a destabilizing **kink** in an α helix. In addition, the **nitrogen atom** of a Pro residue in peptide linkage has **no substituent hydrogen** to participate in hydrogen bonds with other residues. For these reasons, proline is only rarely found within an α helix.

- **Glycine occurs infrequently** in α helices for a different reason: it has more conformational **flexibility** than the other amino acid residues. Polymers of glycine tend to take up coiled structures quite different from an α helix.

- A final factor affecting the stability of an helix in a polypeptide is the identity of the amino acid residues near the **ends of the -helical segment**.

العامل الأخير الذي يؤثر على استقرار الحلزون في البوليببتيد هو هوية بقايا الأحماض الأمينية بالقرب من نهايات الجزء الحلزوني.

- Normally, a small electric dipole exists in each peptide bond. These dipoles are connected through the hydrogen bonds of the helix, resulting in a **net dipole extending along the helix, with** partial positive and negative charges of the helix dipole actually exist near the amino-terminal and carboxyl-terminal ends of the helix, respectively.

عادةً، يوجد ثنائي قطب كهربائي صغير في كل رابطة ببتيدية. ترتبط هذه الثنائيات القطبية من خلال الروابط الهيدروجينية للحلزون، مما ينتج عنه ثنائي قطب صافٍ يمتد على طول الحلزون، مع وجود شحنات موجبة وسلبية جزئية لثنائي قطب الحلزون في الواقع بالقرب من الأطراف الأمينية الطرفية والكربوكسيلية للحلزون، على التوالي

- **The four amino acid residues** at each end of the helix do not participate fully in the helix hydrogen bonds.

لا تشارك بقايا الأحماض الأمينية الأربعة الموجودة في كل طرف من الحلزون بشكل كامل في الروابط الهيدروجينية الحلزونية.

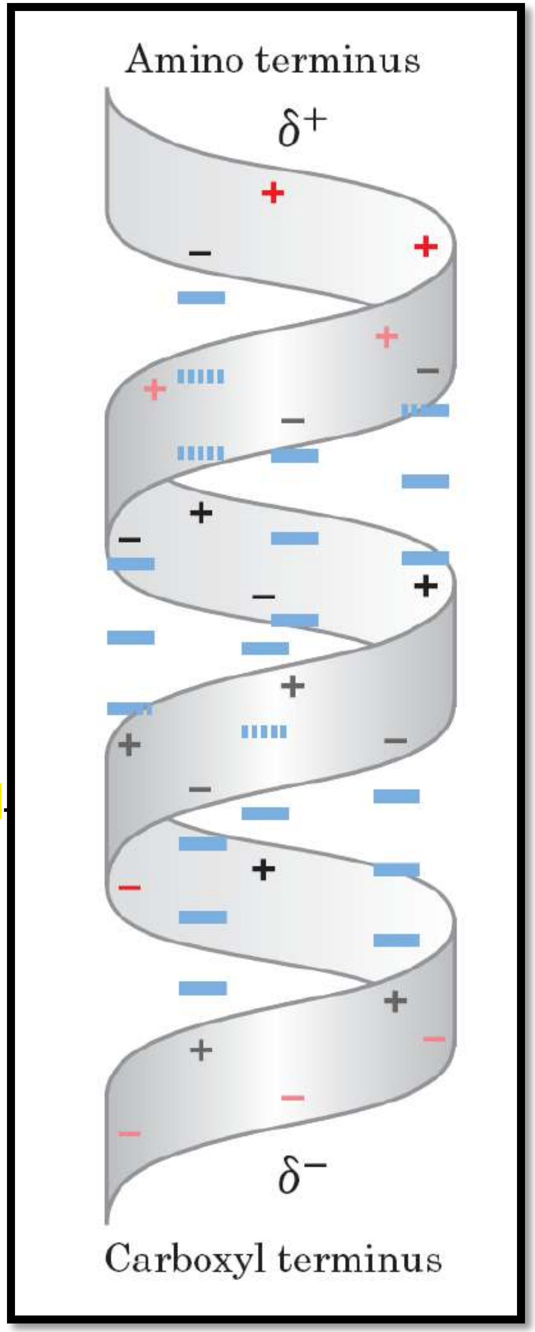
- For this reason, **negatively charged amino acids** are often found near the **amino terminus** of the helical segment, where they have a **stabilizing** interaction with the positive charge of the helix dipole.

- a **positively charged** amino acid at the amino terminal end is **destabilizing**.

حمض أميني مشحون إيجابيا في الطرف الطرفي الأميني يسبب عدم الاستقرار.

- The opposite is true at the carboxyl-terminal end of the helical segment.

والعكس صحيح في الطرف الكربوكسيلي للجزء الحلزوني.



أنواع من القيود تؤثر على استقرار الحلزون 5

5 kinds of restrictions affect the stability of an α helix

- (1) the electrostatic **repulsion (or attraction)** between successive amino acid residues with charged R groups.

التنافر (أو الجذب) الكهروستاتيكي بين بقايا الأحماض الأمينية المتعاقبة ذات المجموعات R المشحونة.

- (2) the **bulkiness** of adjacent R groups

ضخامة المجموعات R المجاورة

- (3) the **interactions between R groups** spaced three (or four) residues apart.

التفاعلات بين المجموعات R بقايا (أو أربعة) متباعدة بمسافة ثلاثة.

- (4) the occurrence of **Pro and Gly** residues

حدوث بقايا البرو و الجلايسين

- (5) the interaction between **amino acid residues at the ends** of the helical segment and the electric dipole inherent to the α helix.

التفاعل بين بقايا الأحماض الأمينية في نهايات القطعة الحلزونية والثنائي القطب الكهربائي المتأصل في القطعة الحلزونية.

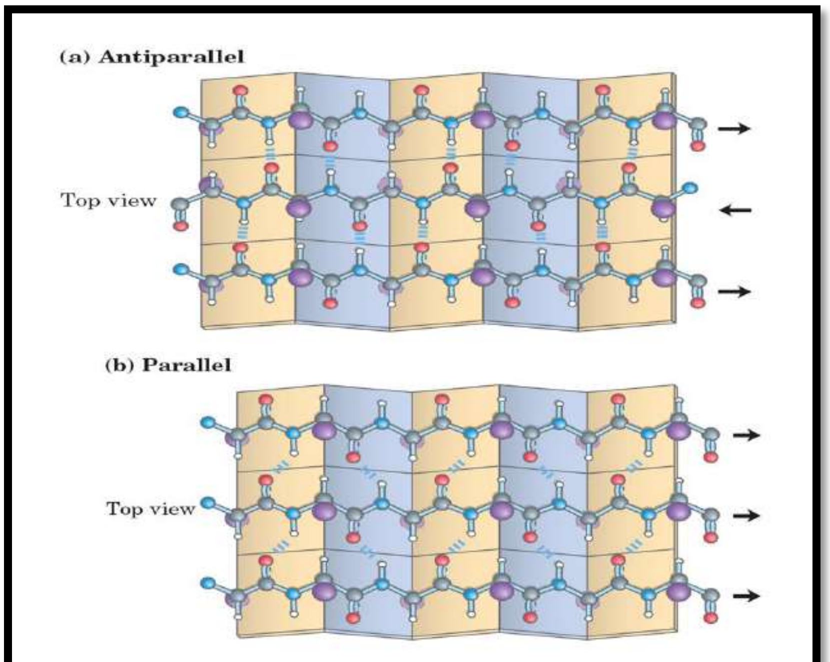
- So, the tendency of a given segment of a polypeptide chain to fold up as an α helix therefore **depends** on the identity and sequence of amino acid residues within the segment.

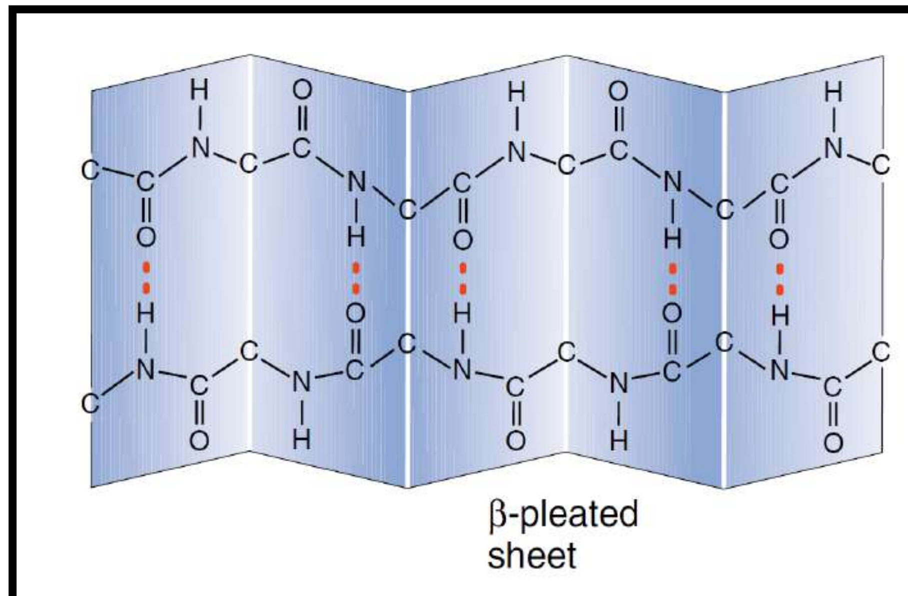
وبالتالي، فإن ميل جزء معين من سلسلة البولييبتيد إلى الانطواء على شكل حلزوني يعتمد على هوية وتسلسل بقايا الأحماض الأمينية داخل الجزء.

يتم تثبيت الصفائح المطوية عن طريق الرابطة الهيدروجينية [بين السلاسل] بين خيوط البولي ببتيد

β pleated Sheets Are Stabilized by [inter-chain] H- Bonding Between Polypeptide Strands

- The β pleated sheet differs markedly from the rod like α helix.
  تختلف الورقة المطوية بشكل ملحوظ عن الورقة الحلزونية على شكل قضيب.
- A polypeptide chain, called a β *strand*, in a β sheet is almost fully **extended rather than being tightly coiled** as in the α helix. سلسلة البولي ببتيد، والتي تسمى خيطًا، في ورقة ممتدة بالكامل تقريبًا بدلاً من أن تكون ملتفة بإحكام كما هو الحال في الحلزون.
- The **side chains** of adjacent amino acids point in **opposite directions**.
  تشير السلاسل الجانبية للأحماض الأمينية المتجاورة إلى اتجاهات متعاكسة.
- A β sheet is formed by linking two or more β strands by hydrogen bonds (**inter-chain** hydrogen bonds)
  (يتم تشكيل الورقة عن طريق ربط سلسلتين أو أكثر بواسطة روابط هيدروجينية (روابط هيدروجينية بين السلاسل
- Adjacent chains in a β sheet can run in opposite directions (**antiparallel β sheet**) or in the same direction (**parallel β sheet**).
  (يمكن للسلاسل المتجاورة في ورقة أن تعمل في اتجاهين متعاكسين (ورقة متوازية) أو في نفس الاتجاه (ورقة متوازية

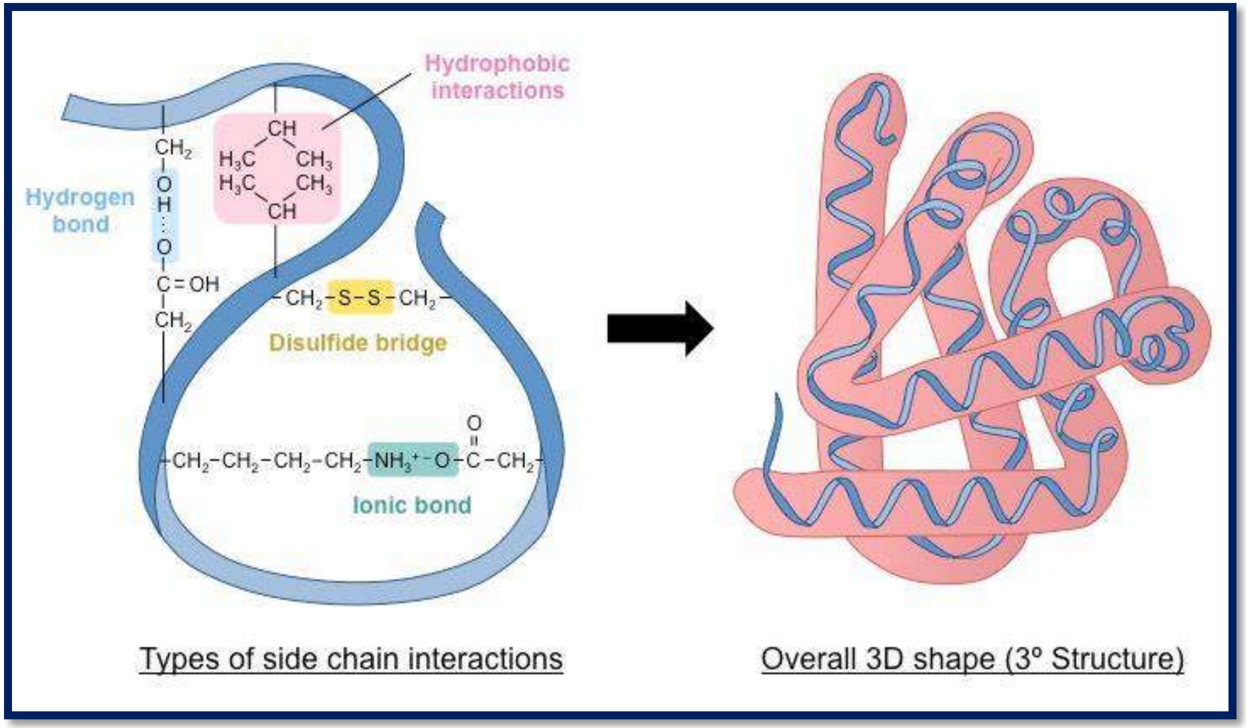




Tertiary Structure

- **Tertiary structure** is the overall 3D arrangement of all atoms in a protein.
البنية الثلاثية هي الترتيب الشامل ثلاثي الأبعاد لجميع الذرات في البروتين.
- Amino acids that are far apart in the polypeptide sequence and that reside in different types of secondary structure may interact within the completely folded structure of a protein. يمكن للأحماض الأمينية المتباعدة في تسلسل البولييبتيد والتي توجد في أنواع مختلفة من البنية الثانوية أن تتفاعل داخل البنية المطوية بالكامل للبروتين.
- Interacting segments of polypeptide chains are held in their characteristic tertiary positions by different kinds of **weak bonding interactions** (and sometimes by **covalent bonds such as S-S bridges**) between the segments.

يتم تثبيت الأجزاء المتفاعلة من سلاسل البولييبتيد في مواضعها الثلاثية المميزة من خلال أنواع مختلفة من تفاعلات الترابط الضعيفة (وأحيانًا عن طريق الروابط التساهمية مثل جسور S-S) بين الأجزاء.



القوى والعوامل واستقرار البنية الثلاثية للبروتين

Forces and factors and stabilize protein tertiary structure

- **Hydrophobic interaction** between hydrophobic (nonpolar) side chains usually end up in clusters at the core of the protein, out of contact with water.
- Once nonpolar amino acid side chains are close together, **van der Waals interactions** help hold them together. **van der Waals interactions are** nonspecific, nondirectional attraction and occur when adjacent atoms come close enough that their outer electron clouds just barely touch.
- **Hydrogen bonds** between polar side chains

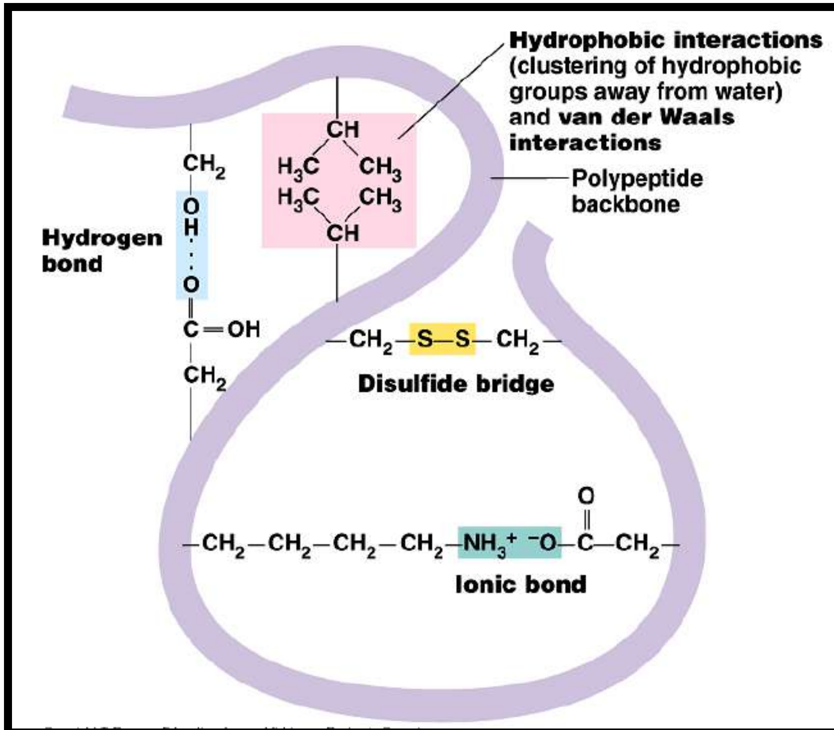
الروابط الهيدروجينية بين السلاسل الجانبية القطبية

- **Ionic bonds** between positively and negatively charged side chains also help stabilize tertiary structure.
- Covalent bonds called **disulfide bridges (S-S bonds)** may further reinforce the shape of a protein.

قد تعمل الروابط التساهمية المسماة بجسور ثاني كبريتيد (روابط S-S) على تعزيز شكل البروتين بشكل أكبر

- **Temperature and pH**

بتيجي بالامتحان ما هي العوامل المؤثرة بنقول الحرارة و البي اتش



All of these different kinds of interactions can contribute to the stability of protein tertiary structure

كل هذه الأنواع المختلفة من التفاعلات يمكن أن تساهم في استقرار البنية الثلاثية للبروتين

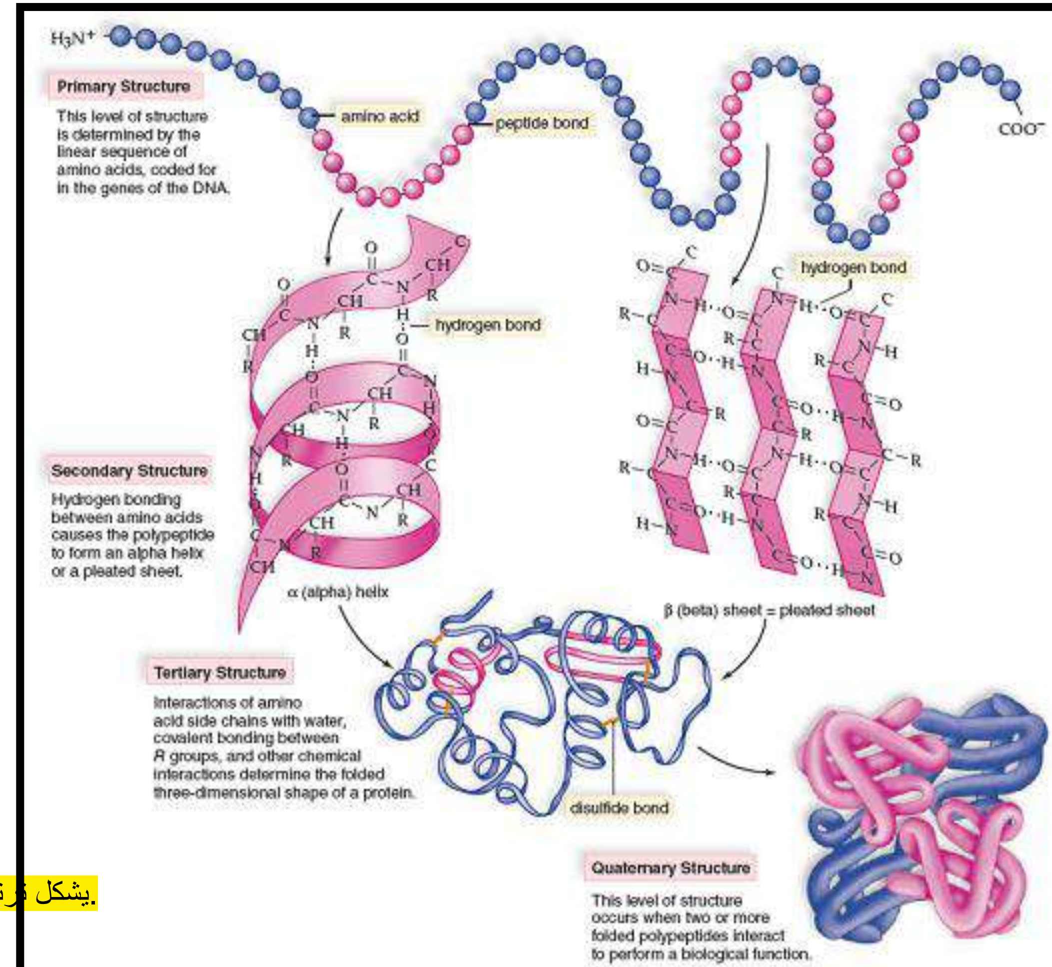
Protein Quaternary Structure

- Some proteins contain two or more separate polypeptide chains, or subunits, which may be identical or different.

تحتوي بعض البروتينات على سلسلتين أو أكثر من سلاسل البولي ببتيد المنفصلة، أو وحدات فرعية، والتي قد تكون متطابقة أو مختلفة.

- The arrangement of these protein subunits in three-dimensional complexes constitutes **quaternary structure**.

يشكل ترتيب هذه الوحدات الفرعية من البروتين في مجمعات ثلاثية الأبعاد بنية رباعية.



The subunits need not be the same. Hemoglobin, for example, is a protein composed of two α-chain subunits and two β- chain subunits.

لا يلزم أن تكون الوحدات الفرعية متماثلة. على سبيل المثال، الهيموجلوبين عبارة عن بروتين يتكون من وحدتين فرعيتين من سلسلة ألفا ووحدتين فرعيتين من سلسلة بيتا.

Lipids

- Lipids are a diverse group of **hydrophobic molecule.**

  .الدهون هي مجموعة متنوعة من الجزيئات الكارهة للماء

- Lipids are a somewhat **loosely defined group** of molecules with one main chemical characteristic: they are **insoluble in water**.

  .الدهون هي مجموعة من الجزيئات غير محددة بشكل واضح ولها خاصية كيميائية رئيسية واحدة: فهي غير قابلة للذوبان في الماء

- The **most familiar** lipids are fats, oils and phospholipids.
- .الدهون الأكثر شيوعًا هي الدهون والزيوت والفوسفوليبيدات
- Other lipids include: **Terpenes, Prostaglandins, Steroids and Waxes**

  تشمل الدهون الأخرى: التربينات والبروستاجلاندينات والستيرويدات والشمع

- Lipids have a very high proportion of nonpolar carbon-hydrogen (C—H) bonds which serve as **long-term energy storage**.

  .تحتوي الدهون على نسبة عالية جدًا من الروابط غير القطبية بين الكربون والهيدروجين (C—H) والتي تعمل كمخزن للطاقة على المدى الطويل

تتكون الدهون من أحماض دهنية معقدة مرتبطة بالجلسرين

Fats consist of complex fatty acids attached to glycerol

- **Fats** are lipid molecules built from a simple skeleton made up of two main kinds of molecules: **fatty acids and glycerol**.

الدهون هي جزيئات دهنية مبنية من هيكل بسيط يتكون من نوعين رئيسيين من الجزيئات: الأحماض الدهنية والجلسرين.

- **Fatty acids** are long-chain hydrocarbons (hydrophobic) with a functional **carboxyl group (COOH)** at one end that gives them the name fatty acid.
- Fatty acids are carboxylic acids **with diverge hydrocarbon chain length** ranging from 4 to 36 carbons long (**C4 to C36**), but the **most common** are even-numbered chains of 14 to 20 carbons.

الأحماض الدهنية هي أحماض كربوكسيلية ذات سلسلة هيدروكربونية متباعدة يتراوح طولها من 4 إلى 36 ذرة كربون (C4 إلى C36)، ولكن الأكثر شيوعًا هي السلاسل ذات الأرقام الزوجية من 14 إلى 20 ذرة كربون.

- **Glycerol** is a 3-carbon polyalcohol (**three —OH groups**).

الجلسرين عبارة عن بولي كحول مكون من ثلاث مجموعات كربون (ثلاث مجموعات OH).

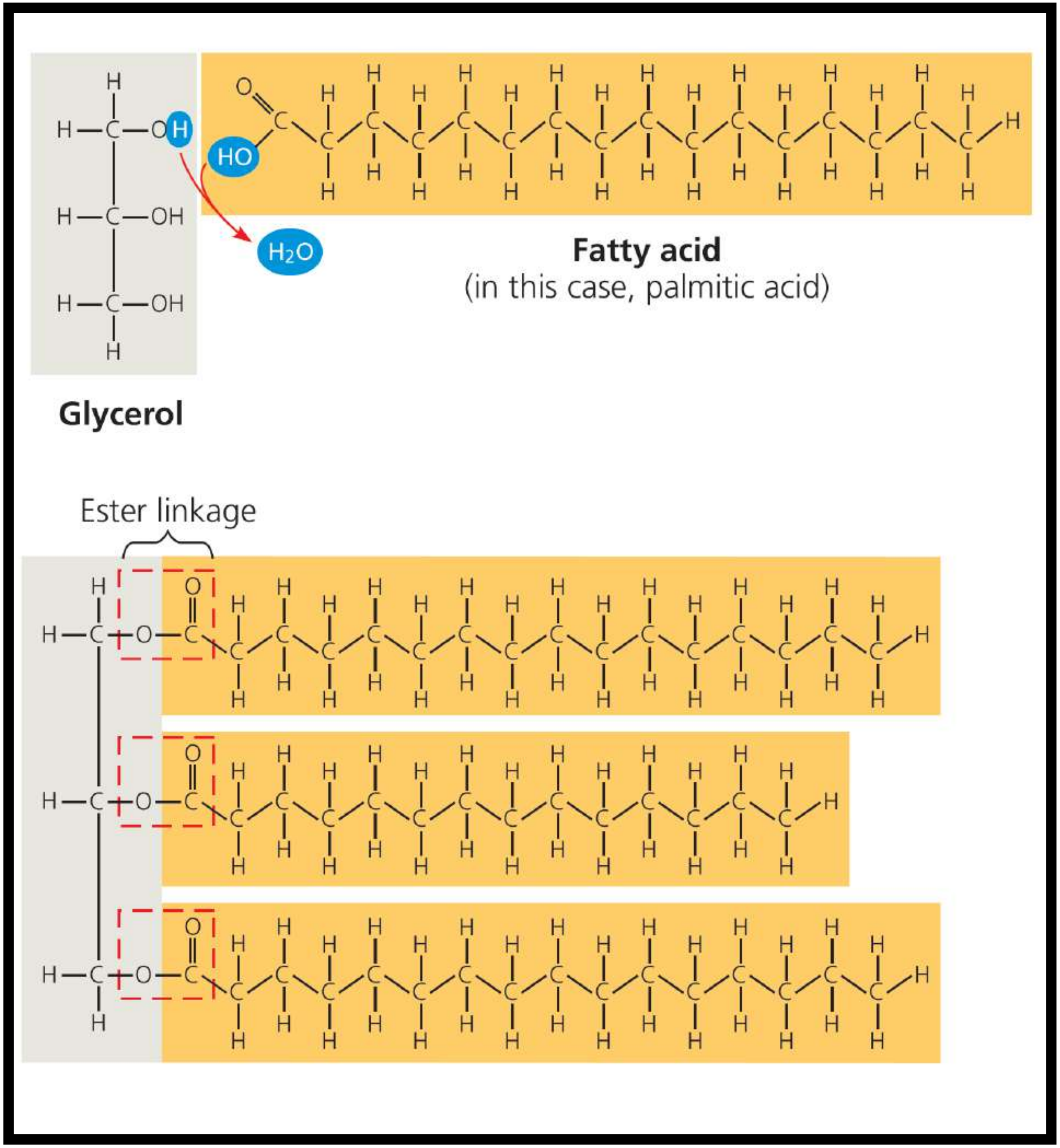
- **Fats** are lipid molecules consist of a **glycerol molecule with three fatty acids** attached through **an ester linkage**, one to each carbon of the glycerol backbone producing fat and commonly called a **triglyceride** (the more accurate chemical name is **triacylglycerol**).

الدهون هي جزيئات دهنية تتكون من جزيء جلسرين مع ثلاثة أحماض دهنية مرتبطة من خلال رابطة إستر، واحد لكل ذرة كربون من العمود الفقري للجلسرين تنتج الدهون وتسمى عادة ثلاثي الجليسريد (الاسم الكيميائي الأكثر دقة هو ثلاثي أسيل الجلسرين).

- The **three fatty acids** of a triglyceride **need not be identical**, and often they are very different from one another. ليس من الضروري أن تكون الأحماض الدهنية الثلاثة المكونة للدهون الثلاثية متطابقة، وغالبًا ما تكون مختلفة جدًا عن بعضها البعض.
- The many C—H bonds of fats serve as a form of **long-term energy storage**.

تعتبر الروابط C—H العديدة الموجودة في الدهون بمثابة شكل من أشكال تخزين الطاقة على المدى الطويل.

كونت رابطة استر
وهي بتتكون ما بين مجموعة كحول
ومجموعة حمض



تسمية الأحماض الدهنية

Nomenclature of fatty acids

- A simplified **nomenclature** for fatty acids compounds specifies the **chain length** and number of **double bonds**, separated by a **colon (:)**

تحدد التسمية المبسطة لمركبات الأحماض الدهنية طول السلسلة وعدد الروابط المزدوجة، مفصولة بعلامة النقطتين (:)

- e.g: The 16-carbon saturated **palmitic acid** is abbreviated **16:0**

هو عدد الكربون 16
عدد الروابط الثنائية 0

- e.g: The 18-carbon **oleic acid**, with one double bond, is **18:1.**

- **Positions** of any double bonds are specified by superscript numbers following **Δ (delta).**

يتم تحديد مواضع أي رابطة مزدوجة بأرقام علوية بعد Δ (دلتا).

رقم الروابط الثنائية بنحطه فوق شعار الدلتا

- A 20-carbon fatty acid with one double bond between **C-9 and C-10** (C-1 being the carboxyl carbon) and another between **C-12 and C-13** is designated **20:2($\Delta^{9,12}$).**

لو عندي 20 فاتي اسيد ووحدة دبل بوند بين كربونة 9 وكربونة 10 وكمان دبل بوند بين كربونة 12 و 13 بتصير التسمية كتالي.

- There is also a **common pattern** in the location of double bonds; in most **monounsaturated** fatty acids the double bond is between C-9 and C-10 **(Δ^9)**, the other double bonds of **polyunsaturated** fatty acids are generally **Δ^{12} and Δ^{15}**.

يوجد أيضًا نمط مشترك في موقع الروابط المزدوجة؛ ففي معظم الأحماض الدهنية الأحادية غير المشبعة تكون الرابطة المزدوجة بين C-9 وC-10 (Δ9)، وتكون الروابط المزدوجة الأخرى للأحماض الدهنية المتعددة غير المشبعة عمومًا Δ12 وΔ15.

- The **double bonds (C=C)** of polyunsaturated fatty acids are almost **never conjugated** (alternating single and double bonds, as in -CH=CH-CH=CH-), but are **separated by a methylene (CH_2) group**: -CH=CH-**CH_2**-CH=CH-.

بنفعش الدبل بوند يكونوا متتاليين لا ينفصل بينهم برابطة احادية

- In **nearly all naturally** occurring unsaturated fatty acids, the double bonds are in the **cis configuration**.

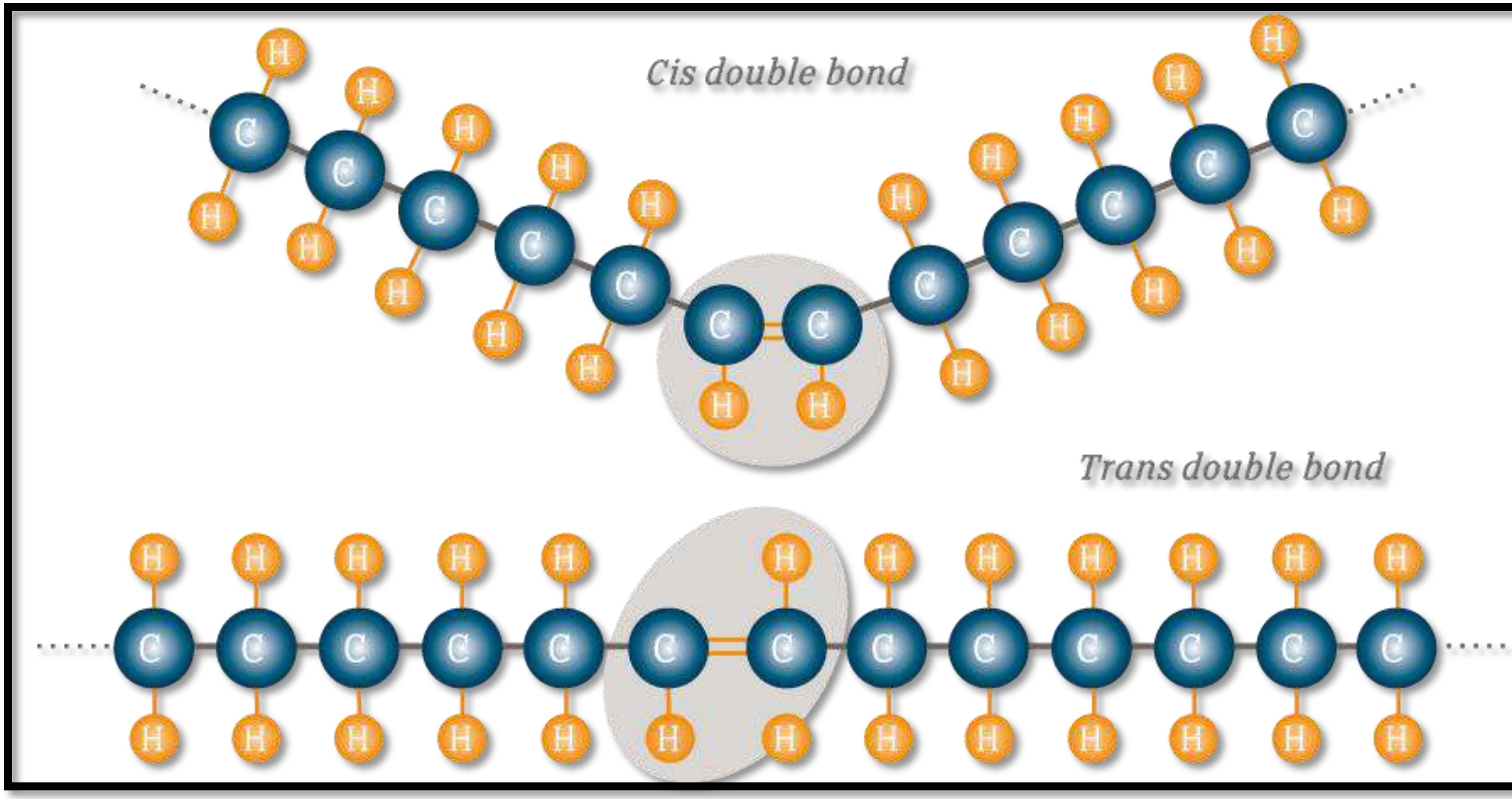
في جميع الأحماض الدهنية غير المشبعة الموجودة بشكل طبيعي تقريبًا، تكون الروابط المزدوجة في تكوين سيس.

الأحماض الدهنية المشبعة وغير المشبعة

Saturated and unsaturated fatty acids

- If all of the internal **carbon atoms** in a fatty acid chain are **bonded to two hydrogen** atoms, we call this **saturated** إذا كانت جميع ذرات الكربون الداخلية في سلسلة الأحماض الدهنية مرتبطة بذرتي هيدروجين، فإننا نسمي هذا مشبعًا
- **Most animal** fats are **saturated** and the **flexibility** hydrocarbon chains allows the fat molecules to pack together **tightly**. معظم الدهون الحيوانية مشبعة، ومرونة سلاسل الهيدروكربون تسمح لجزيئات الدهون بالتجمع معًا بإحكام.
- A fatty acid with **double bonds** between one or more pairs of successive carbon atoms will have fewer hydrogen atoms, and thus is said to be **unsaturated. Monounsaturated** (one double bond) **polyunsaturated (**> one double bond**).**
- Having double bonds changes the behavior of the molecule because **free rotation cannot occur about a C=C double bond** as it can with a C—C single bond thus affecting melting point of the fat. كما يحدث مع الرابطة C=C يؤدي وجود روابط مزدوجة إلى تغيير سلوك الجزيء لأن الدوران الحر لا يمكن أن يحدث حول الرابطة المزدوجة وبالتالي يؤثر ذلك على نقطة انصهار الدهون C—C المفردة.
- Fats containing **polyunsaturated** fatty acids **have low melting points** because their fatty acid **chains bend** at the double bonds, preventing the fat molecules from aligning closely with one another. تتمتع الدهون التي تحتوي على أحماض دهنية متعددة غير مشبعة بنقاط انصهار منخفضة لأن سلاسل الأحماض الدهنية الخاصة بها تنحني عند الروابط المزدوجة، مما يمنع جزيئات الدهون من التوافق بشكل وثيق مع بعضها البعض.
- **Most naturally** occurring unsaturated fatty acids have double bonds with a ***cis* configuration**, that creates a **kink** in the hydrocarbon chain wherever it occurs.
تحتوي معظم الأحماض الدهنية غير المشبعة الطبيعية على روابط مزدوجة ذات تكوين سيس، مما يخلق عقدة في سلسلة الهيدروكربون أينما حدثت.
- When fats are **partially hydrogenated industrially**, this can produce double bonds with a ***trans* configuration** resulting in the so-called ***trans fats***
عندما يتم هدرجة الدهون جزئيًا صناعيًا، يمكن أن يؤدي هذا إلى إنتاج روابط مزدوجة ذات تكوين متحول مما يؤدي إلى ما يسمى بالدهون المتحولة
- ***trans fats*** have been linked to elevated levels of low-density lipoprotein (LDL) and lowered levels of high-density lipoprotein (HDL) which is thought to be associated with an increased risk for **coronary heart disease**.

وقد ارتبطت الدهون المتحولة بارتفاع مستويات البروتين الدهني منخفض الكثافة (LDL) وانخفاض مستويات البروتين الدهني عالي الكثافة (HDL)، والذي يُعتقد أنه مرتبط بزيادة خطر الإصابة بأمراض القلب التاجية.



- Saturated **animal fats**, such as lard and butter, are **solid at room temperature**.

تكون الدهون الحيوانية المشبعة، مثل شحم الخنزير والزبدة، صلبة في درجة حرارة الغرفة.

- In contrast, the fats of **plants and fishes** are generally unsaturated (Usually **liquid at room temperature**), meaning that they are composed of one or more types of unsaturated fatty acids.

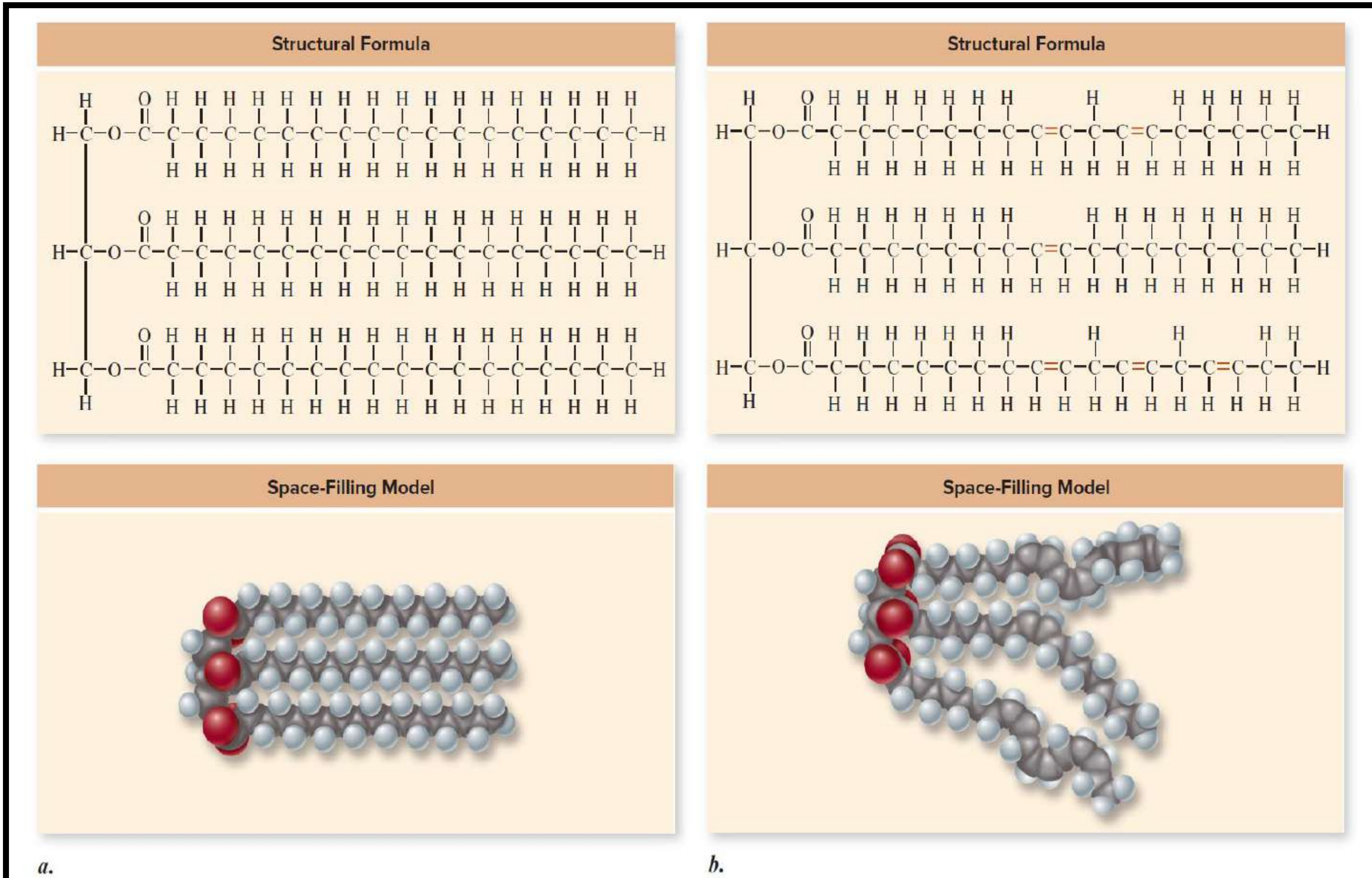
في المقابل، فإن الدهون الموجودة في النباتات والأسماك تكون عمومًا غير مشبعة (عادةً سائلة في درجة حرارة الغرفة)، مما يعني أنها تتكون من نوع واحد أو أكثر من الأحماض الدهنية غير المشبعة.

- The **kinks where the *cis* double bonds** are located in **plant and fish fats** prevent the molecules from packing together closely enough to solidify at room temperature.

إن العقد التي توجد فيها الروابط المزدوجة السيس في الدهون النباتية والأسماك تمنع الجزيئات من التكدس معًا بشكل وثيق بما يكفي للتصلب في درجة حرارة الغرفة.

- The phrase ***hydrogenated vegetable oils*** on food labels means that unsaturated fats have been **synthetically converted to saturated** fats by adding hydrogen, allowing them to solidify.

تعني عبارة "الزيوت النباتية المهدرجة" الموجودة على ملصقات المواد الغذائية أن الدهون غير المشبعة تم تحويلها صناعياً إلى دهون مشبعة عن طريق إضافة الهيدروجين، مما يسمح لها بالتصلب.


Structural Formula
Structural Formula
Space-Filling Model
Space-Filling Model
a.
b.

الدهون توفر الطاقة المخزنة والعزل

Fats Provide Stored Energy and Insulation

- The major function of **fats** (**Triacylglycerols or Triglycerides**) **is energy storage.** The hydrocarbon chains of fats are similar to gasoline molecules and just as rich in energy. الوظيفة الأساسية للدهون (الجليسرولات الثلاثية أو الدهون الثلاثية) هي تخزين الطاقة. وتشبه سلاسل الهيدروكربونات في الدهون جزيئات البنزين وهي غنية بالطاقة بنفس القدر.
- A **gram of fat stores more** than twice as much energy as a gram of a polysaccharide, such as starch. يخزن جرام واحد من الدهون طاقة تزيد عن ضعف الطاقة التي يخزنها جرام واحد من السكاريد المتعدد، مثل النشا.
- Because **plants are relatively immobile**, they can function with bulky energy storage in the **form of starch**. (Vegetable oils are generally obtained from seeds, where more compact storage is an asset to the plant.).

ولأن النباتات غير قادرة على الحركة نسبياً، فإنها تستطيع العمل باستخدام مخزون ضخم من الطاقة في صورة نشا. (عادة ما يتم الحصول على الزيوت النباتية من البذور، حيث يُعتبر التخزين الأكثر إحكاماً من الأصول المفيدة للنبات).

- **Animals**, however, must **carry their energy stores** with them, so there is an advantage to having a **more compact reservoir of fuel—fat**.

ومع ذلك، يجب على الحيوانات أن تحمل مخزوناتها من الطاقة معها، ومن ثم فإن وجود خزان أكثر إحكاما من الوقود - الدهون - يمثل ميزة.

- Humans and other mammals stock their long-term food reserves in **adipose cells**, **which swell and shrink (☺)** as fat is deposited and withdrawn from storage.

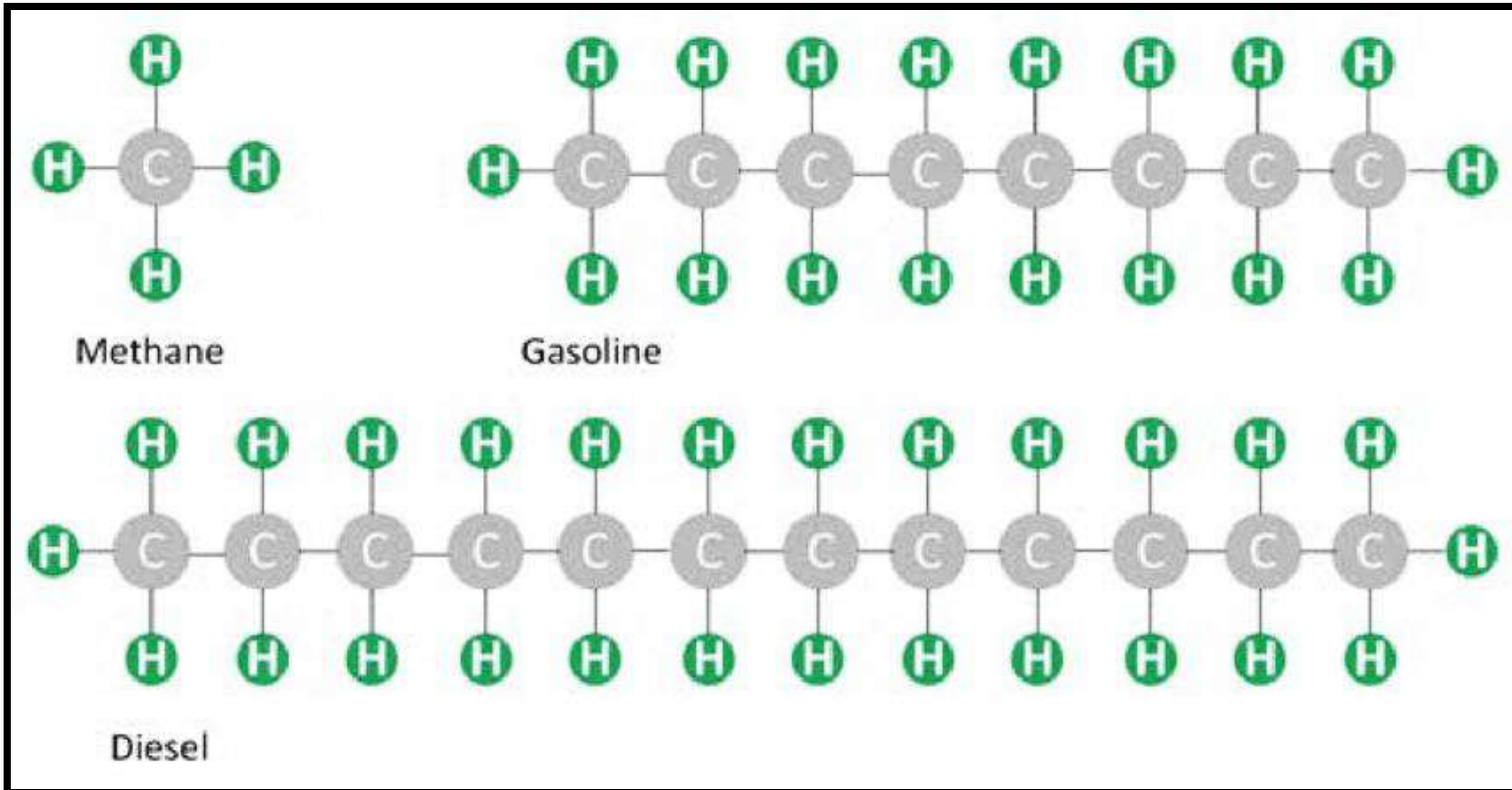
يخزن البشر والثدييات الأخرى احتياطياتهم الغذائية طويلة الأمد في الخلايا الدهنية، والتي تنتفخ وتتقلص (☺) مع تراكم الدهون وسحبها من المخزن.

- In addition to storing energy, **adipose tissue** also **cushions** such vital organs as the **kidneys**, and a layer of fat beneath the **skin insulates the body**.

بالإضافة إلى تخزين الطاقة، تعمل الأنسجة الدهنية أيضًا على حماية الأعضاء الحيوية مثل الكلى، كما تعمل طبقة من الدهون تحت الجلد على عزل الجسم.

- This subcutaneous layer is especially **thick in whales, seals**, and most other marine mammals, **insulating** their bodies **in cold ocean water**.

تكون هذه الطبقة تحت الجلد سميكة بشكل خاص لدى الحيتان والفقمات ومعظم الثدييات البحرية الأخرى، حيث تعمل على عزل أجسامها في مياه المحيط الباردة.


Methane
Gasoline
Diesel

الفوسفوليبيدات هي دهون بنيوية تشكل الأغشية

Phospholipids are Structural Lipids form Membranes

- Phospholipids are among the most important molecules of the cell, as they form the **core of all biological membranes**.

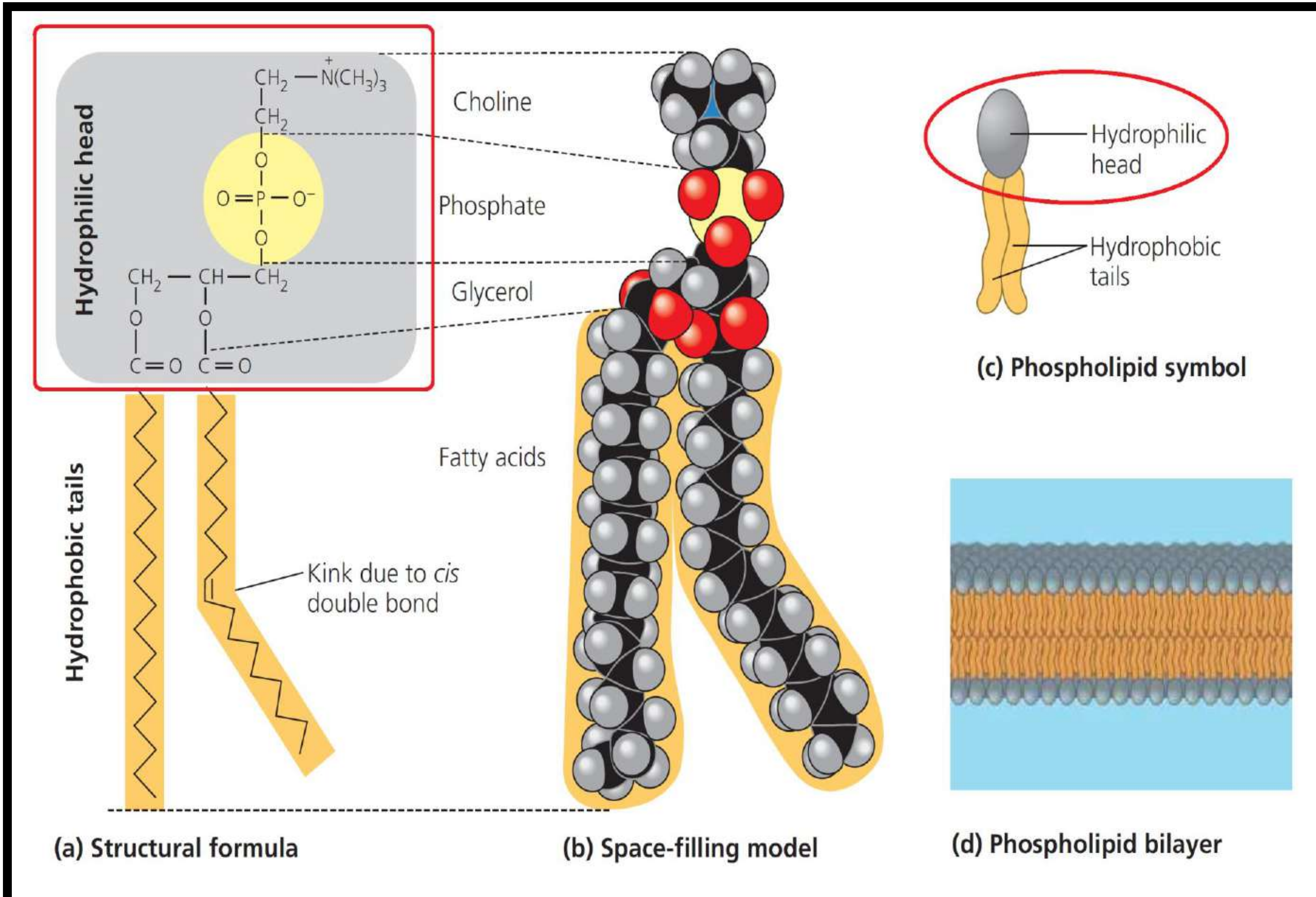
تُعد الفوسفوليبيدات من أهم جزيئات الخلية، حيث أنها تشكل جوهر جميع الأغشية البيولوجية.

- An individual phospholipid is a composite molecule, made up of **three** kinds of subunits: الفسفوليبيد الفردي هو جزيء مركب، يتكون من ثلاثة أنواع من الوحدات الفرعية:
- **1. Glycerol**
- **2. two Fatty acids**, Two fatty acids are attached to the glycerol backbone
- 3. **Phosphate group (—PO_4^{2-})**, attached to one end of the glycerol. The charged phosphate group usually has a charged organic molecule linked to it, such as **choline, ethanolamine, or the amino acid serine.**

مجموعة الفوسفات (—PO42−)، متصلة بطرف واحد من الجلسرين. عادةً ما يكون لمجموعة الفوسفات المشحونة جزيء عضوي مشحون مرتبط بها، مثل الكولين أو الإيثانولامين أو حمض السيرين الأميني.

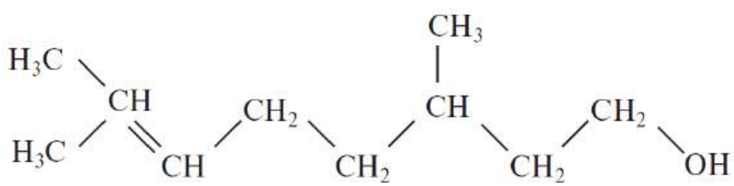
- The phospholipid molecule can be thought of as having **a polar "head"** at one end (the phosphate group) and **two long, very nonpolar "tails"** at the other

يمكن تصور جزيء الفسفوليبيد على أنه يحتوي على "رأس" قطبي في أحد طرفيه (مجموعة الفوسفات) و"ذيلين" طويلين غير قطبيين للغاية في الطرف الآخر

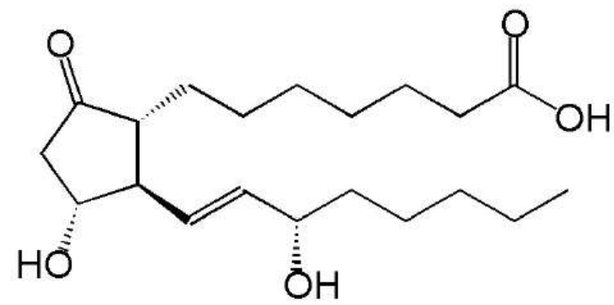

Hydrophilic head
$CH_2 - \overset{+}{N}(CH_3)_3$
CH_2
O
$O=P-O^-$
O
$CH_2 - CH - CH_2$
O
O
C=O
C=O
Choline
Phosphate
Glycerol
Fatty acids
Hydrophobic tails
Kink due to *cis* double bond
Hydrophilic head
Hydrophobic tails
(a) Structural formula
(b) Space-filling model
(c) Phospholipid symbol
(d) Phospholipid bilayer

Terpenes and Prostaglandins

- Organisms contain many **other kinds of lipids** besides fats and phospholipids.
- **Terpenes** are long-chain lipids that are components of many biologically important **pigments**, such as **chlorophyll and the visual pigment retinal**. Rubber is also a terpene.
- Terpenes are linear (**acyclic) or cyclic compounds** largely found as constituents of essential oils
- **Prostaglandins** are a group of about 20 lipids that are modified fatty acids, with **two nonpolar "tails**" attached to **a 5-carbon ring**.
- Prostaglandins act as local **chemical messengers** in many vertebrate tissues.



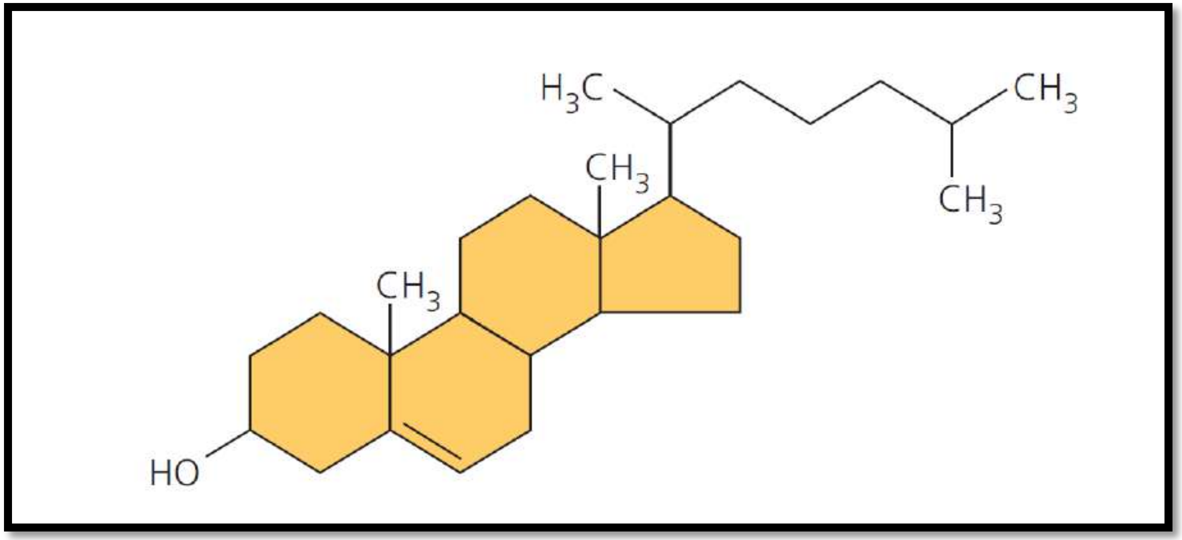
Terpene (citronellol)



Prostaglandins

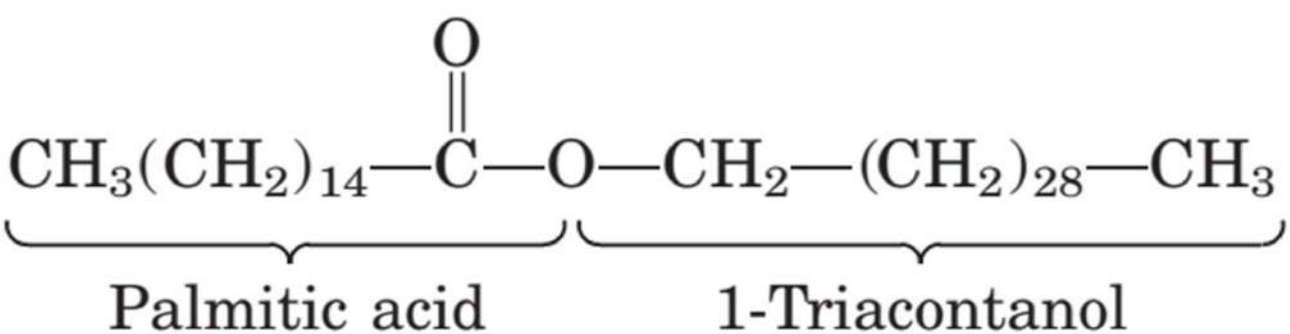
Steroids

- **Steroids**, another class of lipid that chemically different, are carbon skeleton consisting of four-fused carbon rings.
- Different steroids are distinguished by the particular chemical groups attached to this group of rings.
- **Cholesterol**, a type of steroid, is a crucial and common component of animal cell membranes and is also the precursor from which other steroids, such as the vertebrate sex hormones, are synthesized. Most **animal cell membranes** contain the steroid cholesterol.
- In vertebrates, cholesterol is synthesized in the liver and is also obtained from the diet.
- Other steroids, such as **testosterone and estrogen**, function as hormones in multicellular animals.



Waxes Serve as Energy Stores and Water Repellents

- Biological waxes are **esters** of **long-chain** (C14 to C36) saturated and unsaturated fatty acids with **long-chain** (C16 to C30) alcohols (**fatty alcohols).**
- Their melting points (60 to 100 C) are generally higher than those of triacylglycerols.
- In **plankton**, the free-floating organisms, waxes are the chief **storage form** of metabolic fuel.
- Waxes also serve a diversity of other functions related to their **water-repellen**t properties and their **firm consistency**.
- Certain **skin glands** of vertebrates **secrete waxes** to protect hair and skin and keep it elastic, lubricated, and waterproof.
- Birds (**waterfowl**) secrete waxes to keep their feathers **water-repellent**.
- The shiny **leaves of many tropical plant**s are coated with a thick layer of waxes, which prevents excessive **evaporation of water** and protects **against parasites**.



Beeswax, is **an ester of** palmitic acid with fatty alcohol 1-Triacontanol

Nucleic Acid Chemistry: Structure of nucleic acids DNA & RNA

- The Nucleic Acid chemical information was well known to Watson and Crick during their investigation and served as the basis of their model building.

كانت المعلومات الكيميائية للحمض النووي معروفة جيدًا لواتسون وكريك أثناء تحقيقاتهما وكانت بمثابة الأساس لبناء نموذجهما

- Nucleotides (Sometimes called Mononucleotides) are the monomers (building blocks units) of all nucleic acid (DNA and RNA) molecules.

النيوكليوتيدات (تسمى أحيانًا أحاديات النيوكليوتيدات) هي الوحدات البنائية (وحدات البناء) لجميع جزيئات الأحماض النووية (DNA وRNA)

- **Nucleotides** have **three** essential components: **a nitrogenous base**, a **pentose sugar** (a five-carbon sugar), and **a phosphate group.**

تتكون النيوكليوتيدات من ثلاثة مكونات أساسية: قاعدة نيتروجينية، وسكر خماسي الكربون (سكر مكون من خمس ذرات كربون)، ومجموعة فوسفات.

- The **pentose sugars** found in nucleic acids give them their names.

السكريات البنتوزية الموجودة في الأحماض النووية تعطيها أسمائها

- Ribonucleic acids (RNA) contain ribose sugar تحتوي الأحماض النووية الريبونووية (RNA) على سكر الريبوز
- Deoxyribonucleic acids (DNA) contain deoxyribose sugar. تحتوي الأحماض النووية الديوكسي ريبوزية (DNA) على سكر الديوكسي ريبوز

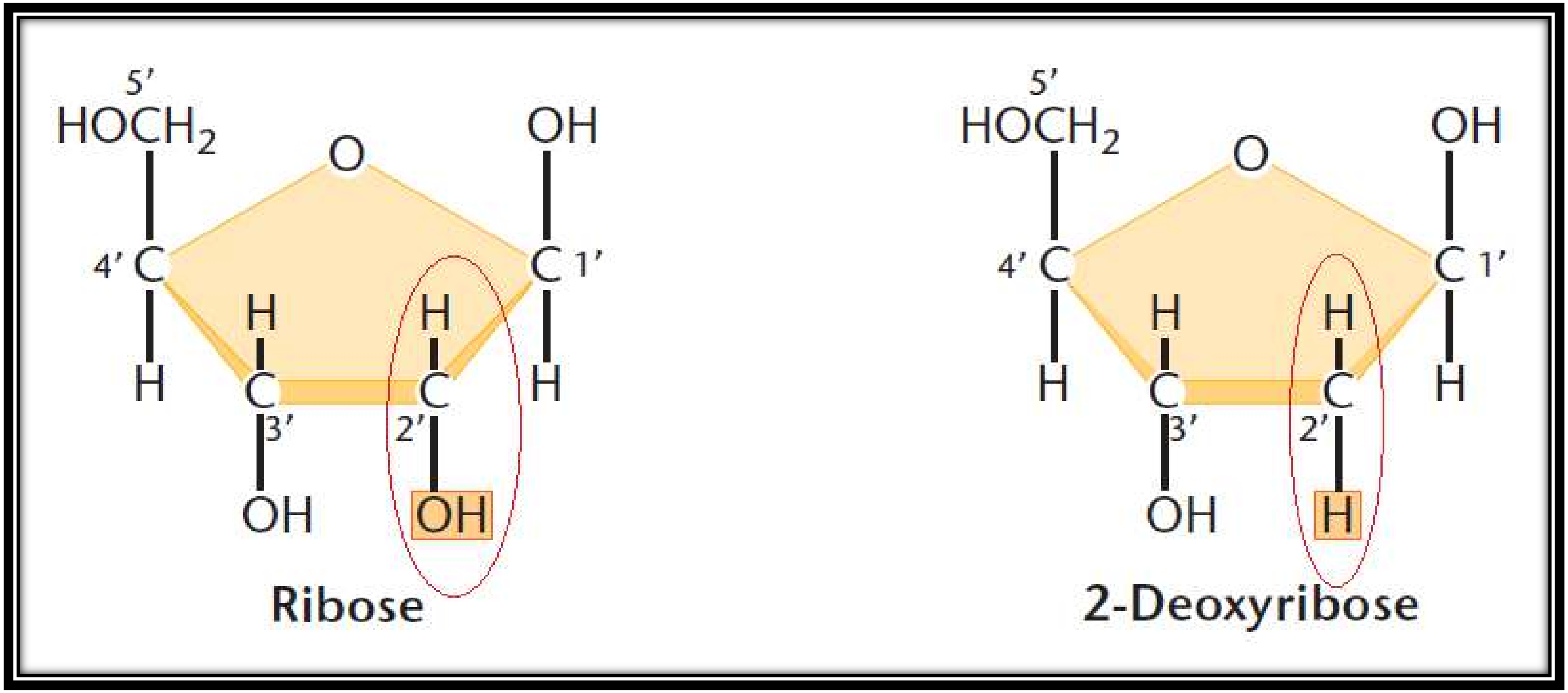
- Each **carbon atom in the ribose** (pentose) sugar is distinguished by a number with a **prime sign (´)** تتميز كل ذرة كربون في سكر الريبوز (البنتوز) برقم يحمل علامة أولية (´)
- Compared with ribose, **deoxyribose has a hydrogen** atom rather than a hydroxyl group at the (C-2´) position, thus distinguishes DNA from RNA.

بالمقارنة مع الريبوز، يحتوي الريبوز منقوص الأكسجين على ذرة هيدروجين بدلاً من مجموعة هيدروكسيل في موضع (C-2´)، وبالتالي يميز الحمض النووي عن الحمض النووي الريبي.

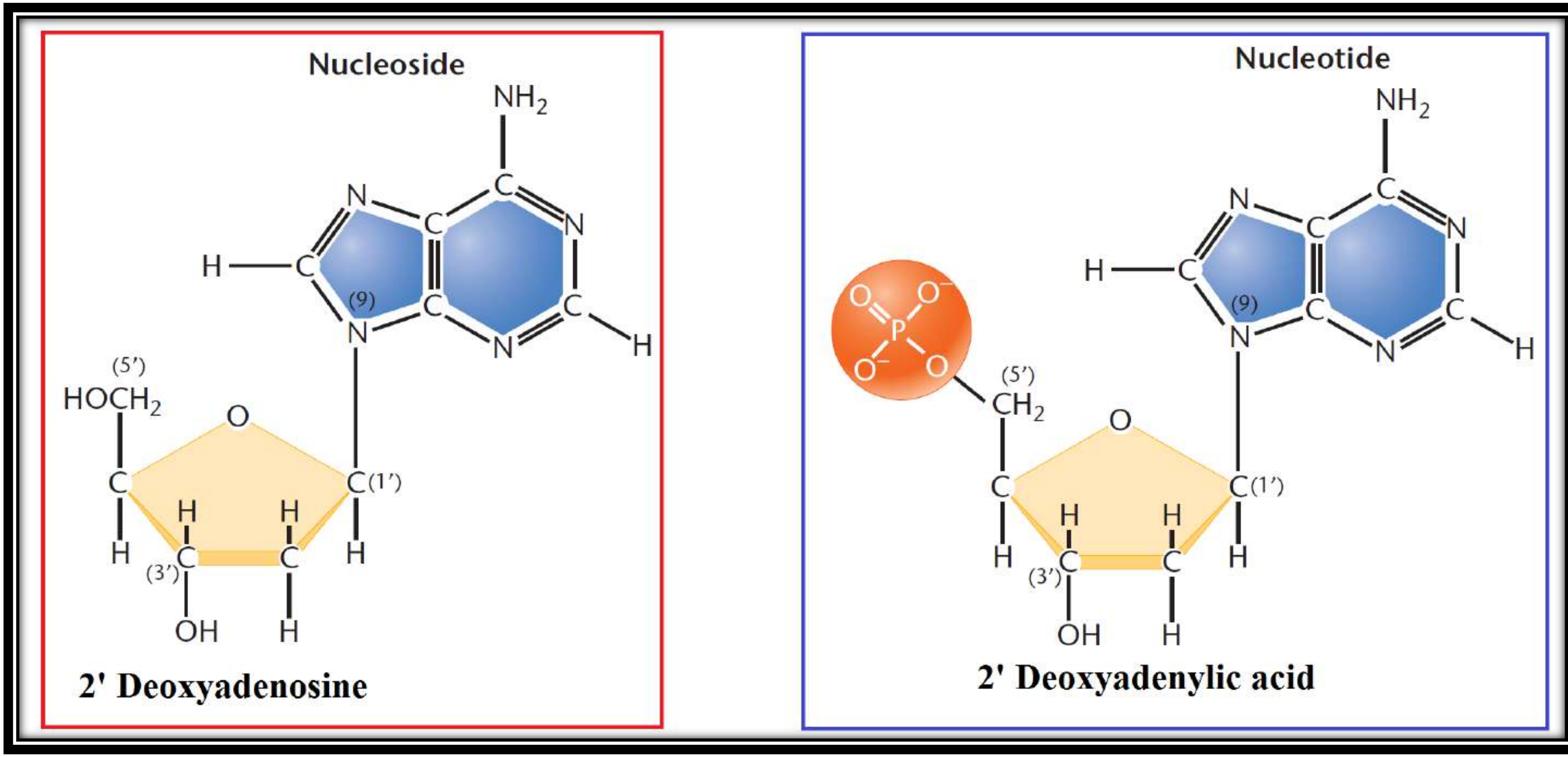
- In the absence of the (C-2´) hydroxyl group, the sugar is more specifically named **2´-deoxyribose.**

يتم تسمية السكر بشكل أكثر تحديدًا باسم ´2-ديوكسي ريبوز، في حالة عدم وجود مجموعة الهيدروكسيل (C-2´)

Ribose vs. 2`-deoxyribose.



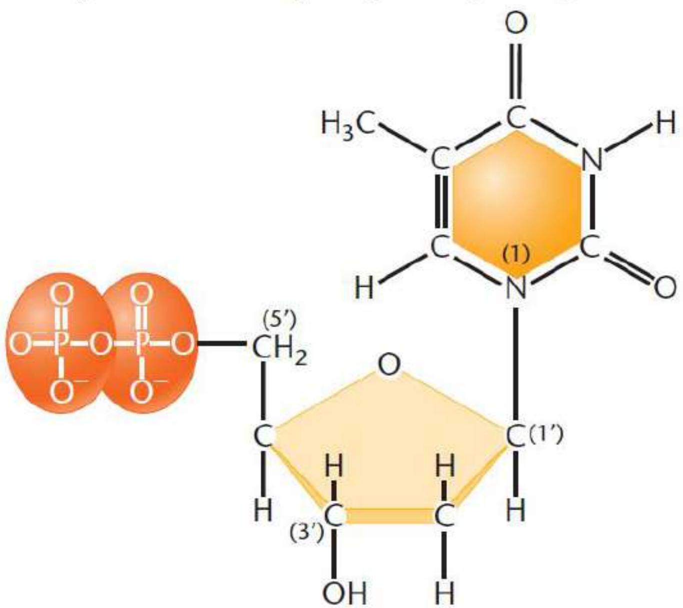
Nucleoside vs. Nucleotide



Nucleoside
=
Pentose sugar + Nitrogen base

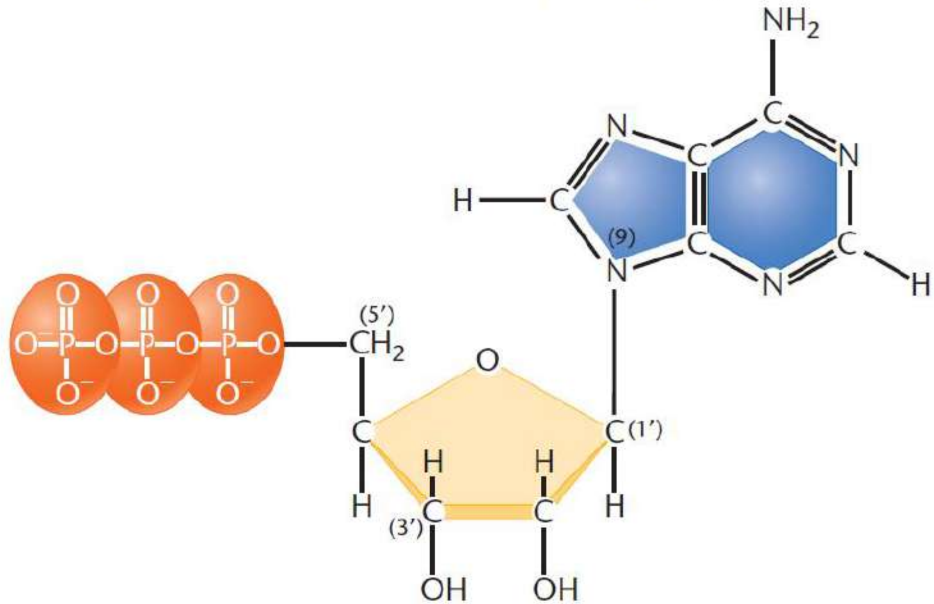
Nucleotide
=
Pentose sugar + Nitrogen base+ Phosphate group

Deoxynucleoside diphosphate (dNDP)



2´deoxythymidine diphosphate (2´dTDP)

Nucleoside triphosphate (NTP)



Adenosine triphosphate (ATP)

Bases and Sugars (Nucleosides) in DNA and RNA

- In DNA: 2′deoxyribose + A, T, G or C
  - dA 2′deoxyadenosine
  - dT 2′deoxythymidine
  - dG 2′deoxyguanosine
  - dC 2′deoxycytidine
- In RNA: ribose + A, U, G, or C
  - A adenosine
  - U uridine
  - G guanosine
  - C cytidine

القواعد النيتروجينية في الأحماض النووية

Nitrogenous bases in nucleic acids

There are two kinds of nitrogenous bases:

Purines : nine-member double ring (A, G)
Pyrimidines: six-member single-ring (C,T, **U**).

Both DNA and RNA contain A, G, and C
only DNA contains the base T
only RNA contains the base **U**.

Each nitrogen or carbon atom of the ring structures of purines and pyrimidines is designated by a number (NO **prime sign (′).**

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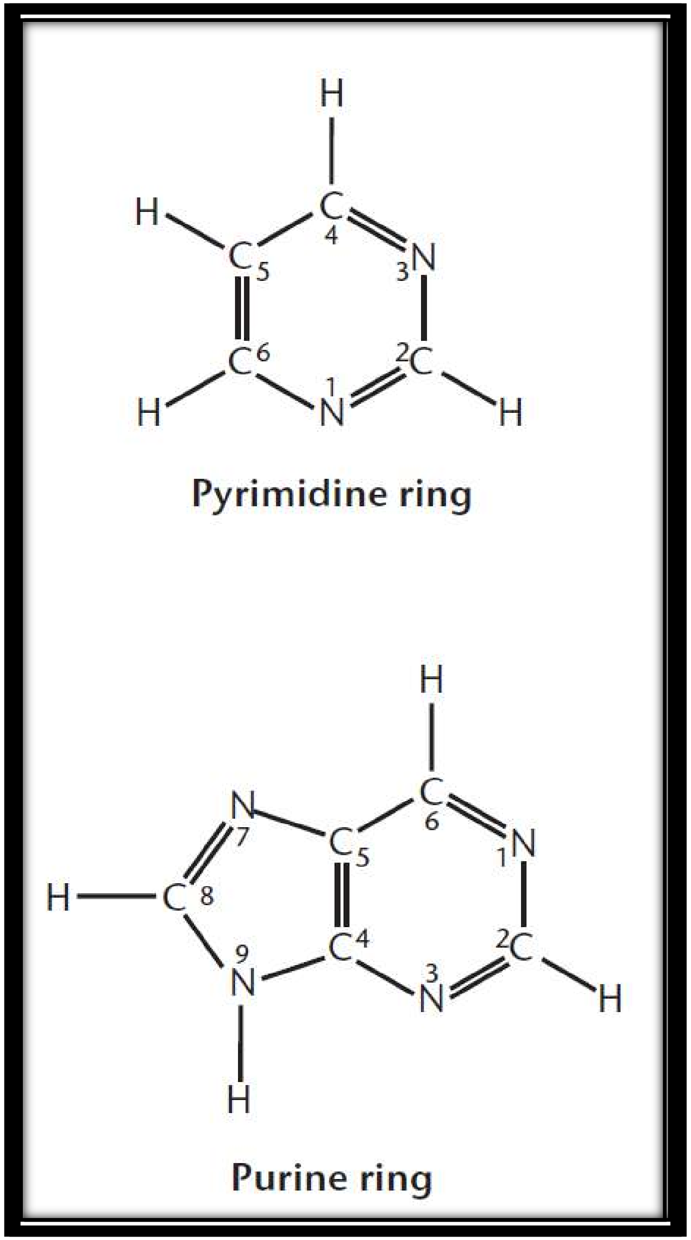
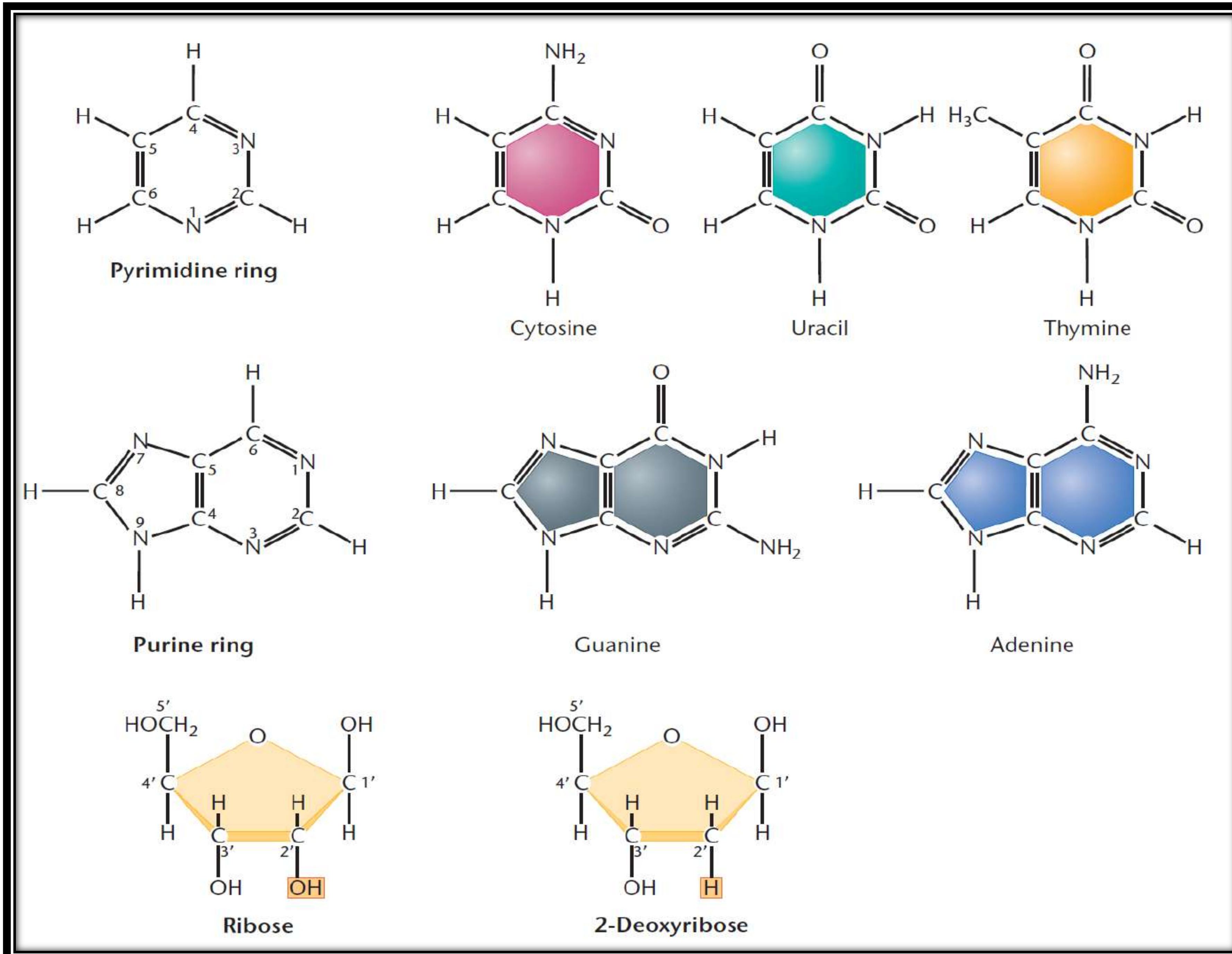



Pyrimidine ring
Cytosine
Uracil
Thymine
Purine ring
Guanine
Adenine
Ribose
2-Deoxyribose

رابطة عالية التحديد بين مكونات النوكليوتيدات

Highly specific bonding between components of nucleotide

- The **bonding** between the components of a nucleotide is **highly specific**.

  إن الرابطة بين مكونات النوكليوتيد محددة للغاية

- The **(C-1´)** atom of the sugar is involved in the chemical linkage to the **nitrogenous base (**purine or pyrimidine)**.**

  تشارك ذرة (C-1´) من السكر في الارتباط الكيميائي بالقاعدة النيتروجينية (البيورين أو البيريميدين)

- For **purine, the N-9** atom is covalently bonded to **(C-1´)** of the sugar.

  بالنسبة للبيورين، فإن ذرة N-9 مرتبطة تساهميًا بـ (C-1´) من السكر

- For **pyrimidine, the N-1** atom is covalently bonded to **(C-1´)** of the sugar.

  بالنسبة للبيريميدين، تكون ذرة N-1 مرتبطة تساهميًا بـ (C-1´) من السكر

- In ribonucleotides, the **phosphate group** may be bonded to the (C-2´) or (C-3´) or (C-5´) atom of the sugar.

  في الريبونوكليوتيدات، قد ترتبط مجموعة الفوسفات بذرة (C-2´) أو (C-3´) أو (C-5´) من السكر

- However binding of **phosphate** to **(C-5´)** atom of the sugar is the **most prevalent** one in biological systems and the one found in DNA and RNA.

ومع ذلك فإن ارتباط الفوسفات بذرة (C-5´) من السكر هو الأكثر انتشارًا في الأنظمة البيولوجية وهو الموجود في الحمض النووي والحمض النووي الريبي.

Nucleotide: nucleoside monophosphate (NMP)

- **Nucleotides** are also described by the term **nucleoside monophosphate (NMP).**

(NMP)يتم وصف النوكليوتيدات أيضًا بمصطلح أحادي فوسفات النوكليوسيد

- The **addition of one or two phosphate groups** results in nucleoside diphosphates (NDPs) and triphosphates (NTP), respectively.

على التوالي، (NTP) وثلاثيات الفوسفات (NDPs) تؤدي إضافة مجموعة أو مجموعتين من الفوسفات إلى تكوين ثنائيات فوسفات النوكليوسيد

- The **2´deoxyribonucleotide triphosphate** (**2´ dNTPs**: 2´ deoxyribonucleotide triphosphate) are the precursor molecule during DNA synthesis.

ديوكسي ريبونوكليوتيد ثلاثي الفوسفات) هو الجزيء السابق أثناء تخليق الحمض النووي dNTPs: 2´ثلاثي فوسفات 2´ديوكسي ريبونوكليوتيد (2

- The **ribonucleotide triphosphate** (NTP) adenosine triphosphate (ATP) and guanosine triphosphate (GTP) are important in **cell bioenergetics** because of the **large amount of energy** involved in adding or removing the terminal phosphate group.

مهمة في الطاقة الحيوية للخلايا بسبب كمية الطاقة الكبيرة المشاركة في إضافة أو إزالة مجموعة الفوسفات الطرفية (GTP) وثلاثي فوسفات الغوانوزين (ATP) وثلاثي فوسفات الأدينوزين (NTP) تعتبر ثلاثي فوسفات الريبونوكليوتيد

- The **hydrolysis of ATP or GTP** to ADP or GDP and inorganic phosphate (Pi) is accompanied by the **release of a large amount of energy** in the cell.

إطلاق كمية كبيرة من الطاقة في الخلية (Pi) والفوسفات غير العضوي GDP أو ADP إلى GTP أو ATP يصاحب تحلل

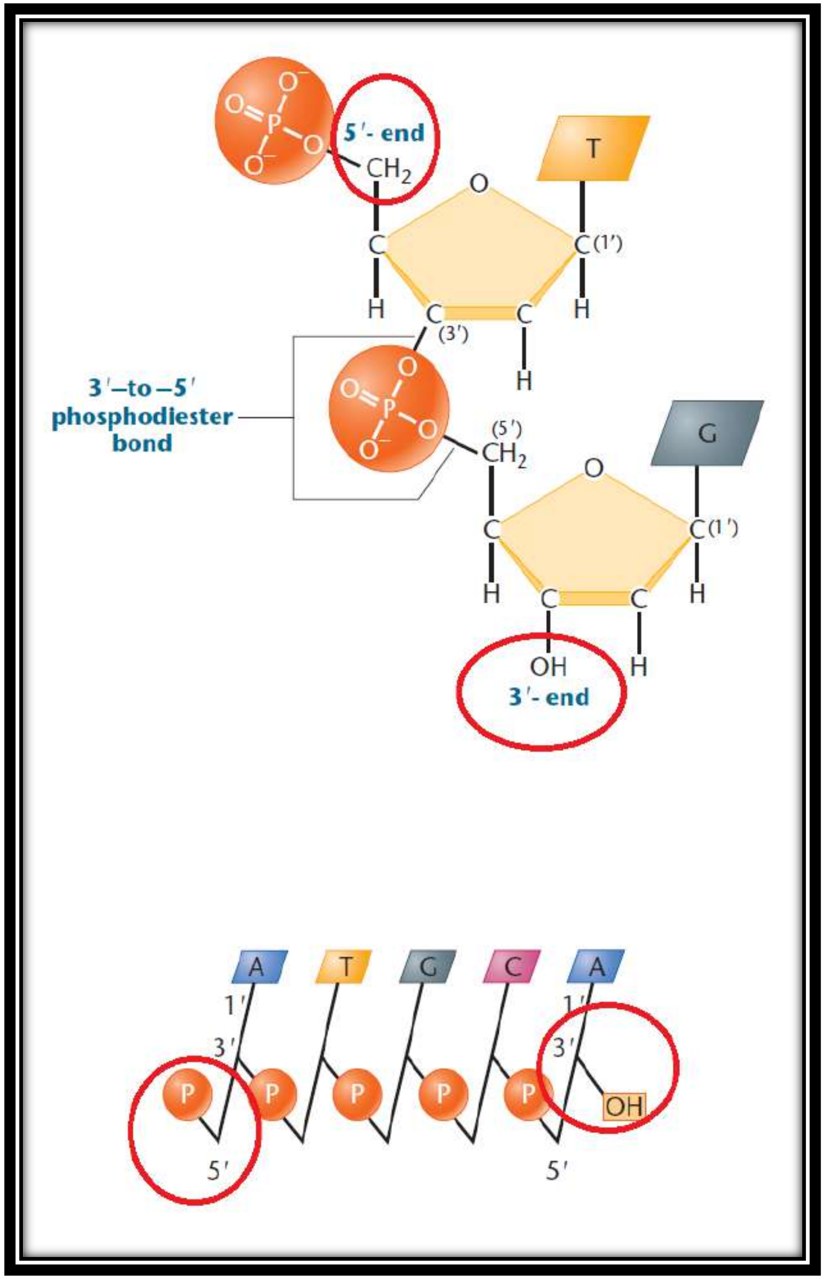
- When these chemical conversions are coupled to other reactions, the energy produced is used to drive them.

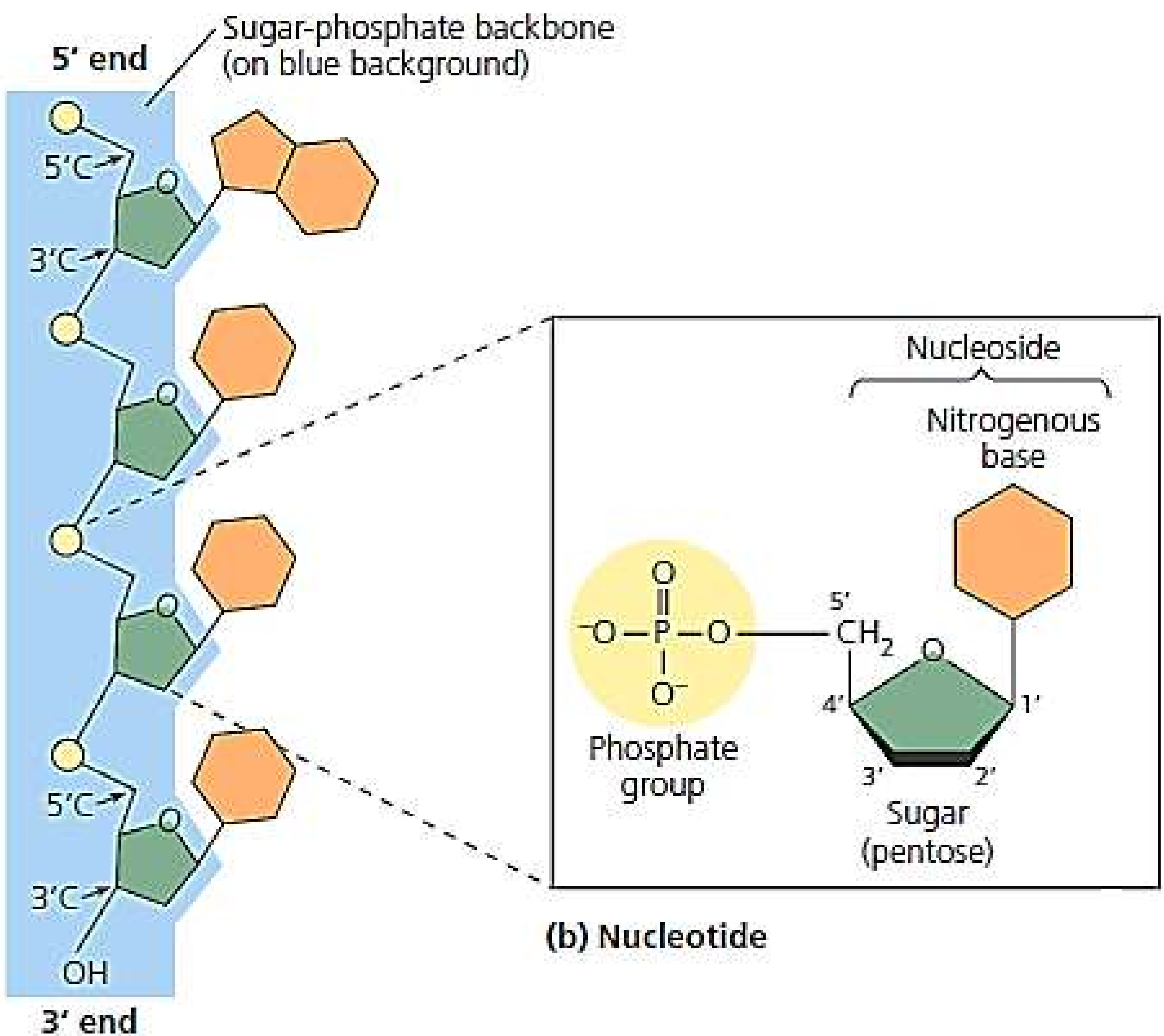
عندما يتم ربط هذه التحويلات الكيميائية بتفاعلات أخرى، يتم استخدام الطاقة المنتجة لتشغيلها

3′ to 5′ Phospho**di**ester Bonds Make the Sugar-Phosphate Backbone

- The linkage between two mononucleotides involves a **phosphate group linked to two sugars.**
- **What is an ester bond??**

- A phospho**di**ester bond is formed as phosphoric acid is joined to two alcohols (the hydroxyl groups on the two sugars) by an ester linkage on both sides.
- Two joined nucleotides (through A phospho**di**ester bond) form a dinucleotide.
- Three nucleotides (through two phospho**di**ester bonds), form a trinucleotide.
- Short chains consisting of up to 20 nucleotides or so are called oligonucleotides
- longer chains, like nucleic acids, are polynucleotides.





(b) Nucleotide

Polynucleotide, or nucleic acid

Notes about Nucleic acids

- Nucleotides are linked by phosphodiester bonds to form Polynucleotides.

- Phosphodiester bond: Covalent bond between the phosphate group (attached to 5′ carbon) of one nucleotide and the 3′ carbon of the sugar of another nucleotide.

- This Phosphodiester bond is very strong, and for this reason DNA is remarkably stable. DNA can be boiled and even autoclaved without degrading!

- 5′ and 3′ : The ends of the DNA or RNA chain are not the same. One end of the chain has a 5′ carbon (C-5′)and the other end has a 3′ carbon (C-3′).
- Long polynucleotide chains account for the large molecular weight of DNA and explain its most important property—storage of vast quantities of genetic information.
- Each nucleotide position in this long chain can be occupied by any one of four nucleotides giving rise to an extraordinary possible variations.
- e.g. a polynucleotide only 1000 nucleotides in length can be arranged $\mathbf{4^{1000}}$ different ways, each one different from all other possible sequences.
- This potential variation in molecular structure is essential for DNA to store the vast amounts of chemical information necessary to direct cellular activities, traits and phenotypes.

Major features of Watson–Crick double helical Model

1. Two long polynucleotide chains are coiled around a central axis, forming a right-handed double helix.

2. The two chains are antiparallel; that is, their **C-5´ to C-3´ (5´→ 3´)** orientations run in opposite directions.

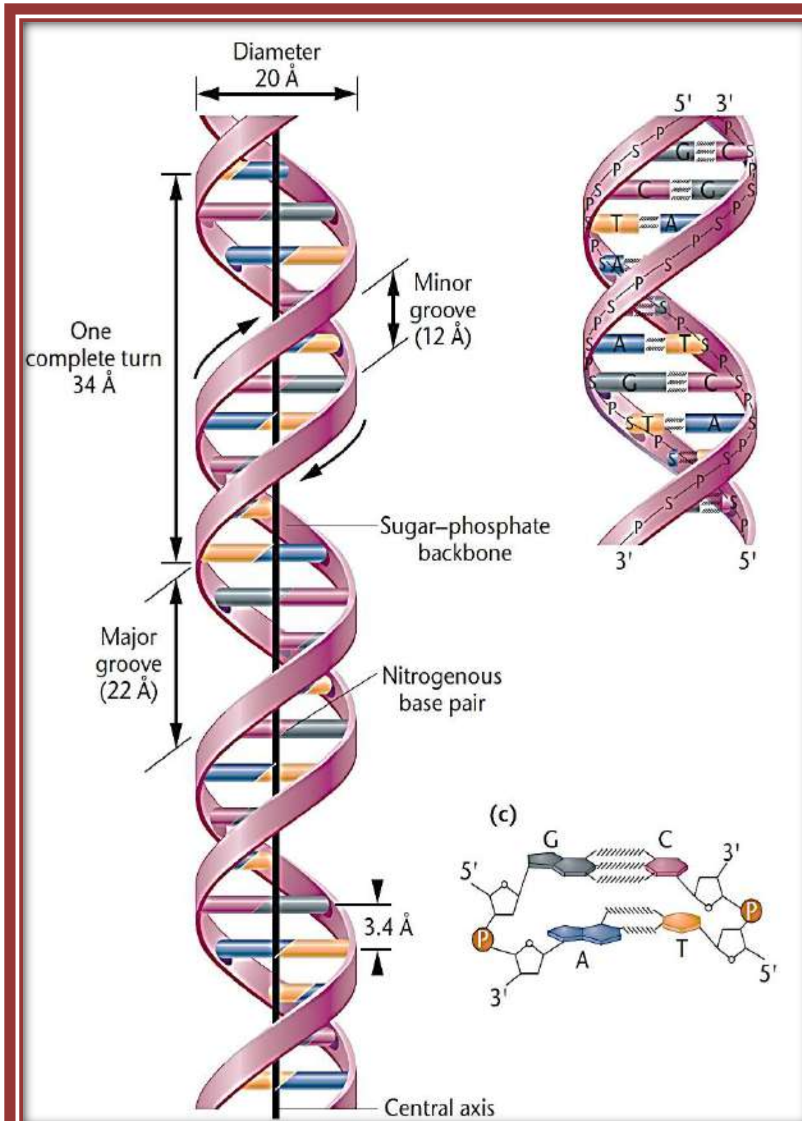
3. The bases of both chains are flat structures, lying perpendicular to the axis; they are "stacked" on one another**, 3.4 Å (0.34 nm) apart**, and located on the inside of the structure.

4. The nitrogenous bases of opposite chains are paired as the result of hydrogen bonds; in DNA, only **A=T** and **C≡G** pairs occur (**complementarity**).

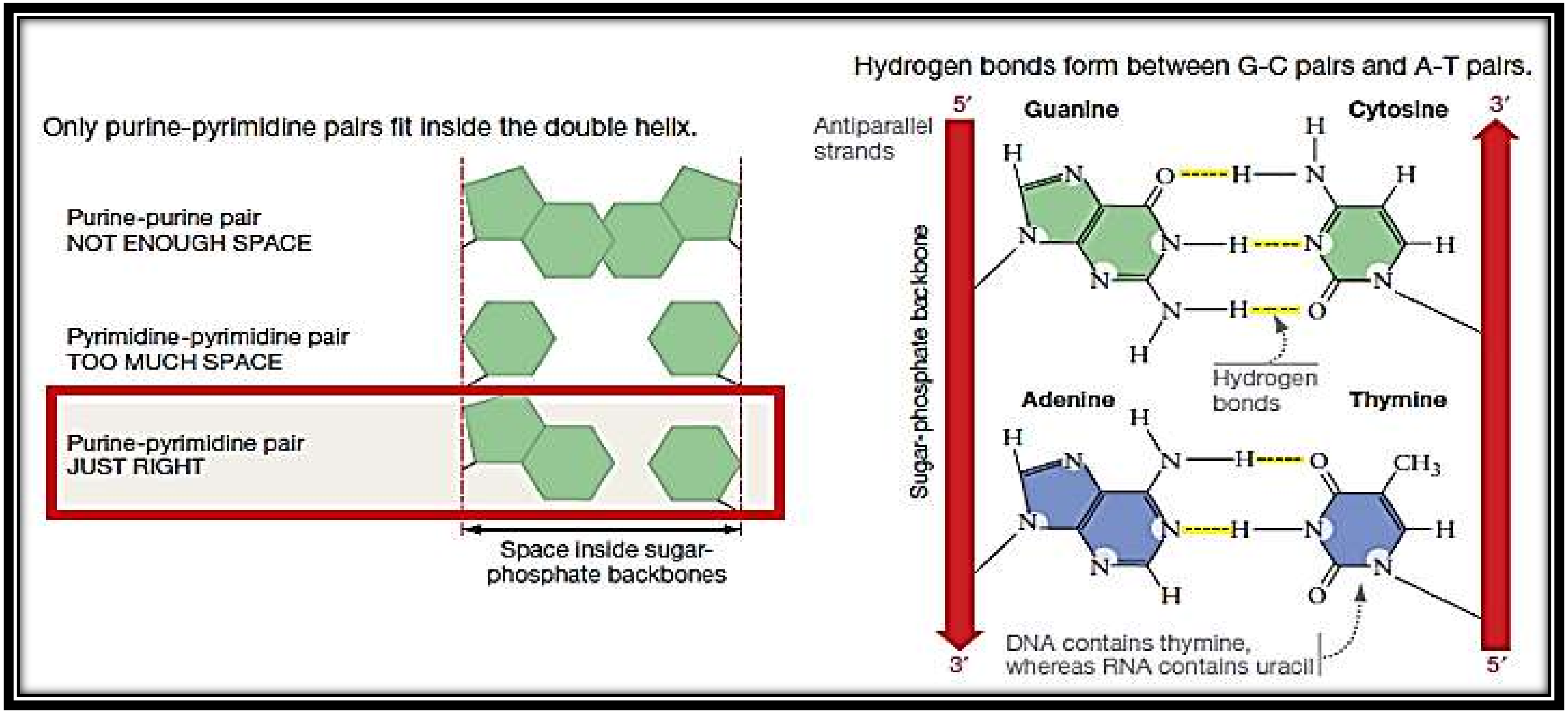
5. Each complete turn of the helix is **34 Å (3.4 nm)** long; thus, **10 bases exist per turn** in each chain.

6. In any segment of the molecule, alternating larger **major grooves and smaller minor grooves** are apparent along the axis.

7. The double helix measures **20 Å (2.0 nm) in diameter.**



Uniform diameter of DNA double helix



The **diameter** of the B-from DNA double helix is 2 nm and is **uniform** throughout. This is achieved only and only if the complementary base pairing occur between a purine and pyrimidine.

Therefore, at any base paring location along the DNA molecule, the two sugar phosphate backbones are always **separated by a combined length of three rings,** two from a purine and one from a pyrimidine.

Alternative forms of DNA exist

- The DNA molecule that Watson and Crick described was in the B-form and was based on X-ray studies of B-DNA performed by Roslaind Franklin, which is present **under aqueous, low-salt conditions.**

- The **B-DNA** form is believed to be the **biologically significant conformation,** that is found in the cell, at 92 % relative humidity.

- **Under different conditions of isolation**, several conformational forms (A,B,C,D,E,P, and Z) of DNA have been recognized. The **primary difference** between the forms is the **direction** that the helix spirals.
- A, B, C, D, E, and P forms of DNA are **right-handed helices**

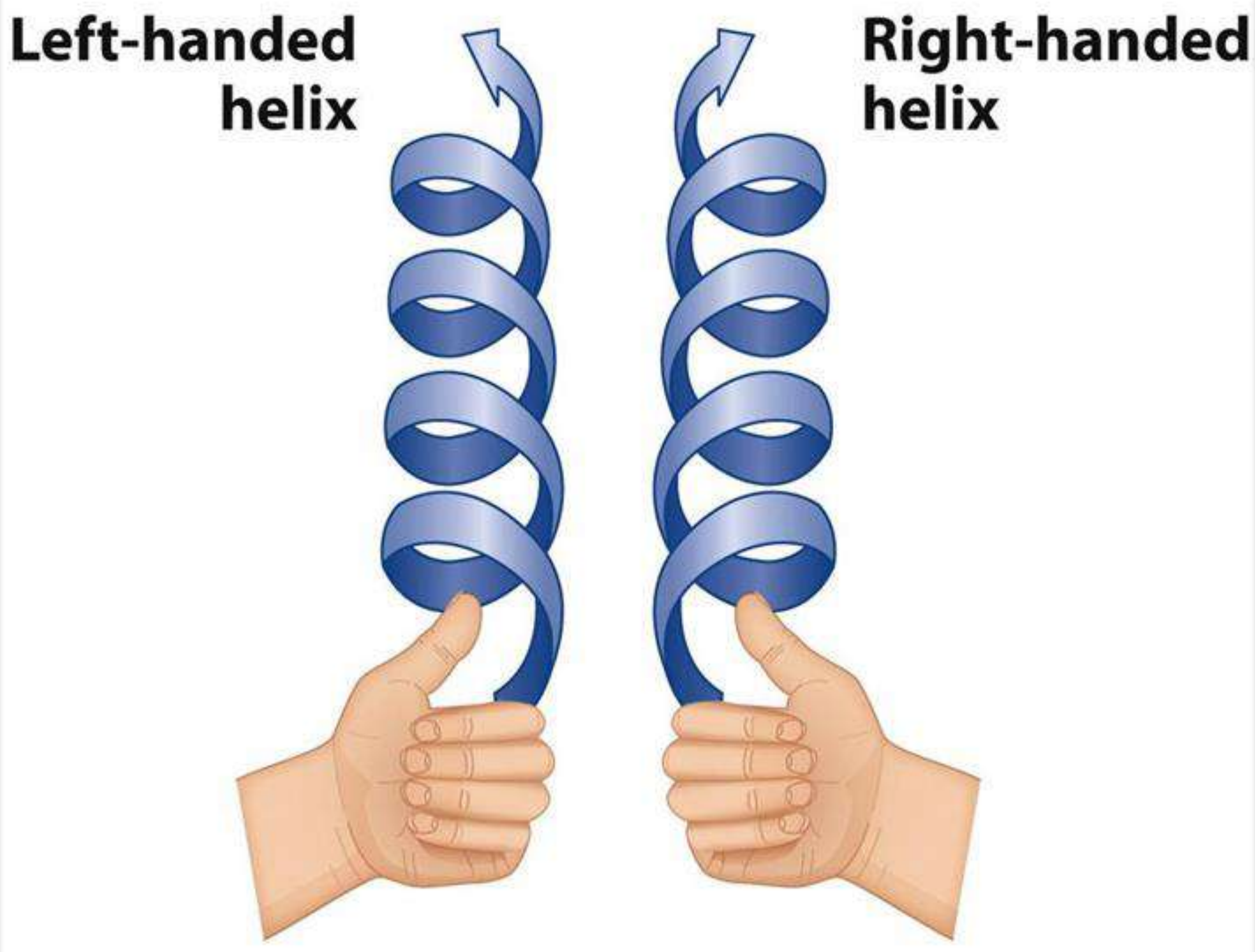
- **Z form is a left-handed double helix** (found in vitro (**synthetic**), very rich in **C-G base pairs**, **under high salt**). The left-handed helix is **18 Å (1.8 nm)** in diameter, contains **12 bp per turn**, and assumes a zigzag conformation (hence its name).

- **A-DNA**, is prevalent under **high-salt or dehydration conditions**, slightly **more compact**, with **11 bp** in each complete turn of the helix, which is 23 Å (2.3 nm) in diameter.

Average structural parameters for some DNA forms

Form	Direction	Helix rise per bp /bp apart	Base pairs/ 360^{o} Turn	Helix Diameter
A	Right	2.6 Å (0.26 nm)	11.0	23A
B	**Right**	**3.4 Å (0.34 nm)**	**10.0**	**20 A**
C	Right	3.3 Å (0.33 nm)	9.3	19A
Z	**Left**	**3.7 Å (0.37 nm)**	**12.0**	**18A**

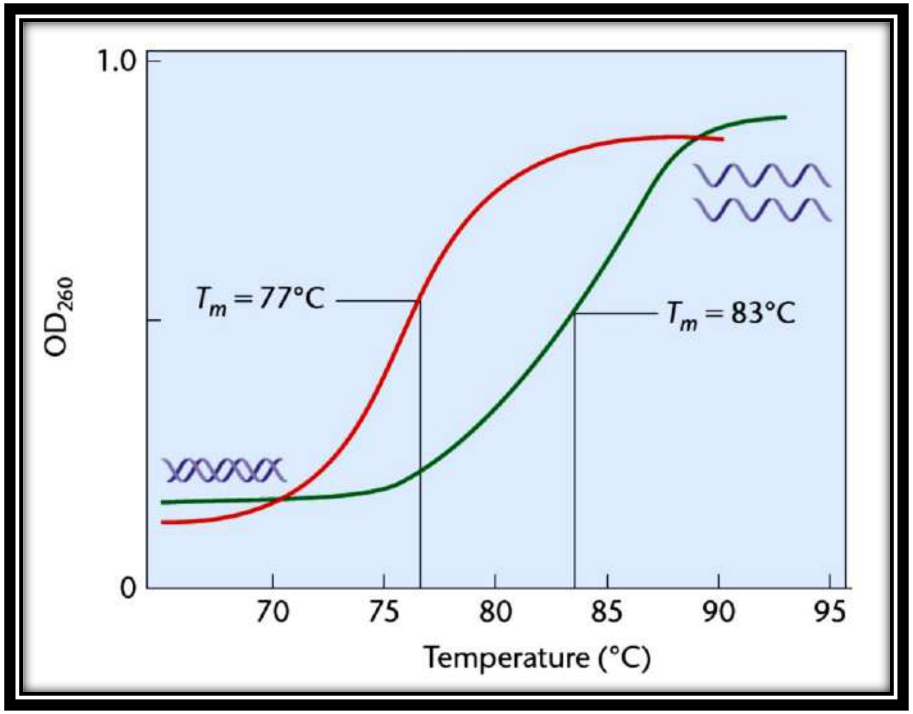
Left-handed and Right- handed DNAs



Lehninger Principles of Biochemistry fifth edition

Optical density @ OD260: Melting Point Curve of DNA

- If **DNA** is subjected to heat, the double helix is **denatured** and unwinds. During unwinding, the viscosity of **DNA decreases and UV absorption increases** (called the **hyperchromic shift**).
- A melting profile, (optical density @260nm: OD260) vs. temperature.
- The midpoint at which 50 percent of the strands have unwound is called the **melting temperature Tm**.
- The molecule with a higher Tm has a higher percentage of C-G base pairs than A-T base pairs

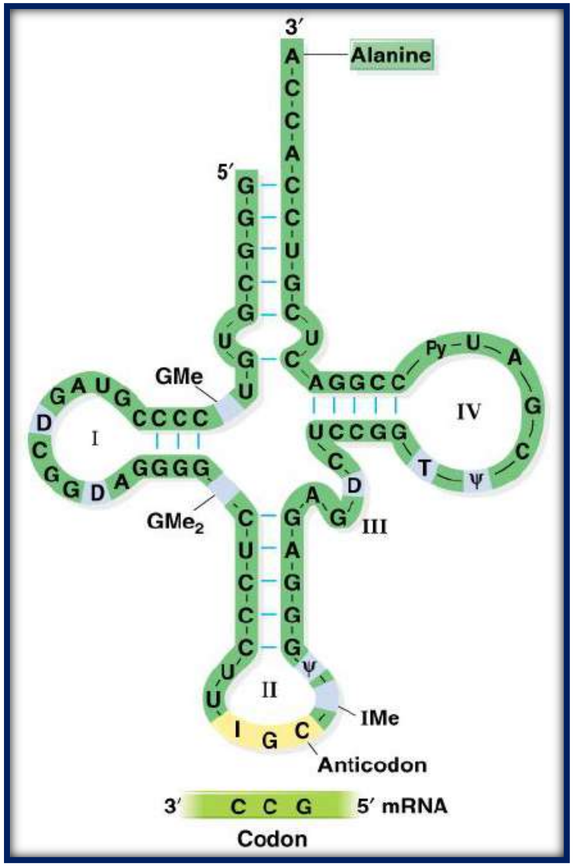


Tm= temperature at which 50% the bp in a double stranded DNA sample have denatured

Tm is proportional to %GC

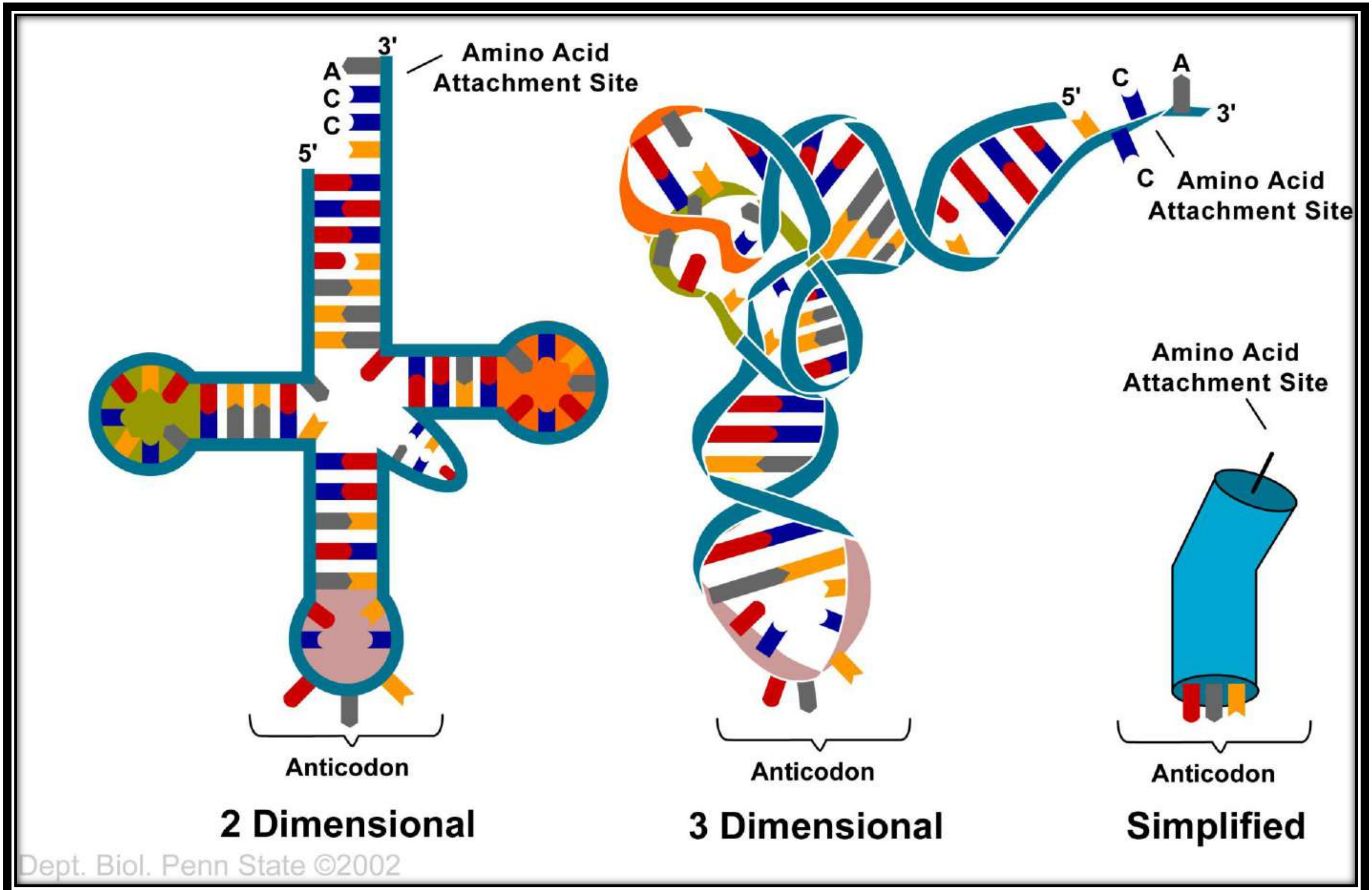
The structure of RNA is chemically similar to DNA, but ??

- The structure of RNA molecules resembles DNA, with several important exceptions.
- Ribose sugar in RNA, instead of 2´ deoxyribose in DNA
- Nitrogenous base uracil in RNA, instead of thymine in DNA
- RNA is single stranded (single stand of polynucleotides, only one **C-5´ end** and **C-3´** end), while DNA is double stranded helix (two **C-5´ ends** and two **C-3´** ends).
- RNA molecules often fold back on themselves to form double-stranded regions of complementary base pairs (only one **C-5´ end** and **C-3´** end).
- Some animal viruses that have RNA as their genetic material contain double-stranded helices (two **C-5´ ends** and two **C-3´** ends).
- There are 3 major classes of cellular RNA molecules function during the expression of genetic information: ribosomal RNA (rRNA), messenger RNA (mRNA), and transfer RNA (tRNA).



- Other unique RNAs exist that perform various genetic and cellular roles, especially in eukaryotes.
- **Telomerase RNA** is involved in DNA replication at the ends (telomeres) of eukaryotic chromosomes
- **Small nuclear RNA (snRNA)** participates in processing (**splicing**) mRNAs
- Antisense RNA, microRNA (miRNA), short interfering RNA (siRNA), and long noncoding RNA (lncRNA) are involved in gene regulation.
- Small nucleolar RNA (snoRNA) and small cytoplasmic RNA (scRNA) are other minor forms of RNA

Secondary Structure of tRNA

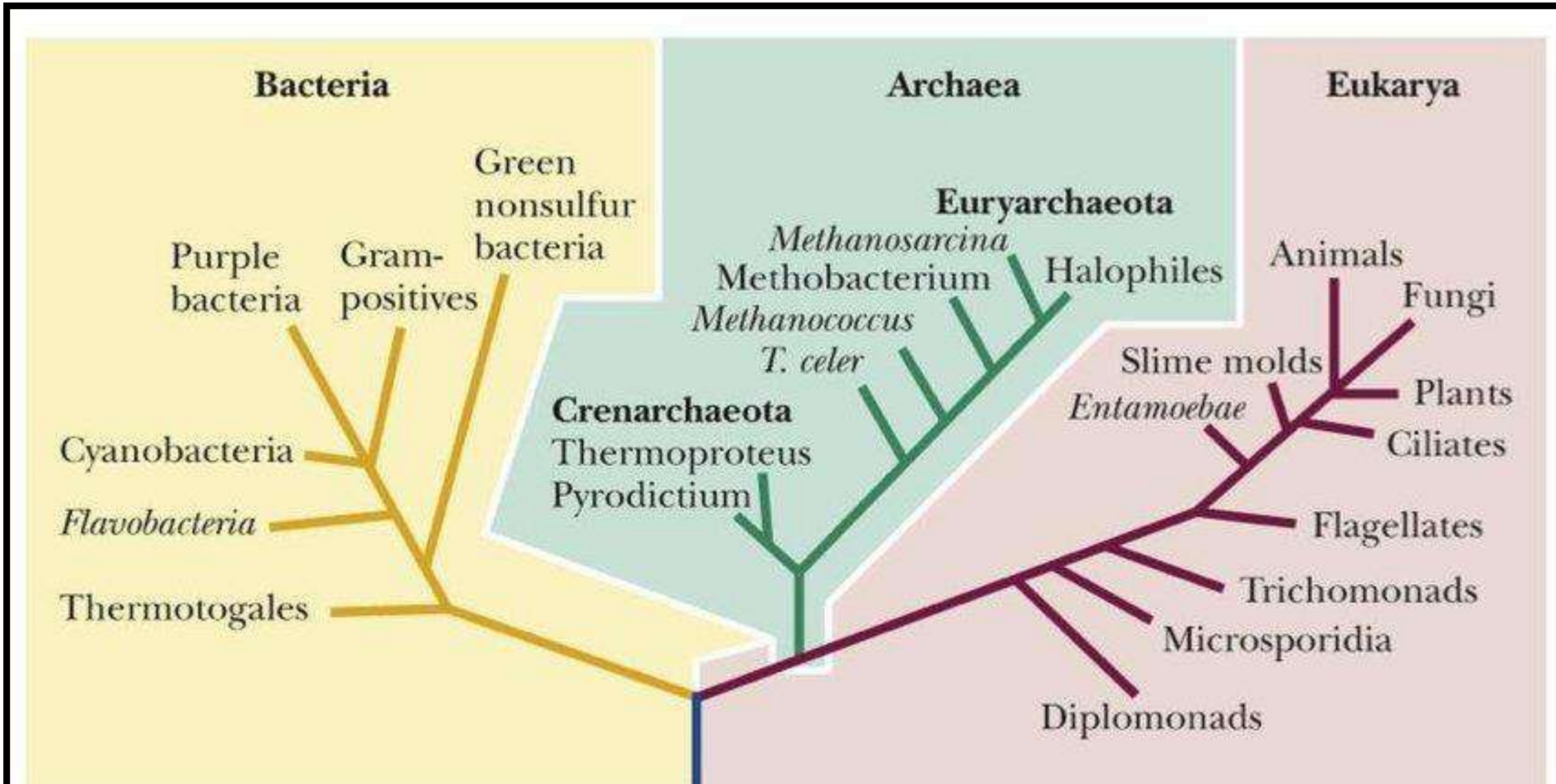


Prokaryotic vs. Eukaryotic Cells

- All cells (prokaryotic and eukaryotic) share certain basic features:
  - bounded by a selective permeable **cell membrane**
  - **Cytosol**, in which subcellular components are suspended.
  - Centrally located genetic material or **chromosomes**, which carry genes in the form of DNA.
  - Have **ribosomes** for making proteins
- A major **difference** between prokaryotic and eukaryotic cells is the **DNA** location
- In a **eukaryotic** cell, most of the DNA is in the **nucleus**,
- In a **prokaryotic** cell, the DNA is concentrated in **a nucleoid region**.
- **Eukaryotic** cells are characterized by **compartmentation** they have internal membranes that compartmentalize their functions.

- **Two distinct types of cells** : prokaryotic and eukaryotic.
- Organisms of the **domains Bacteria and Archaea** consist of prokaryotic cells.

- Organisms of the domain Eukarya—protists, fungi, animals, and plants—all consist of eukaryotic cells.


Bacteria
Archaea
Eukarya
Green
nonsulfur
bacteria
Purple
bacteria
Gram-
positives
Cyanobacteria
Flavobacteria
Thermotogales
Euryarchaeota
Methanosarcina
Methobacterium
Halophiles
Methanococcus
T. celer
Crenarchaeota
Thermoproteus
Pyrodictium
Animals
Fungi
Slime molds
Plants
Entamoebae
Ciliates
Flagellates
Trichomonads
Microsporidia
Diplomonads

Prokaryotic vs. Eukaryotic Cells

- The interior (area) of either type of cell is called the **cytoplasm**; in eukaryotic cells, this term refers only to the region between the nucleus and the plasma membrane.
- Eukaryotic cells are generally **much larger** than prokaryotic cells.
- Size is a general feature of cell structure that relates to function. The logistics of carrying out cellular metabolism sets **limits on cell size**.
- At the **size lower limit**, the smallest cells known are bacteria called **mycoplasmas**, which have diameters between **0.1 and 1.0 µm**.
- These mycoplasmas **(lack a cell wall** around their cell membranes) are perhaps the smallest packages with enough DNA to program metabolism and enough enzymes and other cellular equipment to carry out the activities necessary for a cell to sustain itself and reproduce.
- Typical **bacteria** are **1–5 µm** in diameter, about ten times the size of mycoplasmas.
- **Eukaryotic** cells are typically **10–100 µm** in diameter.

Cell size is limited

- Most cells are **relatively small** for reasons related to the **rate of transport** of substances into and out of them that mainly affected by:
  - (1) surface area available for transport
  - (2) the distance over which transport must occur.
- As the **size of a cell increases**, the length of **time** for transport from the outside membrane to the interior of the cell **increases** as well.
- Larger cells have **higher metabolic rates** (anabolism and catabolism)
- Molecules needed by the cell must be transported through the membrane. Any metabolic waste produced must be removed, also passing through the membrane.
- The **rate** at which this transport occurs depends on both the **distance** to the membrane and the **area of membrane** available.

- This is one reason, an **organism made up of many relatively small cells** has an advantage over one composed of fewer, larger cells.

Surface area-to-volume ratio limit

- Another reason for small cell size is the **surface area-to-volume ratio limit.**
- As a cell's size increases, its volume increases much more rapidly than its surface area. For a spherical cell, the surface area is proportional to (**r^2**), whereas the volume is proportional to (**r^3**).

- Thus, if the radii of two cells differ by a factor of 10, the larger cell will have 10^2, or 100 times, the surface area, but 10^3, or 1000 times, the volume of the smaller cell.

- The **need for a surface area large enough** to accommodate the volume helps explain the microscopic size of most cells
- Larger organisms **do not generally have larger cells** than smaller organisms—they simply have more cells.

- A sufficiently **high ratio of surface area to volume** is especially important in cells that **exchange a lot of material** with their surroundings
- Such cells may have many long, **thin projections** from their surface called **microvilli**, which increase surface area without an appreciable increase in volume.

- Because small cells have more surface area per unit of volume than large ones, **control over cell contents is more effective** when cells are relatively **small**.

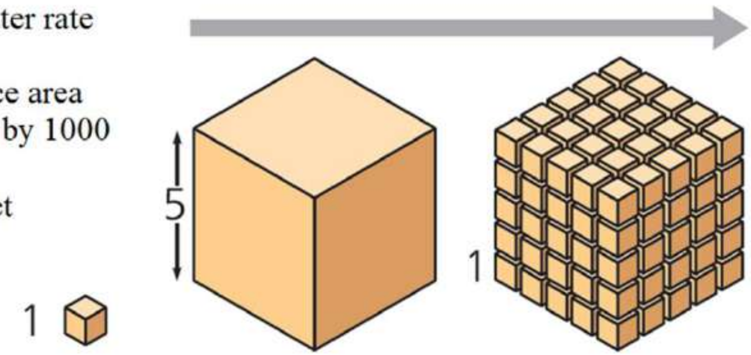
Geometric relationships between surface area and volume

A high surface area-to-volume ratio facilitates the exchange of materials between a cell and its environment.

As a cell gets larger, its volume increases at a faster rate than its surface area.
If the cell radius increases by 10 times, the surface area increases by 100 times, but the volume increases by 1000 times.
A cell's surface area must be large enough to meet the metabolic needs of its volume.

Surface area $(4\pi r^2)$ | Volume $(\frac{4}{3}\pi r^3)$

Surface area increases while total volume remains constant



Total surface area [(height × width of 1 side) × 6 sides × number of cells]	6 units^2	**25 folds** 150 units^2	**125 folds** 750 units^2
Total volume [(height × width × length of 1 cell) × number of cells]	1 unit^3	**125 folds** 125 units^3	**125 folds** 125 units^3
Surface area-to-volume ratio [surface area ÷ volume]	6	$\boxed{1.2}$	6

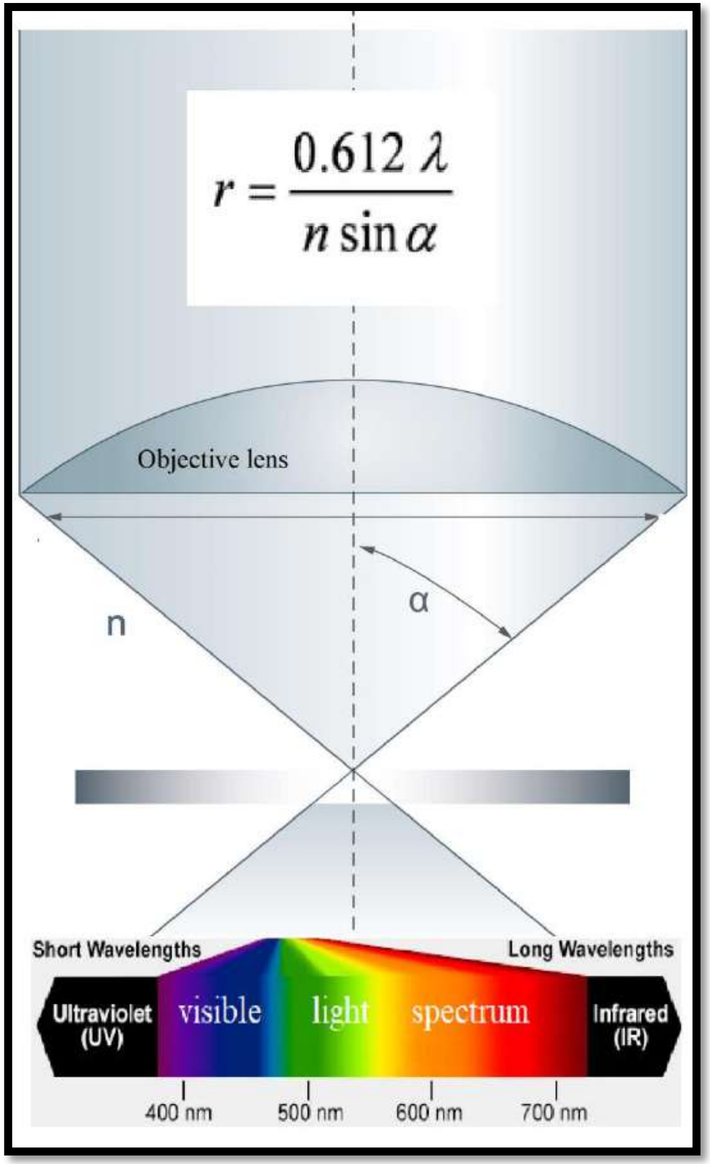
Microscopy: magnification and resolution

- **Microscopes allow visualization of cells and components**
- Microscopes **magnify** small objects to appear bigger.
- The **magnification power** of a light microscope is up to **1500 X** its original size.
- The magnification power of **electron microscopes** can reach up to **1 million X**.
-
- Magnification is not all about **getting details**. At greater magnifications, additional details may not be seen clearly. The **resolution** problem.

- Bigger is only **better when more details** are revealed.
- The fineness of detail that a microscope can reveal is its **resolving power.**
- Resolution is a measure of the clarity of the image.
- **Resolution**: is the minimum distance two points can be apart and still be distinguished as two separate points.
- **Resolution power of human eye** : > 100 μm which allows our eyes to resolve them as two distinct objects rather than one.

Microscope resolution formula

- Where **λ** is the wavelength of light used to image a specimen (a green light of 514 nm)
- Where **n** is the refractive index of the imaging medium (air or oil).
- If using a 'dry' (**non-immersion**) objective lens the air has a refractive index of **1.0.**
- If using an **immersion** objective lens with oil the a refractive index of the imaging medium is **1.52**
- Where **α** is half of the angular aperture of the objective (The maximum angular aperture of an objective is around 144º, **so max α = 72º).**
- Using standard techniques, **the light microscope** cannot resolve detail finer than about 0.2 µm, or **200 nm**, regardless of the magnification



Prokaryotic Cells

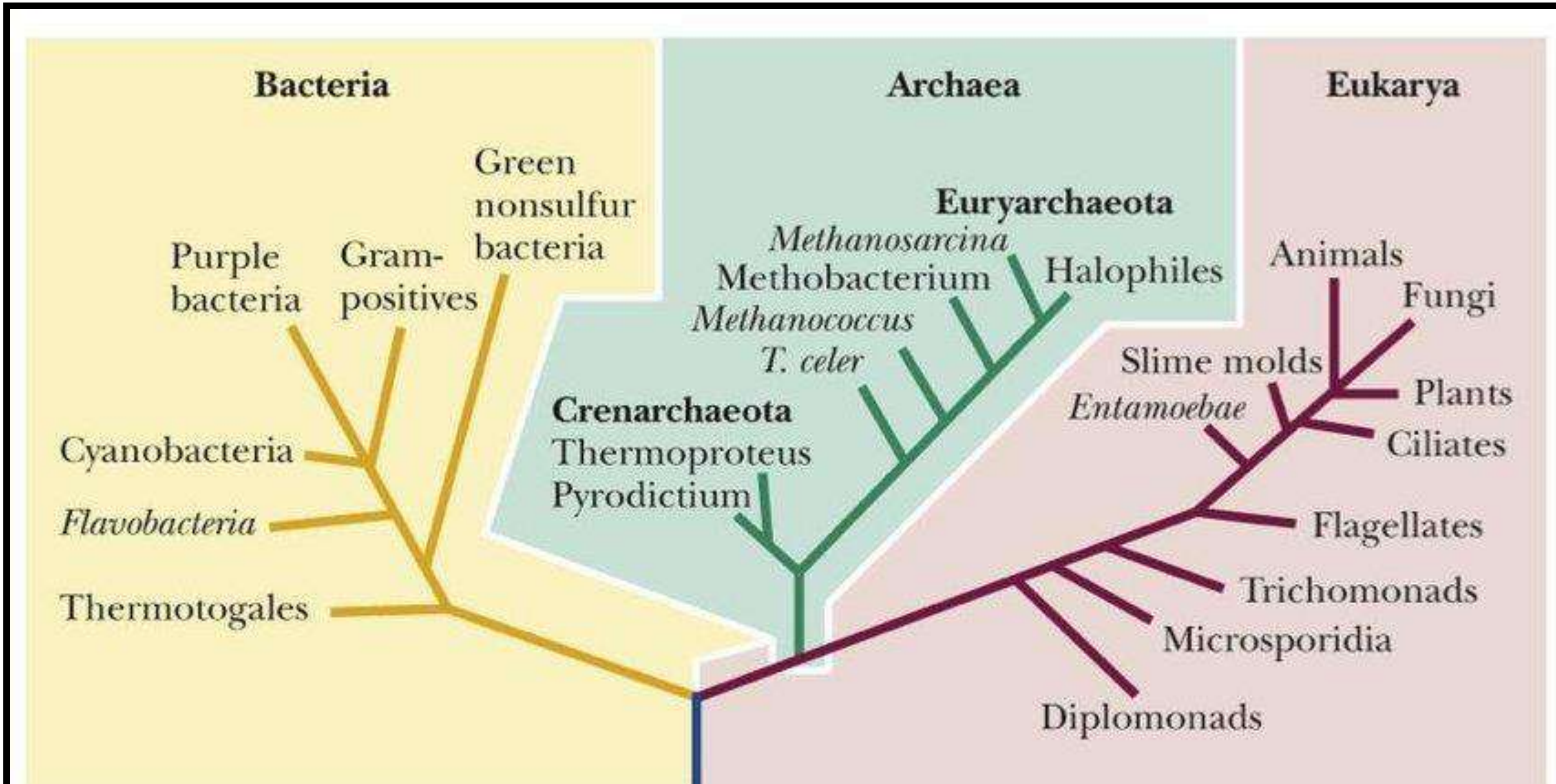
- When cells were **visualized with microscopes**, two basic cellular architectures were recognized that reflects the **presence or absence** of a membrane-bounded **nucleus** that contains genetic material.

- In addition to lacking a nucleus, **prokaryotic cells do not** have an internal membrane system or numerous **membrane-bounded organelles**.

- Prokaryotic cells have relatively **simple organization**, therefore are the simplest organisms.

- Prokaryotic cells are small, consist of **cytoplasm** surrounded by a **plasma membrane** and are encased within a **rigid cell wall**.

- Prokaryotic cells have **no distinct interior compartments**.
- Prokaryotes are very important in the **ecology of living organisms**.
- Some harvest light by **photosynthesis**, others **break down dead** organisms and recycle their components.
- Still others **cause disease** or have uses in many important **industrial processes**.
- Prokaryotes have two main domains: **archaea and bacteria**, the other is Eukarya which includes all eukaryotes



Bacteria
Archaea
Eukarya
Green nonsulfur bacteria
Purple bacteria
Gram-positives
Cyanobacteria
Flavobacteria
Thermotogales
Euryarchaeota
Methanosarcina
Methobacterium
Halophiles
Methanococcus
T. celer
Crenarchaeota
Thermoproteus
Pyrodictium
Animals
Fungi
Slime molds
Plants
Entamoebae
Ciliates
Flagellates
Trichomonads
Microsporidia
Diplomonads

Prokaryotic Cells

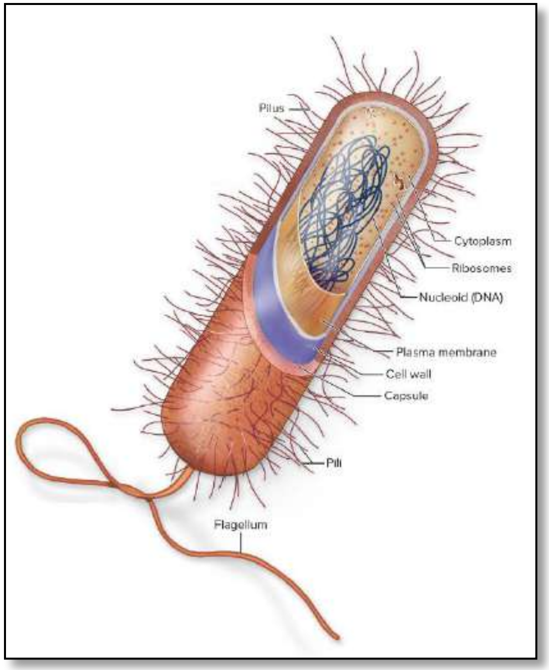
- Prokaryotic cells contain **organelles like ribosomes,** which carry out protein synthesis, but **most lack the membrane-bounded** organelles characteristic of eukaryotic cells.

- The **plasma membrane** of a prokaryotic cell carries out some of the **functions** organelles perform in eukaryotic cells.
-
- For example, some **photosynthetic** bacteria, such as the **cyanobacterium** *Prochloron*, have an extensively folded plasma membrane, with the folds extending into the cell's interior. These membrane folds contain the bacterial pigments connected with photosynthesis.

- Because a prokaryotic cell contains no membrane-bounded organelles, the DNA, enzymes, and other cytoplasmic constituents have access to all parts of the cell.
- Reactions are not compartmentalized as they are in eukaryotic cells, and the whole **prokaryote operates as a single unit**.

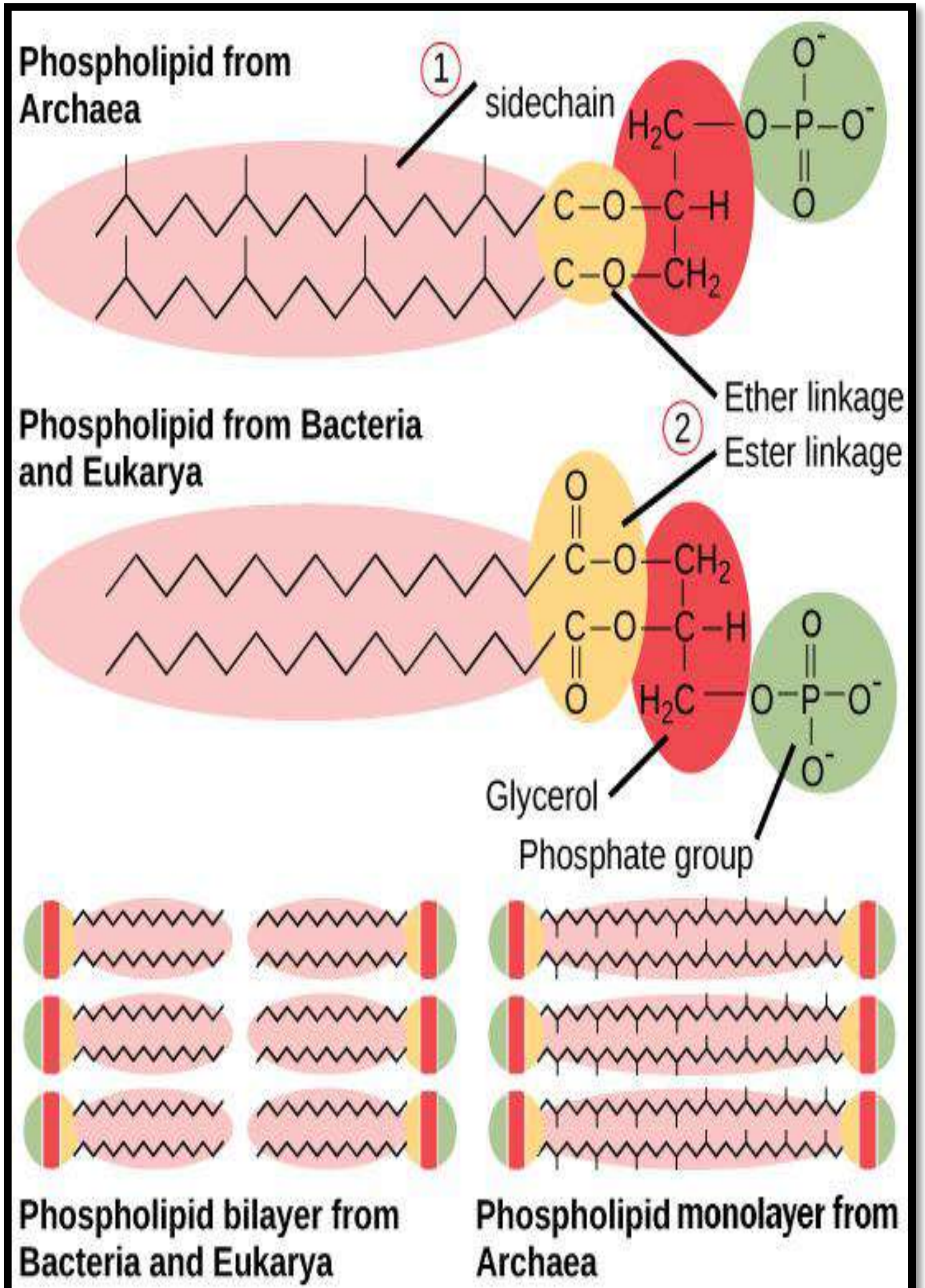
Bacterial cell walls consist of peptidoglycan

- Most bacterial cells are encased by a **strong cell wall**. This cell wall is composed of ***peptidoglycan***, which consists of a carbohydrate matrix (polymers of sugars) that is cross-linked by short polypeptide units.
- Cell walls protect the cell, maintain its shape, and prevent excessive uptake or loss of water.
- The **susceptibility of bacteria to antibiotics** often depends on the structure of their cell walls. The drugs penicillin and vancomycin, for example, interfere with the ability of bacteria to cross-link the peptides in their peptidoglycan cell wall, this destroys the integrity of the structural matrix, which can no longer prevent water from rushing in and swelling the cell to bursting.
- Some bacteria also **secrete a jellylike protective capsule** of polysaccharide around the cell. Many disease-causing bacteria have such a capsule, which enables them to adhere to teeth, skin, food—or practically any surface that can support their growth.

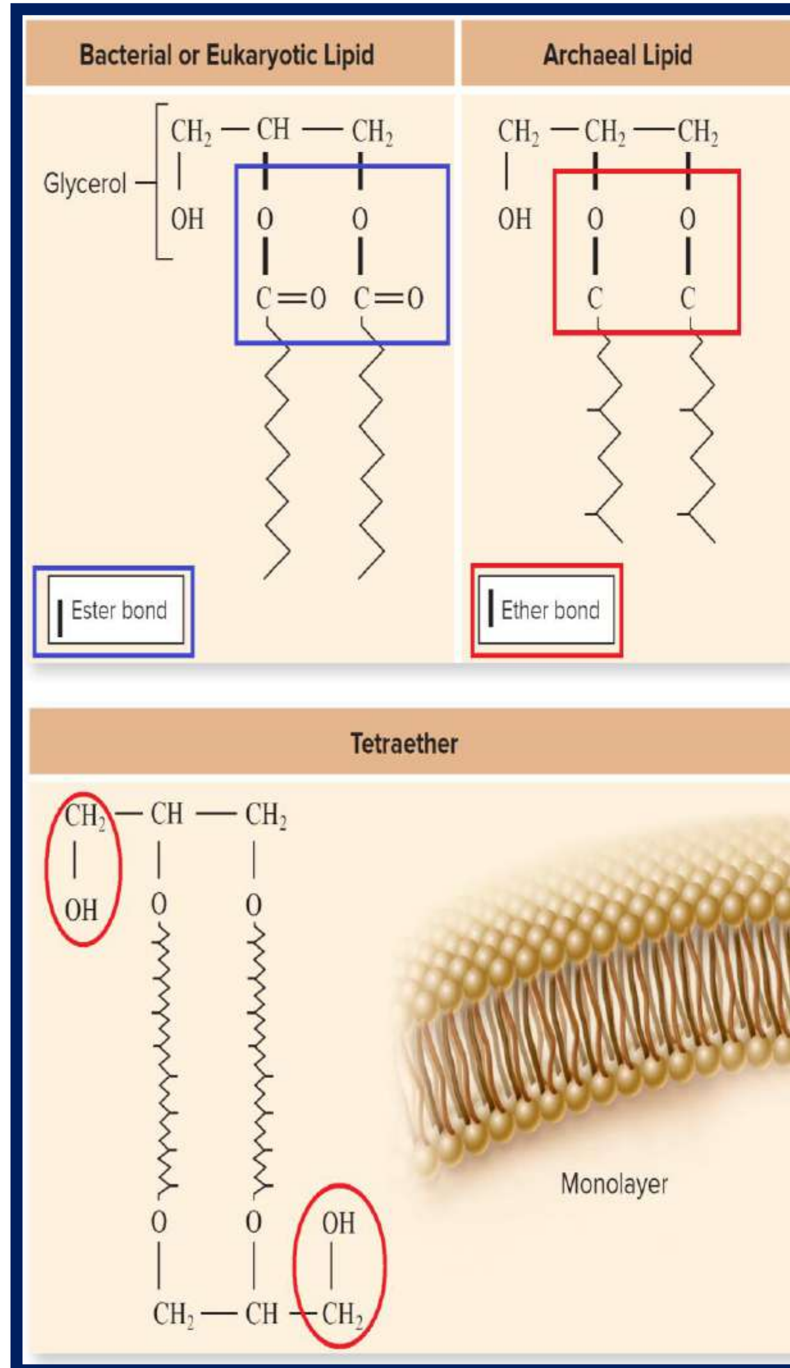


Archaea have unusual membrane lipids

- The **cell walls of archaea** are composed of **various chemical compounds**, including polysaccharides and proteins, and possibly even inorganic components.
- A common feature distinguishing archaea from bacteria is the nature of their **cell membrane lipids** which composed of **glycerol linked to hydrocarbon chains by <u>Ether</u> linkages**, not the ester linkages seen in bacteria and eukaryotes
- These hydrocarbons may also be branched, and they may be organized as **tetraethers** that form a **monolayer** instead of a bilayer.
- The cellular machinery that **replicates DNA and synthesized proteins** in archaea is more closely **related to eukaryotic** systems than to bacterial systems. Even though they share a similar overall cellular architecture with prokaryotes, **archaea appear to be more closely related** on a molecular basis to eukaryotes.
- **Archaea and bacteria are similar** in that both have a prokaryotic cellular structure; however, they **vary considerably** at the biochemical (metabolic) and molecular levels.
- **Archaea and bacteria** differ in four key ways: plasma membrane structure, cell wall structure, DNA replication, and gene expression.



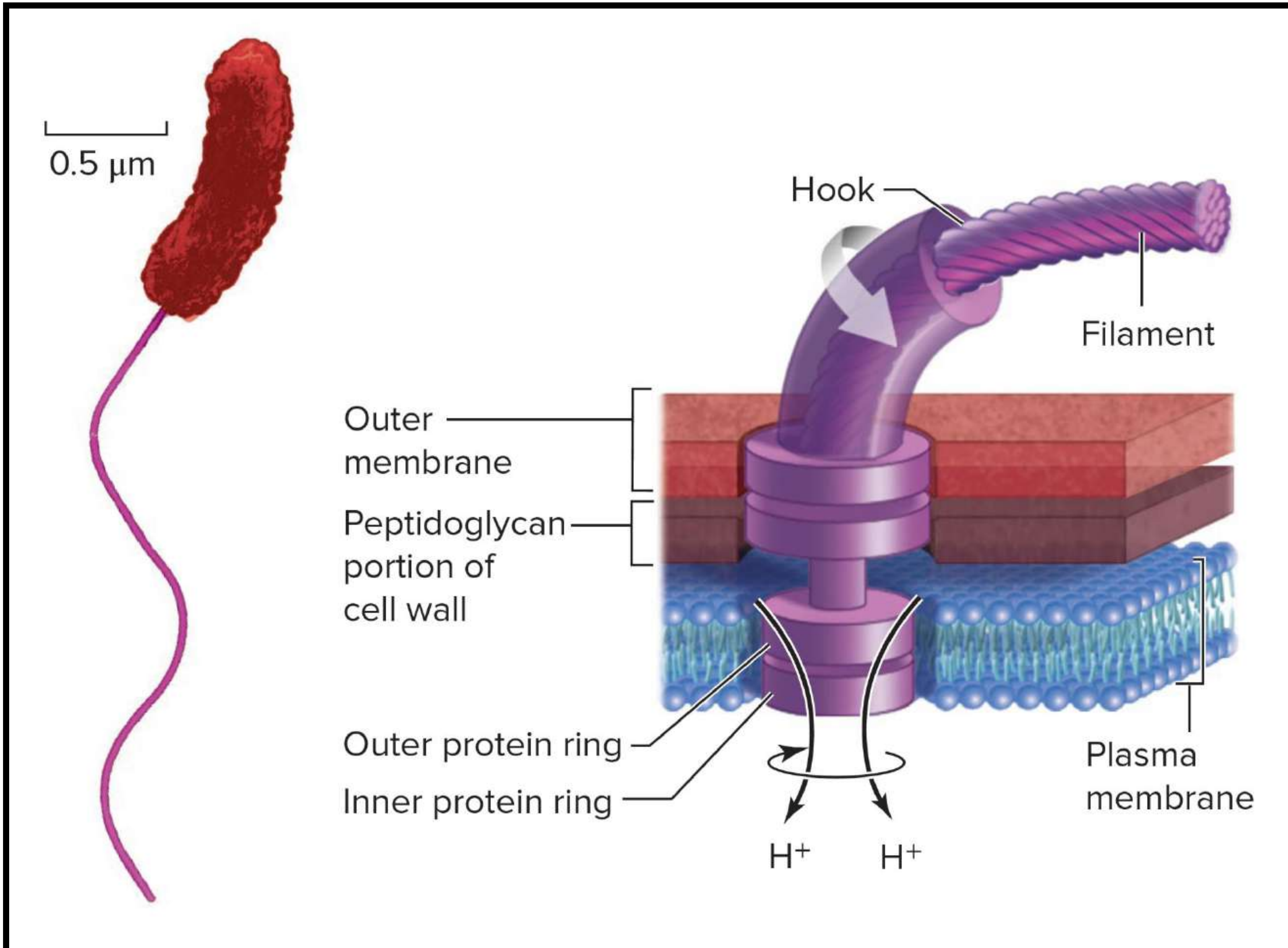
Phospholipid from Archaea
1
sidechain
Ether linkage
Phospholipid from Bacteria and Eukarya
2
Ester linkage
Glycerol
Phosphate group
Phospholipid bilayer from Bacteria and Eukarya
Phospholipid monolayer from Archaea



Bacterial or Eukaryotic Lipid
Archaeal Lipid
Glycerol
Ester bond
Ether bond
Tetraether
Monolayer

Some prokaryotes move by means of rotating flagella

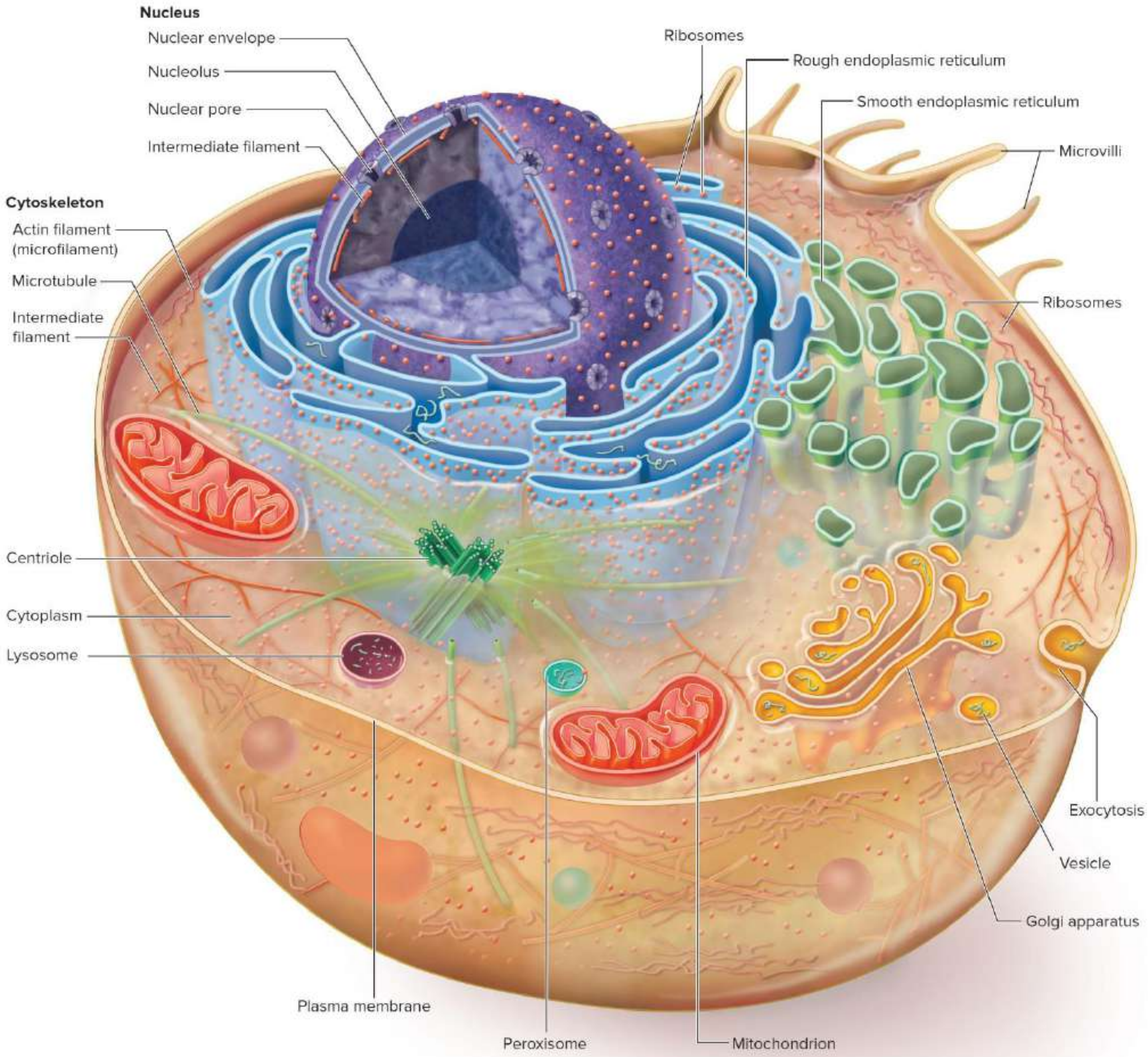
- **Flagella** (singular, *flagellum*) are long, threadlike structures (protein fibers) **protruding** from the **surface of a cell** that are used in **locomotion**. There may be one or more per cell, or none, depending on the species.
- Bacteria can swim at speeds of up to **70 cell lengths per second** by **rotating** their flagella like screws.
- The **rotary motor proteins** are anchored in the plasma membrane and uses the energy stored in a gradient (**Proton-Motive Force**) that transfers protons across the plasma membrane to power the movement of the flagellum (the movement of protons through channels across the membrane is **coupled** to the rotation of flagellum).
- This coupling of an electrochemical gradient to mechanical rotational work is another fascinating feature of the bacterial motor.



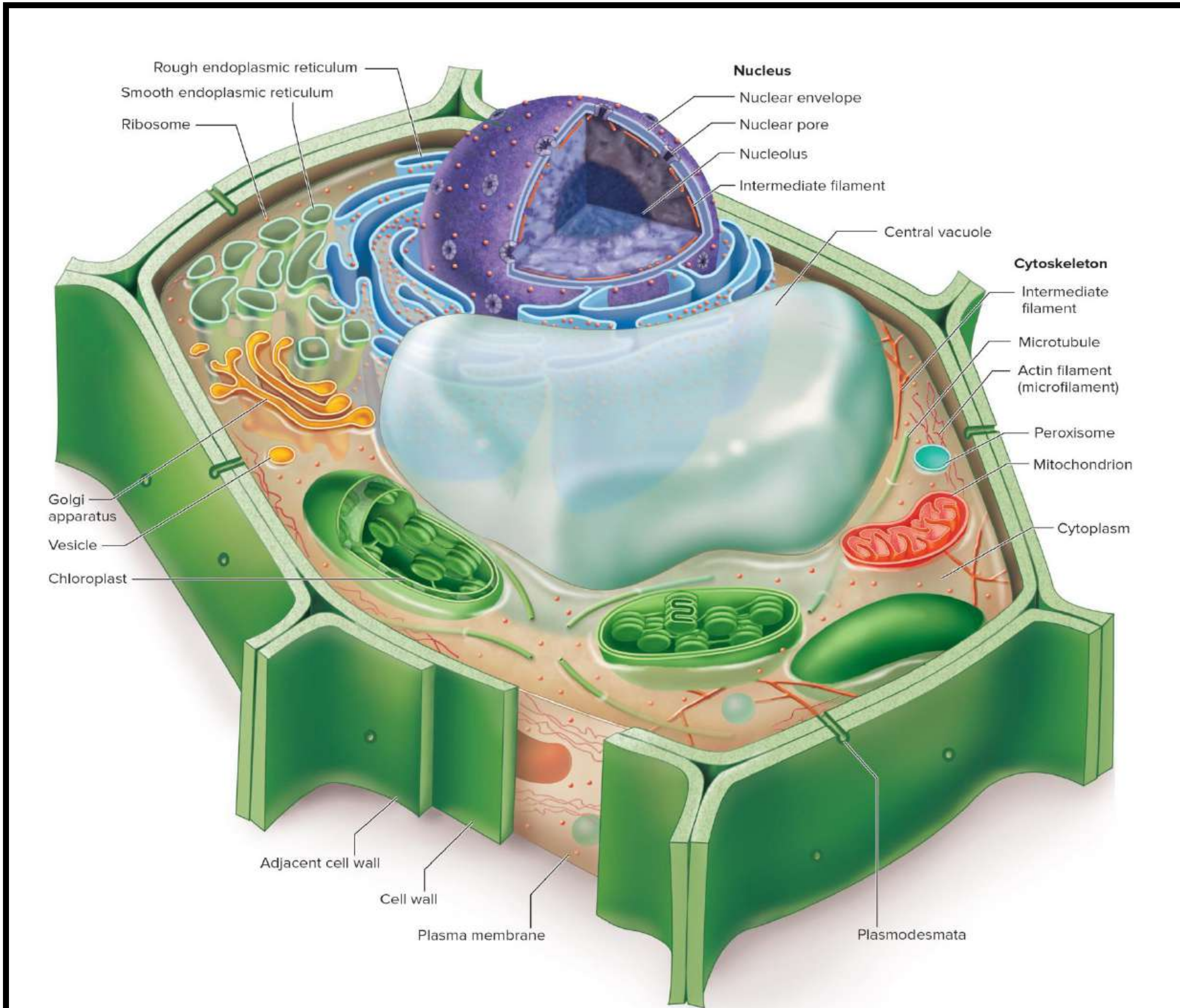
0.5 µm
Hook
Filament
Outer membrane
Peptidoglycan portion of cell wall
Outer protein ring
Inner protein ring
Plasma membrane
H+
H+

A Panoramic View of the Eukaryotic Cell

- **Eukaryotic** cells are far **more complex** than prokaryotic cells.
- The hallmark of the eukaryotic cell is **compartmentalization** and the presence of extensive **endomembrane system** through the cell interior and numerous **membrane-bounded organelles** that form compartments within which multiple biochemical processes can proceed simultaneously and independently.
- **Plant cells** often have a large, membrane-bounded sac called a **central vacuole,** which stores proteins, pigments, and waste materials.
- Inside the nucleus, the **DNA is coiled** tightly around proteins and **packaged** into compact units called **chromosomes.**
- All eukaryotic cells are supported by an internal protein scaffold, the **cytoskeleton.**
- The **nucleus** is the largest and most easily seen organelle within a eukaryotic cell.
- Nucleus is **roughly spherical** in shape, and in animal cells, it is typically located in the central region of the cell, in some cells, a network of fine cytoplasmic filaments seems to support the nucleus in this position.
- The nucleus contains the **genetic information** that enables the synthesis of nearly all proteins of a living eukaryotic cell.
- Most eukaryotic cells possess **a single nucleus**, although the cells of fungi and some other groups may have from several to **many nuclei**. Mammalian erythrocytes (red blood cells) lose their nuclei when they mature.
- Many nuclei exhibit a dark-staining zone called the nucleolus, which is a region where intensive synthesis of ribosomal RNA is taking place.



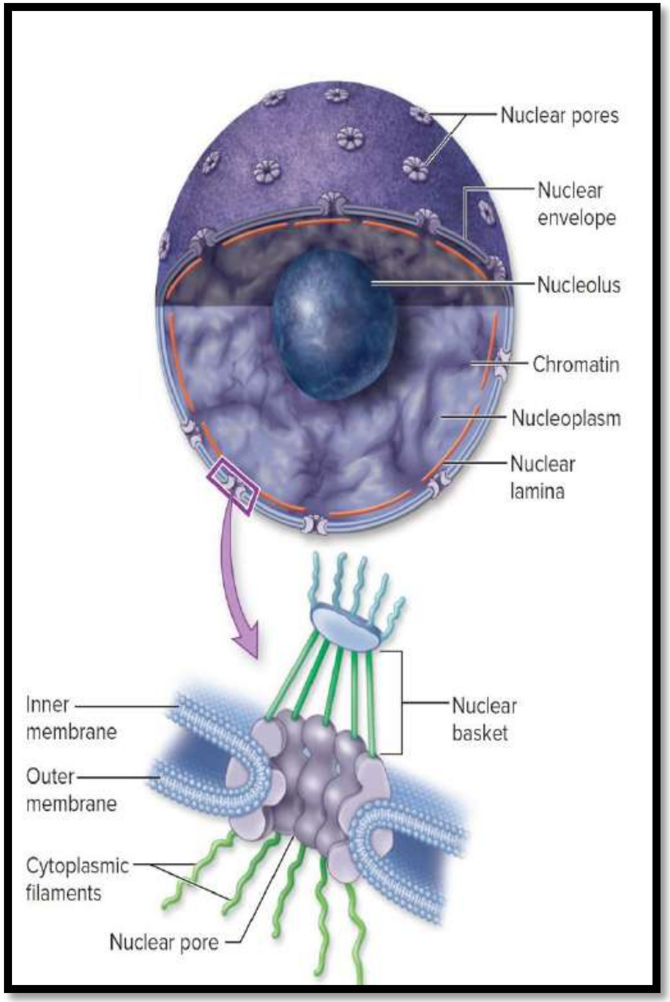
Nucleus
Nuclear envelope
Nucleolus
Nuclear pore
Intermediate filament
Cytoskeleton
Actin filament
(microfilament)
Microtubule
Intermediate
filament
Centriole
Cytoplasm
Lysosome
Ribosomes
Rough endoplasmic reticulum
Smooth endoplasmic reticulum
Microvilli
Ribosomes
Exocytosis
Vesicle
Golgi apparatus
Plasma membrane
Peroxisome
Mitochondrion

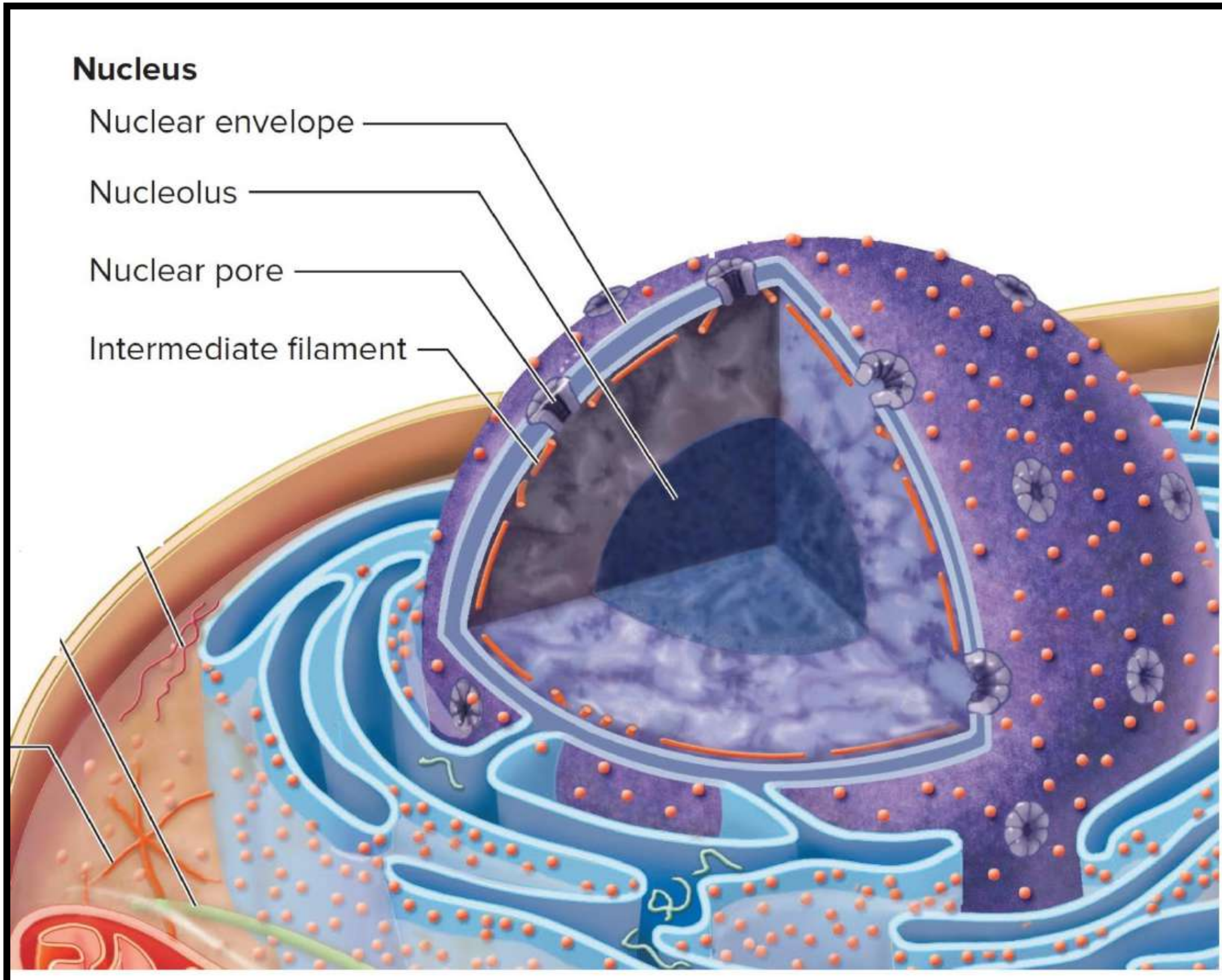


Rough endoplasmic reticulum
Smooth endoplasmic reticulum
Ribosome
Nucleus
Nuclear envelope
Nuclear pore
Nucleolus
Intermediate filament
Central vacuole
Cytoskeleton
Intermediate filament
Microtubule
Actin filament (microfilament)
Peroxisome
Mitochondrion
Cytoplasm
Golgi apparatus
Vesicle
Chloroplast
Adjacent cell wall
Cell wall
Plasma membrane
Plasmodesmata

The nuclear envelope and nuclear pores

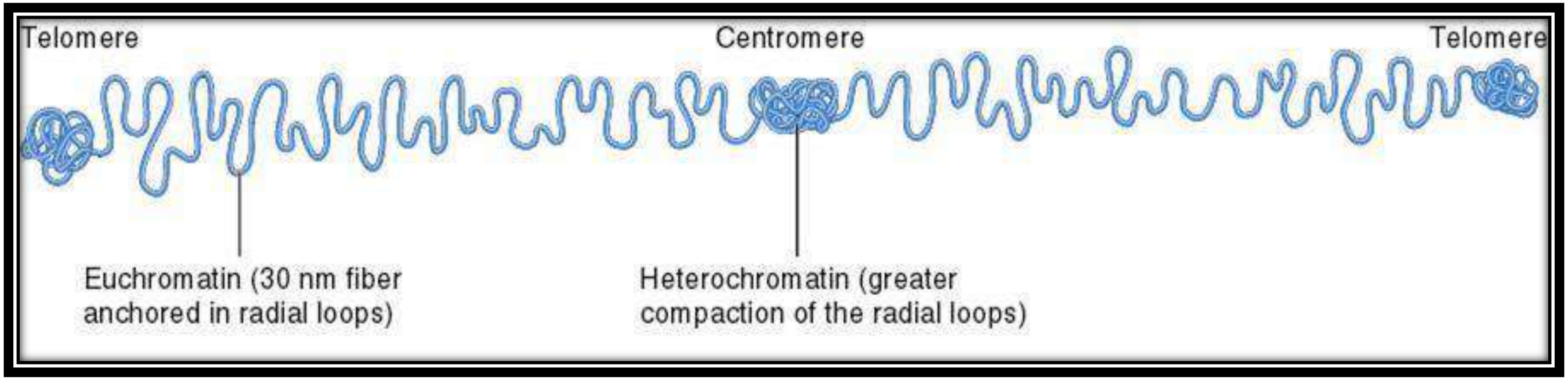
- The **nuclear envelope** is a ***two* phospholipid bilayer membranes**, the **outer membrane** is continuous with the the **endoplasmic reticulum**.
- **Nuclear pores** are **structures** scattered over the surface of the nuclear envelope and **50 to 80 nm** apart at locations where the two membrane layers of the nuclear envelope come together.
- The structure of the **Nuclear pores** consists of a central **framework with eightfold symmetry** that is embedded in the nuclear envelope.
- This **framework** is bounded by a **cytoplasmic face with eight fibers**, and a nuclear face with a complex ring that forms a **nuclear basket** beneath the central ring.
- **Nuclear basket coordinates** the function of several multiprotein complexes involved in chromatin regulation, transcription regulation, proofreading and mRNA export
- The **Nuclear pore** allows ions and small molecules to diffuse freely between nucleoplasm and cytoplasm, while controlling the passage of proteins, RNA and RNA–protein complexes.
- The **inner surface of the nuclear envelope** is covered with a network of fibers that make up the **nuclear lamina** that composed of **intermediate filament** fibers called nuclear lamins.

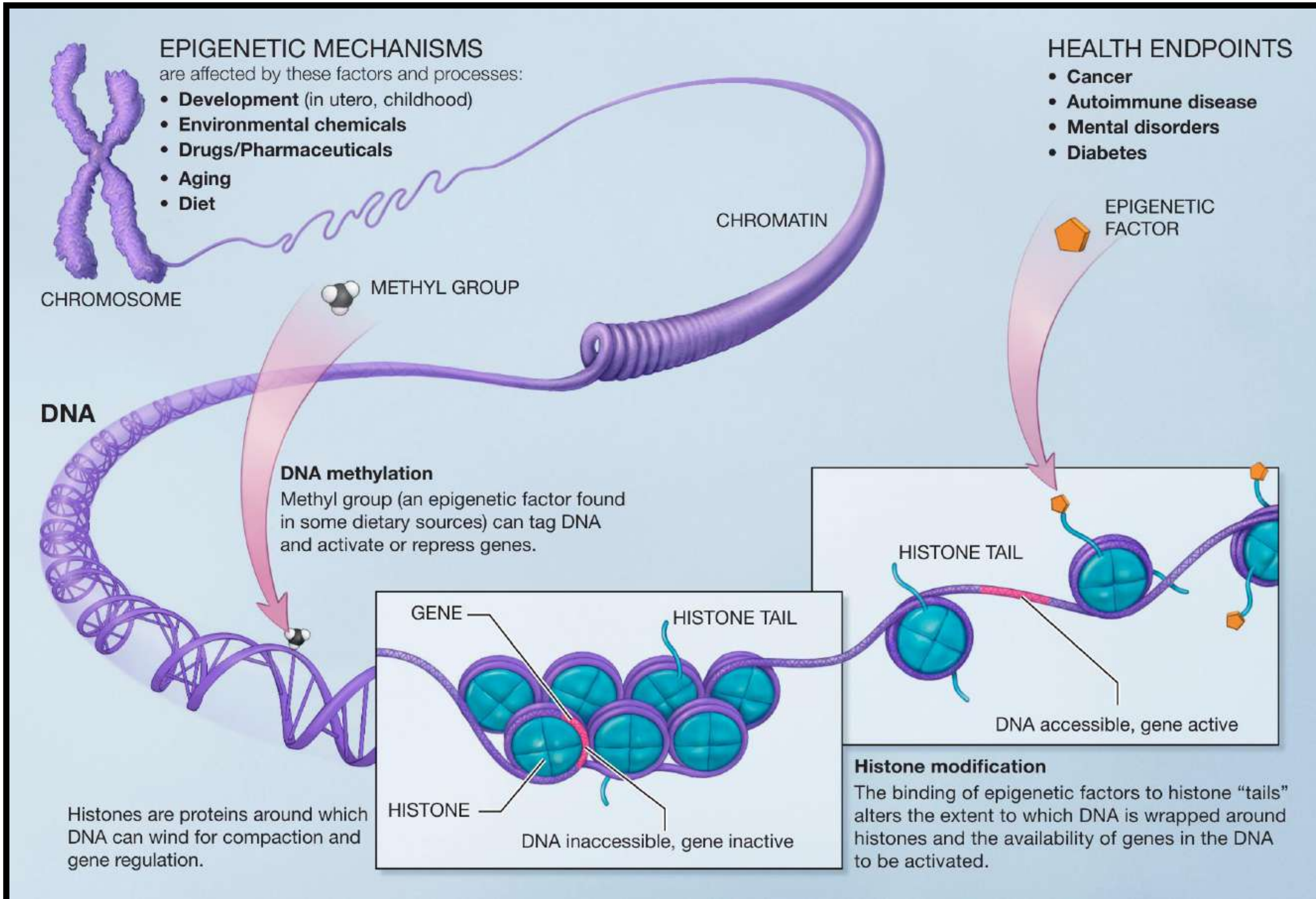


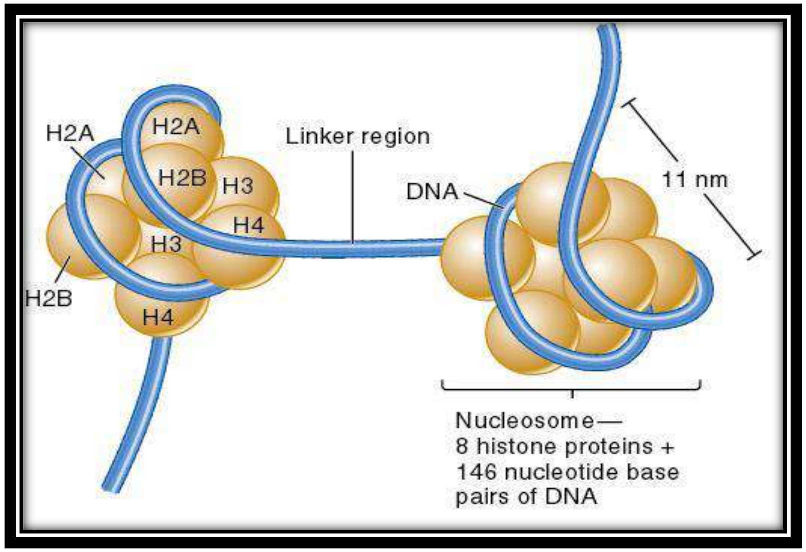

Nucleus
Nuclear envelope
Nucleolus
Nuclear pore
Intermediate filament

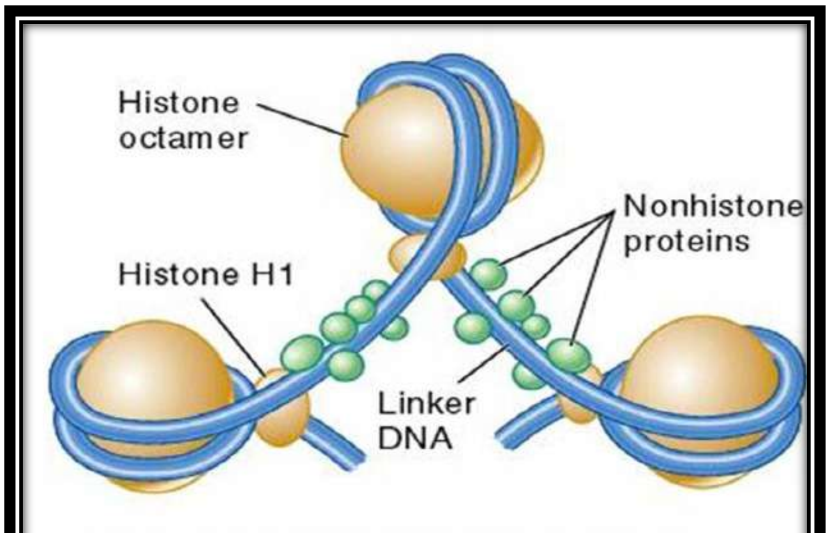
Chromatin: DNA packaging

- In eukaryotes, the DNA is divided into multiple linear chromosomes, which are organized with proteins into a complex structure called **chromatin.**
- The very **structure of chromatin** affects the function of DNA. **Changes** in gene **expression** that do not involve changes in DNA sequence, so-called **epigenetic changes**, involve alterations in chromatin structure.
- Chromatin is usually in a more extended form that is organized in the nucleus.
- When cells divide, the chromatin must be **further compacted** into a more highly condensed state that forms the chromosomes **visible** in the light microscope.
- interphase chromosomes presents as **Heterochromatin or Euchromatin.**
- **Heterochromatin** (less diffuse structure)
  - Tightly compacted regions of chromosomes, *Transcriptionally inactive*
- **Euchromatin (**more diffuse structure), Less condensed regions of chromosomes
  - *Transcriptionally active*

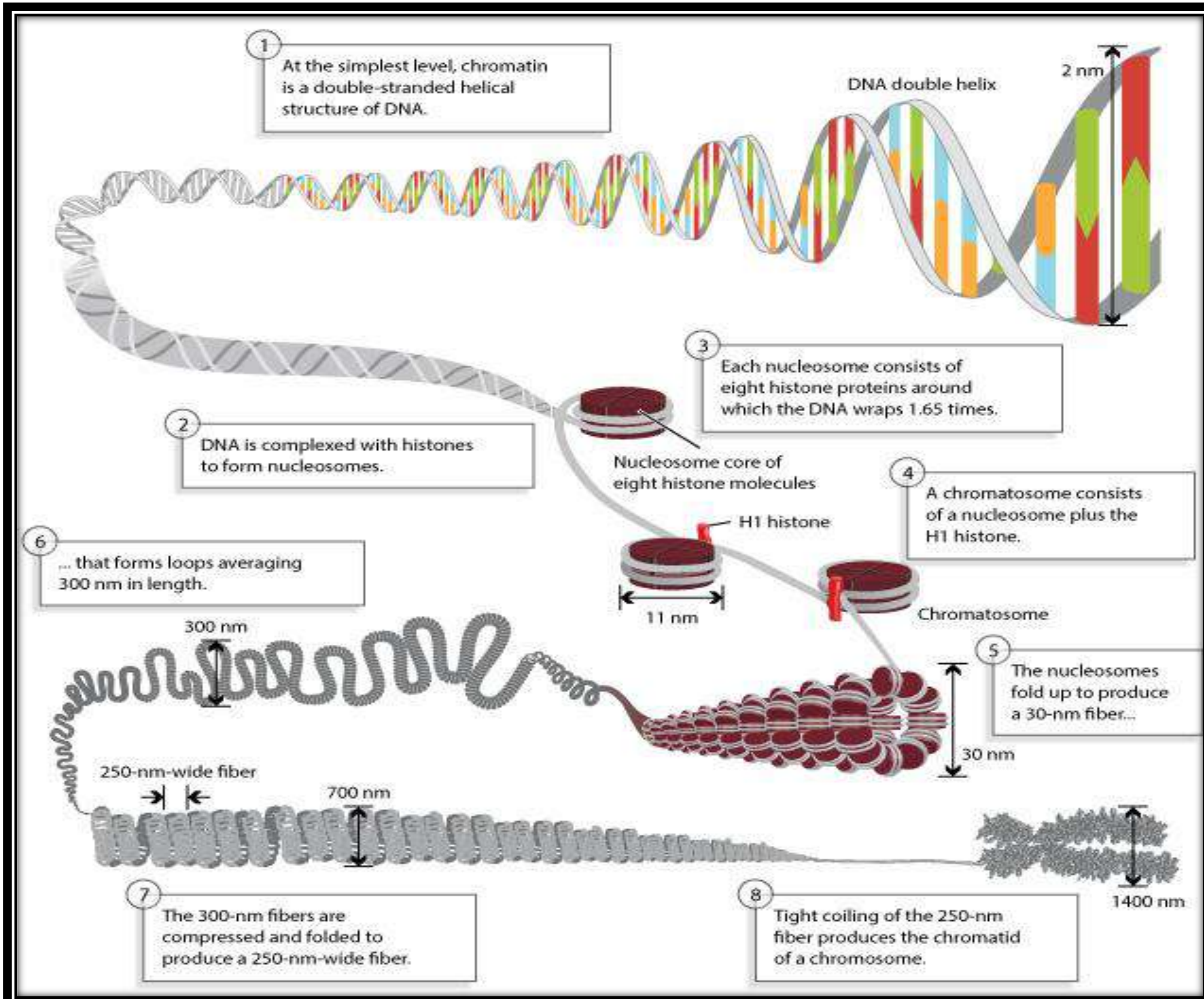



EPIGENETIC MECHANISMS
are affected by these factors and processes:
• Development (in utero, childhood)
• Environmental chemicals
• Drugs/Pharmaceuticals
• Aging
• Diet
HEALTH ENDPOINTS
• Cancer
• Autoimmune disease
• Mental disorders
• Diabetes
CHROMOSOME
CHROMATIN
EPIGENETIC FACTOR
METHYL GROUP
DNA
DNA methylation
Methyl group (an epigenetic factor found in some dietary sources) can tag DNA and activate or repress genes.
HISTONE TAIL
DNA accessible, gene active
GENE
HISTONE TAIL
HISTONE
DNA inaccessible, gene inactive
Histones are proteins around which DNA can wind for compaction and gene regulation.
Histone modification
The binding of epigenetic factors to histone "tails" alters the extent to which DNA is wrapped around histones and the availability of genes in the DNA to be activated.





Nucleosomes showing linker histones and nonhistone proteins


1
At the simplest level, chromatin is a double-stranded helical structure of DNA.
DNA double helix
2 nm
3
Each nucleosome consists of eight histone proteins around which the DNA wraps 1.65 times.
2
DNA is complexed with histones to form nucleosomes.
Nucleosome core of eight histone molecules
4
A chromatosome consists of a nucleosome plus the H1 histone.
H1 histone
6
... that forms loops averaging 300 nm in length.
11 nm
Chromatosome
300 nm
5
The nucleosomes fold up to produce a 30-nm fiber...
30 nm
250-nm-wide fiber
700 nm
1400 nm
7
The 300-nm fibers are compressed and folded to produce a 250-nm-wide fiber.
8
Tight coiling of the 250-nm fiber produces the chromatid of a chromosome.

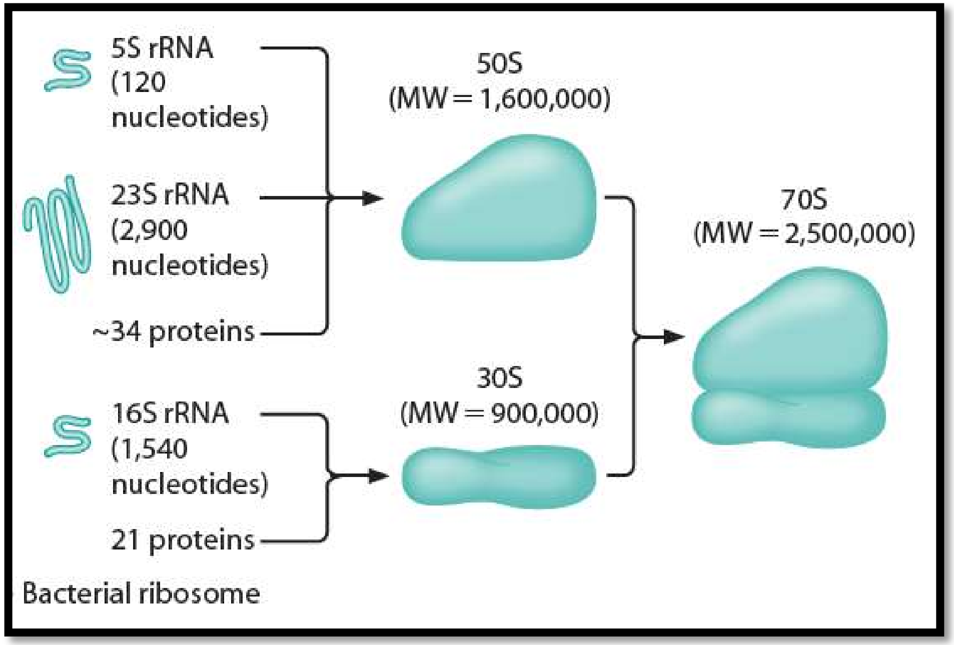
The nucleolus: Ribosomal subunit manufacturing

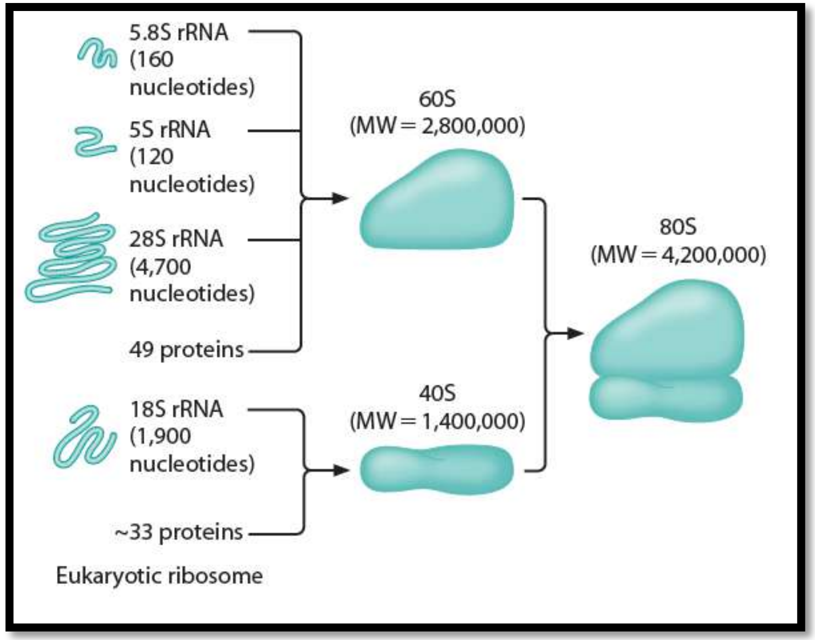
- **Hundreds of copies** of the genes encoding the ribosomal RNAs are clustered together on the chromosome, facilitating ribosome construction by producing RNA molecules from transcribing the cluster. The clusters of ribosomal RNA genes, the RNAs they produce, and the ribosomal proteins all come together within the nucleus during ribosome production.
- These **ribosomal assembly** areas are easily visible within the nucleus as one or more darkstaining regions called **nucleoli** (singular, ***nucleolus***). Nucleoli can be seen under the light microscope even when the chromosomes are uncoiled.
- Ribosome is complex molecular assembly and composed of **two subunits (large and small)** each of which is composed of a combination of **rRNA and proteins**.
- The **large and small** subunits join to form a **functional ribosome** only when they are actively synthesizing proteins.
- Ribosomes are found either **free** in the cytoplasm or associated (**bound**) with internal membranes (Endoplasmic reticulum). Both free and bounded ribosomes and **interchangeable**
- **Free ribosomes synthesize proteins** that are found in the cytoplasm, nuclear proteins, mitochondrial proteins, and proteins found in other organelles not derived from the endomembrane system.
- **Bound ribosomes** synthesize membrane proteins, proteins found in the endomembrane system, and proteins destined for **export** from the cell.

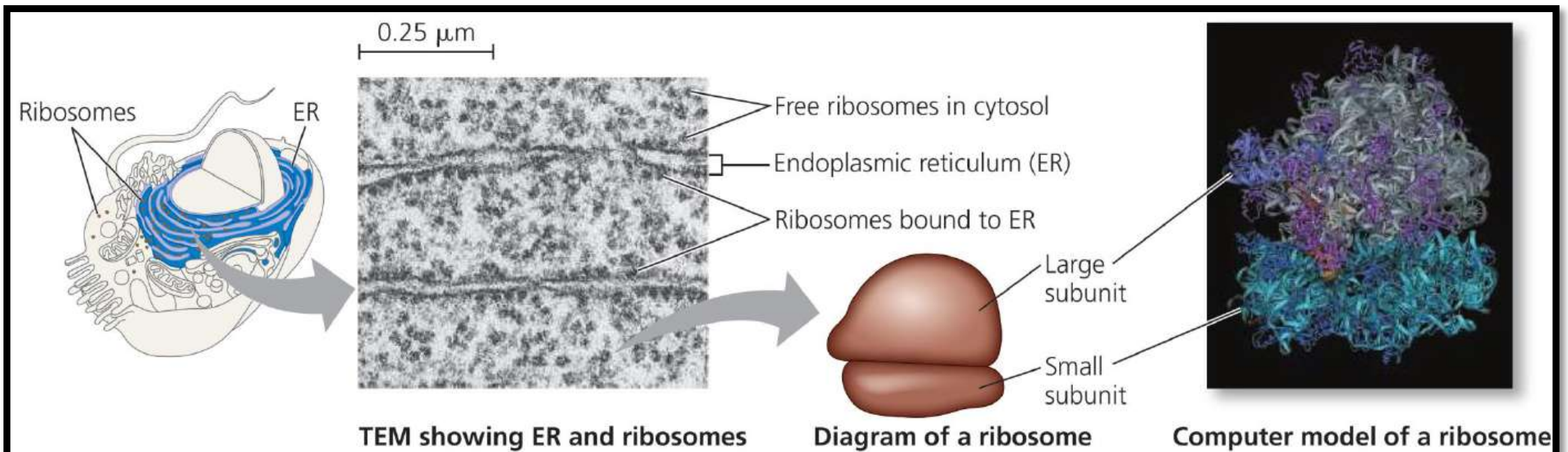
Ribosomal Structure

- Ribosomes can be thought of as "**universal organelles**" because they are found in all cell types from all three domains of life.
- Life is protein-based, and ribosomes are the **factories** that make proteins.
- Ribosome consists of two subunits, **one large and one small.**
- The subunits and rRNA components are most easily isolated and **characterized** on the basis of their **sedimentation behavior** in sucrose gradients, which is a measure of their rate of migration when centrifuged, abbreviated **S for Svedberg coefficient**, which reflects their **density, mass, and shape.**
- In **prokaryotes**, the **monosome** (whole ribosome composed of small and large subunits) **is a 70S particle**, and in **eukaryotes** it is approximately **80S**.
- **Sedimentation coefficients**, which reflect differences in the rate of migration of different-sized particles and molecules, **are not additive**.
- For example, the prokaryotic **70S** monosome consists of a **50S and a 30S** subunit
- The **eukaryotic 80S** monosome consists of a **60S and a 40S** subunit.

Prokaryotic and Eukaryotic Ribosomes

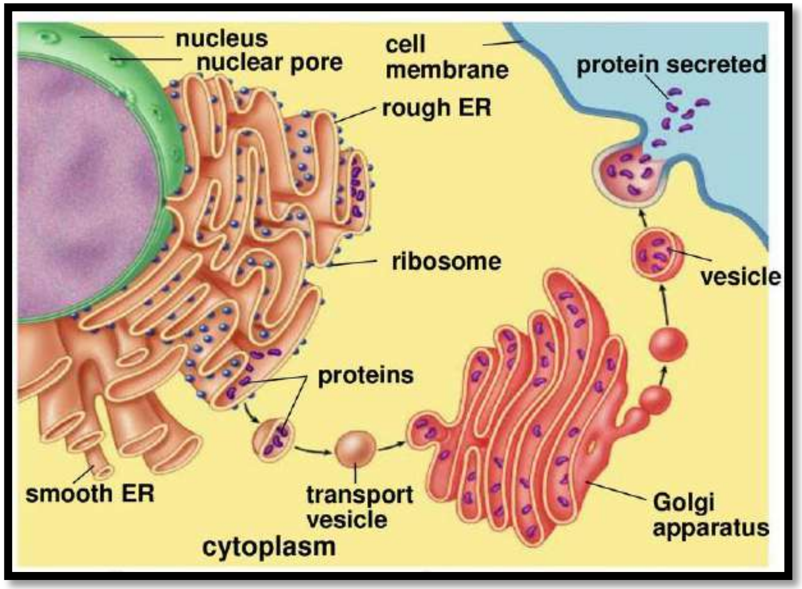






The Endomembrane System

- The **interior of a eukaryotic cell** is packed with membranes that form an **endomembrane system**. This endomembrane system **fills** the cell, **dividing** it into compartments, **channeling** the passage of molecules through the interior of the cell, and **providing surfaces** for the synthesis of lipids and some proteins.
- The endomembrane system in eukaryotic cells is one of the **fundamental distinctions** between eukaryotes and prokaryotes.



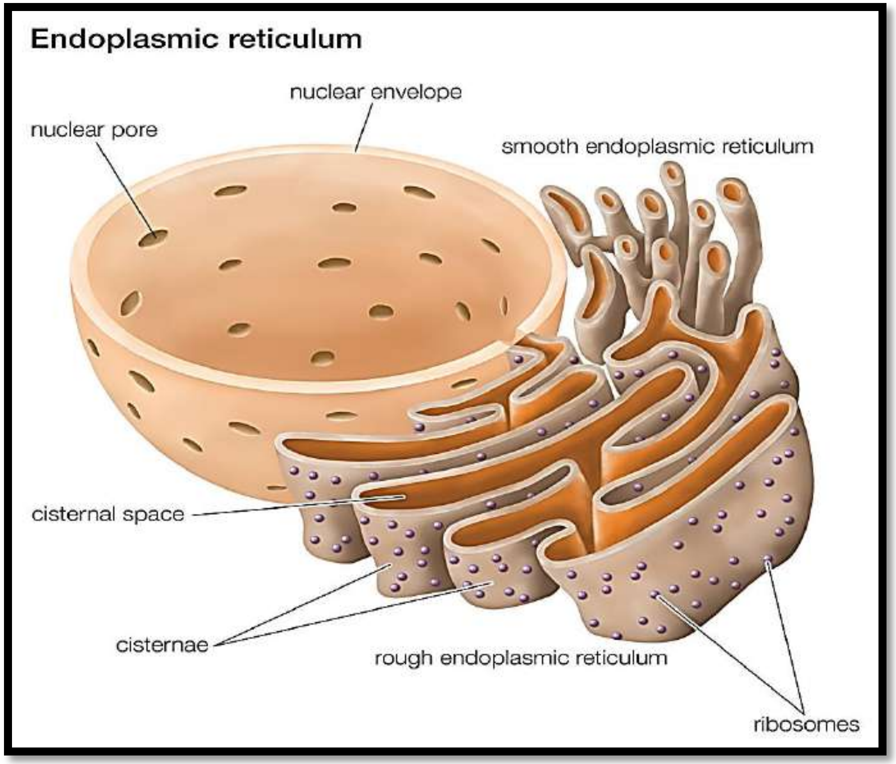
The endomembrane system **is composed of**:

- Nuclear envelope
- Endoplasmic reticulum (ER)
- Golgi apparatus
- Lysosomes
- Vacuoles and Vesicles
- Cell membrane

The **largest** of the internal membranes is the **endoplasmic reticulum (ER).**

The endoplasmic reticulum (ER)

- The **ER is composed** (like membranes) of a phospholipid bilayer embedded with proteins, and may also be connected to the cytoskeleton, which can affect ER structure and growth.
- The **two largest compartments** in eukaryotic cells are the space inside the ER, called **the cisternal space**, or lumen, and the region exterior to it, **the cytosol**, which is the fluid component of the cytoplasm containing dissolved organic molecules and ions.



- The ER is a **network of flattened sacs** and **branching tubules** that extends throughout the cytoplasm in plant and animal cells.
- These sacs and tubules are **all interconnected** by a **single continuous** membrane so that the organelle has only **one large** complexly arranged lumen (**cisternal space**).
- The membrane of ER is continuous with the **outer nuclear membrane**.
- Two regions can be recognized in most cells, known as **smooth ER** and **rough ER.**
- The basic difference is that the **RER is covered in ribosomes**, which give it its rough appearance in the electron microscope.

The smooth ER (SER)

- **Smooth ER (SER)** refers to the regions of the ER with **no or relatively very few** bound ribosomes.
- The **ratio** of SER to RER **is not fixed and** can vary greatly depends on a cell's function.
- Cells that carry out **extensive lipid synthesis**, such as those in the testes, intestine, and brain, have **abundant SER**. Cells that **synthesize secreted proteins**, for example, antibodies, have much **more extensive RER**.
- The membranes of the SER contain many **embedded enzymes**, involved in the **synthesis** of a variety of **carbohydrates and lipids**.
- **Steroid hormones** are also synthesized in the SER of ovaries, testes, and the adrenal gland.
- **Synthesis of phospholipids**. The majority of membrane lipids are assembled in the SER and then sent to whatever parts of the cell need membrane components.
- Store intracellular Ca^{2+} (**sequestering calcium**), which keeps the cytoplasmic level low, allowing Ca^{2+} to be used as a signaling molecule. Ca^{2+} **ions are pumped** from the cytosol into the lumen of the smooth endoplasmic reticulum to more **than 100 times** the concentration found in the cytosol. In muscle cells, for example, Ca^{2+} is used to trigger muscle contraction. In other cells, Ca^{2+} release from SER stores is involved in **diverse signaling pathways**.
- **SER modifies foreign substances** to make them more soluble and less toxic. In the liver, enzymes in the SER carry out this **detoxification** which involves **adding hydroxyl group** to drug making them more soluble and easer to flush from the body.
- The SER is responsible for **some carbohydrate metabolism**. In the liver, for example, the cell breaks down the glycogen. First Glycogen is broken into **glucose-6- phosphate**, an ion that, if released would harm our blood cells. So, enzyme found in the membrane of the SER can remove the phosphate, allowing pure glucose to be released

The rough ER (RER)

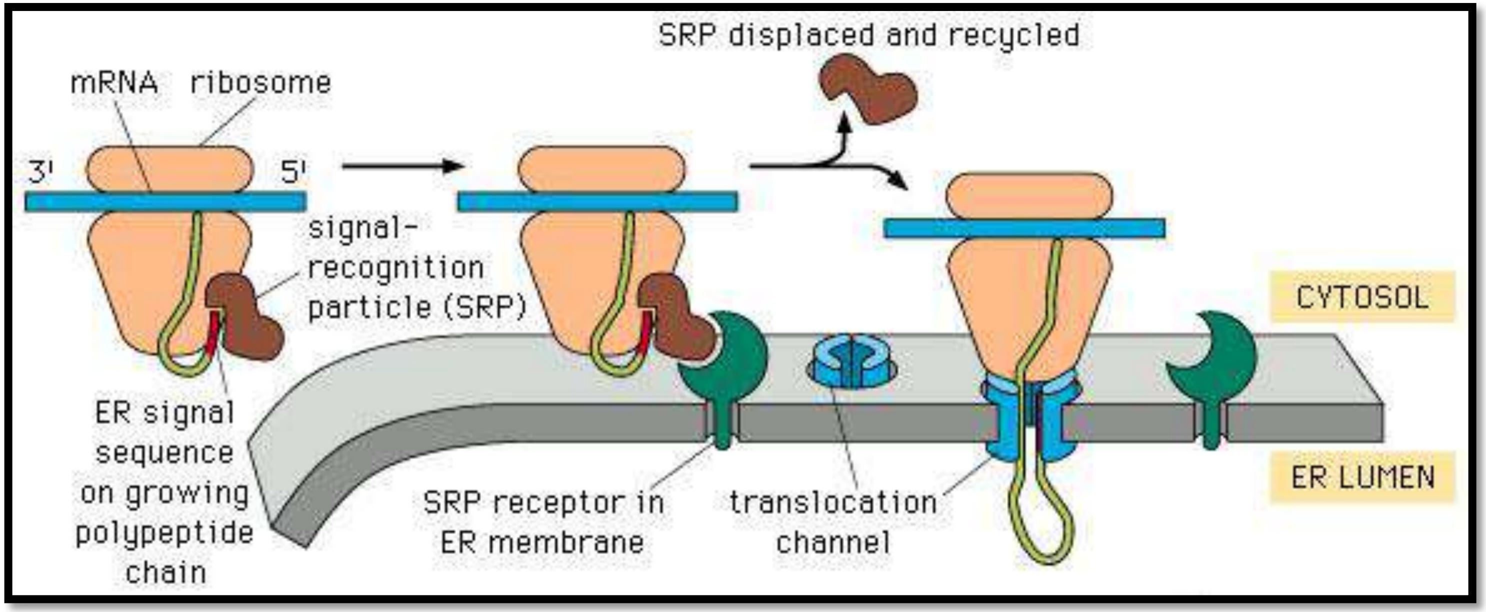
- The rough ER is a site of **protein synthesis**
- The **rough ER** (**RER**) gets its name from the **rough appearance** of its surface because of the **bound ribosomes**.
- The **proteins synthesized** on the surface of the RER are **destined to be exported** from the cell, sent to lysosomes or vacuoles, or vesicles or embedded in the plasma membrane. These proteins **enter the cisternal space** as a first step in the pathway that will sort proteins to their eventual destinations. This **export pathway** also involves **vesicles and the Golgi apparatus**.
- The **sequence of the protein** being synthesized determines whether the ribosome will become associated with the ER or remain a cytoplasmic ribosome.
- **In the RER**, newly synthesized **proteins can be modified** by the addition of short-chain **carbohydrates** to form glycoproteins.
- **Proteins bound for secretion** are separated from other products and packaged into vesicles that move to the Golgi for further modification and packaging for export.
- After secretory proteins are formed, the ER membrane keeps them separate from proteins in the cytosol, which are produced by free ribosomes.
- **Secretory proteins depart** from the ER **are wrapped** in the membranes of vesicles (**transport vesicles**) that bud like bubbles from a specialized region called **transitional ER**.

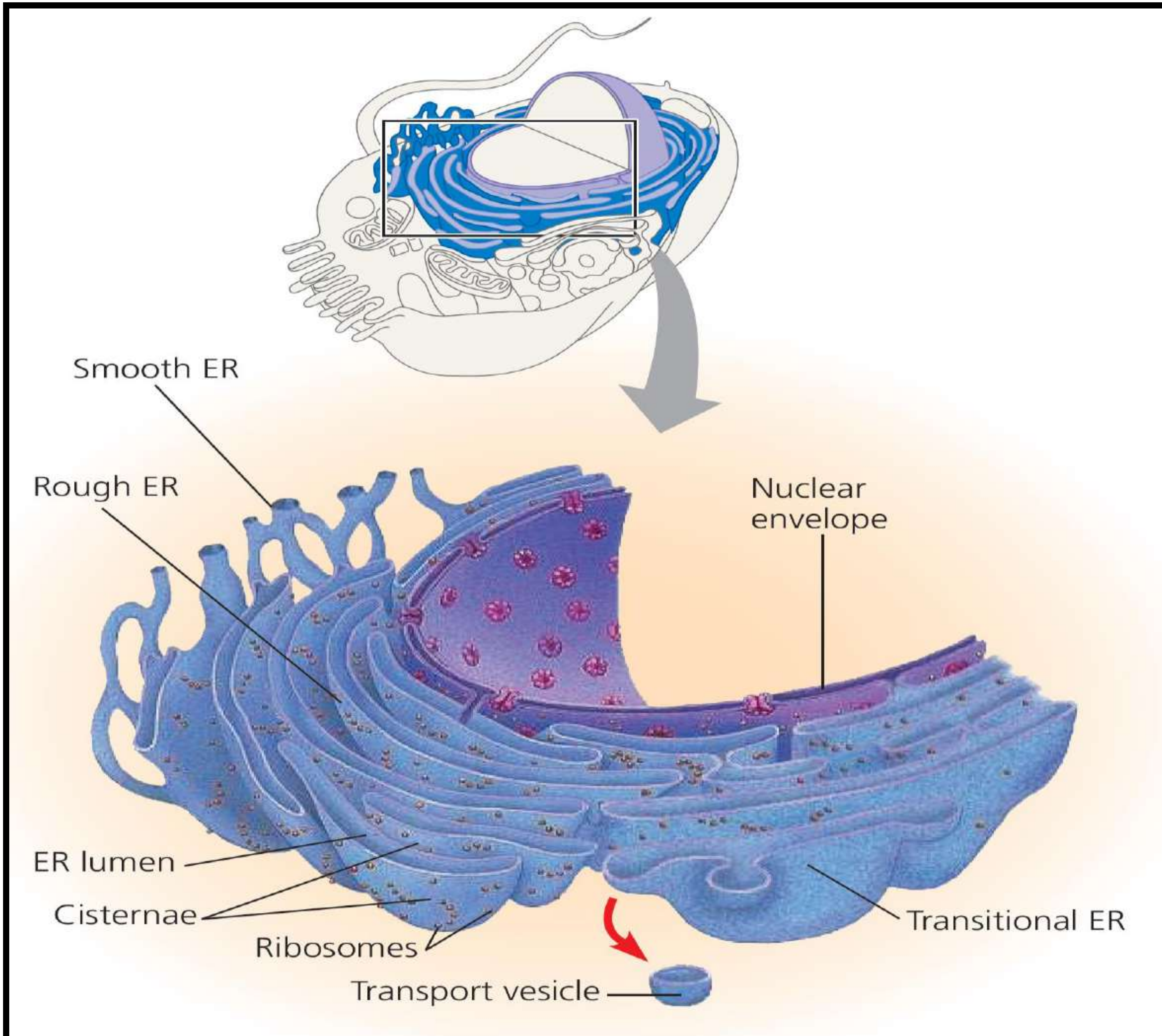
Signal sequence

- **Proteins to be exported** contain special amino acid sequences called **signal sequences**.

- New protein is made **by a free ribosome**, the **signal sequence** of the growing polypeptide attaches to a **recognition factor** that carries the ribosome and its partially completed protein to a "**docking site or receptor**" on the surface of the ER.

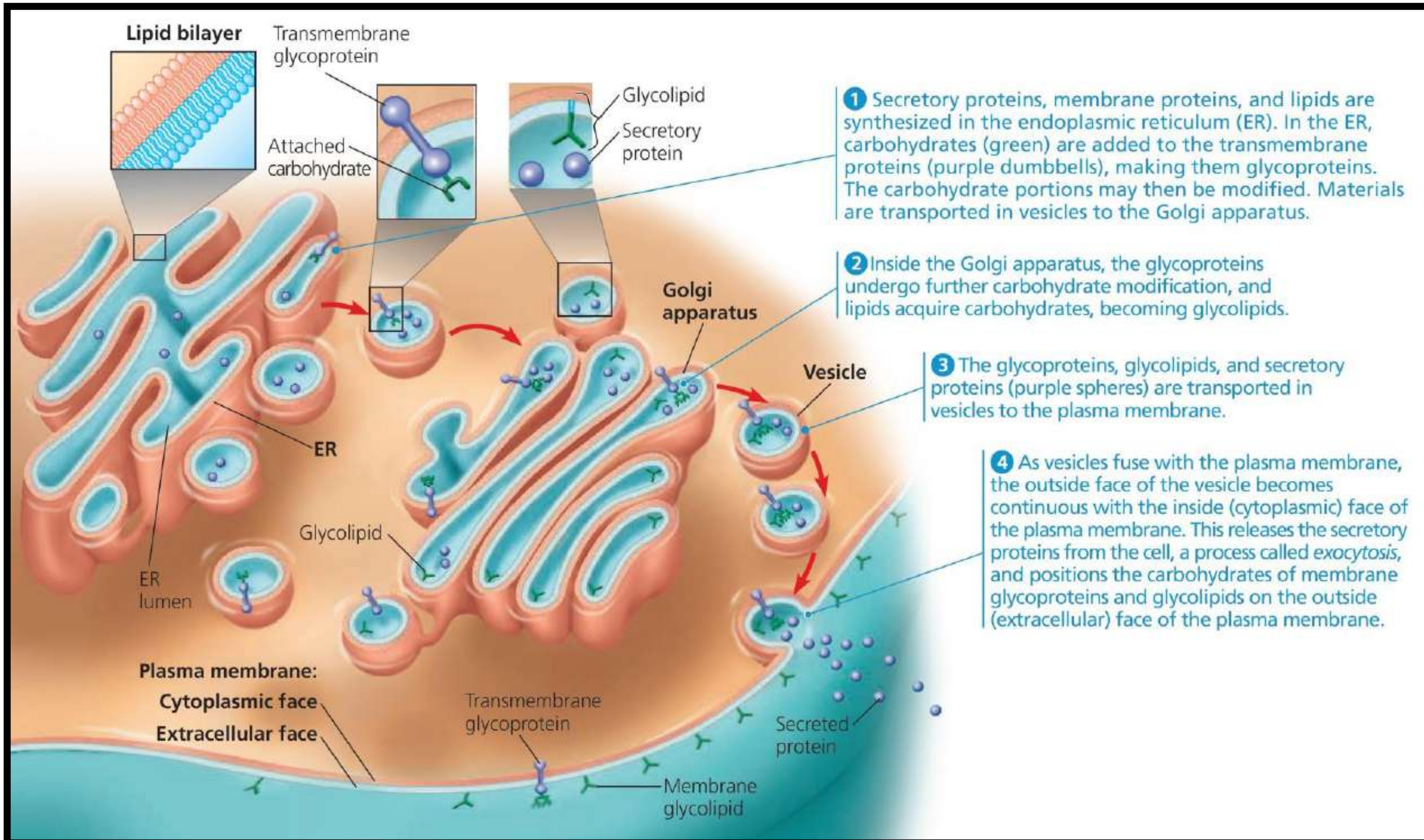
- As the protein is assembled it **passes through the ER membrane** into the interior ER compartment, the cisternal space, from which it is transported by vesicles to the Golgi apparatus




Smooth ER
Rough ER
Nuclear
envelope
ER lumen
Cisternae
Ribosomes
Transport vesicle
Transitional ER

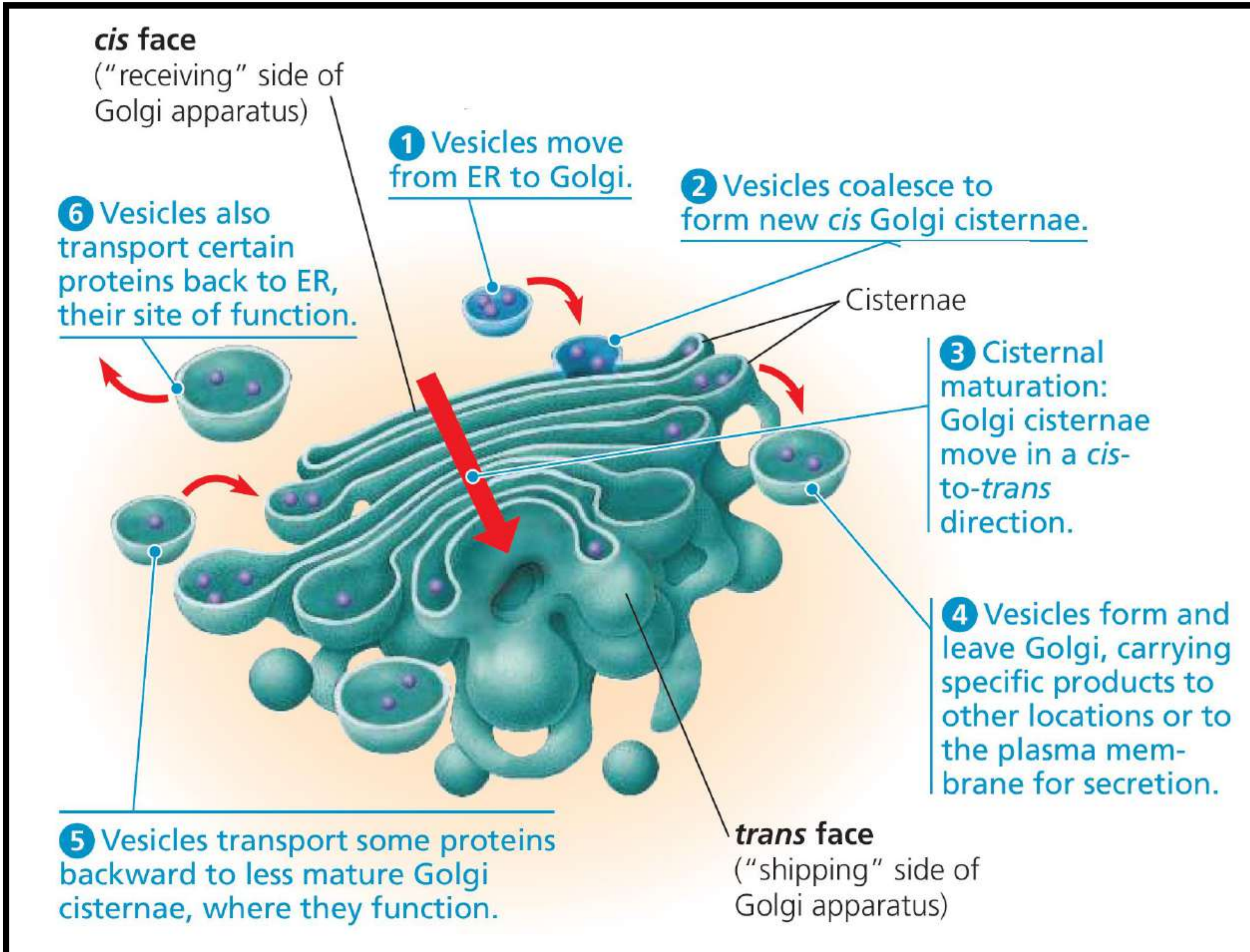
Synthesis and Sidedness of Membranes

- Membranes have **distinct inside and outside faces**.
- The phospholipid bilayers may **differ in lipid composition**, and each protein has directional orientation in the membrane.
- Membrane sidedness is the **asymmetrical arrangement** of proteins, lipids, and their associated carbohydrates in the plasma membrane
- Membrane sidedness **is determined** as it being built.



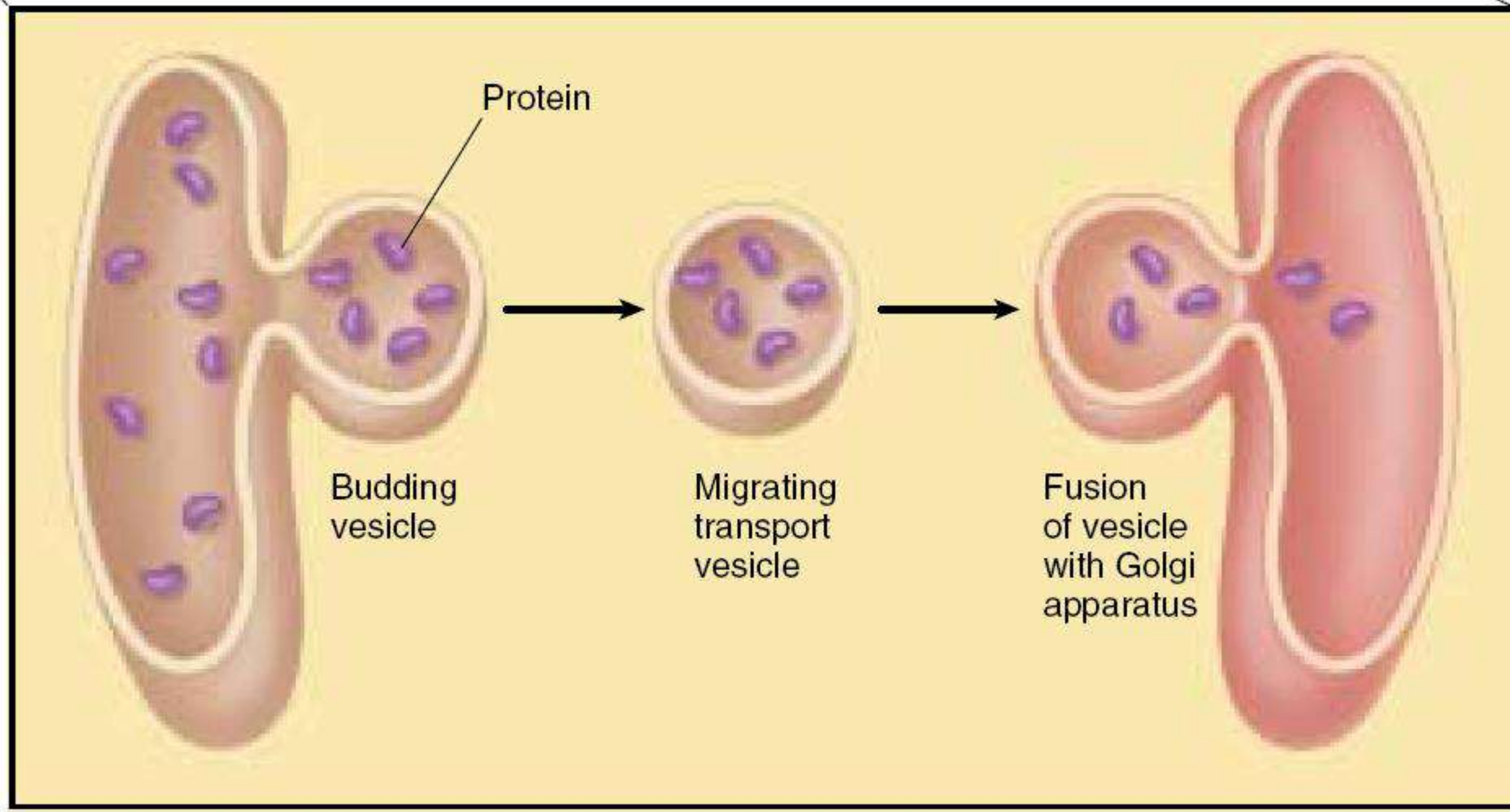
The Golgi apparatus: Receiving & Shipping Center

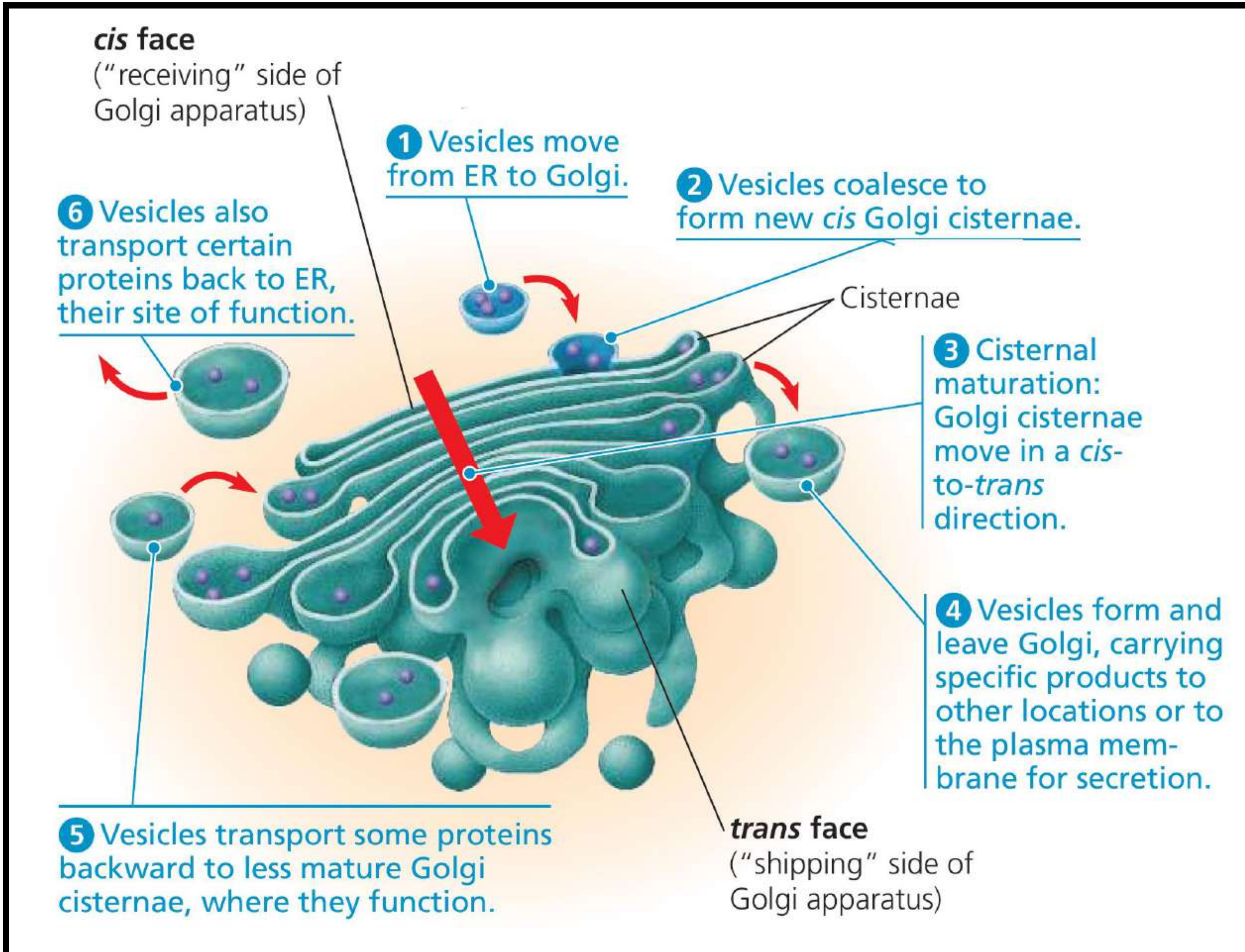
- The Golgi apparatus is a **warehouse** for **receiving**, **sorting**, **packaging, shipping**, and even **manufacturing,** of molecules synthesized at one location and used at another within the cell or even outside of it.
- The Golgi apparatus, named after its discoverer, 1906 Nobel prize winner an Italian physician named **Camillo Golgi**.
- Golgi apparatus is a distinctive stack of **flattened sacks** called **cisternae,** which **vary in number** within the Golgi apparatus from 1 or a few in protists to 20 or more in animal cells, and to **several hundred in plant** cells.
- Unlike the ER cisternae, the Golgi apparatus **sacs are not physically connected**.
- The Golgi apparatus is the **distribution point** of the cell where proteins and lipids made within the RER and SER are **further processed, modified, stored** and then directed to **their final destination**.
- A Golgi apparatus has a **front and a back sides or faces**, each with a distinct membrane composition.
- The **receiving side** is called the ***cis*** **fac**e and is usually located **near the ER**. Materials arrive at the *cis* face in transport vesicles that bud off the ER and exit the ***trans*** **face**, where they are discharged in secretory vesicles .


cis face
("receiving" side of
Golgi apparatus)
1 Vesicles move from ER to Golgi.
2 Vesicles coalesce to form new *cis* Golgi cisternae.
6 Vesicles also transport certain proteins back to ER, their site of function.
Cisternae
3 Cisternal maturation: Golgi cisternae move in a *cis*-to-*trans* direction.
4 Vesicles form and leave Golgi, carrying specific products to other locations or to the plasma membrane for secretion.
5 Vesicles transport some proteins backward to less mature Golgi cisternae, where they function.
trans face
("shipping" side of
Golgi apparatus)

The Golgi apparatus: Receiving & Shipping Center

- Proteins and lipids manufactured on the RER and SER are transported into the Golgi apparatus and **modified during their transit** from the cis region to the trans region.
- The **most common alteration** is the addition or modification of short sugar chains, forming a **glycoprotein and a glycolipid**. Membrane phospholipids may also be altered in the Golgi.
- In addition to its finishing work, the Golgi apparatus **also manufactures** some macromolecules. Many polysaccharides secreted by cells are Golgi products. For example, **pectins (heteropolysaccharide)** and certain **other noncellulose** polysaccharides are made **in the Golgi of plant cells** and then incorporated along with cellulose into their cell walls.
- Like secretory proteins, **nonprotein Golgi products** that will be secreted depart from the trans face of the Golgi inside **transport vesicles** that eventually fuse with the plasma membrane. **The contents are released and the vesicle** is incorporated into the plasma membrane, **adding to the surface area**.
- Before a Golgi apparatus dispatches its products by budding vesicles from the trans face, **it sorts these products** and targets them for various parts of the cell.
- Finally, **transport vesicles budded** from the Golgi may have external molecules on their membranes that recognize "**docking sites**" on the surface of specific organelles or on the plasma membrane, **thus targeting** the vesicles appropriately.


Protein
Budding vesicle
Migrating transport vesicle
Fusion of vesicle with Golgi apparatus



cis face
("receiving" side of
Golgi apparatus)
1 Vesicles move
from ER to Golgi.
2 Vesicles coalesce to
form new *cis* Golgi cisternae.
6 Vesicles also
transport certain
proteins back to ER,
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Cisternae
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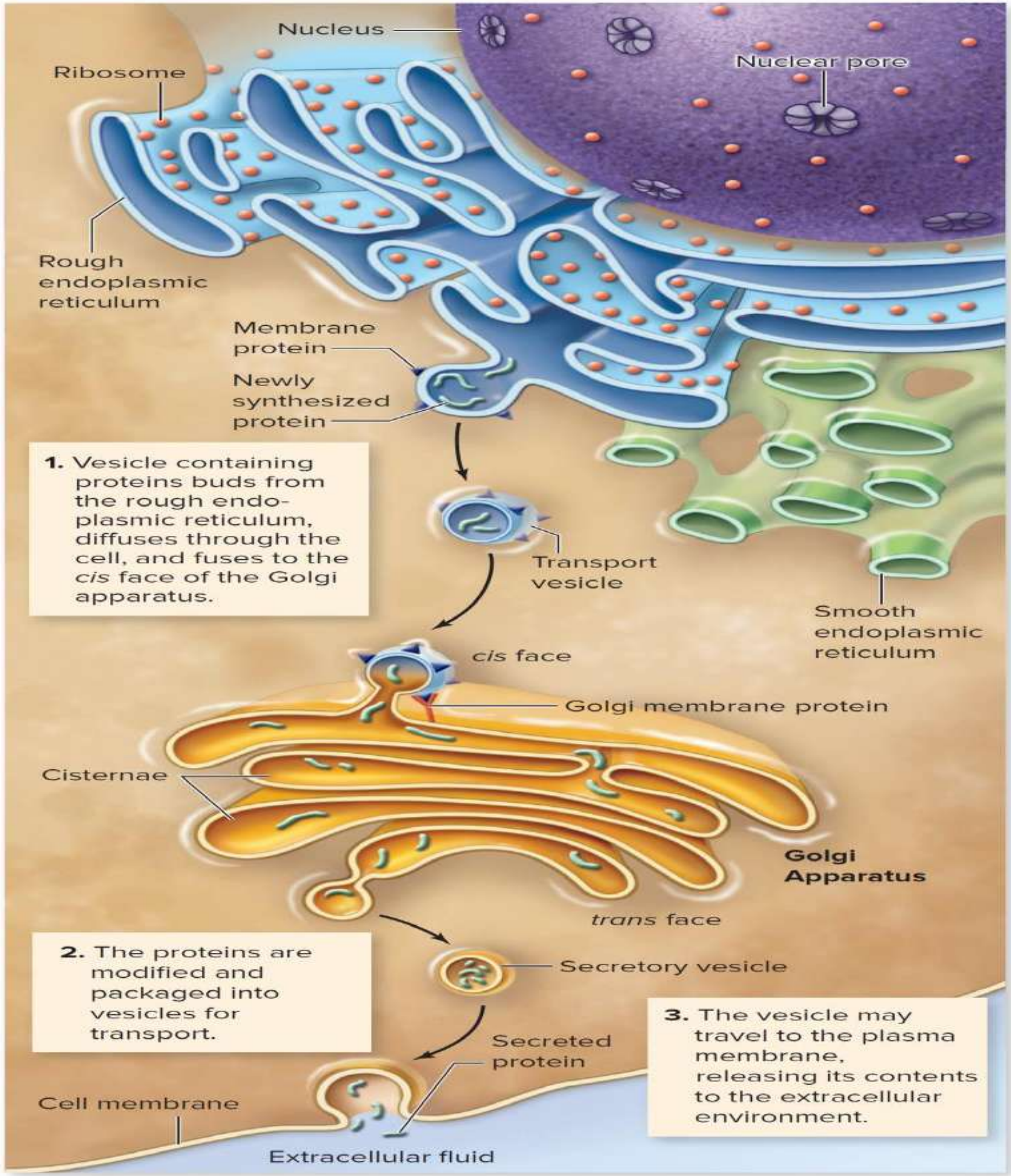
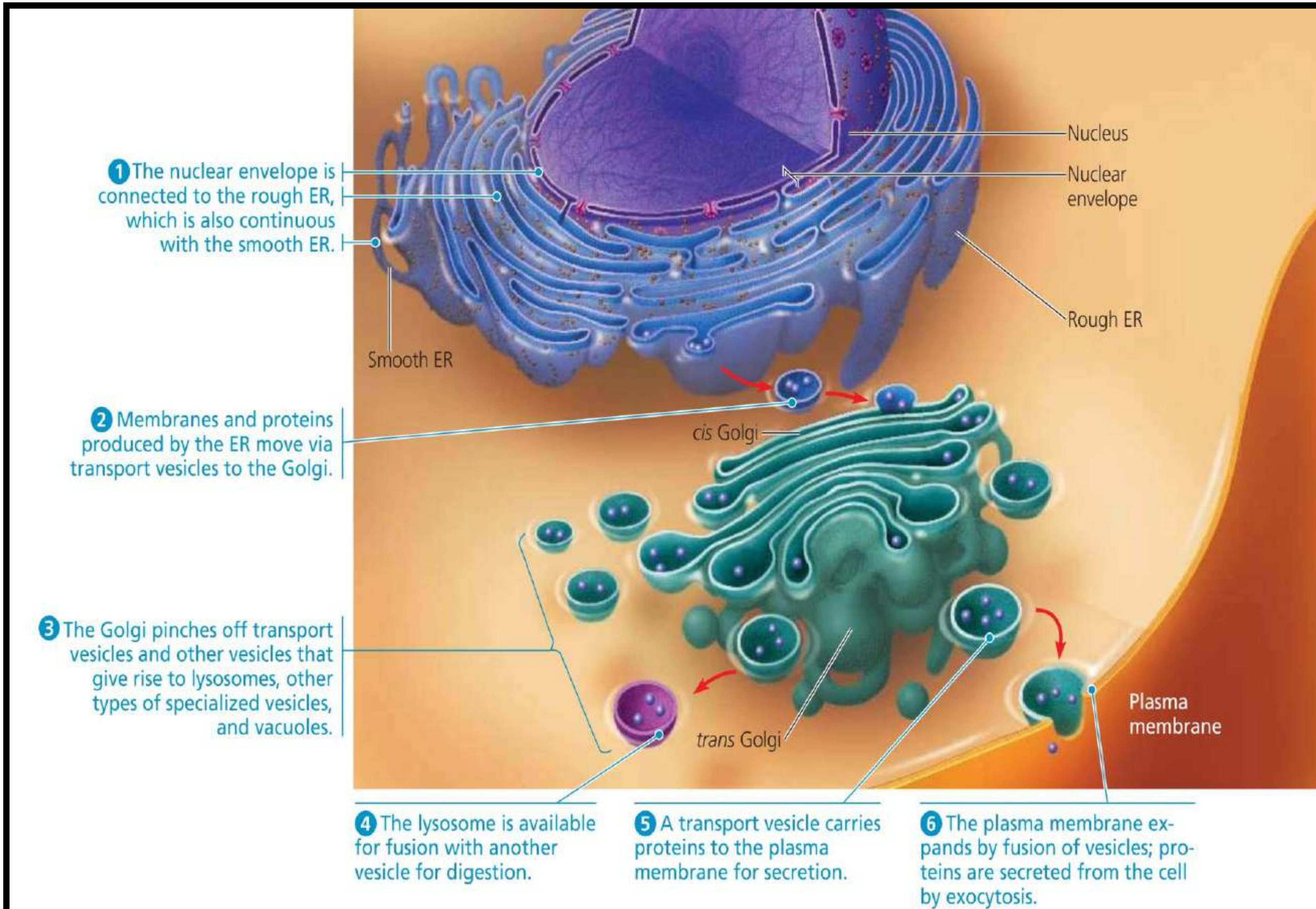
cisternae, where they function.
trans face
("shipping" side of
Golgi apparatus)


Nucleus
Nuclear pore
Ribosome
Rough endoplasmic reticulum
Membrane protein
Newly synthesized protein
1. Vesicle containing proteins buds from the rough endoplasmic reticulum, diffuses through the cell, and fuses to the *cis* face of the Golgi apparatus.
Transport vesicle
Smooth endoplasmic reticulum
cis face
Golgi membrane protein
Cisternae
Golgi Apparatus
trans face
2. The proteins are modified and packaged into vesicles for transport.
Secretory vesicle
3. The vesicle may travel to the plasma membrane, releasing its contents to the extracellular environment.
Secreted protein
Cell membrane
Extracellular fluid



Nucleus
Nuclear envelope
Rough ER
Smooth ER
1 The nuclear envelope is connected to the rough ER, which is also continuous with the smooth ER.
2 Membranes and proteins produced by the ER move via transport vesicles to the Golgi.
cis Golgi
3 The Golgi pinches off transport vesicles and other vesicles that give rise to lysosomes, other types of specialized vesicles, and vacuoles.
trans Golgi
Plasma membrane
4 The lysosome is available for fusion with another vesicle for digestion.
5 A transport vesicle carries proteins to the plasma membrane for secretion.
6 The plasma membrane expands by fusion of vesicles; proteins are secreted from the cell by exocytosis.

تحتوي الليسوسومات على إنزيمات هضمية

Lysosomes contain digestive enzymes

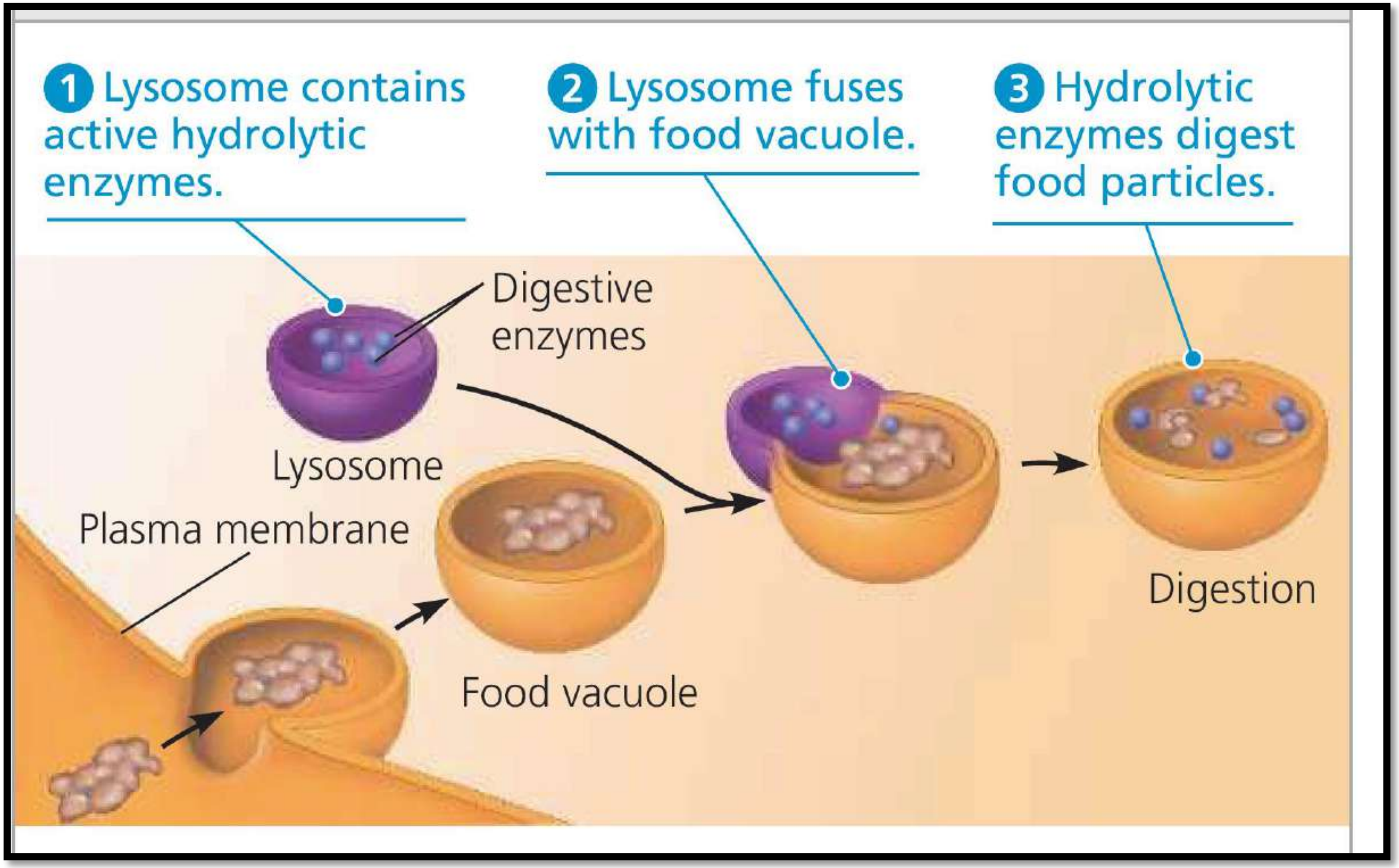
- **Lysosomes** are **digestive vesicles** that arise from the Golgi apparatus and contain high levels of a **variety of enzymes** that can degrade proteins, nucleic acids, lipids, and carbohydrates. الليسوسومات هي حويصلات هضمية تنشأ من جهاز جولجي وتحتوي على مستويات عالية من مجموعة متنوعة من الإنزيمات التي يمكنها تحلل البروتينات والأحماض النووية والدهون والكربوهيدرات
- Lysosomal enzymes work best in the **acidic environment** found in lysosomes. If a lysosome breaks open or leaks its contents, the released enzymes are not very active because the **cytosol has a near-neutral pH**.

تعمل الإنزيمات الليزوزومية بشكل أفضل في البيئة الحمضية الموجودة في الليزوزومات. إذا انفتح الليزوزوم أو تسربت محتوياته، فإن الإنزيمات المنطلقة ليست نشطة للغاية لأن السيتوزول له درجة حموضة محايدة تقريبًا

- Throughout the lives of eukaryotic cells, lysosomal enzymes break down **old organelles (autophagy)** and **recycle** their component molecules, allowing room for newly formed organelles. For example, **mitochondria** are replaced in some tissues every **10 days**, liver cell, for example, recycles half of its macromolecules each week
- Lysosomes carry out **intracellular digestion** in a variety of circumstances.

  تقوم الليسوسومات بعملية الهضم داخل الخلايا في مجموعة متنوعة من الظروف
- Amoebas and many other unicellular protists eat by engulfing smaller organisms or food particles, a process called **phagocytosis**. The food vacuole formed in this way then fuses with a lysosome, whose enzymes digest the food. Digestion products, including simple sugars, amino acids, and other monomers, pass into the cytosol and become nutrients for the cell.
- Some human cells, like **macrophages**, also carry out **phagocytosis**. Macrophages, a type of **WBC** that helps defend the body by engulfing and destroying **bacteria and other invaders** كما تقوم بعض الخلايا البشرية، مثل الخلايا البلعمية، بعملية البلعمة. الخلايا البلعمية، وهي نوع من خلايا الدم البيضاء التي تساعد في الدفاع عن الجسم عن طريق ابتلاع وتدمير البكتيريا وغيرها من الغزاة

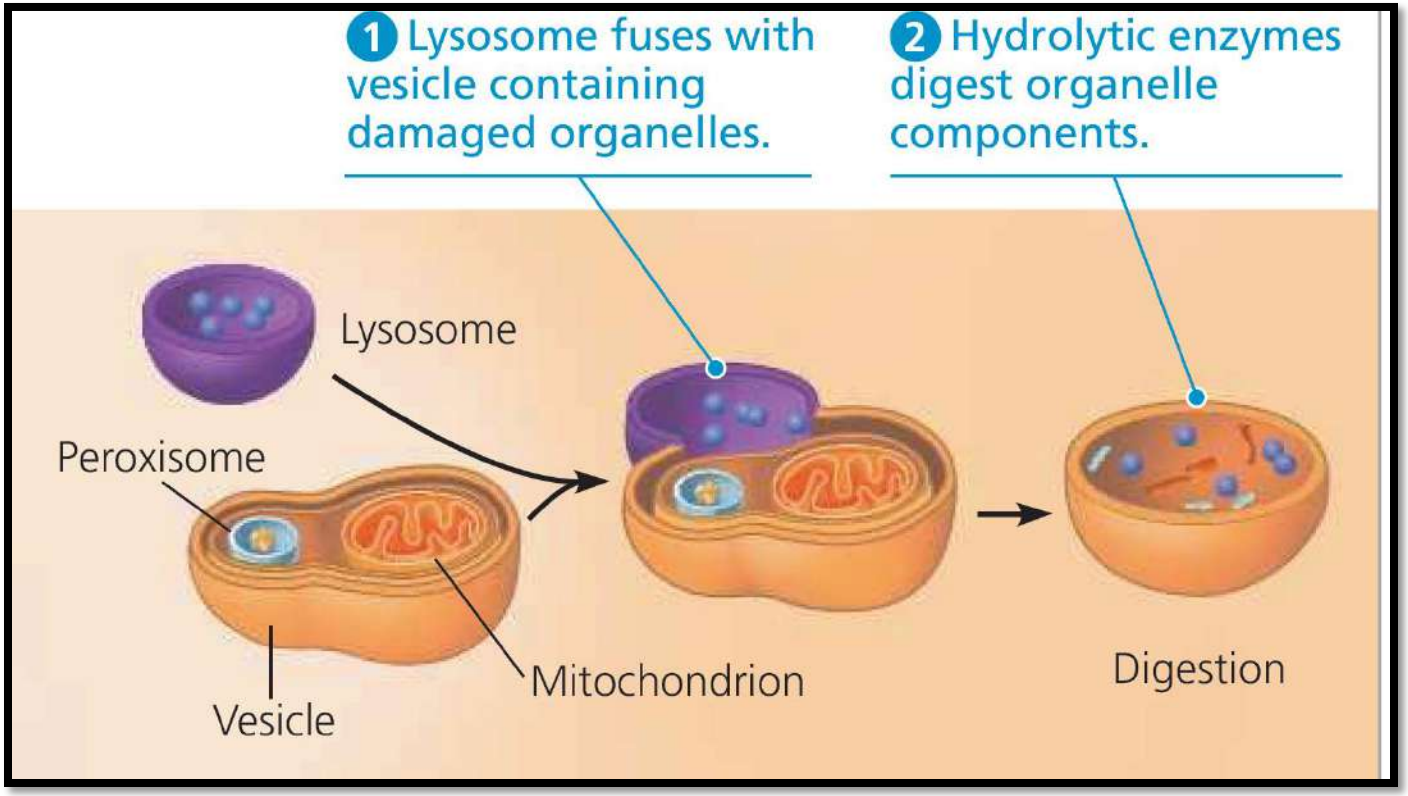
Phagocytosis



Autophagy

- During autophagy, a **damaged organel**le or small amount of cytosol becomes surrounded by a double membrane vesicles and a lysosome fuses with the outer membrane of this vesicle where **t**he lysosomal enzymes break the inner membrane and the enclosed material, and the resulting small organic compounds are released to the cytosol for reuse.

أثناء الالتهام الذاتي، تصبح العضية التالفة أو كمية صغيرة من السيتوزول محاطة بحويصلات ذات غشاء مزدوج ويندمج الليزوزوم مع الغشاء الخارجي لهذه الحويصلة حيث تقوم الإنزيمات الليزوزومية بكسر الغشاء الداخلي والمادة المغلقة، ويتم إطلاق المركبات العضوية الصغيرة الناتجة إلى السيتوزول لإعادة الاستخدام



اضطرابات تخزين الليسوسومات

Lysosomal storage disorders

- A number of **human genetic disorders**, collectively called lysosomal storage disorders, affect lysosomes.

يؤثر عدد من الاضطرابات الوراثية البشرية، والتي يطلق عليها مجتمعة اضطرابات تخزين الليزوزومات، على الليزوزومات

- Lysosomal storage diseases are **inherited metabolic diseases** that are characterized by an abnormal build-up or accumulation of various materials in the body's cells as a result of **enzyme deficiencies**.

أمراض التخزين الليزوزومي هي أمراض أيضية موروثة تتميز بتراكم أو تراكم غير طبيعي لمواد مختلفة في خلايا الجسم نتيجة لنقص الإنزيمات

- **Tay– Sachs disease** is caused by the loss of function of a single lysosomal enzyme (**hexosaminidase**) that necessary to break down a membrane **glycolipid** found in nerve cells. **Accumulation of** glycolipid in the lysosomes affects nerve cell function, leading to a variety of clinical symptoms such as **seizures and muscle rigidity**.

يحدث مرض تاي-ساكس نتيجة لفقدان وظيفة إنزيم ليزوزومي واحد (هيكسوزامينيداز) ضروري لتكسير جليكوليبيد الغشاء الموجود في الخلايا العصبية. يؤثر تراكم الجليكوليبيد في الليزوزومات على وظيفة الخلايا العصبية، مما يؤدي إلى مجموعة متنوعة من الأعراض السريرية مثل النوبات وتيبس العضلات

- **Pompe disease** is a lysosomal storage disorder in which **alpha-glucosidase** is deficient or absent. Deficiency of this lysosomal enzyme results in progressive expansion of **glycogen-filled lysosomes** in multiple tissues, with **cardiac and skeletal muscle, and hepatocytes** being the most severely affected.

مرض بومبي هو اضطراب تخزين الليزوزومات حيث يكون ألفا جلوكوزيداز ناقصًا أو غائبًا. يؤدي نقص هذا الإنزيم الليزوزومي إلى التوسع التدريجي لليزوزومات المليئة بالجليكوجين في أنسجة متعددة، حيث تكون العضلات القلبية والهيكلية وخلايا الكبد الأكثر تضررًا

- **Cystinosis**: Excessive storage of the **amino acid cystine (**the oxidized dimer of the amino acid cysteine) in all cells of the body results in **impaired kidney function**, increased sensitivity to light, and marked growth retardation.

داء السيستين: التخزين المفرط للحمض الأميني السيستين (الثنائي المؤكسد للحمض الأميني السيستين) في جميع خلايا الجسم يؤدي إلى ضعف وظائف الكلى، وزيادة الحساسية للضوء، وتأخر النمو بشكل ملحوظ.

Vacuoles

الفجوات هي حويصلات كبيرة مشتقة من الشبكة الإندوبلازمية وجهاز جولجي

- **Vacuoles are large vesicles** derived from the ER and Golgi apparatus.
- Vacuoles are an integral part of a cell's **endomembrane system** الفجوات هي جزء لا يتجزأ من نظام الغشاء الداخلي للخلية
- Vacuoles membrane (**vacuolar membrane**) is selective in transporting solutes; as a result, the solution inside a vacuole **differs in composition from the cytosol**.

غشاء الفجوات (الغشاء الفجوي) انتقائي في نقل المواد المذابة؛ ونتيجة لذلك، يختلف المحلول داخل الفجوة في التركيب عن السيتوزول

- Vacuoles perform a **variety of functions** in different kinds of cells. تؤدي الفجوات مجموعة متنوعة من الوظائف في أنواع مختلفة من الخلايا
- **Food vacuoles**, formed by phagocytosis. فجوات الغذاء التي تتشكل نتيجة البلعمة
- **Contractile vacuoles:** Many unicellular protists living in **fresh water** have contractile vacuoles that **pump excess water** out of the cell, thereby maintaining a suitable concentration of ions and molecules inside the cell.

الفجوات الانقباضية: تمتلك العديد من الكائنات وحيدة الخلية التي تعيش في المياه العذبة فجوات انقباضية تضخ الماء الزائد خارج الخلية، وبالتالي تحافظ على تركيز مناسب من الأيونات والجزيئات داخل الخلية

- **In plants and fungi**, certain vacuoles carry out **enzymatic hydrolysis**, a function shared by lysosomes in animal cells. في النباتات والفطريات، تقوم بعض الفجوات بالتحلل الأنزيمي، وهي وظيفة مشتركة مع الليزوزومات في الخلايا الحيوانية
- In plants, small vacuoles (**storage vacuoles**) can hold reserves of important organic compounds, such as the proteins stored in seeds. في النباتات، يمكن للفجوات الصغيرة (فجوات التخزين) أن تحتفظ باحتياطيات من المركبات العضوية المهمة، مثل البروتينات المخزنة في البذور
- Vacuoles may also help protect the plant against herbivores by storing compounds that are **poisonous or inedible** to animals. يمكن أن تساعد الفجوات أيضًا في حماية النبات من الحيوانات العاشبة من خلال تخزين المركبات السامة أو غير الصالحة للأكل بالنسبة للحيوانات
- Some plant vacuoles contain **pigments**, such as the red and blue pigments of petals that help attract pollinating insects to flowers. تحتوي بعض فجوات النبات على أصباغ، مثل الصبغات الحمراء والزرقاء الموجودة في البتلات والتي تساعد في جذب الحشرات الملقحة إلى الزهور
- Mature plant cells generally contain a **large central vacuole**, which develops by merging or fusion of smaller vacuoles. The solution inside the central vacuole, called **cell sap**, is the plant cell's **main storehouse** of inorganic ions, including potassium and chloride, as well as water.

،تحتوي الخلايا النباتية الناضجة عمومًا على فجوة مركزية كبيرة، تتطور عن طريق دمج أو اندماج فجوات أصغر. المحلول الموجود داخل الفجوة المركزية، والذي يسمى عصارة الخلية هو المخزن الرئيسي للخلية النباتية للأيونات غير العضوية، بما في ذلك البوتاسيوم والكلوريد، بالإضافة إلى الماء

الميتوكوندريا والبلاستيدات الخضراء: مولدات الخلايا

Mitochondria and Chloroplasts: Cellular Generators

- **Mitochondria and chloroplasts** share structural and functional **similarities**.

تتشابه الميتوكوندريا والبلاستيدات الخضراء في البنية والوظيفة

- Structurally, they are both surrounded by a **double membrane**, and both contain their **own DNA** and **protein synthesis** machinery.

من الناحية البنيوية، كلاهما محاط بغشاء مزدوج، وكلاهما يحتوي على آلية خاصة به لتخليق الحمض النووي والبروتين

- Functionally, they are both involved in **energy metabolism**, changing energy from one form to another. من الناحية الوظيفية، يشارك كلاهما في عملية التمثيل الغذائي للطاقة، وتحويل الطاقة من شكل إلى آخر
- **Mitochondria** (singular, mitochondrion) are the sites of **cellular respiration**, the metabolic process that uses oxygen to drive the **generation of ATP** by extracting energy from sugars, fats, and other fuels.

الميتوكوندريا (مفردها ميتوكوندريا) هي مواقع التنفس الخلوي، وهي العملية الأيضية التي تستخدم الأكسجين لدفع توليد ATP عن طريق استخراج الطاقة من السكريات والدهون والوقود الأخرى

- Mitochondria are **found in nearly all eukaryotic cells**, including those of plants, animals, fungi, and most protists. Some cells have a **single large mitochondrion**, but more often a cell has **hundreds or even thousands** of mitochondria. The number correlates with the cell's **level of metabolic activity**. Cells that **move** or **contract** have proportionally **more mitochondria** per volume than less active cells.

توجد الميتوكوندريا في كل الخلايا حقيقية النواة تقريبًا، بما في ذلك خلايا النباتات والحيوانات والفطريات ومعظم الكائنات الأولية. تحتوي بعض الخلايا على ميتوكوندريا كبيرة واحدة، ولكن في أغلب الأحيان تحتوي الخلية على مئات أو حتى آلاف الميتوكوندريا. يرتبط العدد بمستوى النشاط الأيضي للخلية. تحتوي الخلايا التي تتحرك أو تنقبض على عدد أكبر نسبيًا من الميتوكوندريا لكل حجم مقارنة بالخلايا الأقل نشاطًا

- **Chloroplasts** contain the green pigment **chlorophyll**, along with enzymes and other molecules and found in plants and algae, are the sites of **photosynthesis** that **converts solar energy to chemical energy** by absorbing sunlight and using it to drive the synthesis of organic compounds (sugars) from carbon dioxide and water.

تحتوي البلاستيدات الخضراء على الصبغة الخضراء الكلوروفيل، إلى جانب الإنزيمات والجزيئات الأخرى الموجودة في النباتات والطحالب، وهي مواقع التمثيل الضوئي الذي يحول الطاقة الشمسية إلى طاقة كيميائية عن طريق امتصاص ضوء الشمس واستخدامه لدفع عملية تخليق المركبات العضوية (السكريات) من ثاني أكسيد الكربون والماء

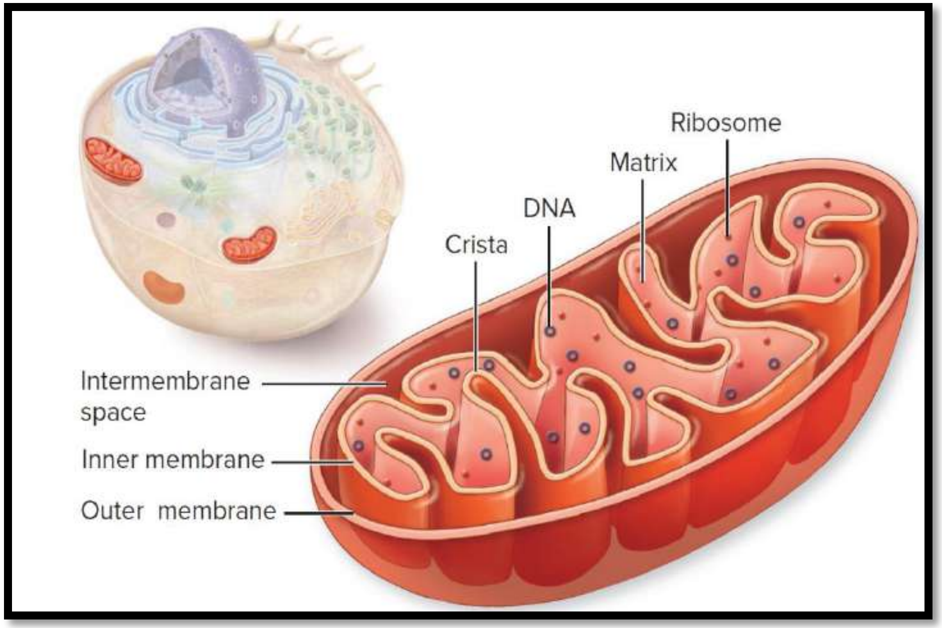
الميتوكوندريا تستقلب السكر لتوليد ATP

Mitochondria metabolize sugar to generate ATP

- **Mitochondria** (singular, *mitochondrion*) are typically **tubular or sausage-shaped** organelles about the size of bacteria that are found **in almost all** types of eukaryotic cells الميتوكوندريا (مفردها ميتوكوندريا) هي عضيات أنبوبية أو على شكل نقانق بحجم البكتيريا تقريبًا وتوجد في جميع أنواع الخلايا حقيقية النواة تقريبًا
- Mitochondria are **bounded by two membranes**: a smooth outer membrane, and an **inner folded membrane** with numerous adjacent /tangent layers called **cristae** (singular, *crista*). تحيط بالميتوكوندريا غشائين: غشاء خارجي أملس، وغشاء داخلي مطوي مع العديد من الطبقات المتجاورة/المماسة تسمى كريستا (مفردها كريستا)
- The cristae divide the mitochondrion into **two compartments**: a **matrix,** lying inside the inner membrane; and an outer compartment, or **intermembrane space,** lying between the two mitochondrial membranes.

تقسم القمم الميتوكوندريا إلى حجرتين: مصفوفة تقع داخل الغشاء الداخلي؛ وحجرة خارجية، أو فراغ بين الغشاءين، تقع بين غشائي الميتوكوندريا

On the surface of the inner membrane, and also embedded within it, are **proteins that carry out oxidative metabolism**, the oxygen-requiring process by which energy in macromolecules is used to produce ATP .



على سطح الغشاء الداخلي، وأيضًا داخله، توجد بروتينات تقوم بعملية التمثيل الغذائي التأكسدي، وهي العملية التي تتطلب الأكسجين والتي يتم من خلالها استخدام الطاقة في الجزيئات الكبيرة لإنتاج ATP

Mitochondria

- Mitochondria have their **own DNA**; this DNA contains several **genes** that produce proteins essential to the mitochondrion's role in **oxidative metabolism**. Thus, the mitochondrion, in many respects, acts as a cell within a cell, containing its own genetic information specifying proteins for its unique functions.

تمتلك الميتوكوندريا حمضها النووي الخاص؛ ويحتوي هذا الحمض النووي على العديد من الجينات التي تنتج البروتينات الضرورية لدور الميتوكوندريا في التمثيل الغذائي التأكسدي. وبالتالي، تعمل الميتوكوندريا، في كثير من النواحي، كخلية داخل خلية، وتحتوي على معلوماتها الجينية الخاصة التي تحدد البروتينات لوظائفها الفريدة

- The mitochondria **are not fully autonomous**. Most of the genes that encode the enzymes used in oxidative metabolism are **located in the cell nucleus**.

لا تتمتع الميتوكوندريا بالاستقلالية الكاملة. فمعظم الجينات التي تشفر الإنزيمات المستخدمة في عملية التمثيل الغذائي التأكسدي توجد في نواة الخلية

- A eukaryotic cell does not produce brand-new mitochondria each time the cell divides. Instead, the **mitochondria themselves divide in two**, doubling in number, and these are partitioned between the new cells.

لا تنتج الخلية حقيقية النواة ميتوكوندريا جديدة في كل مرة تنقسم فيها الخلية. بدلاً من ذلك، تنقسم الميتوكوندريا نفسها إلى اثنتين، ويتضاعف عددها، ويتم توزيعها بين الخلايا الجديدة

- Most of the components required for **mitochondrial division are encode**d by **genes in the nucleus** and are translated into proteins by cytoplasmic ribosomes.

يتم ترميز معظم المكونات المطلوبة لانقسام الميتوكوندريا بواسطة الجينات الموجودة في النواة ويتم ترجمتها إلى بروتينات بواسطة الريبوسومات السيتوبلازمية

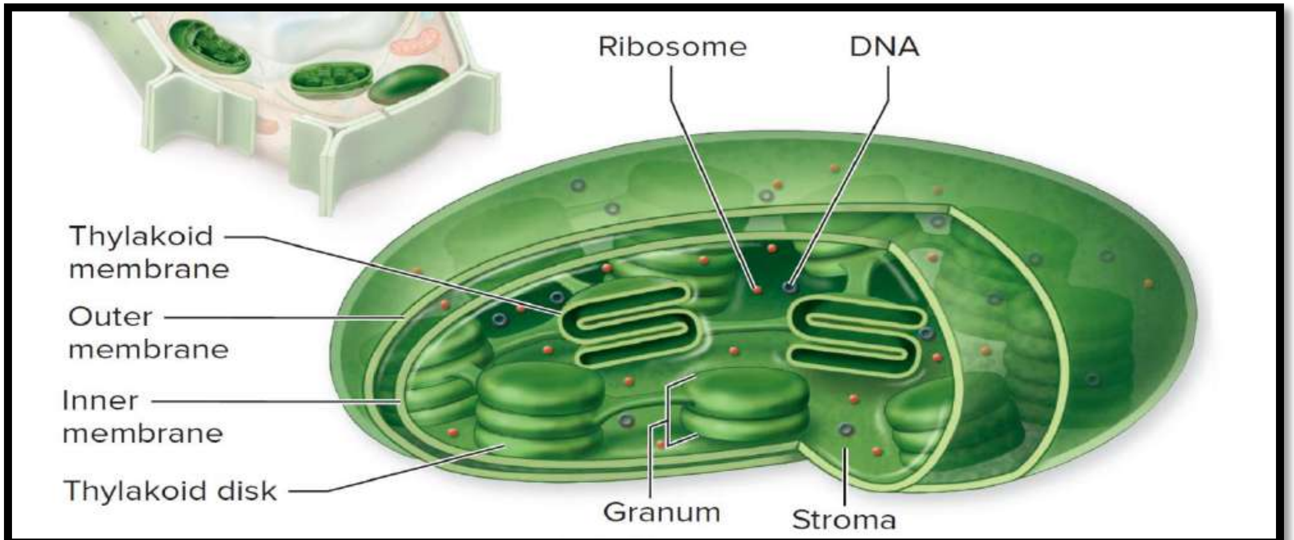
- Mitochondrial replication is, therefore, impossible without nuclear participation, and **mitochondria thus cannot be grown in a cell-free** culture.

لذلك، فإن تكرار الميتوكوندريا أمر مستحيل بدون مشاركة النواة، وبالتالي لا يمكن زراعة الميتوكوندريا في ثقافة خالية من الخلايا

والسكريات ATP تستخدم البلاستيدات الخضراء الضوء لتوليد

Chloroplasts use light to generate ATP and sugars

- Eukaryotic **autotroph organisms** (e.g plants) that carry out photosynthesis typically contain from one to several hundred **chloroplasts that** contain the photosynthetic pigment **chlorophyll**. تحتوي الكائنات الحية ذاتية التغذية حقيقية النواة (مثل النباتات) التي تقوم بعملية التمثيل الضوئي عادةً على من واحد إلى عدة مئات من البلاستيدات الخضراء التي تحتوي على صبغة التمثيل الضوئي الكلوروفيل
- The chloroplast is surrounded by **two membranes**. In addition to the outer and inner membranes, which lie in close association with each other, chloroplasts have closed compartments (**third membranous system**) of stacked membranes called **grana (singular, *granum*)**, which lie inside the inner membrane. Each granum may contain from a few to several dozen disk-shaped structures called **thylakoids.** On the surface of the thylakoids are the **light-capturing photosynthetic** pigments.
- Surrounding the thylakoid is a **fluid matrix called the *stroma*** *that includes the* enzymes used to synthesize glucose during photosynthesis. يحيط بالثيلاكويد مصفوفة سائلة تسمى السدى والتي تحتوي على الإنزيمات المستخدمة في تخليق الجلوكوز أثناء عملية التمثيل الضوئي
- All plastids are produced by the division of existing plastids.
يتم إنتاج جميع البلاستيدات عن طريق انقسام البلاستيدات الموجودة



The Cytoskeleton

- The cytoplasm of all eukaryotic cells is **crisscrossed by a network** of protein fibers that supports the shape of the cell and **anchors** organelles to fixed locations.

يتقاطع سيتوبلازم جميع الخلايا حقيقية النواة مع شبكة من الألياف البروتينية التي تدعم شكل الخلية وتثبت العضيات في مواقع ثابتة

- This network, called the cytoskeleton, **is almost dynamic system**, constantly assembling and disassembling. هذه الشبكة، التي تسمى الهيكل الخلوي، هي نظام ديناميكي تقريبًا، يتم تجميعه وتفكيكه باستمرار
- Individual fibers consist of polymers of **identical protein subunits** that attract one another and spontaneously assemble into long chains. Fibers disassemble in the same way, as one subunit after another breaks away from one end of the chain.

تتكون الألياف الفردية من بوليمرات من وحدات بروتينية متطابقة تجتذب بعضها البعض وتتجمع تلقائيًا في سلاسل طويلة. تتفكك الألياف بنفس الطريقة، حيث تنفصل وحدة فرعية تلو الأخرى عن أحد طرفي السلسلة

قد تحتوي الخلايا حقيقية النواة على الأنواع الثلاثة التالية من ألياف الهيكل الخلوي، وكل منها يتكون من نوع مختلف من الوحدات الفرعية:

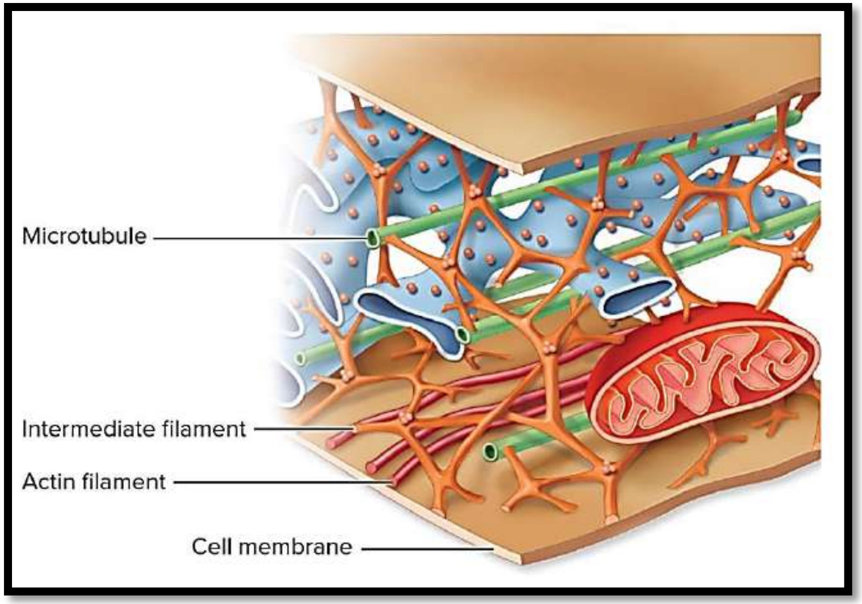
Eukaryotic cells may contain the following three types of cytoskeletal fibers, each formed from a different kind of subunit:

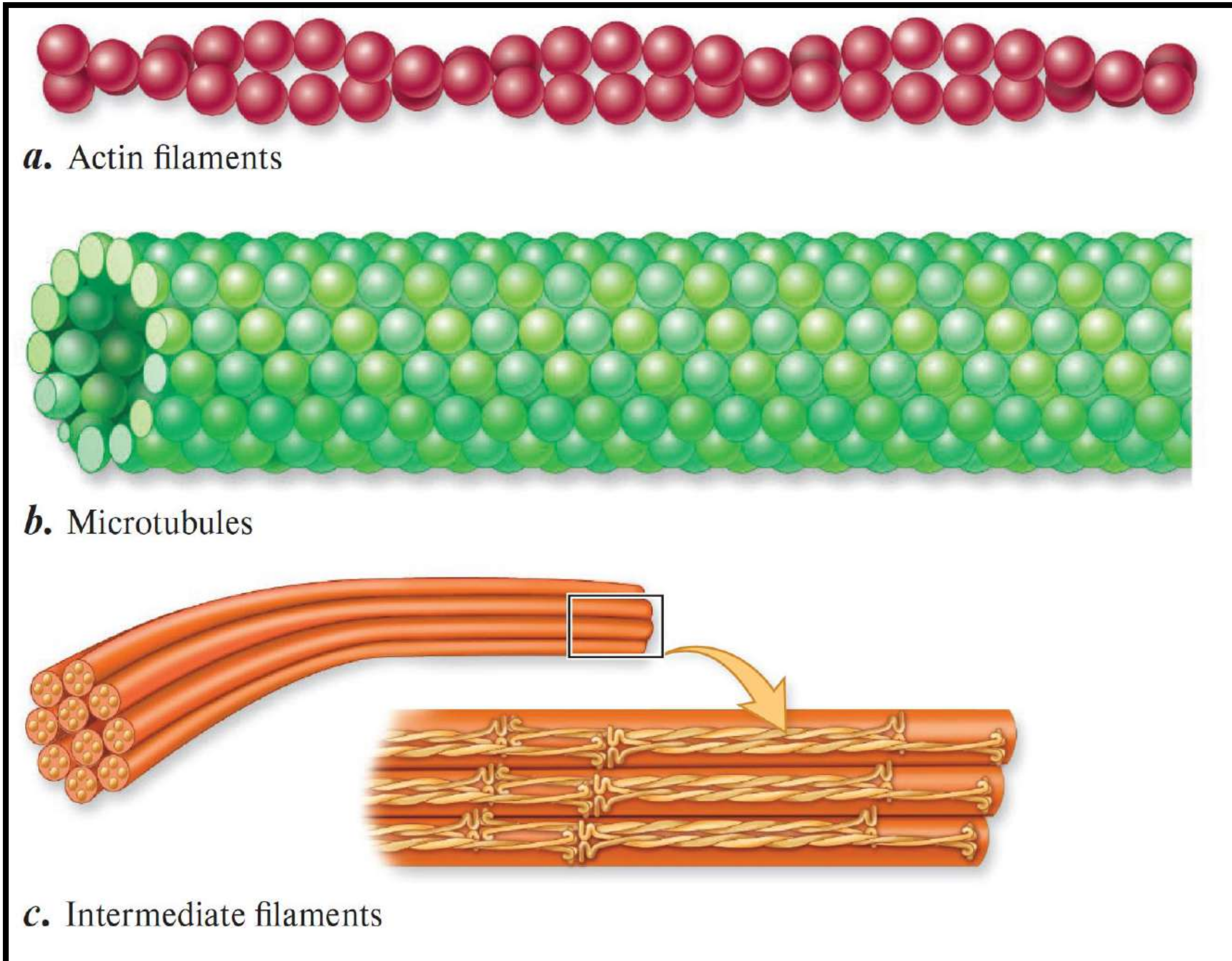
Microtubules (the thickest; about **25 nm** in diameter). الأنابيب الدقيقة (الأكثر سمكًا؛ حوالي 25 نانومتر في القطر

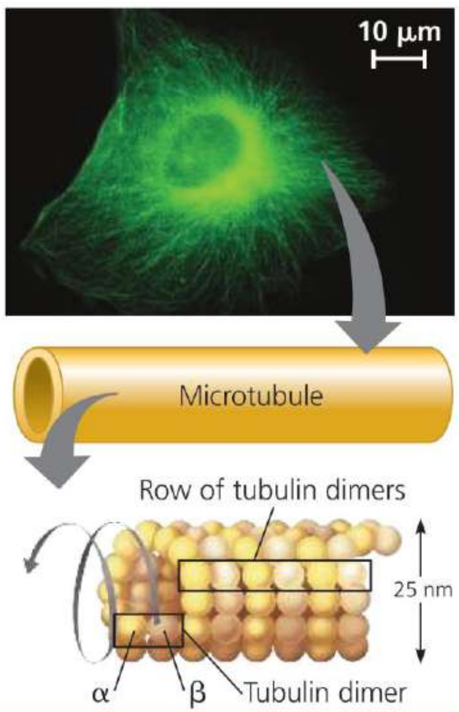
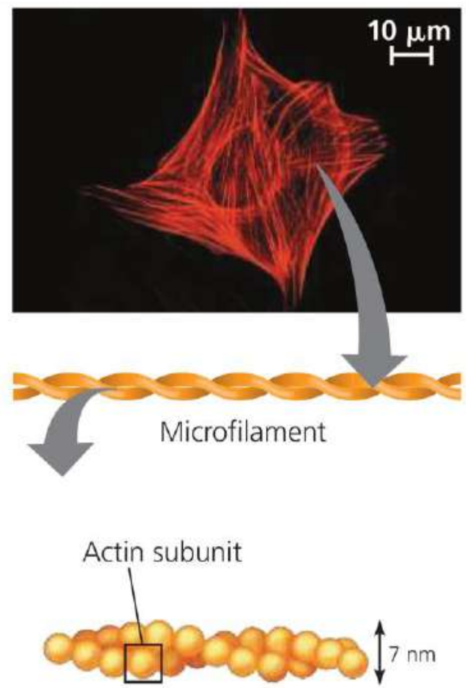
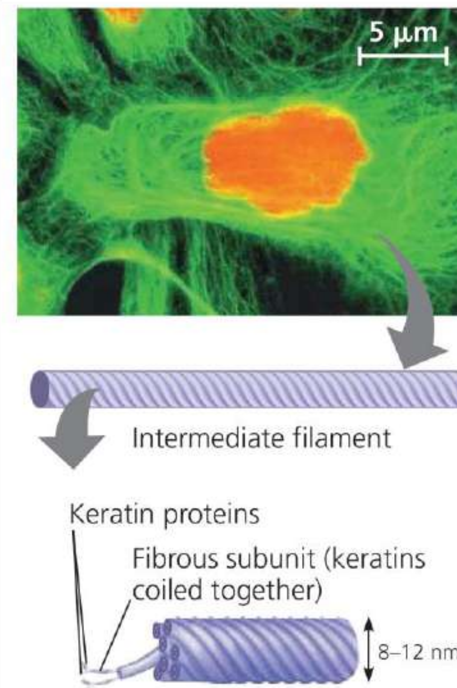
Microfilaments, sometimes called actin filaments (the thinnest: a about **7 nm** in diameter) الخيوط الدقيقة، والتي تسمى أحيانًا خيوط الأكتين (الأرق: يبلغ قطرها حوالي 7 نانومتر)

Intermediate filaments. (are fibers with diameters in a middle range : **8–12 nm**

الخيوط المتوسطة. (هي ألياف بأقطار تتراوح في نطاق متوسط: 8-12 نانومتر




a. Actin filaments
b. Microtubules
c. Intermediate filaments

The Structure and Function of the Cytoskeleton			
Property	**Microtubules (Tubulin Polymers)**	**Microfilaments (Actin Filaments)**	**Intermediate Filaments**
Structure	Hollow tubes	Two intertwined strands of actin	Fibrous proteins coiled into cables
Diameter	25 nm with 15-nm lumen	7 nm	8–12 nm
Protein subunits	Tubulin, a dimer consisting of an α-tubulin and a β-tubulin	Actin	One of several different proteins (including keratins)
Main functions	Maintenance of cell shape; cell motility; chromosome movements in cell division; organelle movements	Maintenance of cell shape; changes in cell shape; muscle contraction; cytoplasmic streaming (plant cells); cell motility; cell division (animal cells)	Maintenance of cell shape; anchorage of nucleus and certain other organelles; formation of nuclear lamina
Fluorescence micrographs of fibroblasts. Connective tissue cells called fibroblasts are a favorite cell type for cell biology studies because they spread out flat and their internal structures are easy to see. In each fibroblast shown here, the structure of interest has been tagged with fluorescent molecules. In the third micrograph, the DNA in the nucleus has also been tagged (orange).			

وظيفة الهيكل الخلوي: الدعم والحركة

Function of the Cytoskeleton: Support and Motility

- The most obvious **function of the cytoskeleton** is to give **mechanical support** to the cell and **maintain its shape** especially important for animal cells, which lack walls.

الوظيفة الأكثر وضوحًا للهيكل الخلوي هي تقديم الدعم الميكانيكي للخلية والحفاظ على شكلها وهو أمر مهم بشكل خاص للخلايا الحيوانية، التي تفتقر إلى الجدران

- The cytoskeleton provides **anchorage for many organelles and even cytosolic enzyme** molecules. The cytoskeleton is dynamic, it can be quickly dismantled in one part of the cell and reassembled in a new location, changing the shape of the cell.

يوفر الهيكل الخلوي مرساة للعديد من العضيات وحتى جزيئات الإنزيمات السيتوبلازمية. الهيكل الخلوي ديناميكي، ويمكن تفكيكه بسرعة في جزء واحد من الخلية وإعادة تجميعه في مكان جديد، مما يغير شكل الخلية

- Some types of **cell motility (movement)** also involve the cytoskeleton.

تتضمن بعض أنواع حركة الخلايا أيضًا الهيكل الخلوي

- The term ***cell motility* includes both changes in cell location and movements** of cell parts. Cell motility generally requires interaction of the cytoskeleton with **motor proteins**. يشمل مصطلح حركة الخلية كلاً من التغيرات في موقع الخلية وحركات أجزائها. تتطلب حركة الخلية عمومًا تفاعل الهيكل الخلوي مع البروتينات الحركية

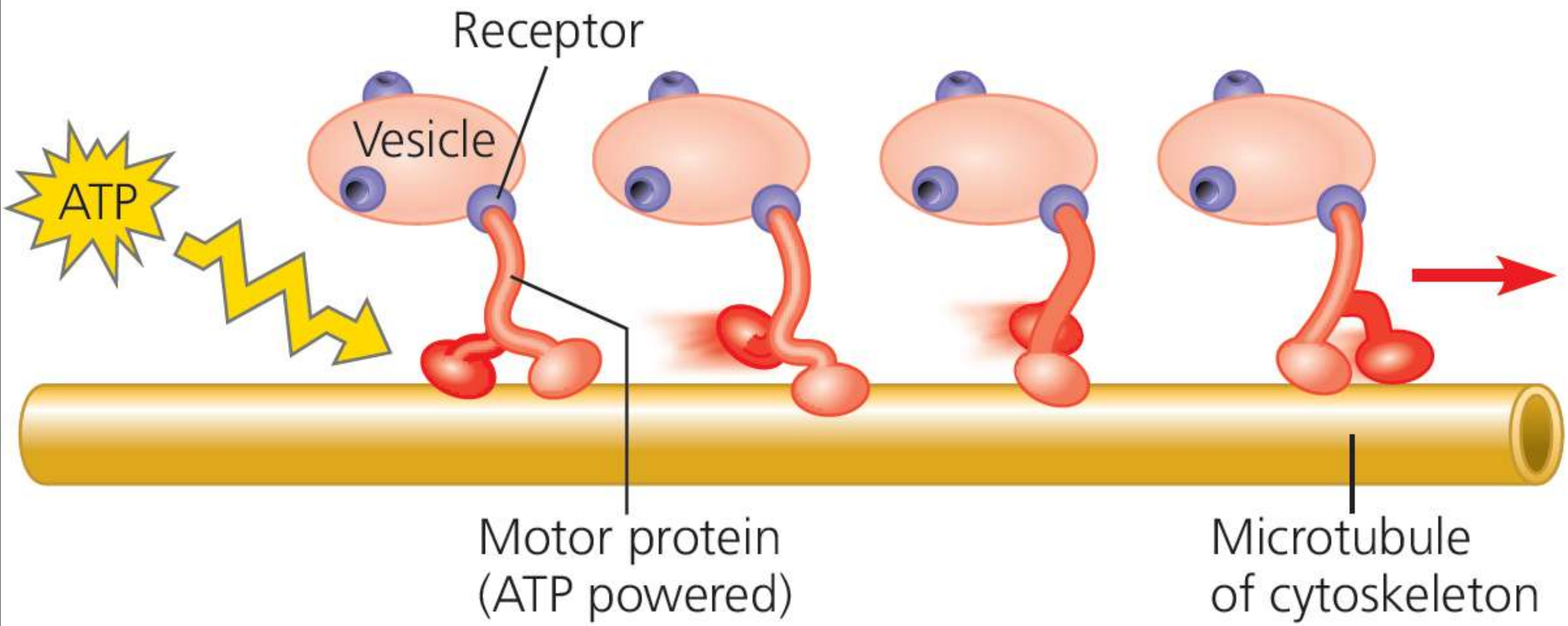
- There are many such examples: Cytoskeletal elements and motor proteins work together with plasma membrane molecules to allow whole cells to move along fibers outside the cell. هناك العديد من الأمثلة على ذلك: تعمل العناصر الهيكلية الخلوية والبروتينات الحركية مع جزيئات الغشاء البلازمي للسماح للخلايا بأكملها بالتحرك على طول الألياف خارج الخلية

- Inside the cell, **vesicles and other organelles often use motor protein** “feet” to “walk” to their destinations **along a track** provided by the cytoskeleton. For example, this is how vesicles containing **neurotransmitter** molecules migrate to the tips of axons, the long extensions of nerve cells that release these molecules as chemical signals to adjacent nerve cells .

- The cytoskeleton also **manipulates the plasma membrane**, bending it inward to form food vacuoles or other phagocytic vesicles.

ويقوم الهيكل الخلوي أيضًا بالتلاعب بالغشاء البلازمي، فيثنيه إلى الداخل لتشكيل فجوات غذائية أو حويصلات بلعمية أخرى

Motor proteins and the cytoskeleton.



A motor protein that attaches to a receptor on a vesicle can "walk" the vesicle along a microtubule or microfilament

Microtubules

الأنابيب الدقيقة، وهي أكبر العناصر الهيكلية الخلوية، هي أنابيب مجوفة يبلغ قطرها حوالي 25 نانومتر، وتتكون كل منها من حلقة مكونة من 13 خيطًا بروتينيًا

- **Microtubules**, the largest of the cytoskeletal elements, are **hollow tubes** about **25 nm** in diameter, each composed of a ring of 13 protein **protofilaments**.
- Microtubules **vary greatly in length**. Some are less than 200 nm long (**cytosolic MTs**); others, such as **axonemal MTs** (cilia flagella) , can be many micrometers in length

تختلف الأنابيب الدقيقة بشكل كبير في الطول. بعضها يقل طوله عن 200 نانومتر (أنابيب دقيقة في السيتوبلازم)؛ والبعض الآخر، مثل الأنابيب الدقيقة المحورية (أهداب الأسواط)، يمكن أن يصل طوله إلى عدة ميكرومترات.

- Globular proteins consisting of **noncovalently dimers** of **α- and β-tubulin** subunits (heterodimer) polymerize to form the 13 protofilaments.

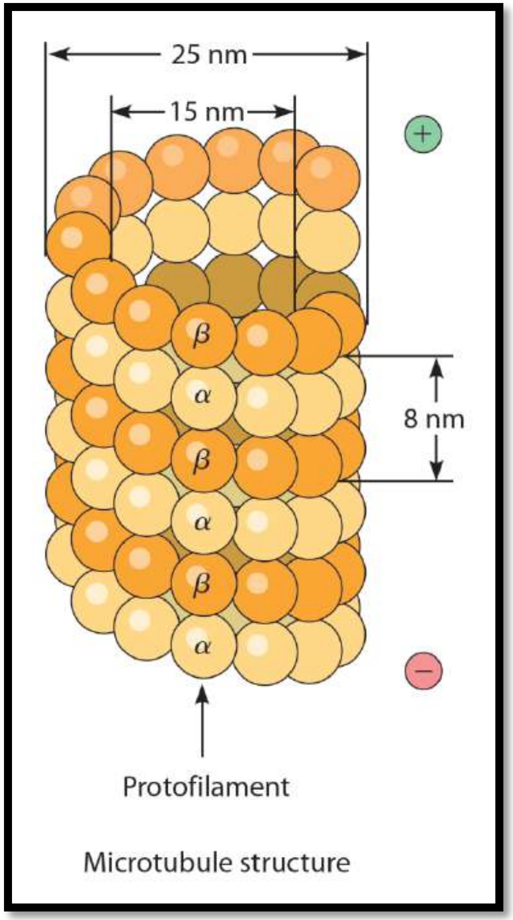
تتبلمر البروتينات الكروية المكونة من ثنائيات غير تساهمية من وحدات ألفا وبيتا توبيولين (ثنائي غير متجانس) لتكوين الخيوط الأولية الثلاثة عشر

- The protofilaments are arrayed side by side around a central core, giving the microtubule its characteristic tube shape.

تتجمع الخيوط الأولية جنبًا إلى جنب حول قلب مركزي، مما يمنح الأنبوب الدقيق شكله الأنبوبي المميز

- In many cells, microtubules form from **nucleation centers (MTOC)** near the center of the cell and radiate toward the periphery. في العديد من الخلايا، تتشكل الأنابيب الدقيقة من مراكز النواة (MTOC) بالقرب من مركز الخلية وتنتشر نحو المحيط
- The two most important types of **MTOCs** are the **basal bodies** associated with cilia, and the **centrosome** associated with spindle formation. هما الأجسام القاعدية المرتبطة بالأهداب، والجسيم المركزي المرتبط بتكوين المغزل MTOCs النوعان الأكثر أهمية من
- The **average half-life** of a microtubule ranges from as long as 10 minutes in a nondividing animal cell to as short as 20 seconds in a dividing animal cell.

يتراوح متوسط عمر النصف للأنابيب الدقيقة من 10 دقائق في الخلية الحيوانية غير المنقسمة إلى 20 ثانية في الخلية الحيوانية المنقسمة

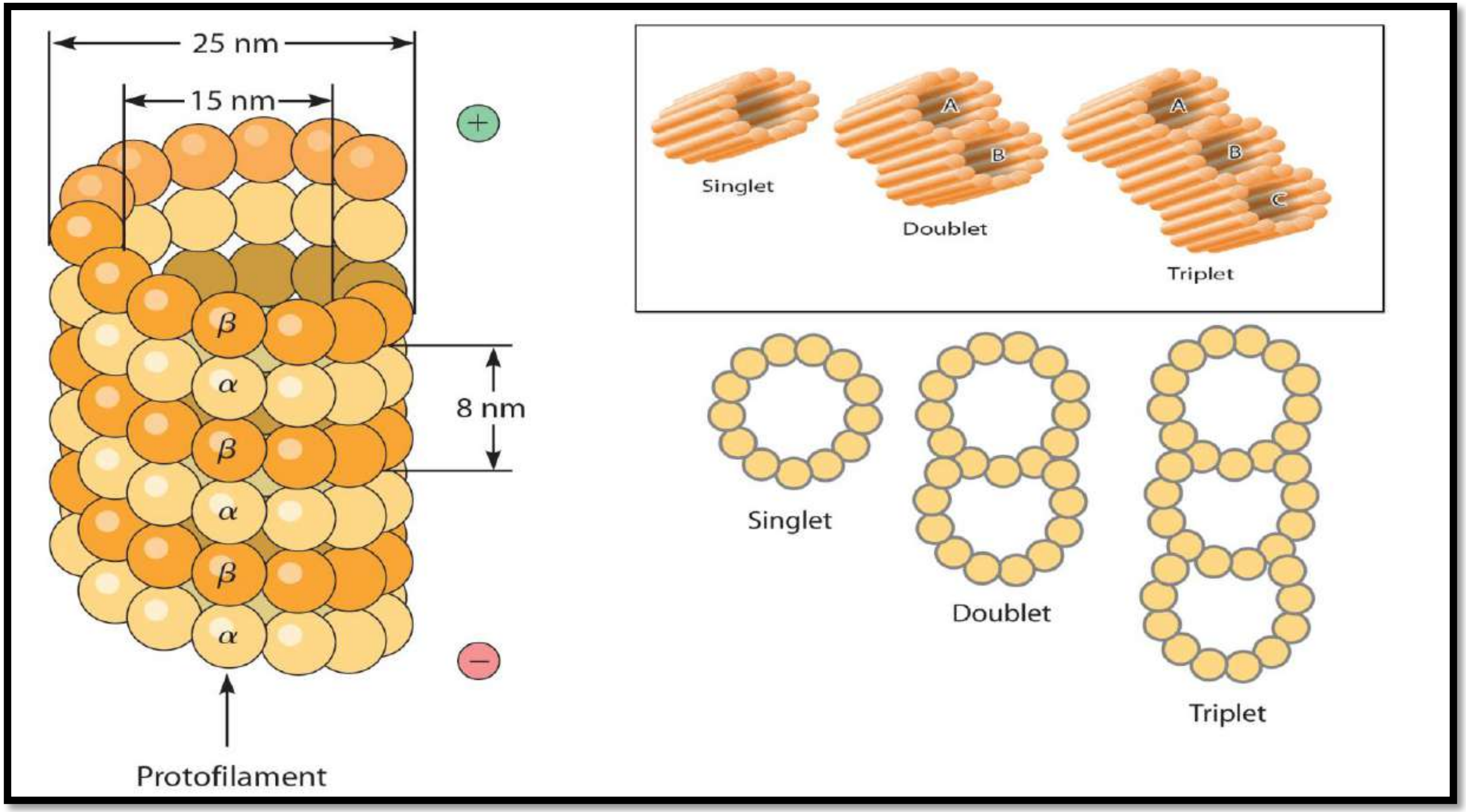


Microtubules forms

Microtubules can form as **singlets** (13 protofilaments around a hollow lumen), **doublets**, or **triplets**.

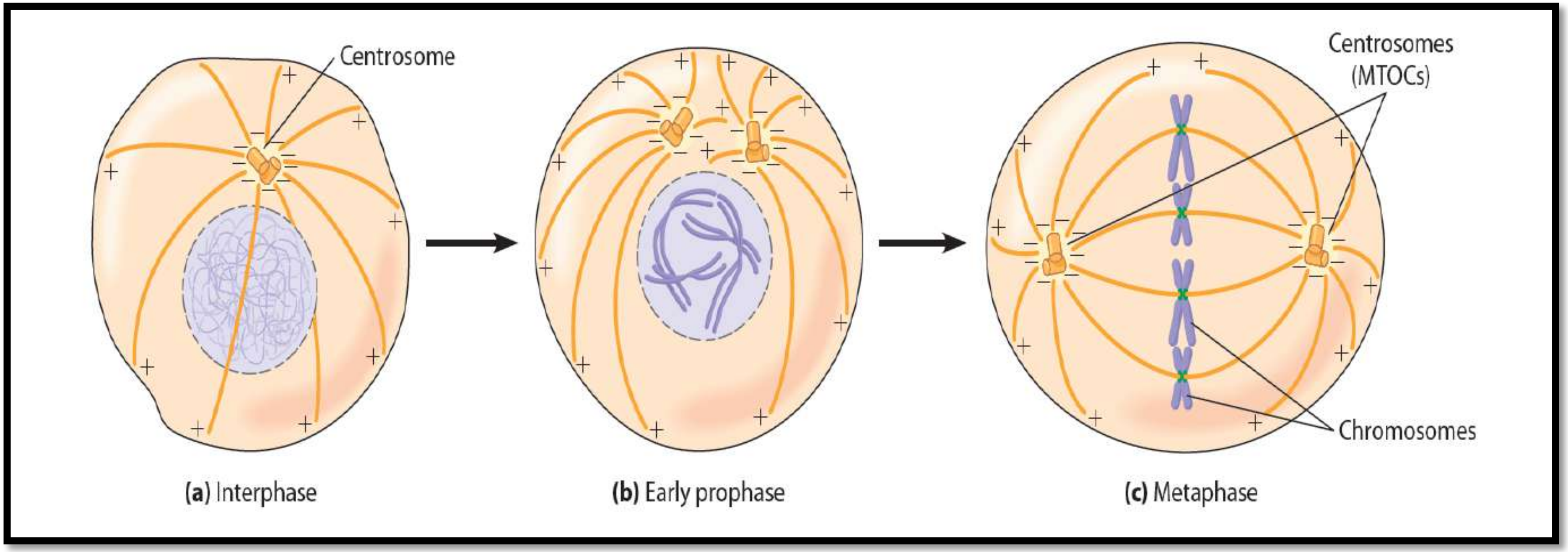
Doublets and triplets contain **one complete 13-protofilament** microtubule (the *A tubule*) and one or two additional **incomplete** (< 13 protofilaments) tubules (called *B* and *C tubules*) usually consisting of **10 -11** protofilaments.

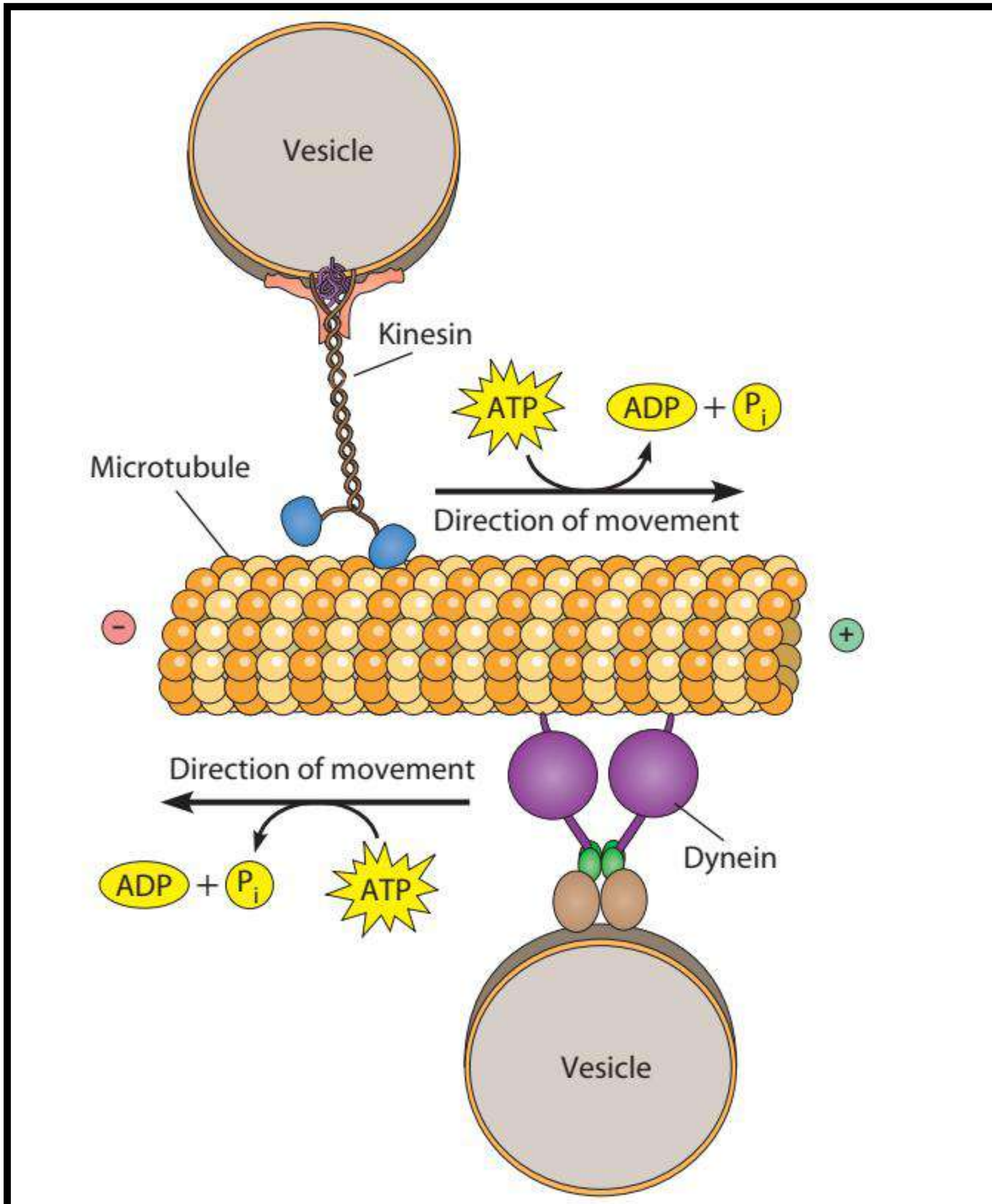
Doublets are found in cilia & flagella; while triplets are found in basal bodies & centrioles.



Microtubule Polarity

- The ends of the microtubule are designated **as plus (+)** (away from the nucleation center) or **minus (−)** (toward the nucleation center).
- Microtubules **grow at each end** by the polymerization of **tubulin hetero dimers**, and shrink at each end by the release of tubulin hetero dimers (depolymerization).
- Both processes (polymerization and de polymerization) always occur more **rapidly at one end**, the **plus end**. The other, less active, end is the minus end.
- Special motor proteins (**powered by ATP**), move cellular organelles around the cell on microtubular "tracks".
- **Kinesin** proteins move organelles **toward the "+" end** (toward the cell periphery), and **dynein** proteins move them toward **the "−" end**.

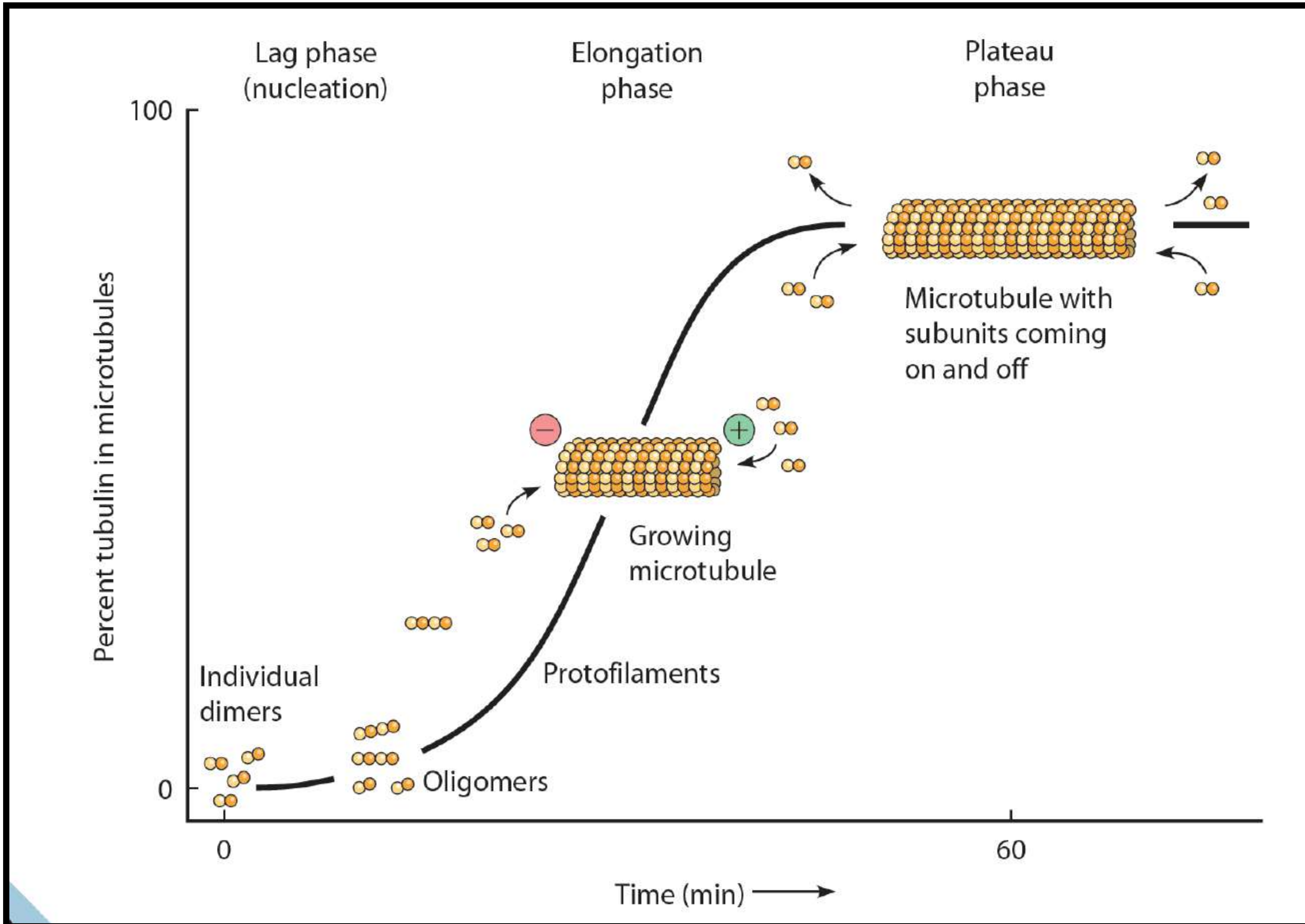



Vesicle
Kinesin
ATP
ADP + P_i
Microtubule
Direction of movement
−
+
Direction of movement
ADP + P_i
ATP
Dynein
Vesicle

Microtubules are build from Tubulin Heterodimers

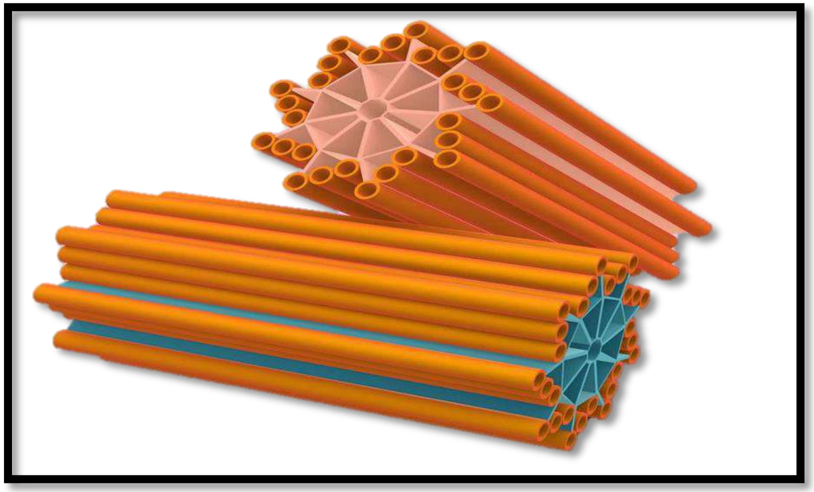
- The basic building subunit of a protofilament is a **tubulin heterodimer** (α -tubulin & β –tubulin). MTOCs organize and polarize the MT within cells.
- Individual α and β-tubulin molecules are 4–5 nm in daimeter, and they have **nearly identical** 3D structures, and each has **a GTP-binding site** at the N-terminus.
- As soon as individual α -tubulin and β -tubulin molecules are synthesized, they **bind noncovalently** to each other to produce an **α,β tubulin heterodimer**.
- **GTP is required** for MT assembly. Each tubulin heterodimer binds two GTP molecules. The **α** -tubulin binds one GTP; the other GTP is bound by **β** -tubulin
- ***Kinetics of Microtubule Assembly***
- Microtubules form by the **reversible** polymerization of α,β tubulin heterodimer at their ends. A critical step in the formation of MTs is the **aggregation** of α,β tubulin heterodimer into clusters **called oligomers that** serve as "nuclei" from which new microtubules can grow, and this process is referred to as **nucleation or lag phase** which proceeds at **slow rate.**
- Once an MT has been nucleated, it **grows** by **addition** of an α,β tubulin heterodimer subunits **at either end**, via a process called **elongation**, which is **faster** than lag phase.
- Finally, MTs increase to a point where the **concentration of free tubulin** (individual or dimers) becomes **limiting (critical concentration).** This leads to the **plateau phase**, where MT assembly is balanced by disassembly.

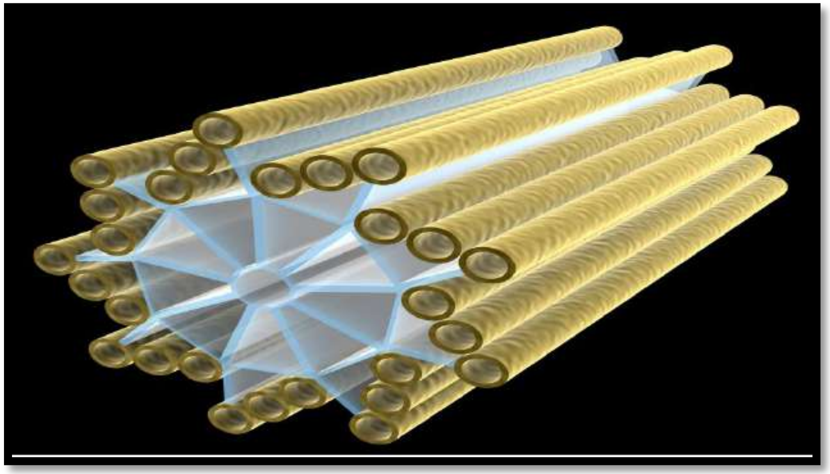
Kinetics of Microtubule Assembly



Centrioles and basal bodies are complex MT structures

- **Centrioles** are barrel-shaped structures found in the cells of animals and most protists. **Centrioles** occur in **pairs**, usually located at right angles (**perpendicular**) to each other near the nuclear membranes in a region referred as a **centrosome**.
- **Centrioles** (each about 250 nm (0.25 μm) in diameter are composed of **nine sets of triplet MTs** arranged in a ring in "**9+0" pattern**.
- **Nontubulin** proteins are present to connect the microtubule triplets to each others.
- The **basal body** is structurally very similar to a centriole, with **nine sets of triplets MT** in **a "9+0**" pattern. **Basal bodies** are the cellular structure responsible for **anchoring** cilium or flagellum.
- In humans and in many animal species the **basal body** of the fertilizing sperm's flagellum enters the egg and becomes a **centriole**.





Cilia and Flagella

- Some eukaryotic cells have **flagella** (singular, *flagellum*) and **cilia** (singular, *cilium*), both are cellularextensions that contain microtubules.

تحتوي بعض الخلايا حقيقية النواة على أسواط (مفردها سوط) وأهداب (مفردها هدب)، وكلاهما امتدادات خلوية تحتوي على أنابيب دقيقة

- **Eukaryotic** cells have a completely **different kind of flagellum** than prokaryotes, consisting of a circle of nine microtubule pairs (**doublets**) surrounding two central **singlet** microtubules (**9 + 2 pattern or structure)**. Also eukaryotic flagella **undulates**, or waves up and down, rather than rotates.

تحتوي الخلايا حقيقية النواة على نوع مختلف تمامًا من الأسواط عن بدائيات النواة، حيث تتكون من دائرة من تسعة أزواج من الأنابيب الدقيقة (ثنائيات) تحيط بأنبوبين دقيقين مركزيين (نمط أو بنية 9 + 2). كما أن الأسواط حقيقية النواة تتلوى أو تتأرجح لأعلى ولأسفل، بدلاً من الدوران

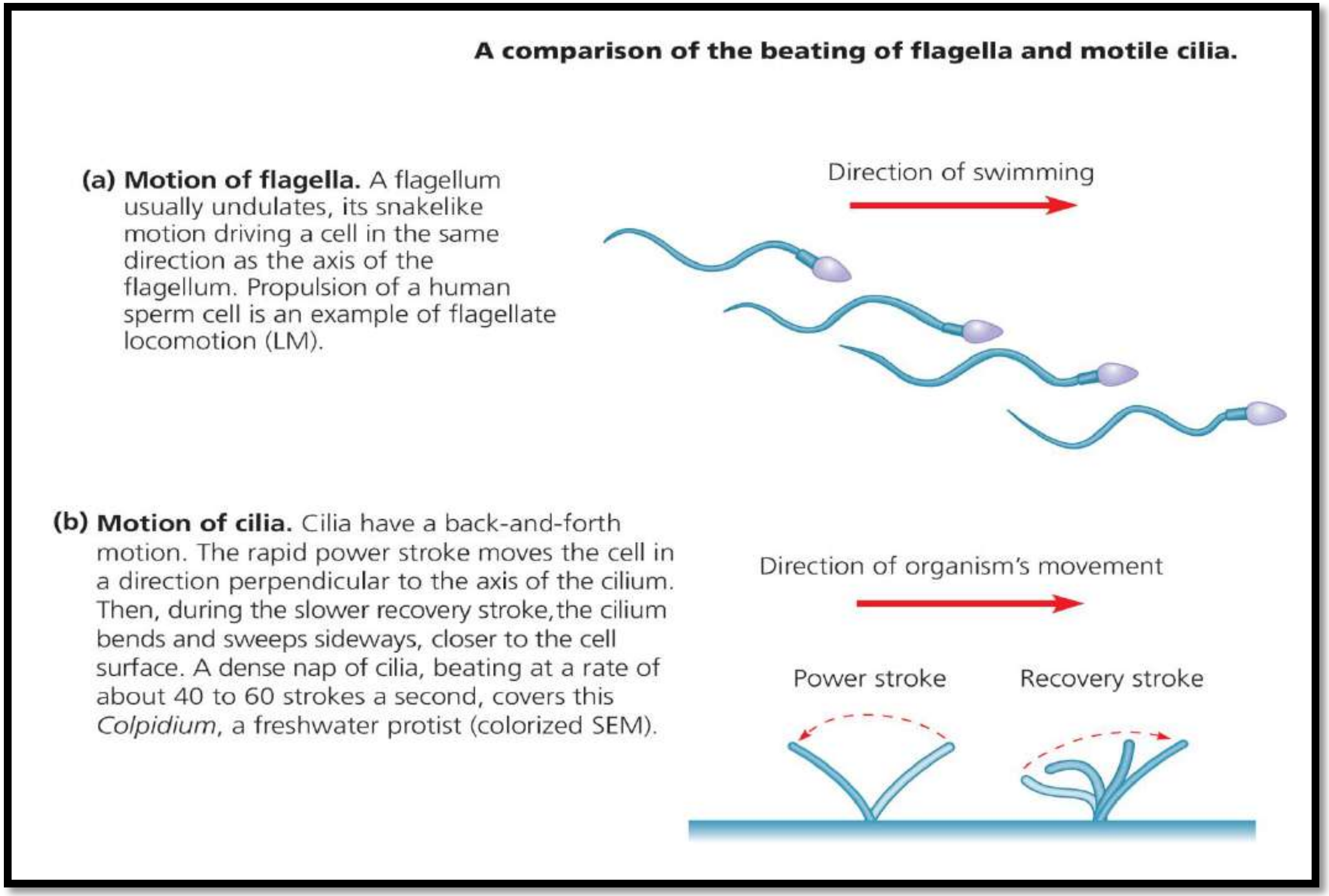
- The MTs of cilia and flagellum are **derived from a basal body (nine MT triplets)**, situated just below the point where the cilia or flagellum protrudes from the surface of the cell.

يتم اشتقاق أطراف الأهداب والسوط من جسم قاعدي (تسعة ثلاثيات أطراف أهداب)، يقع أسفل النقطة التي تبرز منها الأهداب أو السوط من سطح الخلية

- Many unicellular protists are propelled through water by cilia or flagella that act as locomotor appendages. تتحرك العديد من الكائنات وحيدة الخلية عبر الماء بواسطة الأهداب أو الأسواط التي تعمل كملحقات حركية
- The sperm of animals, algae, and some plants have flagella. تحتوي الحيوانات المنوية والطحالب وبعض النباتات على أسواط
- When cilia or flagella extend from cells that are **attached** tightly together in a sheet that is part of a tissue layer, **they can move fluid over the surface of the tissue**, e.g. the ciliated lining of the trachea sweeps mucus containing trapped debris out of the lungs, and in a woman's reproductive tract, the cilia lining the oviducts help move an egg toward the uterus.
- The **sensory cells of the vertebrate ear** also contain **conventional cilia** surrounded by **complex cilia** (actin-based stereocilia); so sound waves bend these structures and provide the initial sensory input for hearing

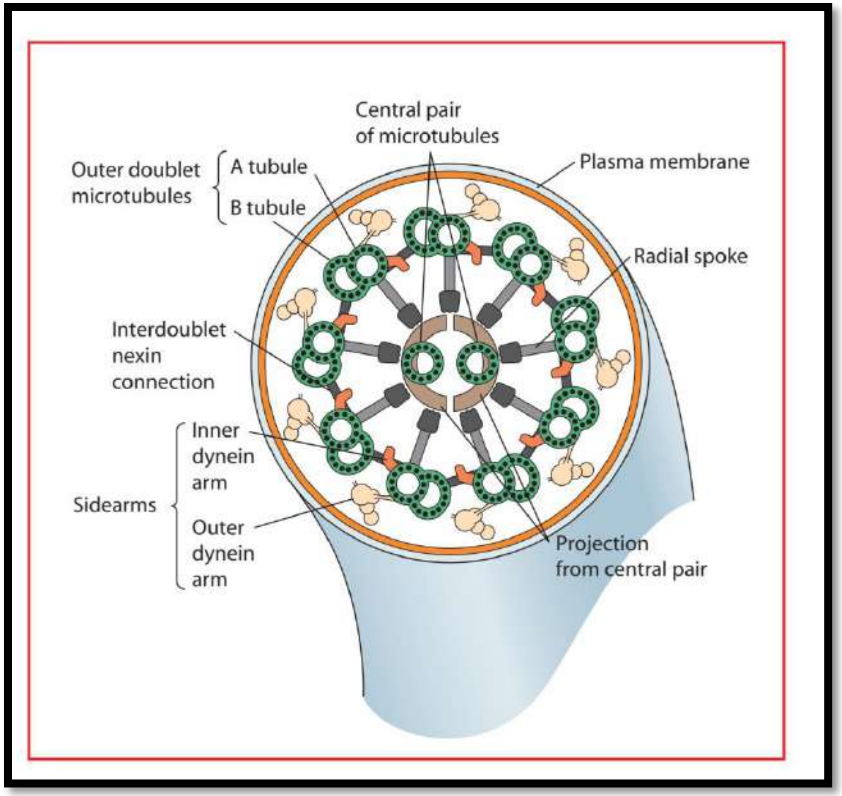
تحتوي الخلايا الحسية في أذن الفقاريات أيضًا على أهداب تقليدية محاطة بأهداب معقدة (أهداب حسية قائمة على الأكتين)؛ لذا فإن الموجات الصوتية تنحني هذه الهياكل وتوفر المدخلات الحسية الأولية للسمع

- **Cilia** usually occur in **large numbers** on the cell surface. **Flagella** are usually **limited** to just one or a few per cell, but longer than cilia.
- Flagella and cilia differ in their beating patterns.
- A **flagellum** has an **undulating motion** like the tail of a fish.
- In contrast, **cilia** have **alternating power** and recovery strokes, much like the oars of a racing crew boat
-

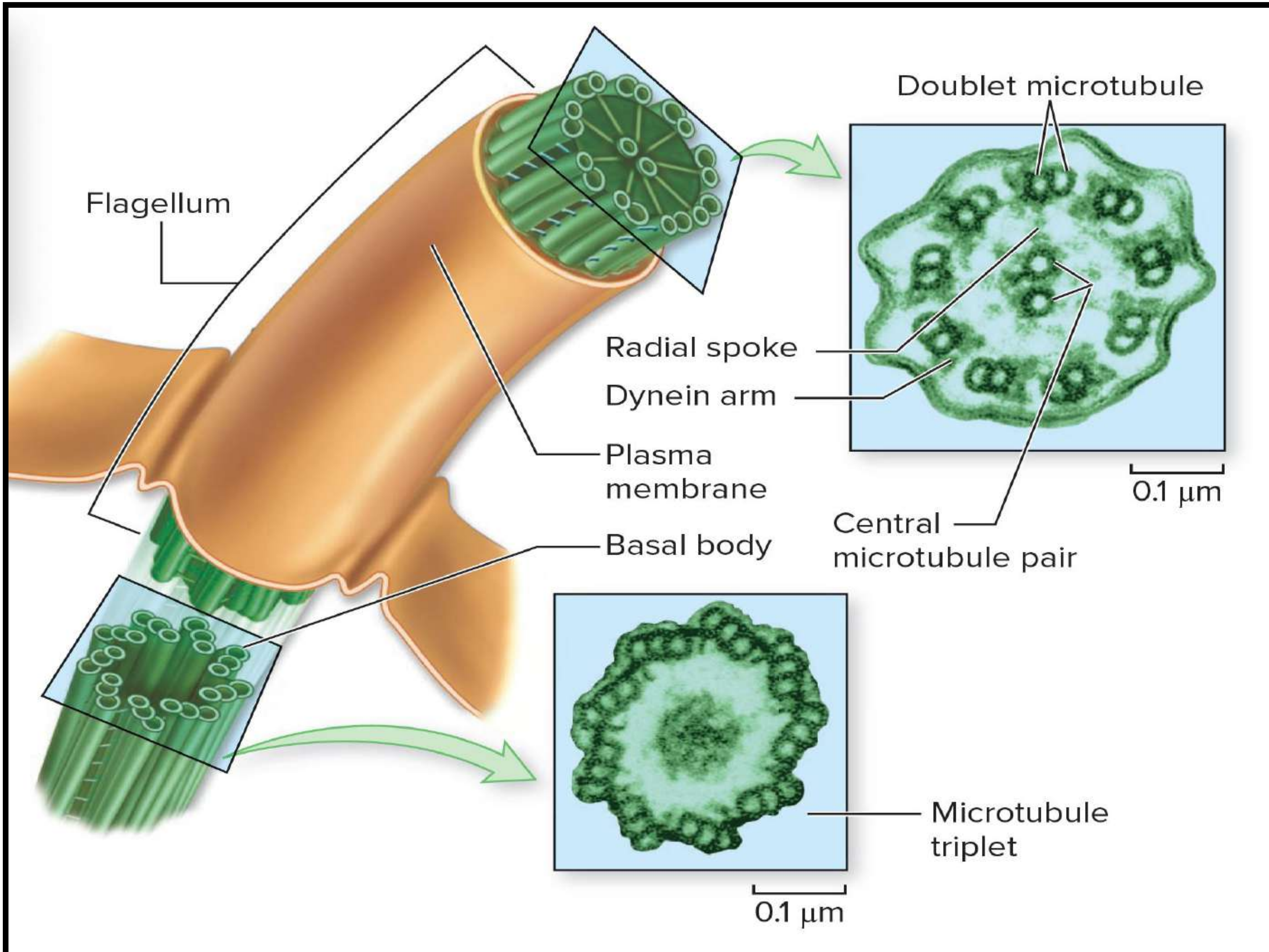


9+2 structure pattern bending movements of cilia & flagella

- Bending involves large motor proteins called **dyneins (axonemal dynein)** that are attached along each outer MT doublet.
- A typical dynein protein has **two "feet"** that "walk" along the microtubule of the adjacent doublet, **using ATP for energy**.
- One foot maintains contact, while the other releases and reattaches one step farther along the MT.
- The **outer doublets and two central singlet** MT are held together by flexible cross-linking proteins (**radial spokes**).

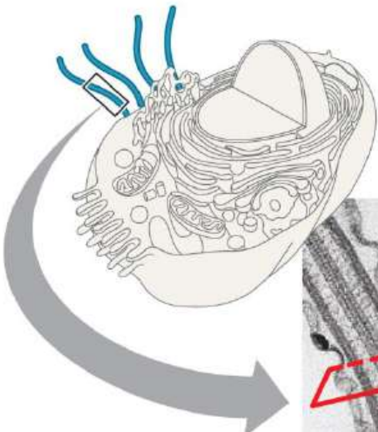


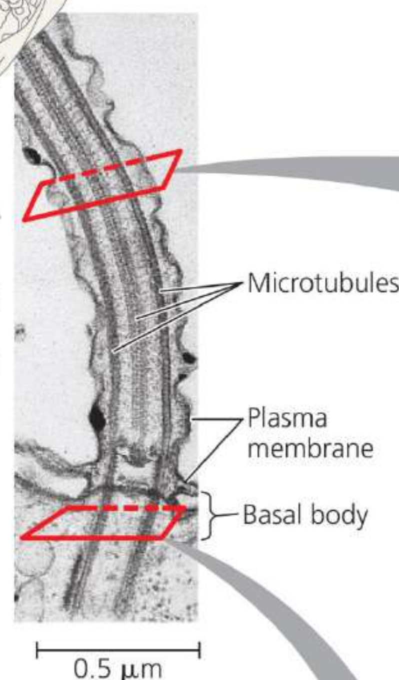
- If the **MT doublets were not held** in place by the radial spokes, the walking action would make them **slide past each other**.
- Instead, with the holding function of radial spokes, the movements of the dynein feet cause the flagellum to **bend**.



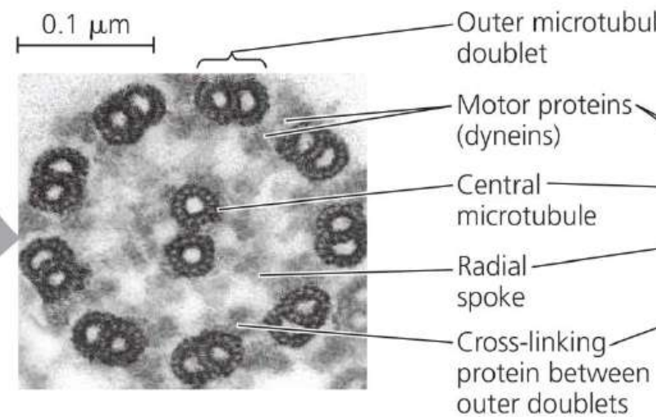
Flagellum
Doublet microtubule
Radial spoke
Dynein arm
Plasma
membrane
Central
microtubule pair
0.1 μm
Basal body
Microtubule
triplet
0.1 μm

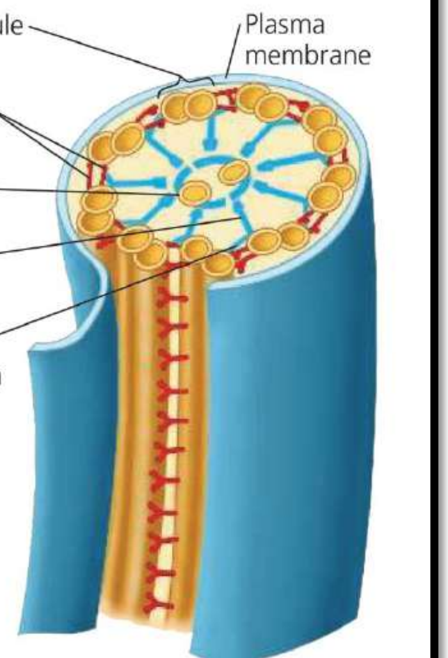
Structure of a flagellum or motile cilium.





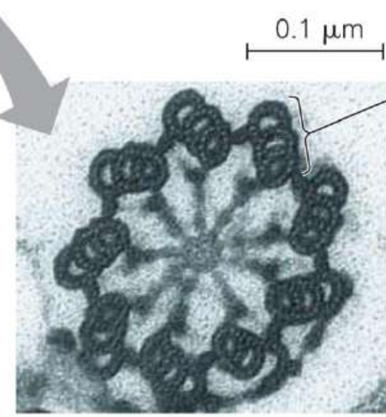
(a) A longitudinal section of a motile cilium shows microtubules running the length of the membrane-sheathed structure (TEM).



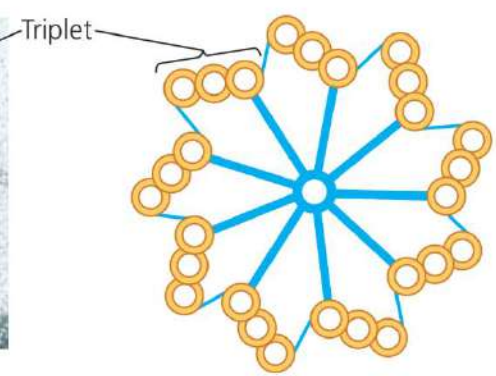


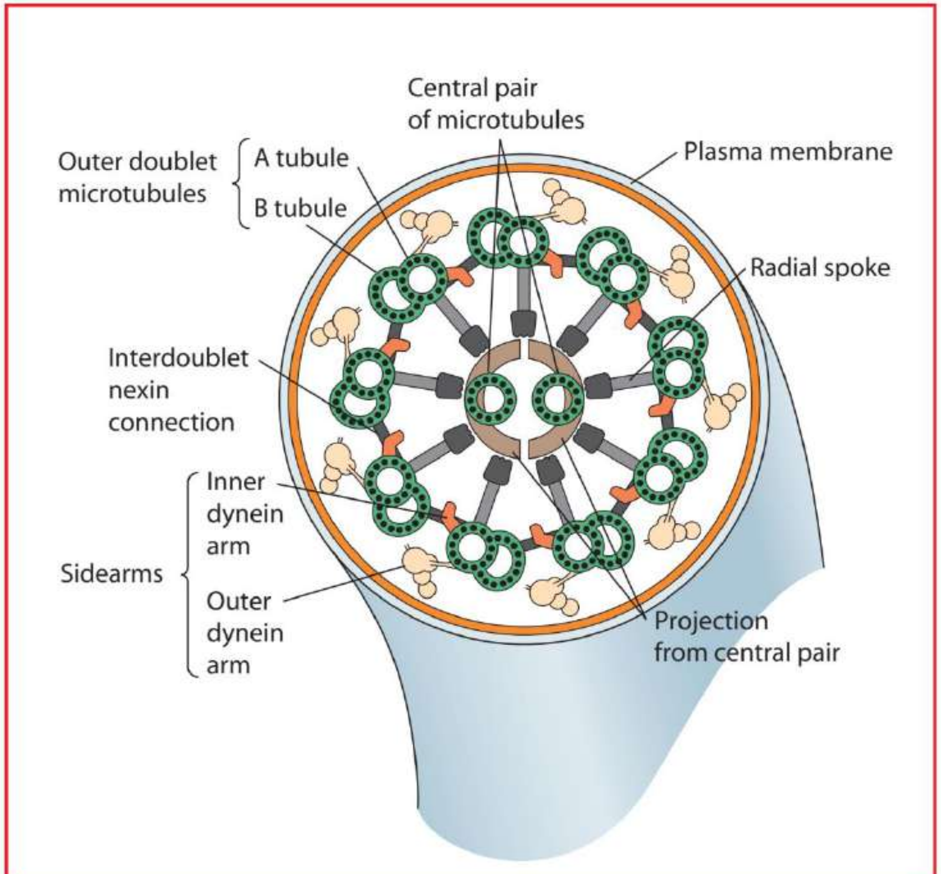
(b) A cross section through a motile cilium shows the "9 + 2" arrangement of microtubules (TEM). The outer microtubule doublets are held together with the two central microtubules by flexible cross-linking proteins (blue in art), including the radial spokes. The doublets also have attached motor proteins called dyneins (red in art).

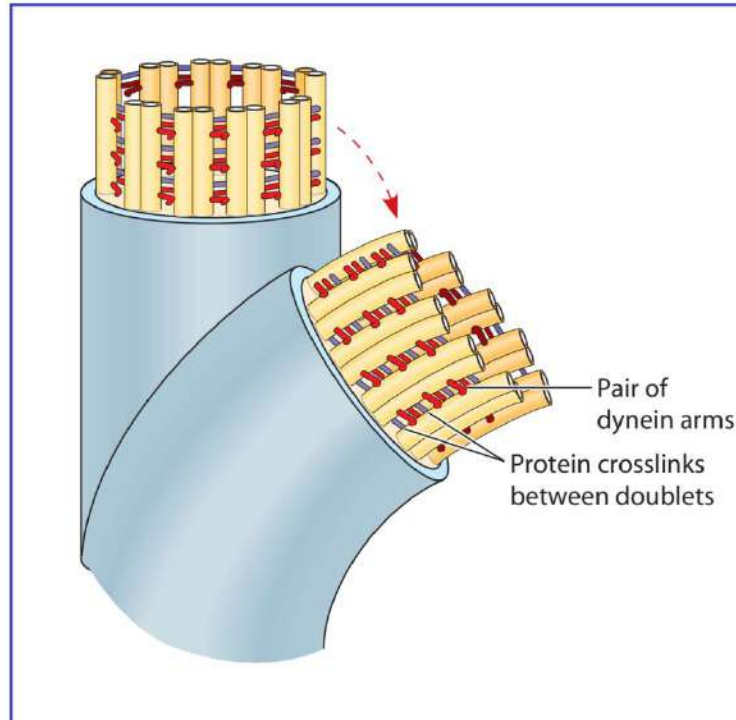
(c) Basal body: The nine outer doublets of a cilium or flagellum extend into the basal body, where each doublet joins another microtubule to form a ring of nine triplets. Each triplet is connected to the next by nontubulin proteins (thinner blue lines in diagram). This is a "9 + 0" arrangement: The two central microtubules are not present because they terminate above the basal body (TEM).



Cross section of basal body




Central pair
of microtubules
Outer doublet
microtubules
A tubule
B tubule
Plasma membrane
Radial spoke
Interdoublet
nexin
connection
Inner
dynein
arm
Sidearms
Outer
dynein
arm
Projection
from central pair

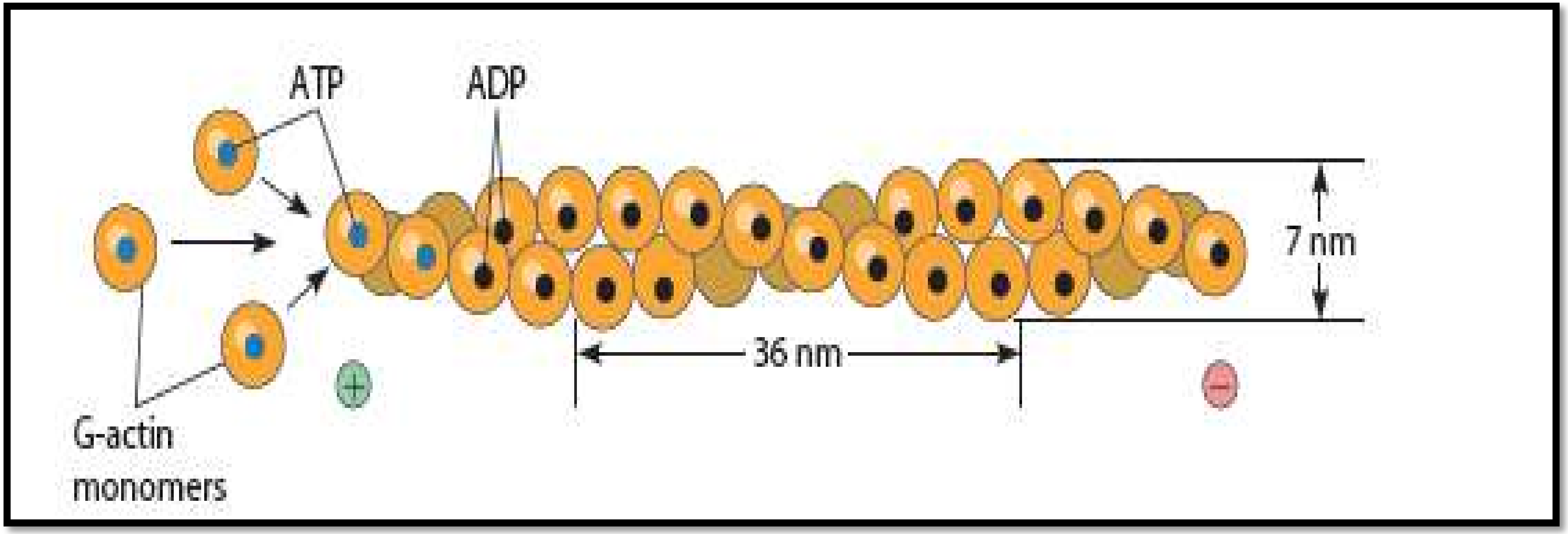

Pair of
dynein arms
Protein crosslinks
between doublets

Microfilaments (Actin Filaments)

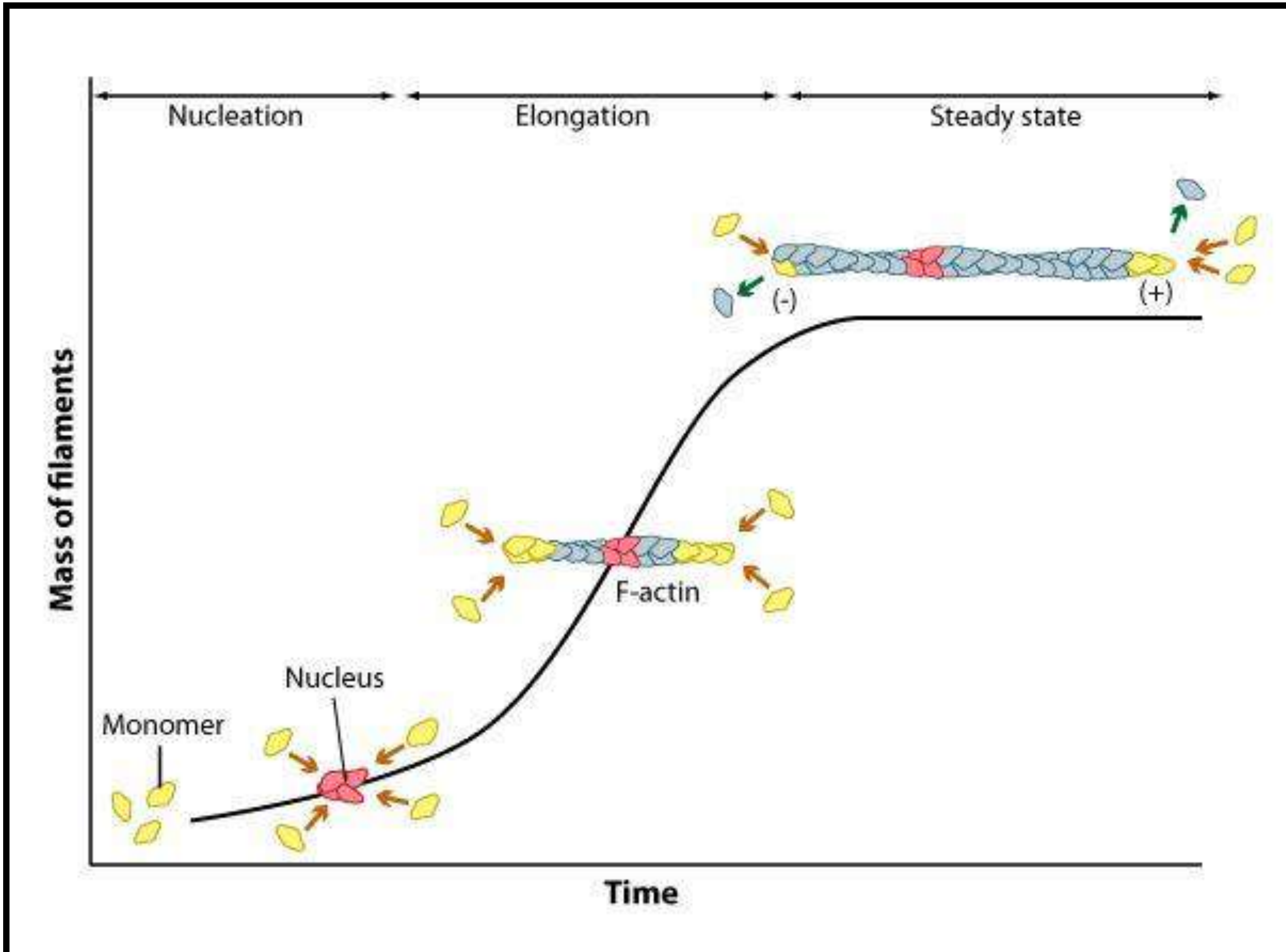
- **Microfilaments (MF)** are thin solid rods and present in all eukaryotic cells.
- MF are also called **actin filaments** because they are built from molecules of **G-actin**, a globular protein.
- Under the right conditions, **G-actin molecules polymerize to form microfilaments**; in this form, actin is referred to **as action filament or F-actin (filamentous actin).**
- A microfilament is a **twisted double chain** of G-actin subunits.
- Besides occurring as free actin (**G-actin**) and linear filaments (**F-actin**) , microfilaments can form structural networks (**actin network**).
- A 3D network formed by microfilaments just to the inside of the plasma membrane (***cortical microfilaments***) helps support the cell's shape , which gives the outer cytoplasmic layer of a cell, called the **cortex**, the **semisolid consistency of a gel**, in contrast with the more fluid state of the interior cytoplasm.
- Microfilaments are best known for their role in the **contraction of muscle cells**.
- MFs are **not limited to muscle cells**, and occur in almost all eukaryotic cells and are involved in numerous other phenomena, including a variety of **locomotory** and **structural functions.**

G-Actin Monomers Polymerize into F-Actin Microfilaments

- **G-actin monomers** can polymerize **reversibly** into filaments with a **lag phase (**filament nucleation**)**, which begins with formation of dimers or trimers, called ***nucleation seeds***, followed by a more **rapid** polymer **elongation phase**.
- The **F-actin filaments** that form are composed of **two linear strands of polymerized G-actin wound around each other** in a helix.
- Within a microfilament, **all the actin** monomers are oriented in the **same direction**, so that an MF, like a microtubule, has certain **polarity**.
- **In vitro**, rate polymerization proceeds **much faster** at the **plus (+)** end , than the rate at **minus (-)** end.



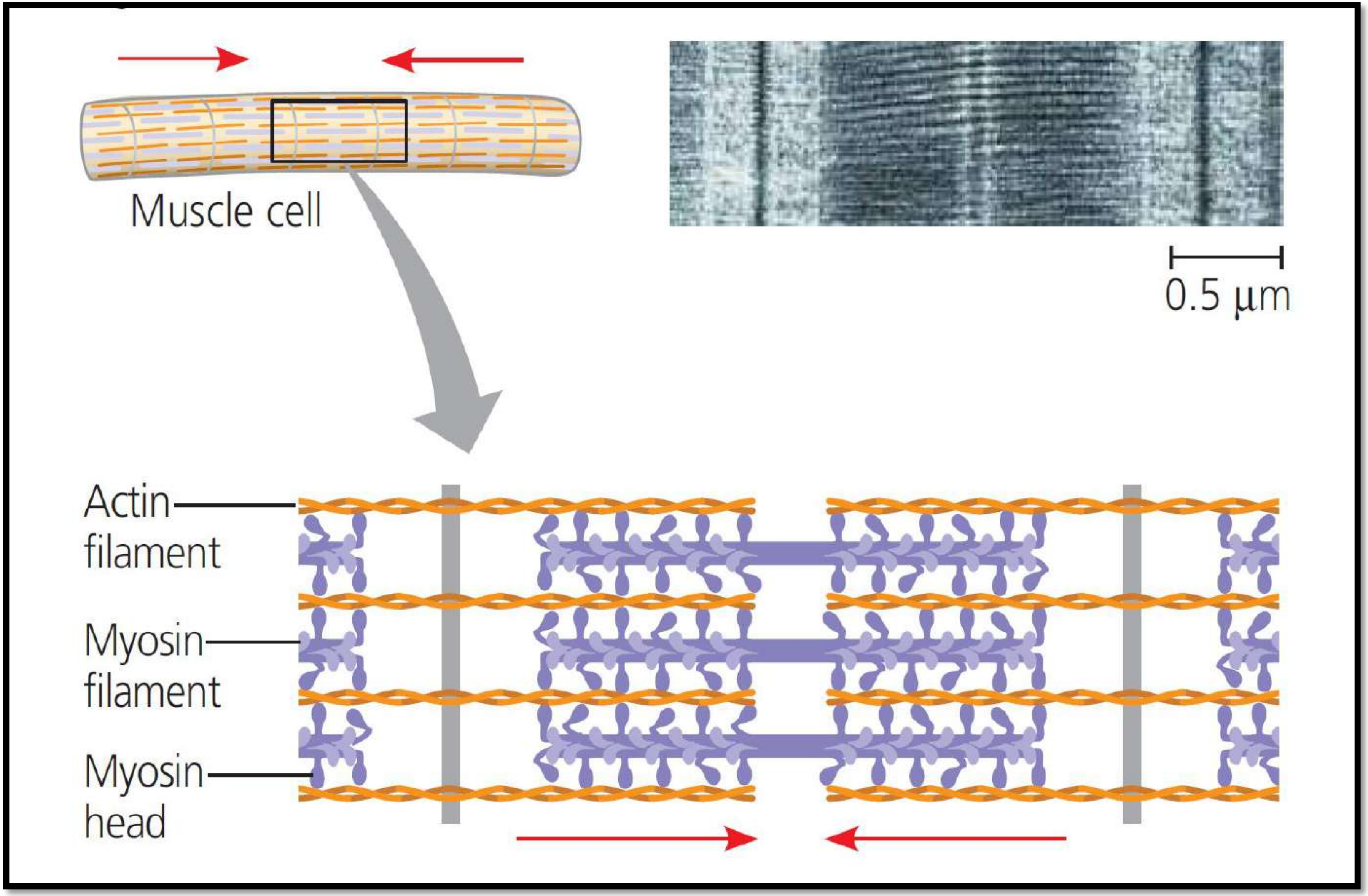
Kinetics of Microfilaments Assembly



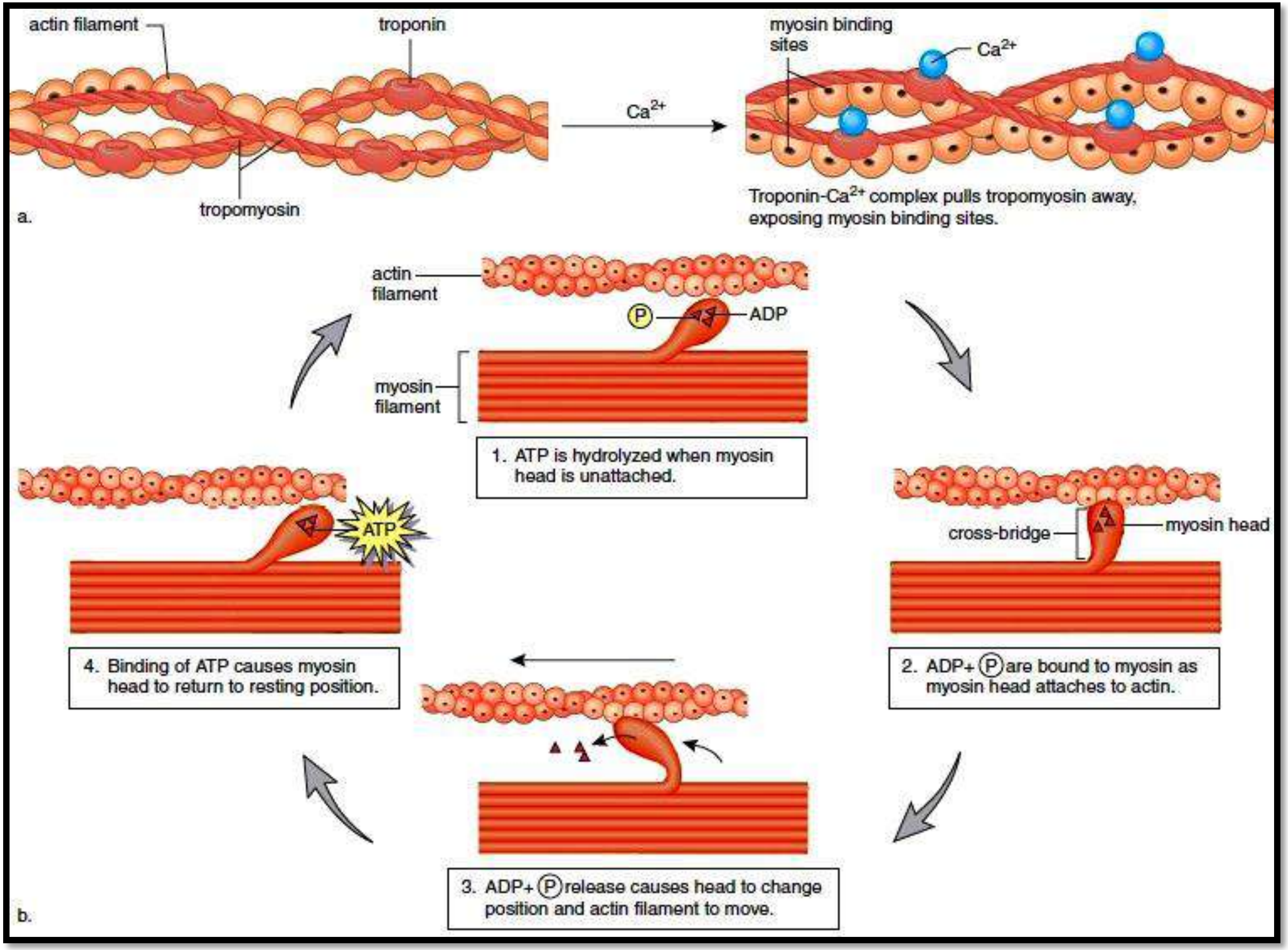
Microfilaments functions

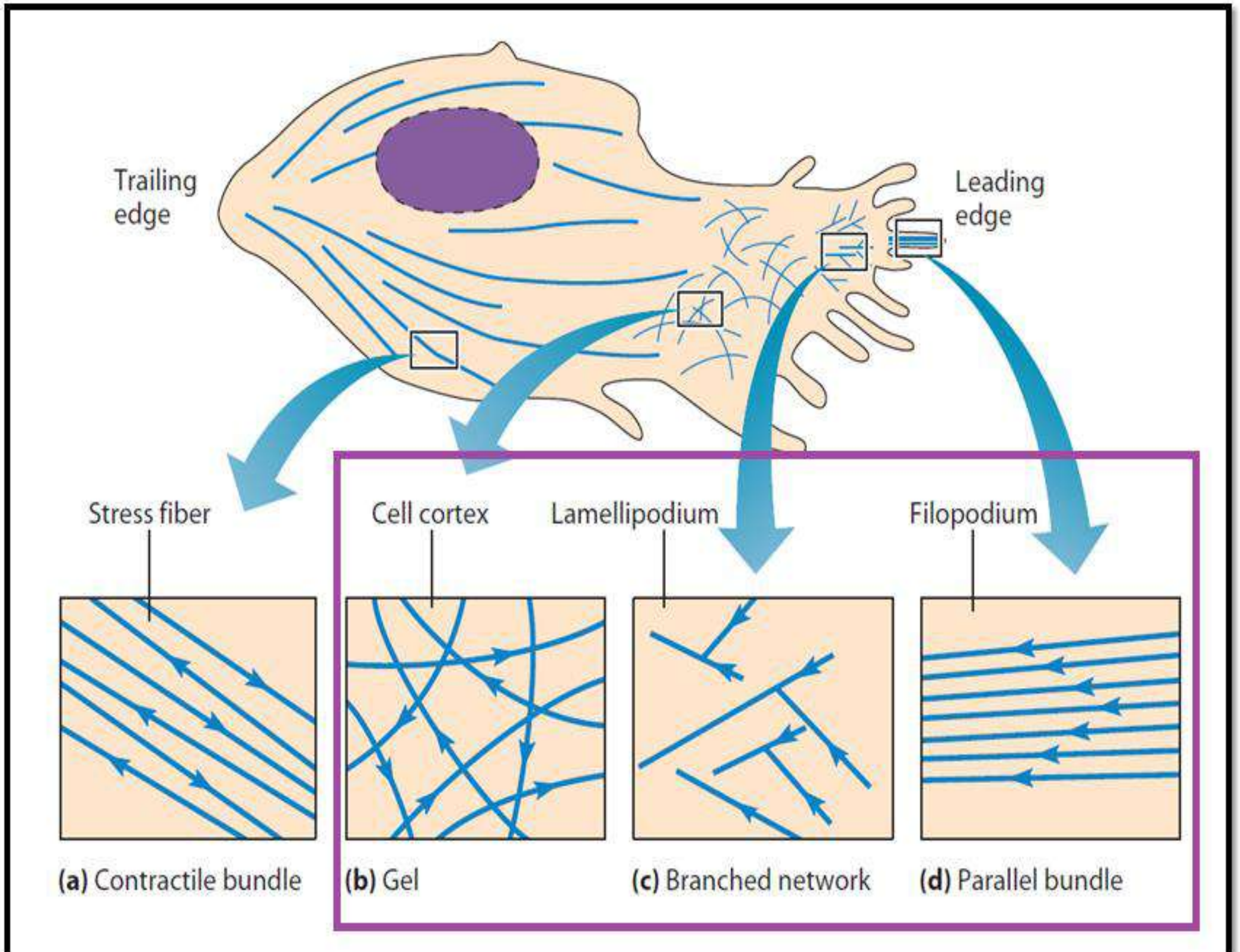
- *Examples of **locomotory** function of microfilaments:*
- **Muscle contraction**: Thousands of **actin** filaments (some times called thin filaments) and thicker filaments made of a protein called **myosin** interact to cause contraction of muscle cells.
- Cell migration via **pseudopodia formation:** the unicellular protist *Amoeba* and some of our white blood cells. These cell crawl along a surface by extending cellular extensions called **pseudopodia** and moving toward them.
- **Cytoplasmic streaming movement:** In plant cells, actin-protein interactions contribute to **cytoplasmic streaming**, a circular flow of cytoplasm within cells, which speeds the movement of organelles and the distribution of materials within the cell.
- **Cytokinesis:** MFs also produce the **cleavage furrows** that divide the cytosol of animal cells during **cytokinesis**.
- *Examples of **structural** function of microfilaments:*
- **Cell cortex**: MFs are important in developing and maintaining cell shape. Most animal cells, have a **dense network of microfilaments** within the cell **cortex** just beneath the plasma membrane. The **cortex** provides structural rigidity on the cell surface and facilitates shape changes and cell movement.
- **Microvilli:** Parallel bundles of MFs also make up the structural core of **microvilli**, the fingerlike extensions found on the surface of many animal cells.

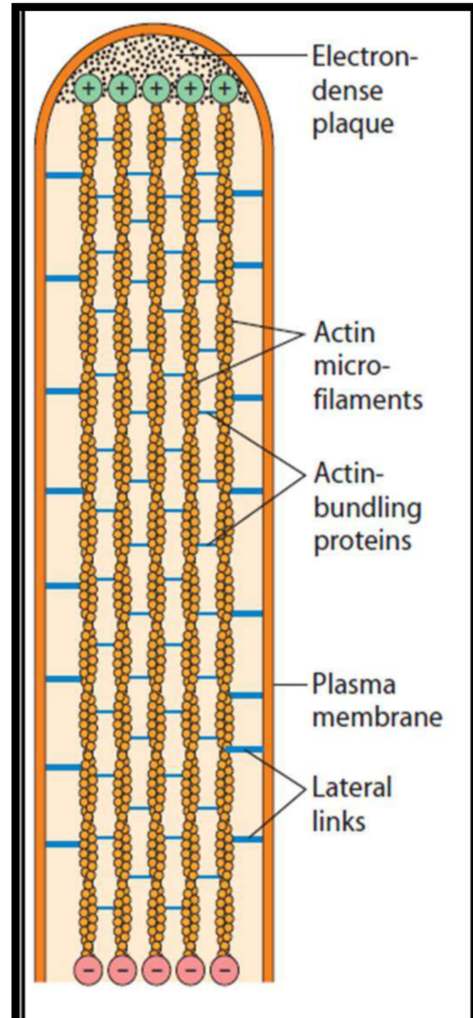
Actin-myosin in Muscle contraction



Role of Ca^{2+} in Muscle contraction







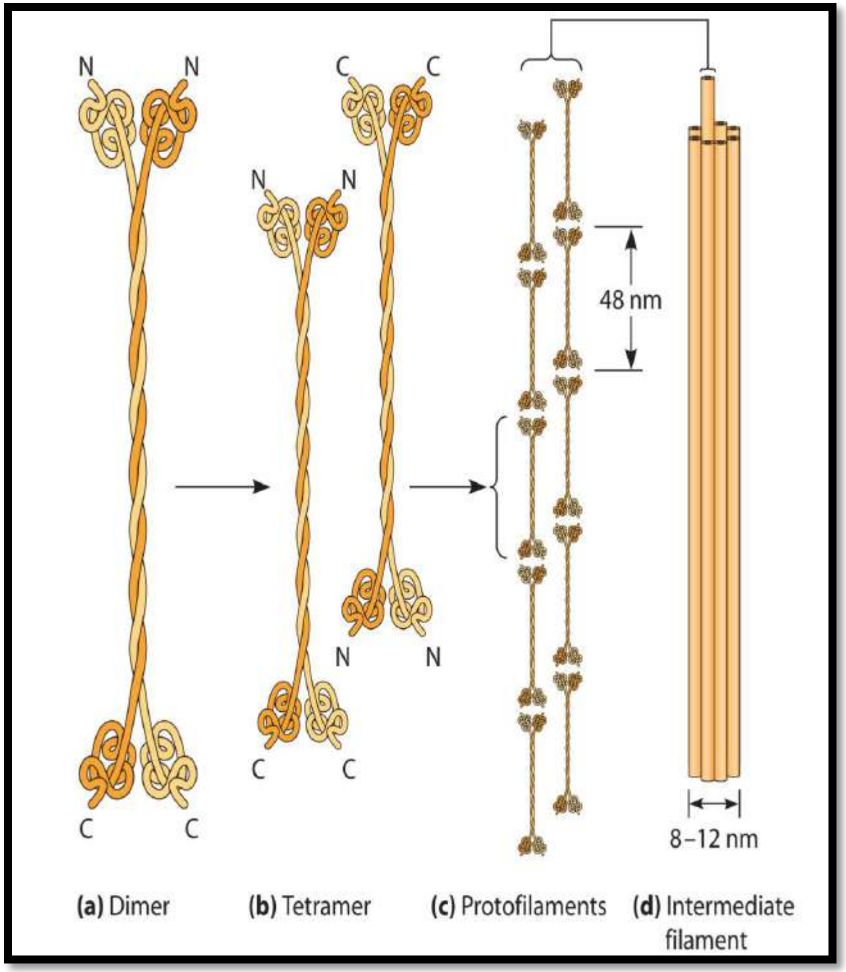
(b) Structure of a microvillus

Intermediate Filaments (IFs)

- IFs have a **diameter of about 8–12 nm**, which makes them intermediate in size between microtubules and microfilaments.
- Intermediate filaments are **not found in the cytosol of plant cells**, but they are abundant in many animal cells, where IFs occur **singly** or in **bundles** and appear to play a structural or **tension-bearing role.** Intermediate filaments are **the strong element** of the cytoskeleton in animal cells
- The basic subunits of IFs are **two intertwined polypeptides forming fibrous dimers** (**not globular like tubulin and G actin**).
- In contrast to microtubules and microfilaments, **IFs are tissue specific** so differ markedly in amino acid composition from tissue to tissue.
- The two polypeptides are identical for all IFs except **keratin** filaments, which are obligate **heterodimers of type I and type II polypeptides**.
- Intermediate filaments are the **most stable** and the **least soluble constituents** of the cytoskeleton. Once formed, intermediate filaments **are stable** and usually do not break down
- Given their stability, IFs likely serve as a **scaffold** to support the entire cytoskeletal framework.
- In contrast to MTs and MFs, **IFs do not appear to be polarized**.

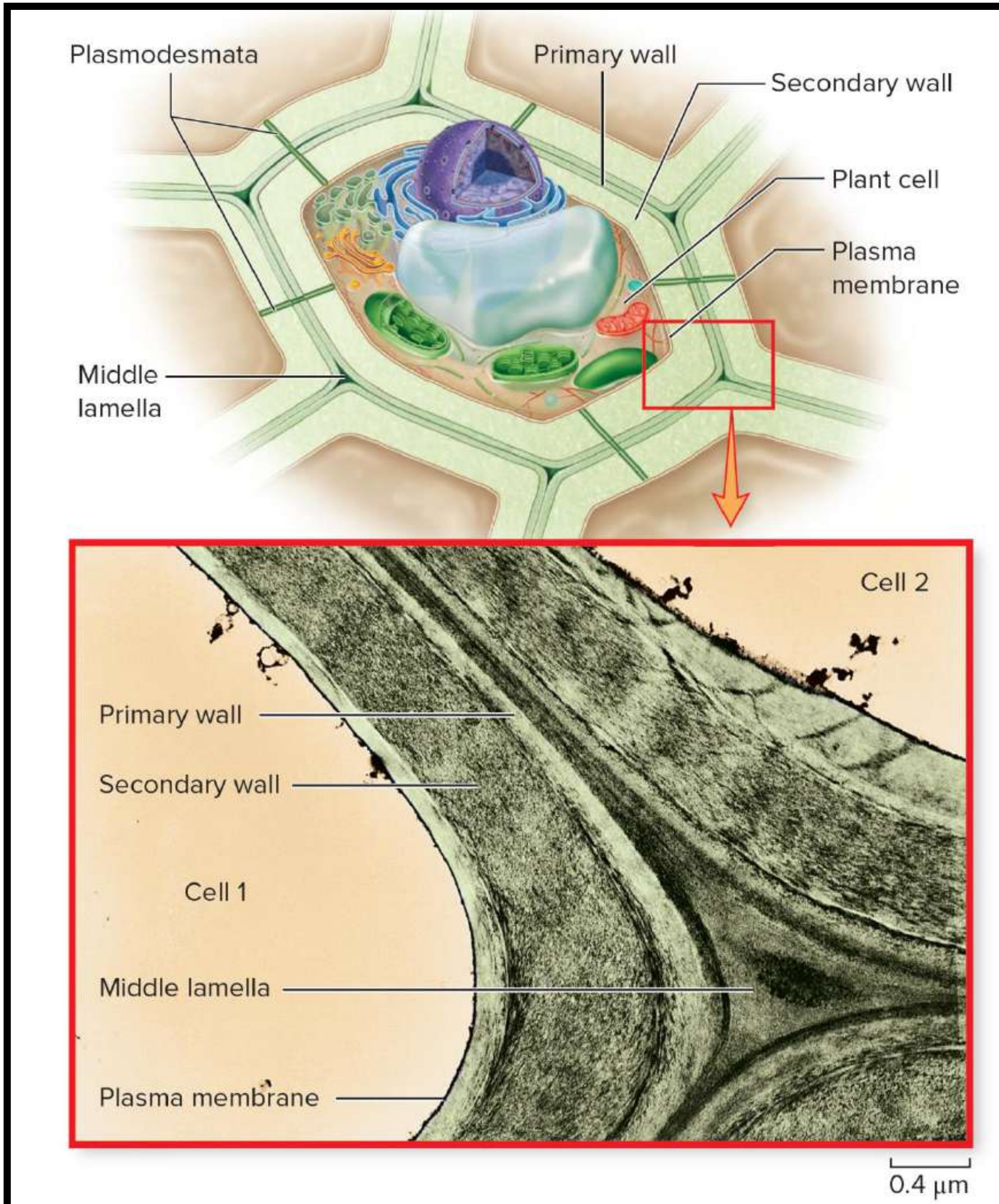
Function of IFs

- Epithelial cells are rich in keratin filaments.
- Nerve cells (nerve axon)
-
- The nucleus typically sits within a cage made of intermediate filaments.
- Other intermediate filaments make up the nuclear lamina, which lines the interior of the nuclear envelope



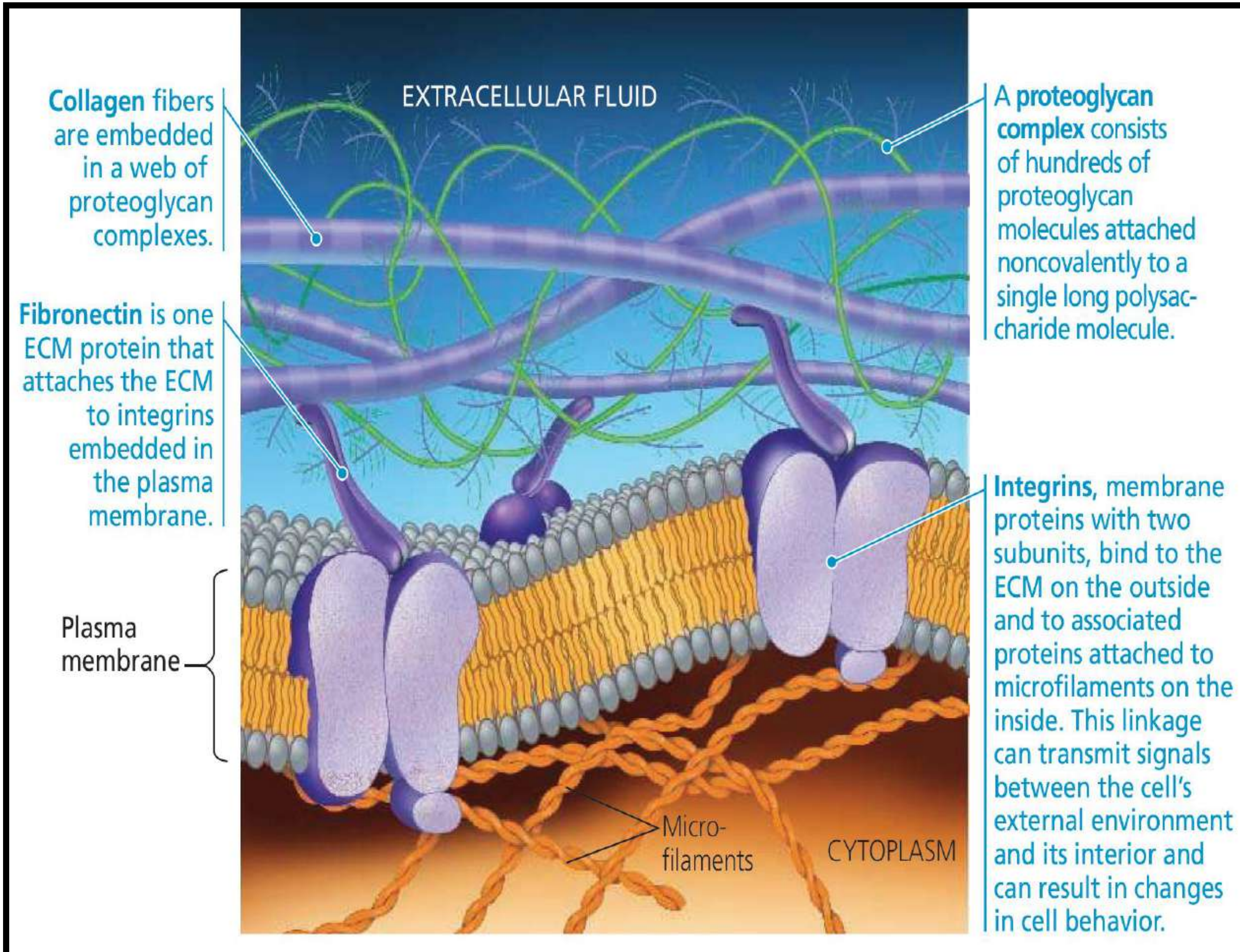
Extracellular structure of plant cells: Cell Wall

- The cells of plants, fungi, and many types of protists **have cell walls**, which **protect** and **support** the cells. The cell walls of these eukaryotes are **chemically and structurally different** from prokaryotic cell walls.
- In **plants and protists**, the cell walls are composed of fibers of the polysaccharide **cellulose**, whereas the cell walls in **fungi** are composed of **chitin**.
- In plants, **primary walls** that thin and flexible are laid down when the cell is still growing (**A young plant cell**).
- Between primary walls of adjacent cells is the **middle lamella**, a thin layer rich in sticky polysaccharides called **pectins**. The middle lamella **glues** adjacent cells together.
- When the **cell matures and stops growing**, it strengthens its wall. Some plant cells do this simply by secreting **hardening substances** into the primary wall. Other cells add a **secondary cell wall** deposited inside the primary walls (between the plasma membrane and the primary cell wall)
- The **secondary cell wall**, often deposited in several laminated layers, has a strong and durable matrix that affords the cell protection and support. **Wood**, for example, consists mainly of secondary walls.


Plasmodesmata
Primary wall
Secondary wall
Plant cell
Plasma membrane
Middle lamella
Cell 2
Primary wall
Secondary wall
Cell 1
Middle lamella
Plasma membrane
0.4 μm

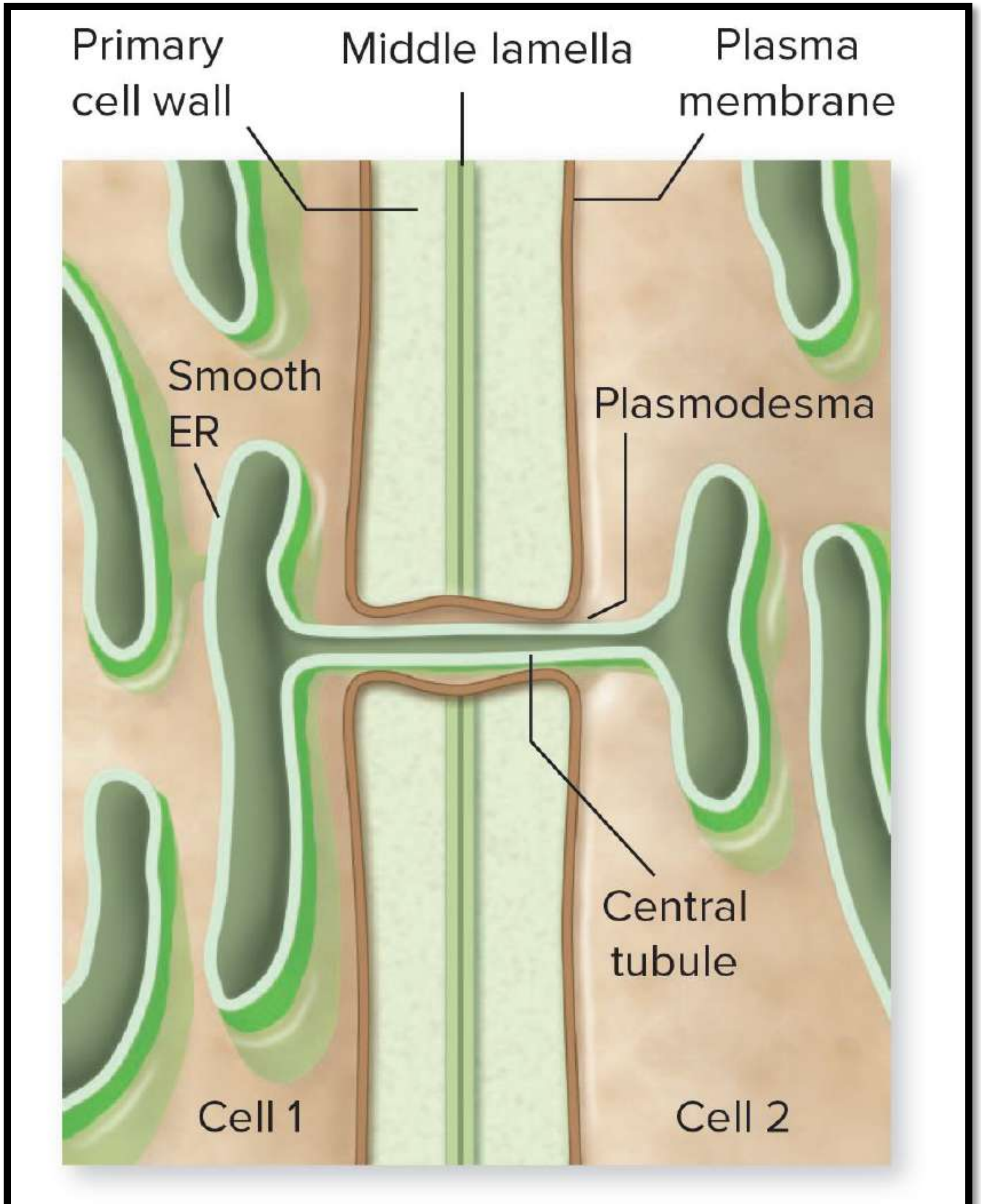
The Extracellular Matrix (ECM) of Animal Cells

- Although **animal cells lack walls** similar to those of plant cells, but **they do have** a rich and complex mixture of **fibrous proteins**, glycoproteins and proteoglycan molecules forming **the extracellular matrix (ECM).**
- The **most abundant** protein in the ECM of most animal cells is the **fibrous** protein called **collagen** (~40% of the total protein in human body). Another but **less abundant** in ECM is the fibrous protein **elastin** which forms strong fibers outside the cells
- The collagen and elastin fibers are **embedded** within a complex network of **glycoproteins and proteoglycans** secreted by the cells forming a protective layer over the cell surface.
- Some cells are attached to the ECM by ECM glycoproteins such as **fibronectin**.
- **Fibronectin and other ECM** proteins bind to cell-surface receptor proteins called **integrins** that are built into the plasma membrane and **span the membrane** and bind on their cytoplasmic side to associated proteins attached mainly to **microfilaments** (actin filaments) and sometimes to **intermediate filaments** of the cytoskeleton.
- Integrins are in a position to **transmit signals** between the ECM and the cytoskeleton and thus **integrate or associate changes** occurring outside and inside the cell.
- By this way of integration between the ECM and the cells, the ECM can help coordinate the behavior of all the cells in a particular tissue.


EXTRACELLULAR FLUID
Collagen fibers are embedded in a web of proteoglycan complexes.
Fibronectin is one ECM protein that attaches the ECM to integrins embedded in the plasma membrane.
Plasma membrane
A proteoglycan complex consists of hundreds of proteoglycan molecules attached noncovalently to a single long polysaccharide molecule.
Integrins, membrane proteins with two subunits, bind to the ECM on the outside and to associated proteins attached to microfilaments on the inside. This linkage can transmit signals between the cell's external environment and its interior and can result in changes in cell behavior.
Micro-filaments
CYTOPLASM

Cell-to-Cell Interactions: plant cell plasmodesmata

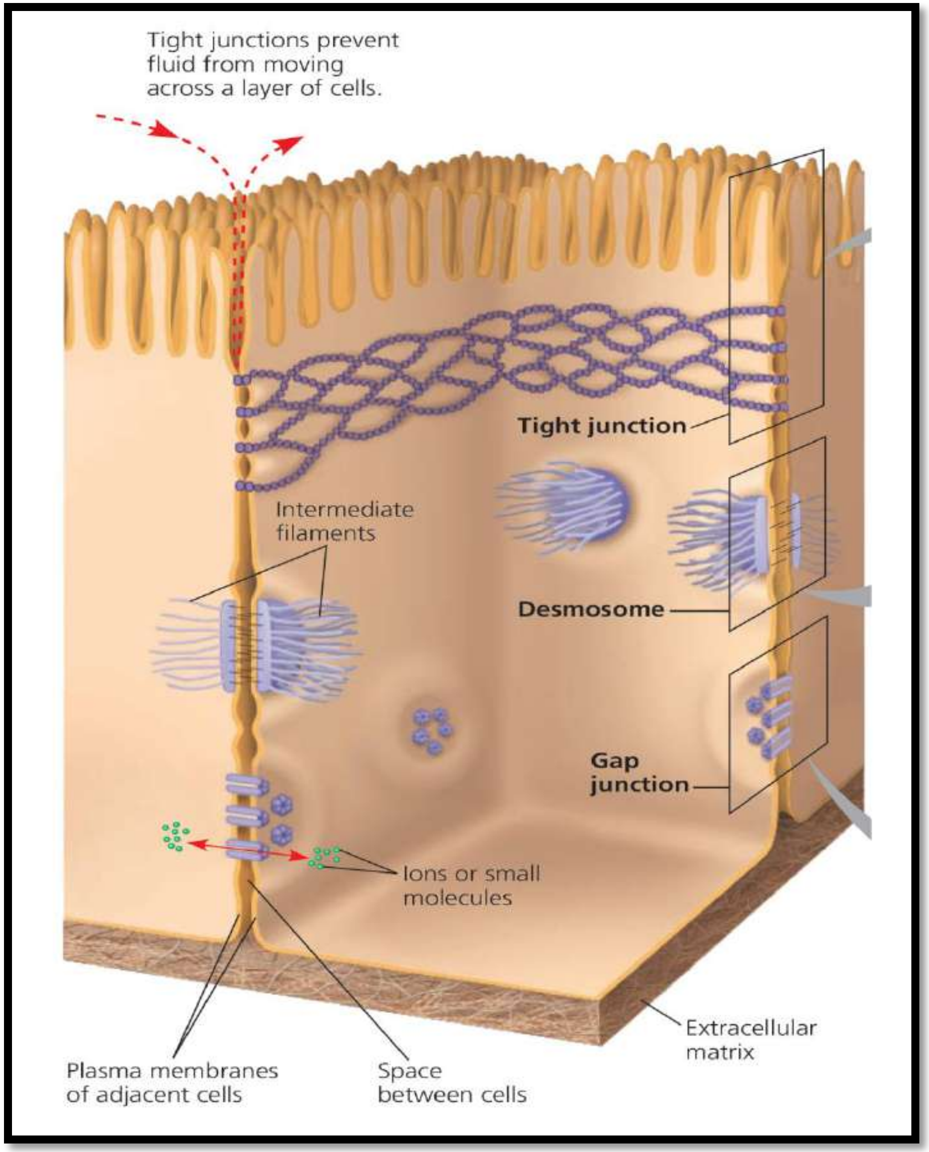
- Cells in an animal or plant are organized into tissues, organs, and organ systems, where **neighboring cells** often adhere, interact, and communicate via sites of **direct physical contact**.
- ***Plasmodesmata in Plant Cells***
- In plants, the nonliving cell walls separate every cell from all others, however many **cell–cell junctions** occur at **holes or gaps in the walls**, where the plasma membranes of adjacent cells can come into contact with one another.
- The **cytoplasmic connections** that form across the touching plasma membranes are called **plasmodesmata** (singular, *plasmodesma*).
- The plasma membranes of adjacent cells line the channel (central tubule) of each plasmodesma and connects the endoplasmic reticulum of each two of adjacent plant cells together, thus **plasmodesmata unify most of the plant into one living continuum** (a continuous sequence) allowing water and small solutes to pass freely from cell to cell .
- Because the channels of **plasmodesmata** are filled with cytosol, the cells share the **same internal chemical environment**.


Primary
cell wall
Middle lamella
Plasma
membrane
Smooth
ER
Plasmodesma
Central
tubule
Cell 1
Cell 2

Animal Cell-to-Cell Interactions: Tight Junctions, Desmosomes, and Gap Junctions

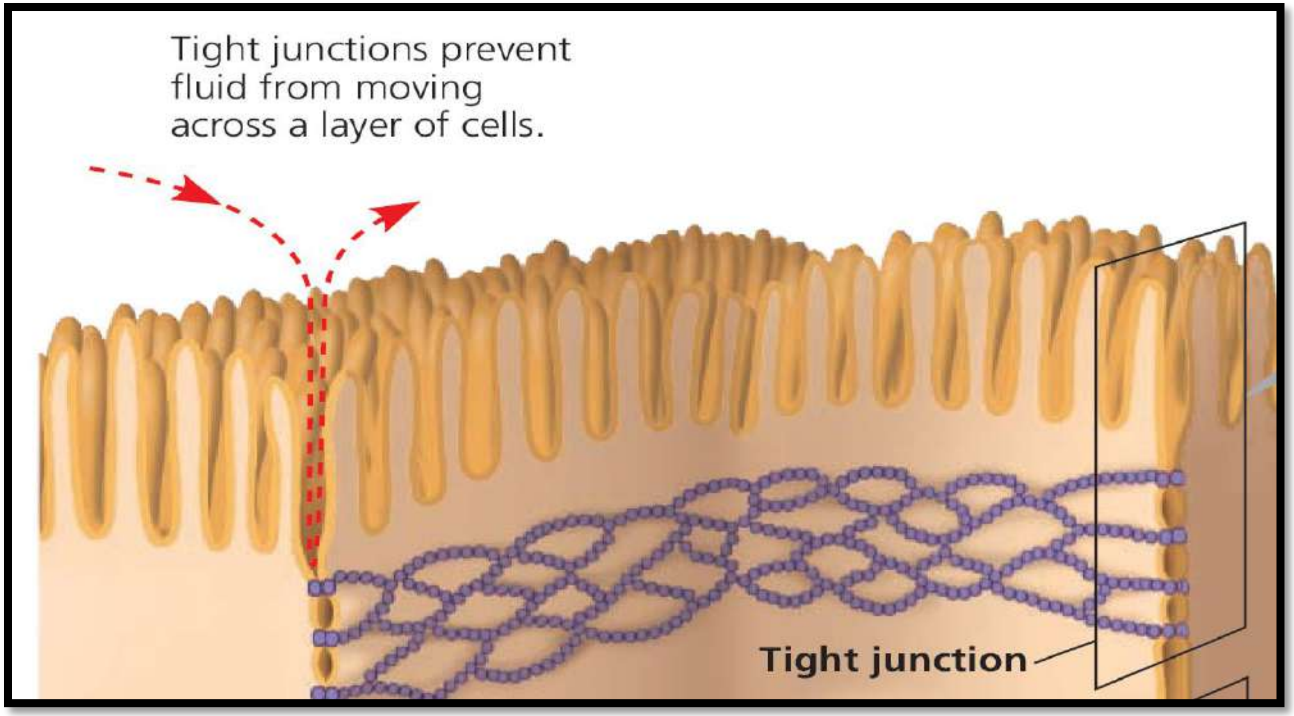
- In animals, there are three main types of **cell-cell interaction or cell junctions**:

- ***Tight junctions***
- ***Desmosomes***
- ***Gap junctions***
- All three types of cell junctions are especially **common in epithelial tissue**, which lines the external and internal surfaces of the body.



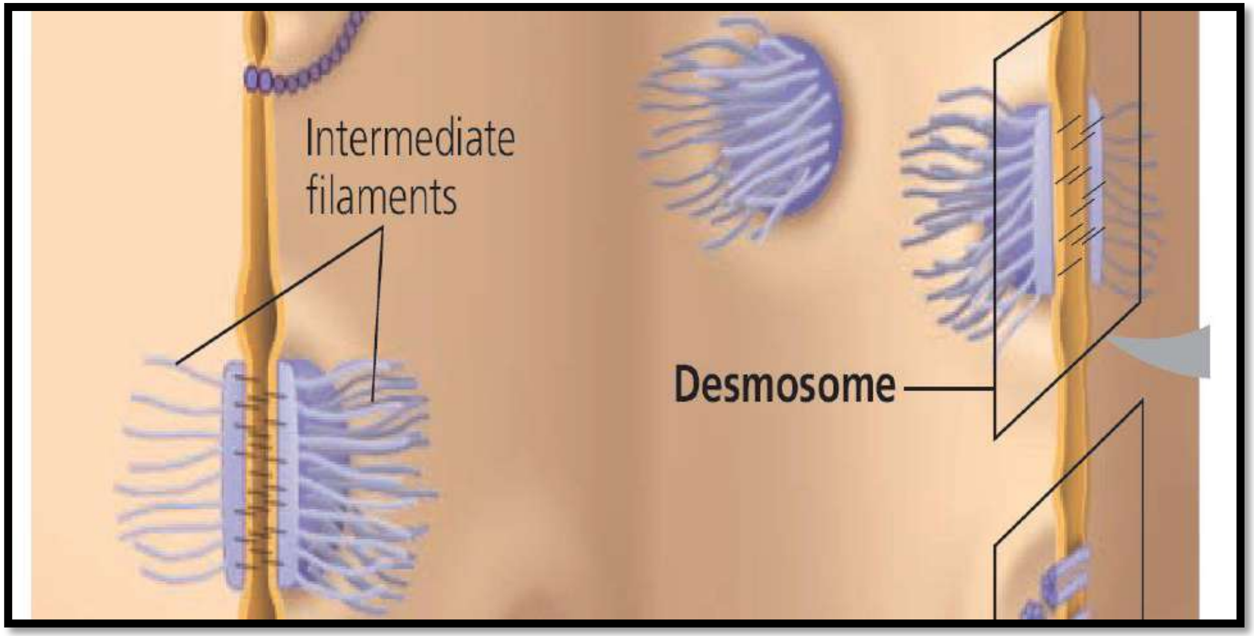
Tight junctions

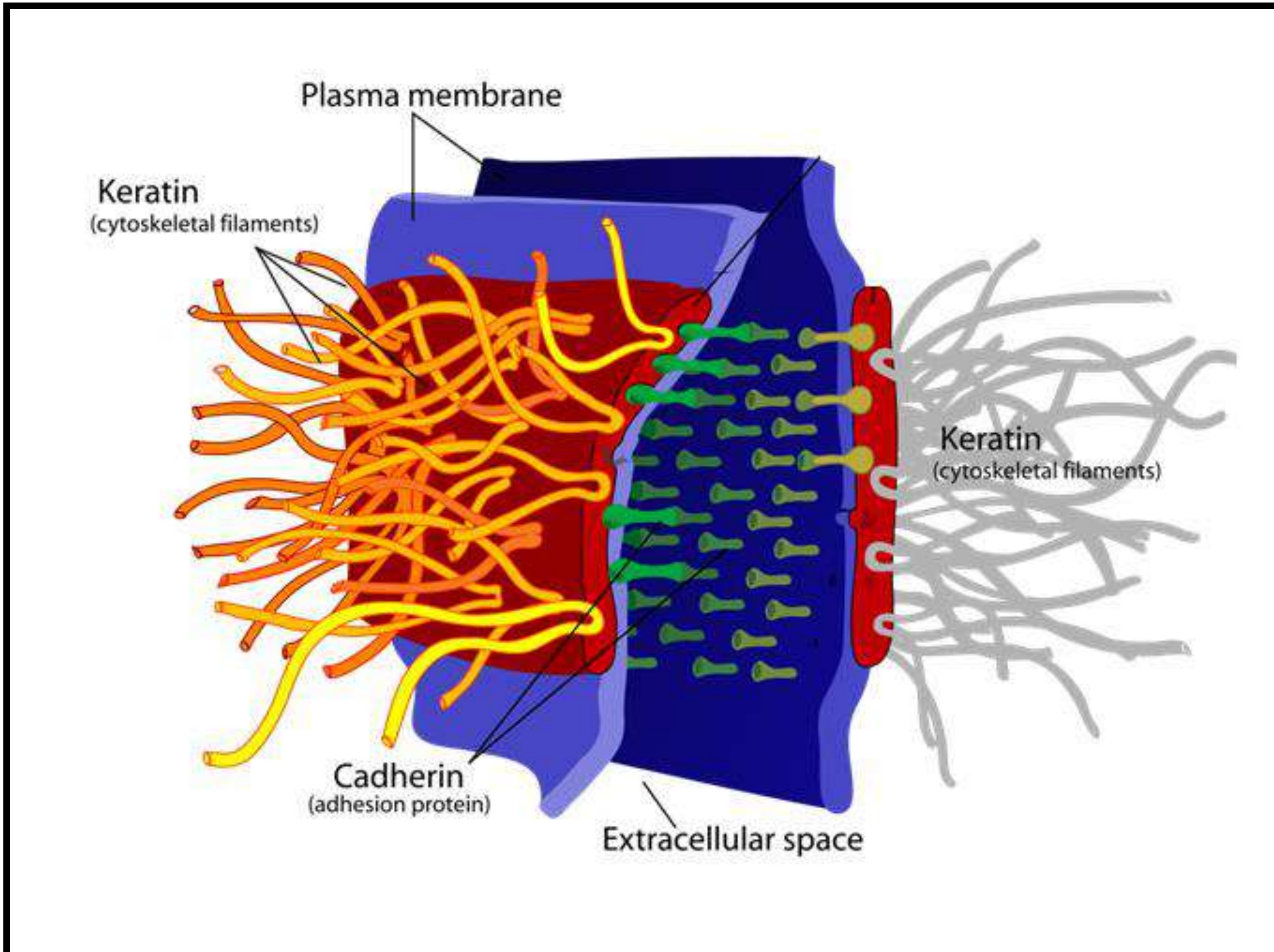
- At **tight junctions**, the plasma membranes of neighboring cells are **very tightly pressed or squeezed** against each other, bound together by specific proteins thus forming **continuous seals** or barrier around animal cells that **prevents leakage** of extracellular fluid across a layer of epithelial cells.
- **Tight junctions** contain proteins called **Claudins** that have the ability to **occlude or block** substances from passing between cells.
- For example, tight junctions between skin cells make us **watertight** (no water enters or passes through.) .



Desmosomes : Adhesive or anchoring junctions

- **Desmosomes are adhesive junctions or anchoring junctions** that mechanically attach the cytoskeleton of a cell to the cytoskeletons of other cells or to the extracellular matrix. These junctions are **found in tissues subject to mechanical stress**, such as muscle and skin epithelium.
- Desmosomes are a **cadherin-based junction.** Cadherin is a **transmembrane** protein with an extracellular domain that can interact with the extracellular domain of a cadherin in an adjacent cell to join the cells together.
- Desmosomes function like **rivets, fastening** cells together into strong sheets.
- **Intermediate filaments (**strong **keratin** proteins) **anchor** desmosomes in the cytoplasm.

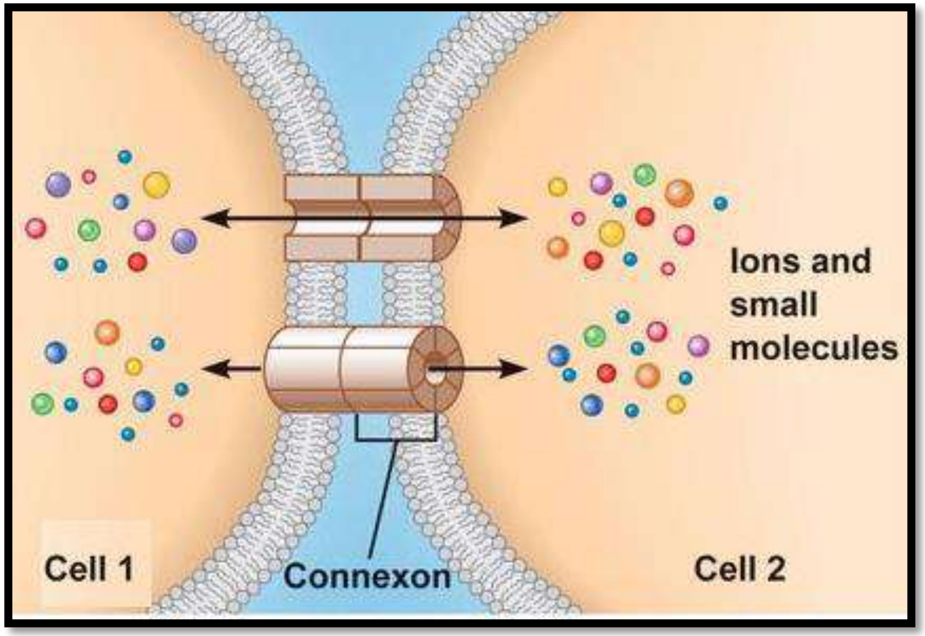


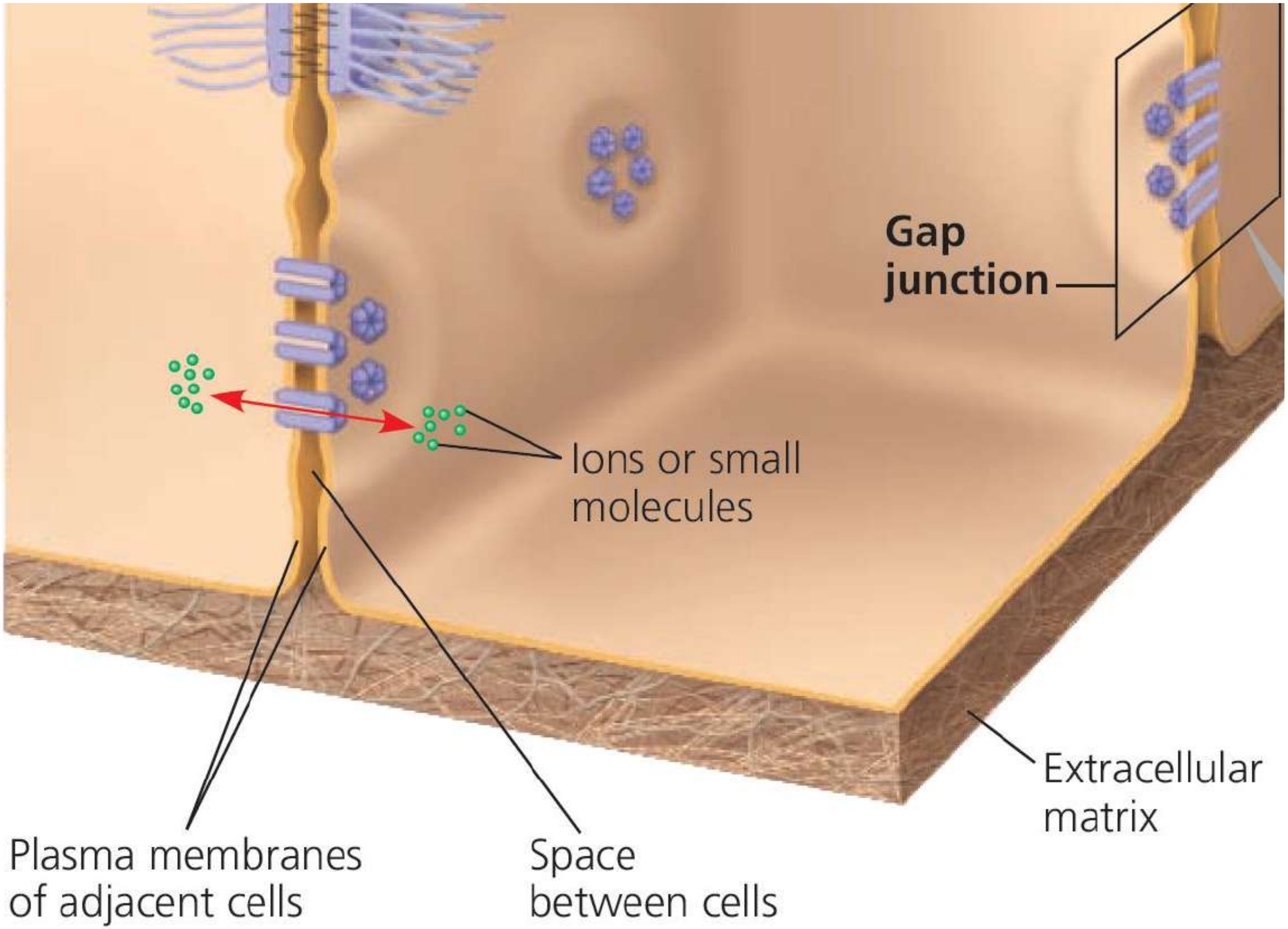

Plasma membrane
Keratin
(cytoskeletal filaments)
Keratin
(cytoskeletal filaments)
Cadherin
(adhesion protein)
Extracellular space

Gap junctions: a communicating junctions

- **Gap junctions** (also called *communicating junctions*) provide **cytoplasmic channels** from one animal cell to an adjacent cell.
- Gap junctions are formed by complexes of **six identical transmembrane proteins** extending from the membranes of the two cells and **arranged in a circle** creating a **channel through** the plasma membrane where ions, sugars, amino acids, and other small molecules may pass, **but not proteins**.
- Gap junctions are necessary for communication between cells in many types of tissues, such as heart muscle, and in animal embryos.

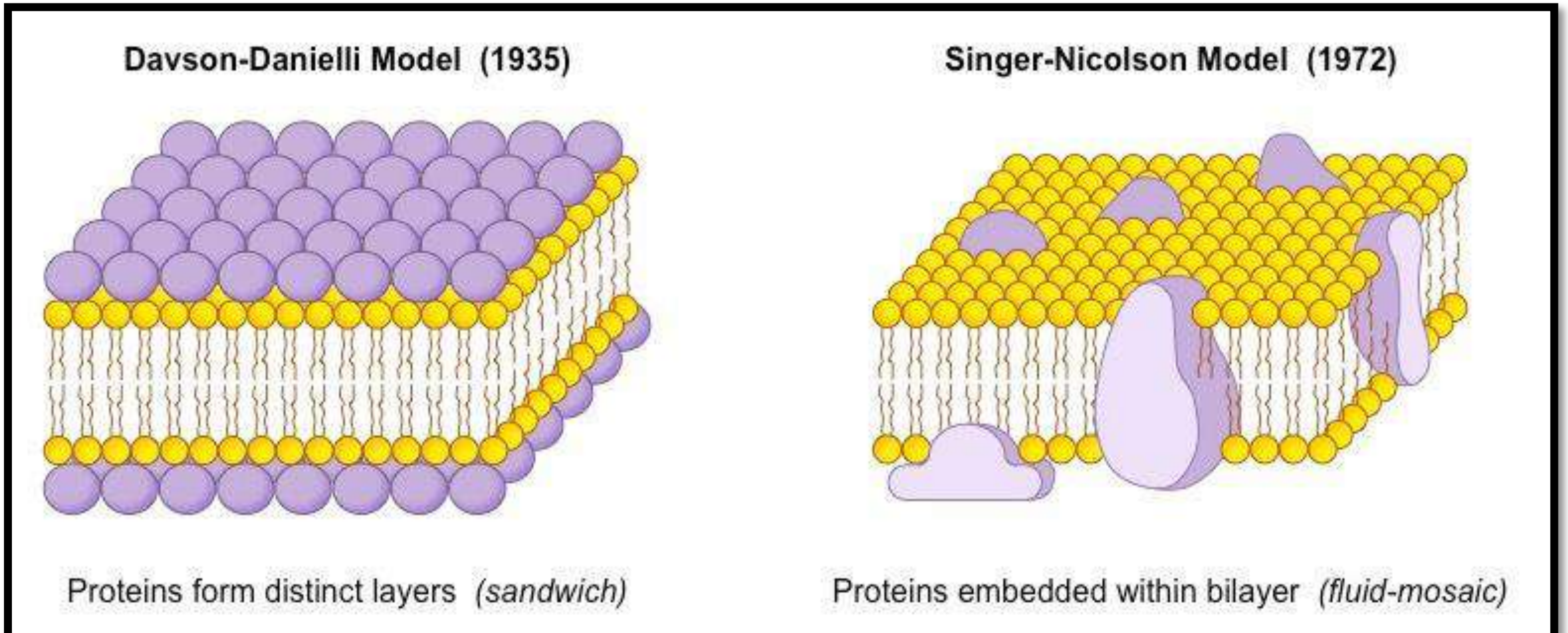
Gap junction channels are **dynamic structures** that can **open or close** (gating) in response to a variety of factors, including $Ca2^{+}$ and H^{+} ions.
This **gating serves** at least one important function. When a **cell is damaged**, its plasma membrane often becomes leaky. Ions in high concentrations outside the cell, such as Ca2+, flow into the damaged cell and **close its gap junction channels**. This isolates the cell and prevents the damage from spreading




Gap
junction
Ions or small
molecules
Extracellular
matrix
Plasma membranes
of adjacent cells
Space
between cells

The 1935 Davson–Danielli model: Sandwich model

- The **first model** that attempted to describe the position of membrane proteins within the lipid bilayer was proposed by **Davson and Danielli in 1935**: (**The sandwich model)**
- The sandwich model describes a **phospholipid bilayer that lies between two** layers of globular proteins (Sandwich as the lipid layer was sandwiched between two protein layers) or vis versa two layers of protein flanked a central phospholipid bilayer.
- Davson–Danielli Sandwich model was the believed and predominated model **until 1972 when Singer and Nicolson** described the correct cell membrane structural model: **The fluid mosaic model.**

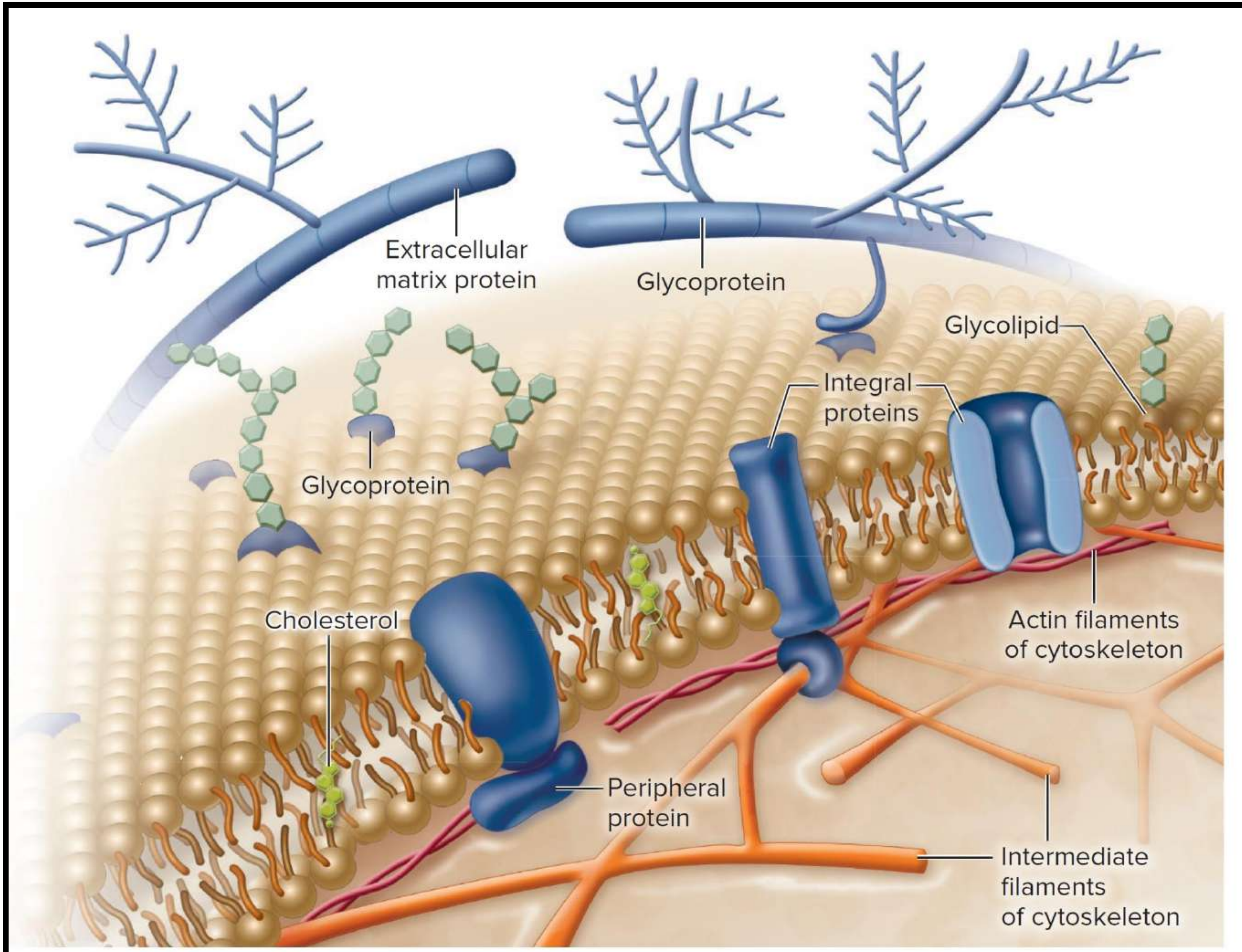


Cell membrane: The fluid mosaic model

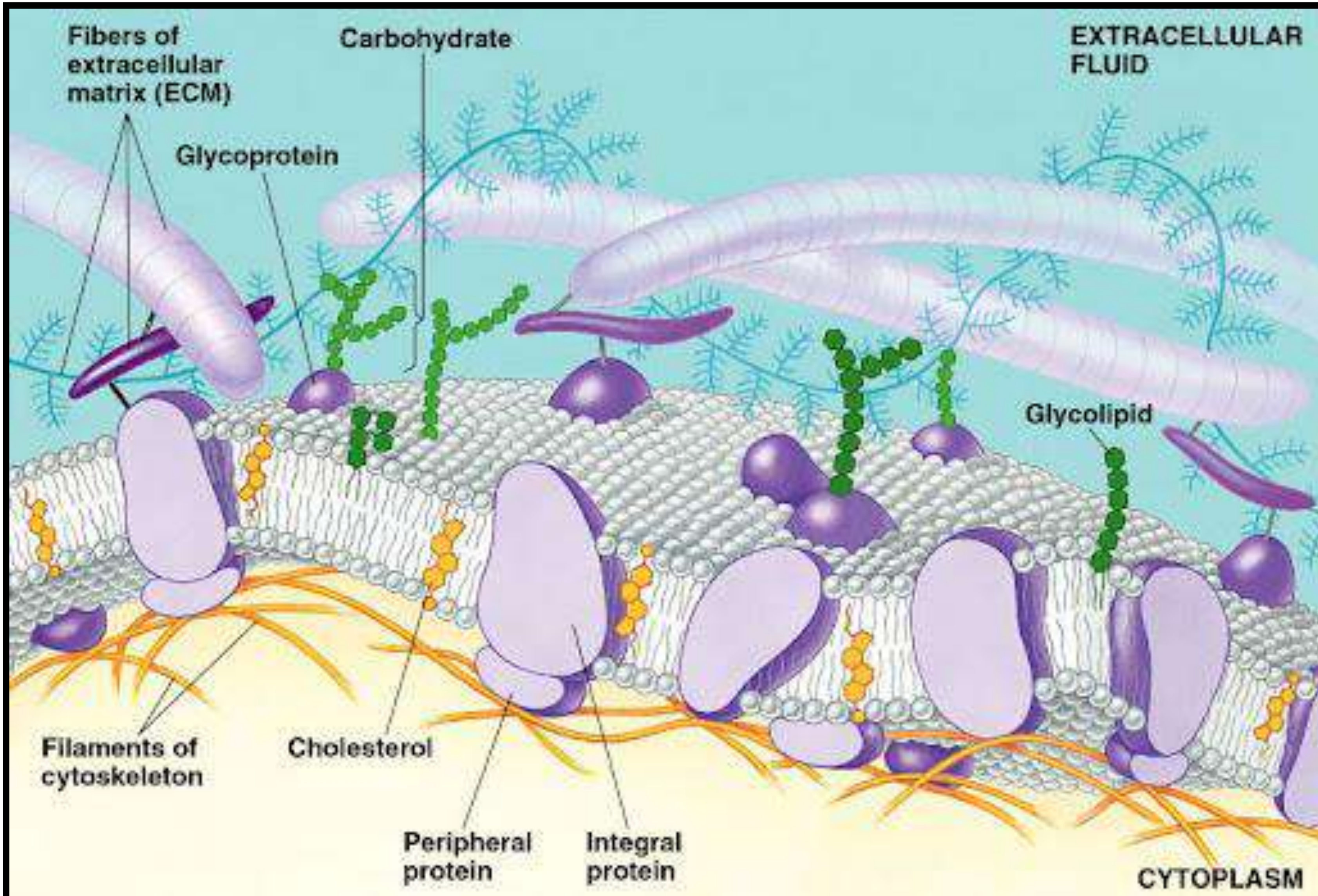
- Cellular membranes are **fluid mosaics of lipids and proteins**
- **Lipids** and **proteins** are the major components of membranes, although **carbohydrates** are also important.
- The most abundant lipids in most membranes are **phospholipids** (an amphipathic molecule).
- Most membrane **proteins are amphipathic**.
- Singer and Nicolson proposed that the **globular proteins** are inserted into the **phospholipids** bilayer, with their **nonpolar segments** in contact with the **nonpolar interior** of the bilayer and their **polar portions** protruding out from the membrane surface, thus maximizes contact of hydrophilic regions of a protein with water in the cytosol and extracellular fluid
- Structure of cell membrane revealed two categories of membrane proteins based on their degree of association with the membrane.
- **Integral proteins** are embedded in the membrane,
- **Peripheral proteins** are associated with the surface of the membrane

Cellular membranes consist of four component groups

- Eukaryotic membranes share the same fundamental architecture and in animals are assembled from **four components**:
- **1. Phospholipid bilayer.**
- **2. Proteins (peripheral and integral)**
  - Peripheral proteins: are usually loosely bound to the membrane surface and attached to the hydrophilic part of the Phospholipid molecules or to other integral proteins
  - Integral proteins (partially embedded and totally embedded or transmembrane proteins)
- Many integral membrane proteins are **not fixed in position**. They can move about, just as the phospholipid molecules do.
- **3. Cholesterol**
- Animal cell membranes contain cholesterol. Plant cells have other sterols, but little or no cholesterol.
- **4. Carbohydrates**
- Carbohydrates of the membrane are the sugar molecules added by ER and/or Glogi apparatus to membrane proteins and lipids, converting them into **glycoproteins** and **glycolipids**. Different cell types exhibit different varieties of these glycoproteins and glycolipids on their surfaces, which act as cell identity markers (**Cell-surface markers**).



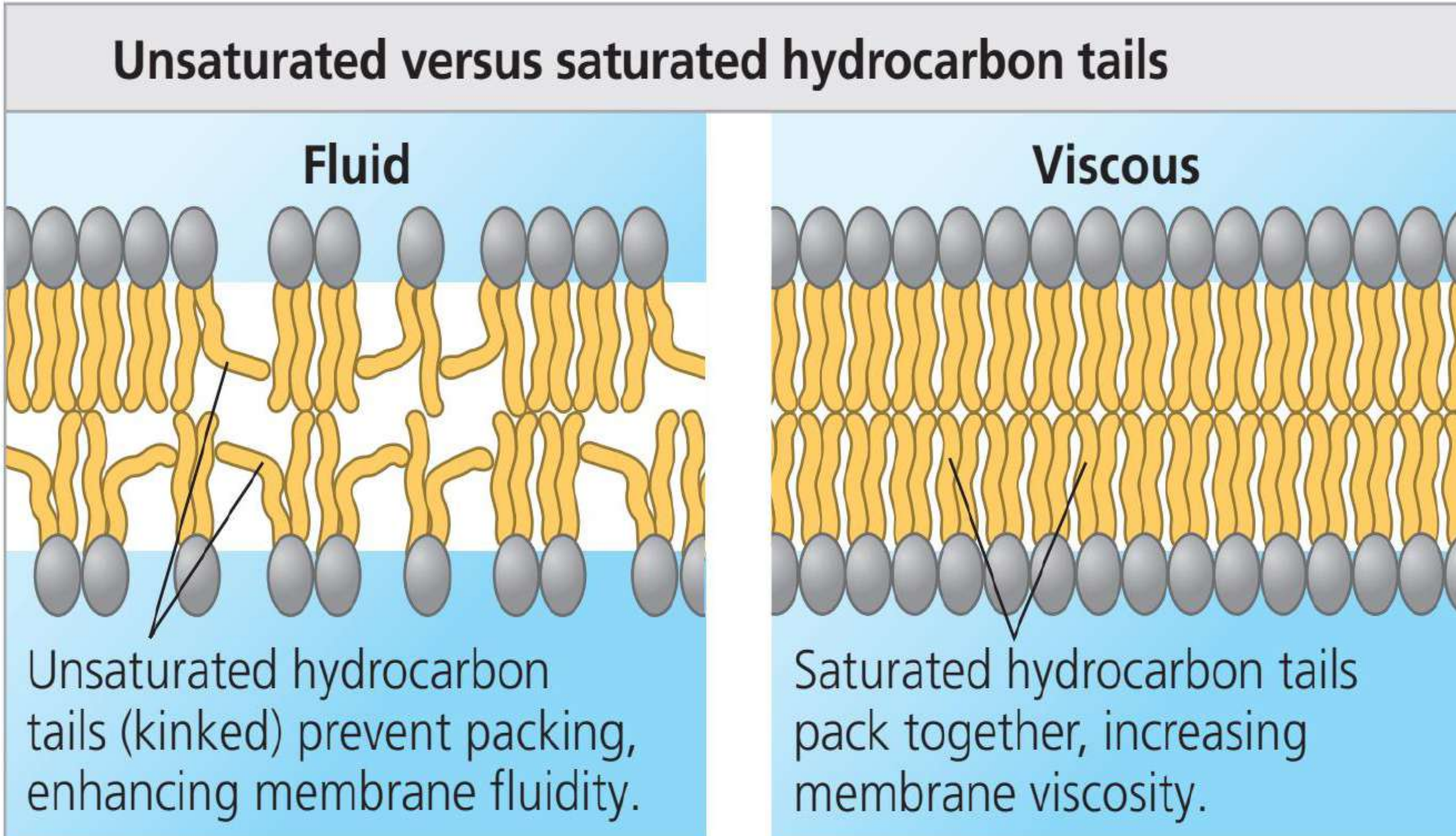
Extracellular
matrix protein
Glycoprotein
Glycolipid
Integral
proteins
Glycoprotein
Cholesterol
Actin filaments
of cytoskeleton
Peripheral
protein
Intermediate
filaments
of cytoskeleton


Fibers of extracellular matrix (ECM)
Carbohydrate
EXTRACELLULAR FLUID
Glycoprotein
Glycolipid
Filaments of cytoskeleton
Cholesterol
Peripheral protein
Integral protein
CYTOPLASM

The Fluidity of Membranes: phospholipids

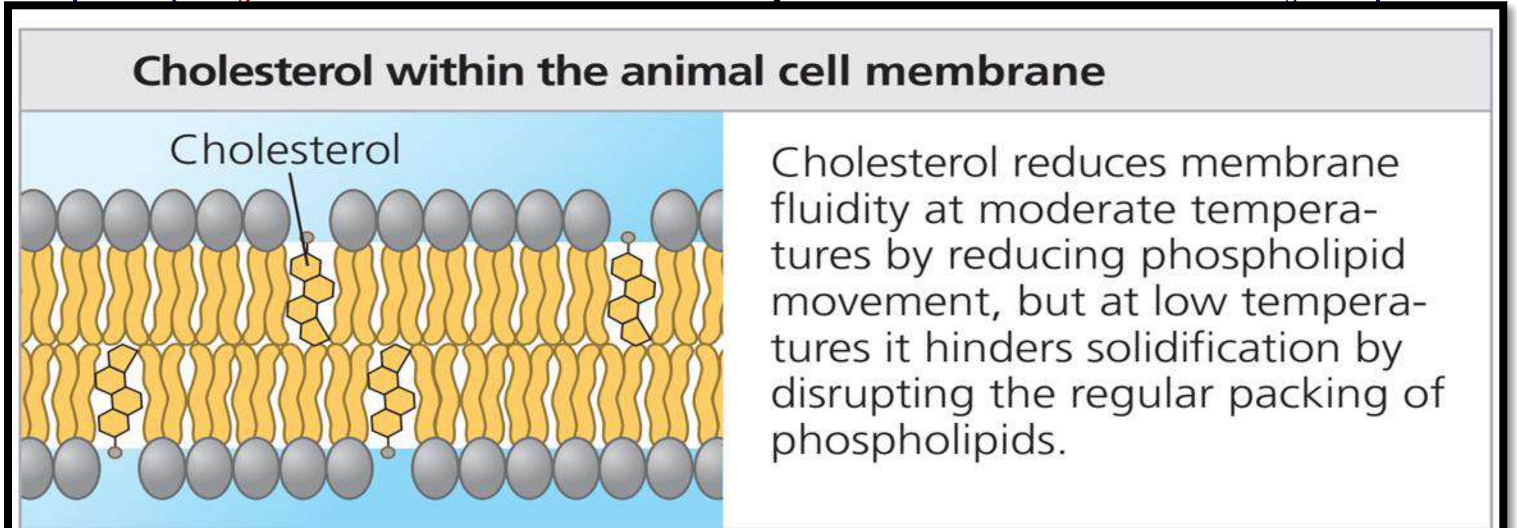
- Membranes are not static sheets of molecules locked rigidly in place. A membrane is held together mainly by **hydrophobic interactions**, which are much **weaker than** covalent bonds
- Most of the **lipids and some proteins** can shift about sideways—that is, in the plane of the membrane. **Very rarely**, also, a **lipid may flip-flop across** the membrane, switching from one phospholipid layer to the other.
- Proteins are much larger than lipids and **move more slowly**, when they do move.
- **Many membrane proteins** seem to be held immobile by their attachment to the cytoskeleton or to the extracellular matrix.
- A membrane remains fluid as temperature decreases until the **phospholipids** settle into a **closely packed arrangement** and the membrane **solidifies**.
- The **temperature** at which a membrane **solidifies** depends on the types of lipids it is made of.
- As the temperature decreases, the membrane remains fluid to a **lower temperature** if it is rich **in unsaturated phospholipids**. Because of kinks in the tails where double bonds are located, unsaturated hydrocarbon tails cannot pack together as closely as saturated hydrocarbon tails, making the membrane more fluid

Factors that affect membrane fluidity



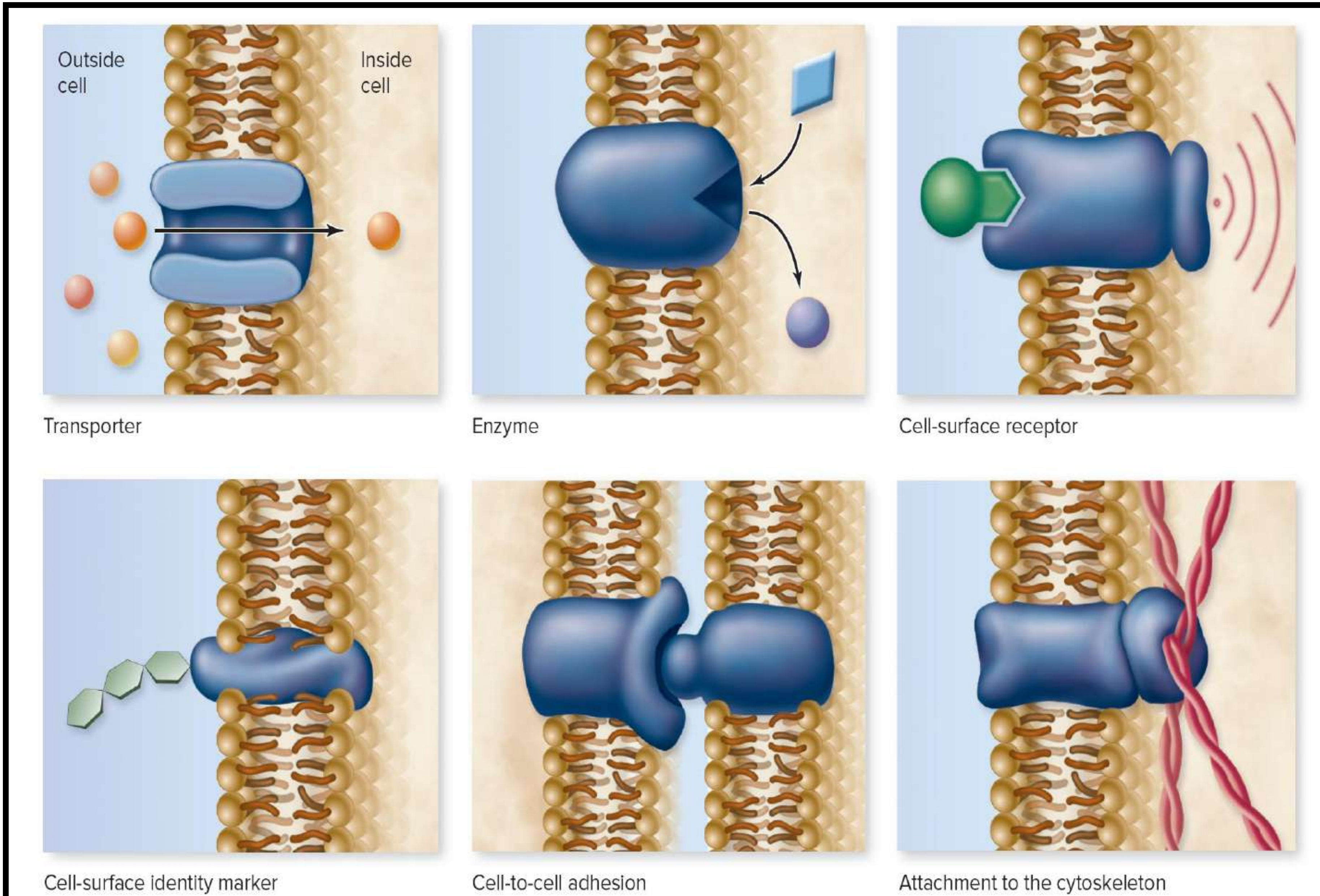
The Fluidity of Membranes: Cholesterol

- **Cholesterol**, which is **stuck between phospholipid** molecules in the plasma membranes of animal cells, has **different effects** on membrane fluidity at different temperatures.
- At relatively **high temperatures—at** 37°C, the body temperature of humans, for example—cholesterol makes the **membrane less fluid** by restricting phospholipid movement.
- However, because **cholesterol also hinders** the close packing of phospholipids, it **prevents** the membrane to **solidify at low temperatures** . Thus, cholesterol can be thought of as a "fluidity buffer" for the membrane, resisting changes in membrane fluidity that can be caused by changes in temperature.
- Compared to animals, **plants have very low levels of cholesterol**; rather, related steroid lipids (**Phytosterols or Plant sterols**) buffer membrane fluidity in plant cells



Membrane Proteins: Multifunctional Components

- **1. Transporters (Transport) .** Membranes are very selective, allowing only certain solutes to enter or leave the cell, through either channels or carriers composed of proteins.
- **2. Enzymes.** Cells carry out many chemical reactions on the interior surface of the plasma membrane, using protein enzymes attached to the membrane.
- **3.Cell-surface receptors for Signal transduction.** Membranes are sensitive to chemical messages, which are detected by receptor proteins on their surfaces.
- **4. Cell-surface identity markers.** Membranes carry cell-surface markers that identify them to other cells. Most cell types carry their own ID tags, specific combinations of cell-surface proteins and protein complexes such as glycoproteins that are characteristic of that cell type.
- **5. Cell-to-cell adhesion proteins.** Cells use specific proteins to glue themselves to one another. Some act by forming temporary interactions, and others form a more permanent bond.
- **6. Attachments to the cytoskeleton and to ECM.** Surface proteins that interact with other cells are often anchored to the cytoskeleton by linking proteins.


Outside cell
Inside cell
Transporter
Enzyme
Cell-surface receptor
Cell-surface identity marker
Cell-to-cell adhesion
Attachment to the cytoskeleton

حركة المرور عبر الغشاء

Traffic across membrane

- All cells obtain the molecules and ions they need from their surrounding extracellular fluid. تحصل جميع الخلايا على الجزيئات والأيونات التي تحتاجها من السائل خارج الخلايا المحيط بها
- There is an **continuous traffic of molecules and ions** in and out of the cell through its plasma membrane e.g: glucose, Na^+, Ca^{2+} هناك حركة مستمرة للجزيئات والأيونات داخل وخارج الخلية من خلال غشاءها البلازمي مثل: الجلوكوز،
- In eukaryotic cells, there is also **transport in and out of membrane-bounded** intracellular compartments such as the nucleus, endoplasmic reticulum, and mitochondria. e.g : proteins, mRNA, Ca^{2+}, ATP.

في الخلايا حقيقية النواة، هناك أيضًا نقل داخل وخارج المقصورات داخل الخلايا المحاطة بالغشاء مثل النواة والشبكة الإندوبلازمية والميتوكوندريا. على سبيل المثال: البروتينات، mRNA، Ca2+، ATP

- **Two problems are to be considered in traffic across membranes**

هناك مشكلتان يجب مراعاتهما في حركة المرور عبر الأغشية

1-Relative concentrations

التركيزات النسبية

- Normally molecules and ions move spontaneously down their concentration gradient or **downhill** (from a region of higher to a region of lower concentration)

تتحرك الجزيئات والأيونات عادةً بشكل تلقائي إلى أسفل منحدر تركيزها أو إلى أسفل (من منطقة ذات تركيز أعلى إلى منطقة ذات تركيز أقل)

- Molecules and ions can be moved against their concentration gradient or **uphill**, but this process, requires the **expenditure of energy (usually from ATP).**

يمكن تحريك الجزيئات والأيونات ضد تدرج تركيزها أو صعودًا، ولكن هذه العملية تتطلب إنفاق الطاقة (عادةً من ATP)

***2-Lipid bilayers are impermeable to most essential molecules and ions*.**

الطبقات الدهنية الثنائية غير منفذة لمعظم الجزيئات والأيونات الأساسية

- The lipid bilayer is **permeable to water molecules and a few other small, uncharged**, molecules like oxygen (O_2) and carbon dioxide (CO_2). These move freely in and out of the cell.

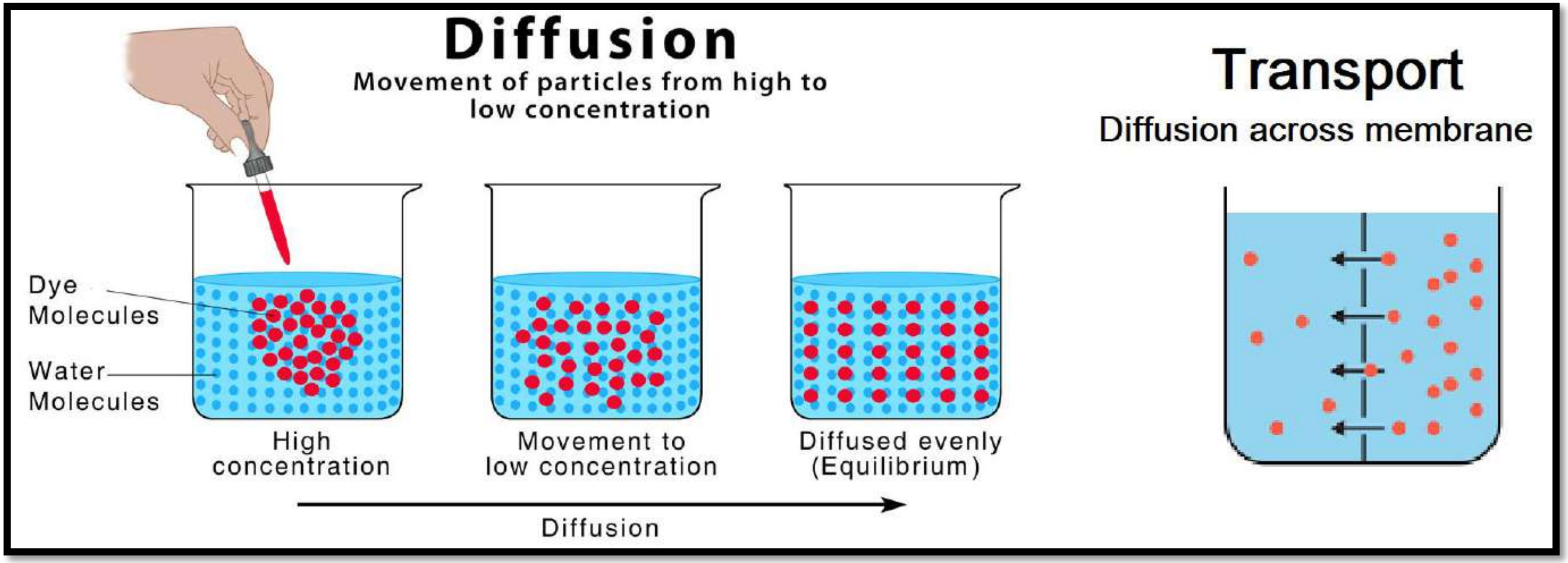
الطبقة الدهنية الثنائية نفاذة لجزيئات الماء وبعض الجزيئات الصغيرة الأخرى غير المشحونة مثل الأكسجين (O2) وثاني أكسيد الكربون (CO2). تتحرك هذه الجزيئات بحرية داخل وخارج الخلية.

- Lipid bilayers are **impermeable** to: ions such as K+, Na+, Ca2+ Cl-, HCO3- , small hydrophilic molecules like glucose and macromolecules like proteins and RNA.

الطبقات الدهنية الثنائية غير منفذة لـ: الأيونات مثل K+ وNa+ وCa2+ وCl- وHCO3- والجزيئات الصغيرة المحبة للماء مثل الجلوكوز والجزيئات الكبيرة مثل البروتينات والحمض النووي الريبي

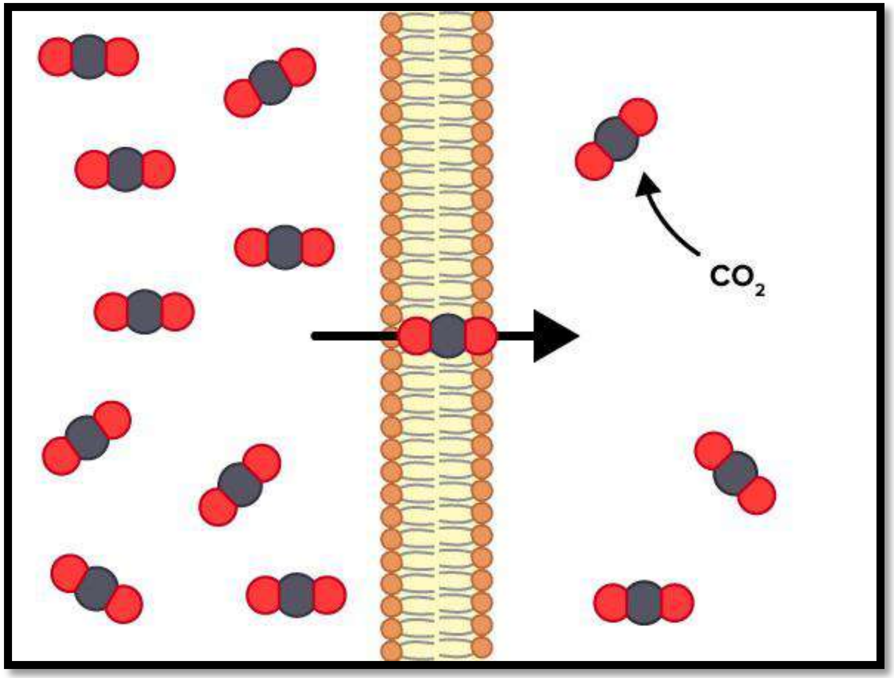
Diffusion vs transport

- **Diffusion** is the random movement of molecules down their concentration gradient to spread out into the available space (only its own, without regard to other molecules). The direction of the diffused molecule is **unaffected** by the concentration gradients of **other substances.**
- **Diffusion is spontaneous** because it decreases the amount of energy in the system and increases disorder or **increases the entropy.**
- Diffusion is **passive process** because the cell does not use energy.
- When the diffused molecules pass or move **across membrane** this is called transport



Passive transport

- **Passive transport** is movement of a substance down their concentration gradient (**downhill**) across a biological membrane with **no use of energy**.
- The concentration gradient itself represents **potential energy and driving force** for passive transport, assuming the membrane is permeable for such substance or molecule.
- Biological membranes are **selectively permeable** and therefore have different effects on the rates of transport of various molecules.

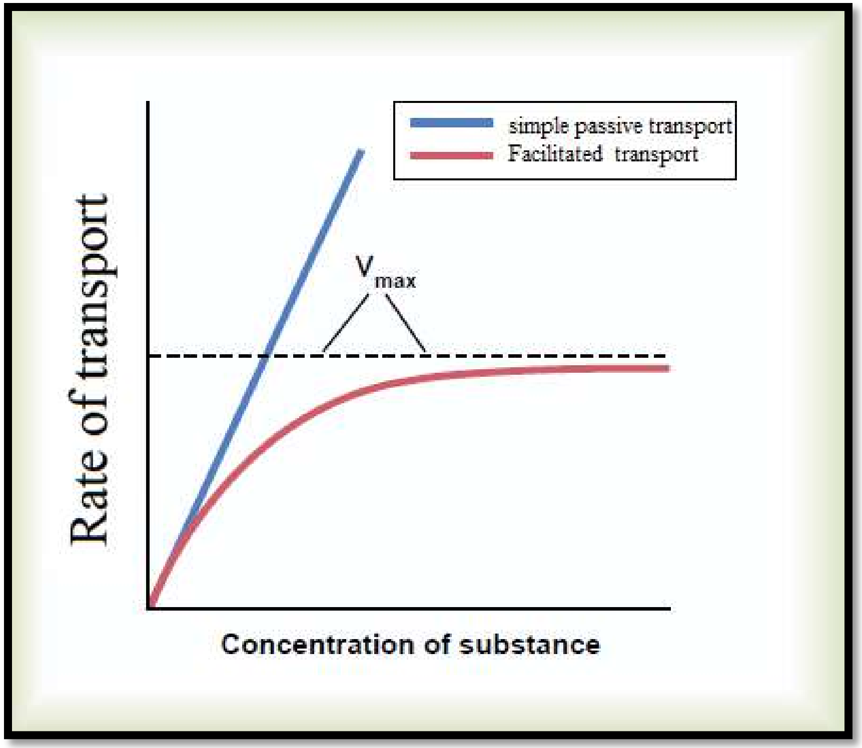


Facilitated transport: Passive Transport Aided by Proteins

- Many polar molecules and ions blocked by the lipid bilayer of the membrane **can pass passively (downhill)** with the help of transport proteins that span the membrane. This phenomenon is called **facilitated transport**.
- Most transport proteins are **very specific**: they transport some substances but not others.
- Transport proteins are either **channel proteins** or **carrier proteins**.
- **Channel proteins** simply provide hydrophilic **corridors /passageway** that allow specific molecules or ions to cross the membrane e.g water molecules or small ions .
- **Aquaporins** are specialized channel proteins that facilitate the massive levels of movement of **water (osmosis**) that occur in plant cells and in animal cells
- **Carrier proteins**, e.g. glucose transporter, seem to **undergo a distinctive change in shape** triggered by the binding and release of the transported molecule. Such changes somehow translocate the solute-binding site across the membrane**. S**ugars and amino acids are also transported by carrier proteins
- **Facilitated transport** via channel protein or carrier proteins is a type of passive transport that result in the net movement of a substance **down its concentration gradient (downhill)**.

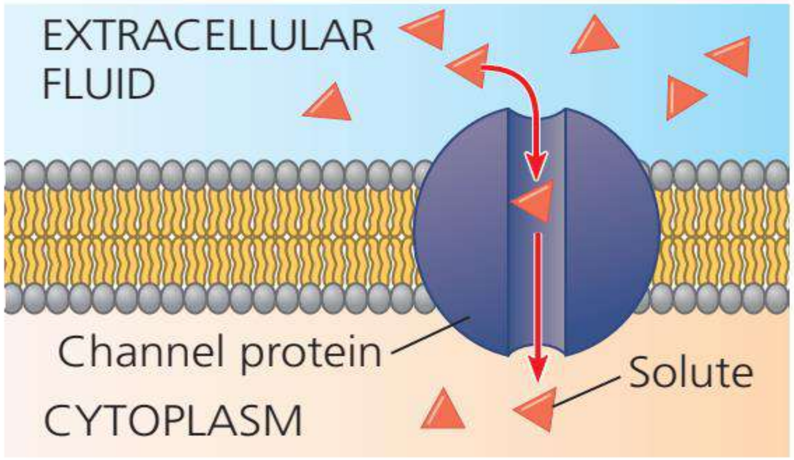
Saturation of carrier proteins

- Facilitated transport through carrier protein is a form of passive transport and therefore **requires a concentration difference** across the membrane.
- Carrier protein must bind to the molecule they transport, so the **relationship** between **concentration and rate of transport differs** from that due to simple passive transport.
- As concentration increases, transport by simple passive transport shows a **linear increase** in rate of transport.
- But with Facilitated transport through carrier protein, as concentration increase more of the carriers are bound to the transported molecule. At high enough concentrations all carriers will **be occupied**, and the rate of transport will be **constant**. This means that the carrier exhibits ***saturation***.

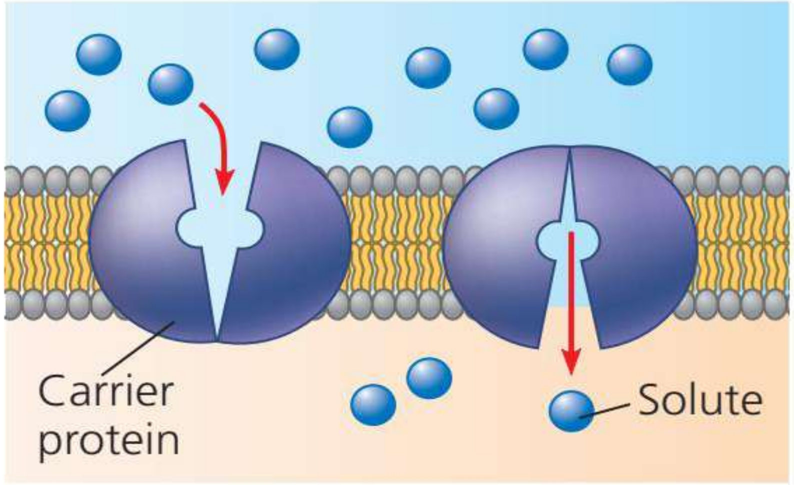


Two types of transport proteins that carry out facilitated transport

A channel protein has a channel through which water molecules or a specific solute can pass.



A carrier protein alternates between two shapes, moving a solute across the membrane during the shape change.



In both cases (channel protein or carrier protein), the protein can transport the **solute in either direction**, but the net movement is down the concentration gradient of the solute.

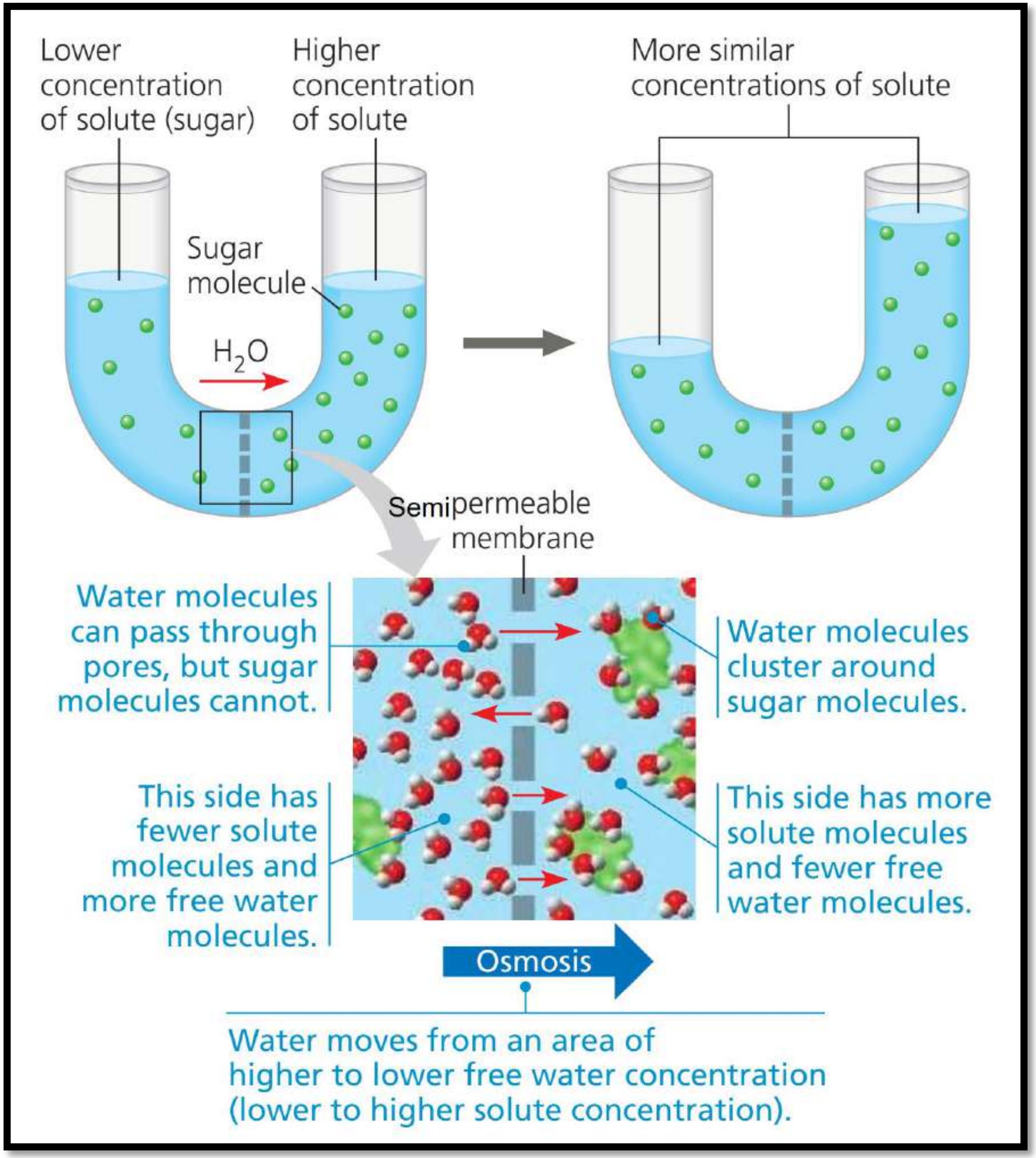
Gated Channels

- Many ion channels (Channel proteins that transport ions) function as **gated channels**, which open or close in response to a stimulus (**electrical, chemical or mechanical**)

- **Electrically gated ion channels**
- e.g. a potassium ion channels of a nerve cell is an electrically gated ion channel that opens in response to an electrical stimulus, allowing a stream of potassium ions to leave the cell.
- **Chemically gated ion channels**
- Chemically (ligand) gated ion channels like Na^+ channels that opens in response to chemical ligand (neurotransmitter acetylcholine) binding allowing a stream of Na^+ ions move across the membrane.
- **Mechanically gated ion channels**:
- e.g K+ channels in stereocilia, the movement of cilia opens potassium gated channels that starts further steps in generating action potential.

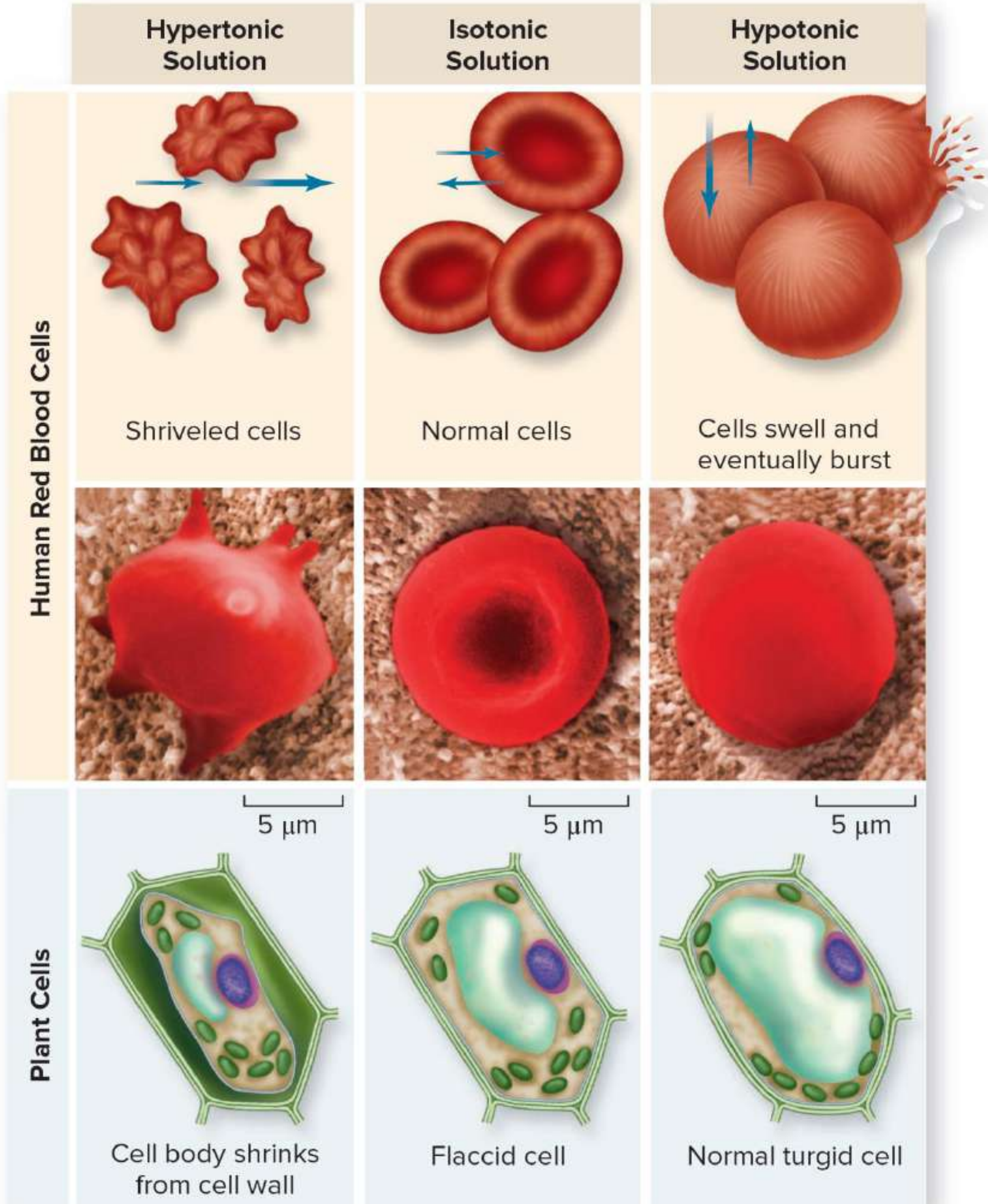
Osmosis

- **Osmosis** is **the movement of water** across **semipermeable** membranes
- In aqueous solution (water + dissolved solutes) both water and solutes tend to diffuse downhill (down their concentration gradients).
- When two regions are separated by a membrane, what happens depends on whether the solutes can pass freely through that membrane (selective permeability). Most solutes, including ions and sugars, are **unable to cross the lipid bilayer**. So, the concentration gradient of these solutes can lead to the **movement of water**.
- When a **semipermeable** membrane (**allows water only**) separates two solutions with different concentrations of solutes, the concentrations of free water molecules on the two sides of the membrane also differ.
- The **side with higher solute** concentration has **tied up more wa**ter molecules in hydration shells and thus **has fewer free water** molecules.
- As a consequence of this difference, **free water molecules move down** their concentration gradient, **toward the higher solute** concentration.
- This **net movement of water across** a semipermeable membrane toward a higher solute concentration is called **osmosis**


Lower concentration of solute (sugar)
Higher concentration of solute
More similar concentrations of solute
Sugar molecule
H_2O
Semipermeable membrane
Water molecules can pass through pores, but sugar molecules cannot.
Water molecules cluster around sugar molecules.
This side has fewer solute molecules and more free water molecules.
This side has more solute molecules and fewer free water molecules.
Osmosis
Water moves from an area of higher to lower free water concentration (lower to higher solute concentration).

osmotic concentration (osmolarity/ Osmolality)

- **Osmotic concentration:** represents the concentration of *all* solutes in a solution.
- Osmolarity number of solute particles in 1 L of solvent
- Osmolality number of solute particles in 1 kg of solvent.
- If two solutions have **unequal** osmotic concentrations, the solution with the **higher** concentration is **hypertonic or hyperosmotic**, and the solution with the **lower** concentration is **hypotonic or hypoosmotic**).
- When two solutions have **the same** osmotic concentration, the solutions are **isotonic or isosmotic.**
- The direction and extent of any movement of water across the plasma membrane is determined by comparing the **osmotic strength** of the cytoplasm and the extracellular fluid.
- Water **moves out of a cell in a hypertonic solution** (that is, the cytoplasm of the cell is hypotonic, compared with the extracellular fluid). This loss of water causes the cell to shrink.
- The **amount of water** that enters or leaves the cell depends on the difference the osmotic concentrations of the cytoplasm and the extracellular fluid. This is measured as **osmotic pressure**.
- **Osmotic strength or pressure**: is the tendency of a solution to take in a pure water by osmosis.



Hypertonic Solution
Isotonic Solution
Hypotonic Solution
Human Red Blood Cells
Shriveled cells
Normal cells
Cells swell and eventually burst
5 µm
5 µm
5 µm
Plant Cells
Cell body shrinks from cell wall
Flaccid cell
Normal turgid cell

Active transport Across Membranes

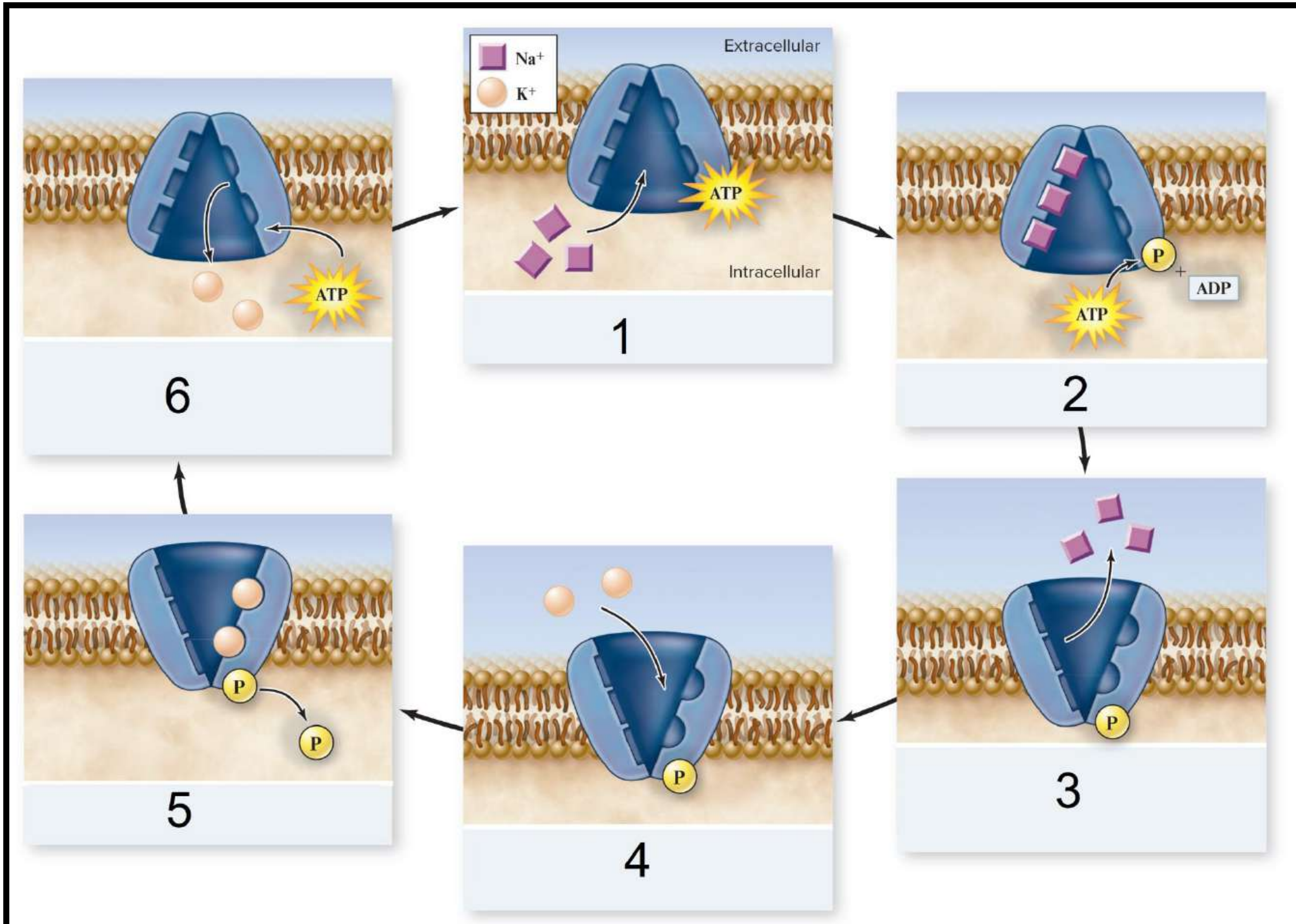
- **Active transport uses energy** (typically from ATP) to move solutes across a cell membrane against their gradients (**uphill**).
- Active transport is described as **pumping** a solute across a membrane against its gradient where the cell must expend energy. The use of **energy** from ATP in active transport may be **direct (primary active transport) or indirect (secondary active transport)**.
- Active transport involves **highly selective protein carriers, not channels**, within the membrane that bind to the transported substance, which could be an ion or a simple molecule, such as a sugar, an amino acid, or a nucleotide. If the carrier protein transport **a single type** of molecule, these carrier proteins are called **uniporters**
- If the carrier protein transport **two different molecules together**, these carrier proteins are called **symporters or antiporters**
- **Symporters** transport two molecules in **the same direction**, and
- **antiporters** transport two molecules in **opposite directions**.
- **Active transport enables a cell to take up additional molecules** of a substance that is already present in its cytoplasm in concentrations higher than in the extracellular fluid. Active transport also enables a cell to move substances out of its cytoplasm and into the extracellular fluid, despite higher external concentrations.

The Na^+ / K^+ pump works directly on ATP

- More than **one-third** of all of the **energy expended** by non-dividing an animal cell is used in the **active transport of Na+/K+ ions.**
- Most animal cells have a **low internal concentration of Na+,** relative to their surroundings, and a **high internal concentration of K+.**
- **A**nimal cells maintain these concentration differences or gradients by actively pumping three Na^+ out and two K^+ in, generating **electrochemical gradient**.
- These gradients of Na+ and K+ are important in the creation of an electrical potential across the membrane (**action potential**) , critical to the function of nerve cells.
- The **carrier protein** that transports these two ions across the cell membrane is known as the **sodium–potassium pump** (Na+/K+ pump). This carrier protein uses **ATP** to move these two ions.
- In Na+/K+ pump, the energy is used to **change the conformation** of the carrier protein, which **changes its affinity** for either Na+ ions or K+ ions.
- The Na+/K+ pump works through series of conformational changes in the transmembrane protein

The Na^+ / K^+ pump works directly on ATP

- **Step 1.** With sodium-potassium pump opens inward, one ATP molecule is attached (not phosphorylated) **three Cytoplasmic Na+ bind** with high affinity to the cytoplasmic side of the pump protein .
- **Step 2**. Binding of 3 Na+ ions **stimulates phosphorylation** (ATP is hydrolyzed to ADP, transferring a phosphate to the pump), the pump protein is now phosphorylated.
- **Step 3.** Phosphorylation leads to a **change in protein shape (opens outward),** exposing the three Na+ to the outside. In this conformation (opens outward), the pump has a **low affinity for Na+,** allowing the three bound Na+ ions to be released into the extracellular fluid (outward).
- **Step 4.** The phosphorylated protein that **opening outside has a high affinity for K+,** so after the release of the 3 Na+, two K+ bind to the extracellular side of the pump
- **Step 5.** The binding of the K+ **triggers dephosphorylation** (the release of the phosphate group), and a conformational change back to the binding pocket facing the cytoplasm (opens inward).
- **Step 6.** dephosphorylation **restores the protein's original shape**, which has a **lower affinity for K+** , so the two K+ are released inward , and again the pump returning to a state with a low affinity for K+ and **high affinity for Na+** and three new Na+ can bind to initiate another cycle.
- In every cycle, **one ATP is utilized**, three Na+ leave the cell and two K+ enter.

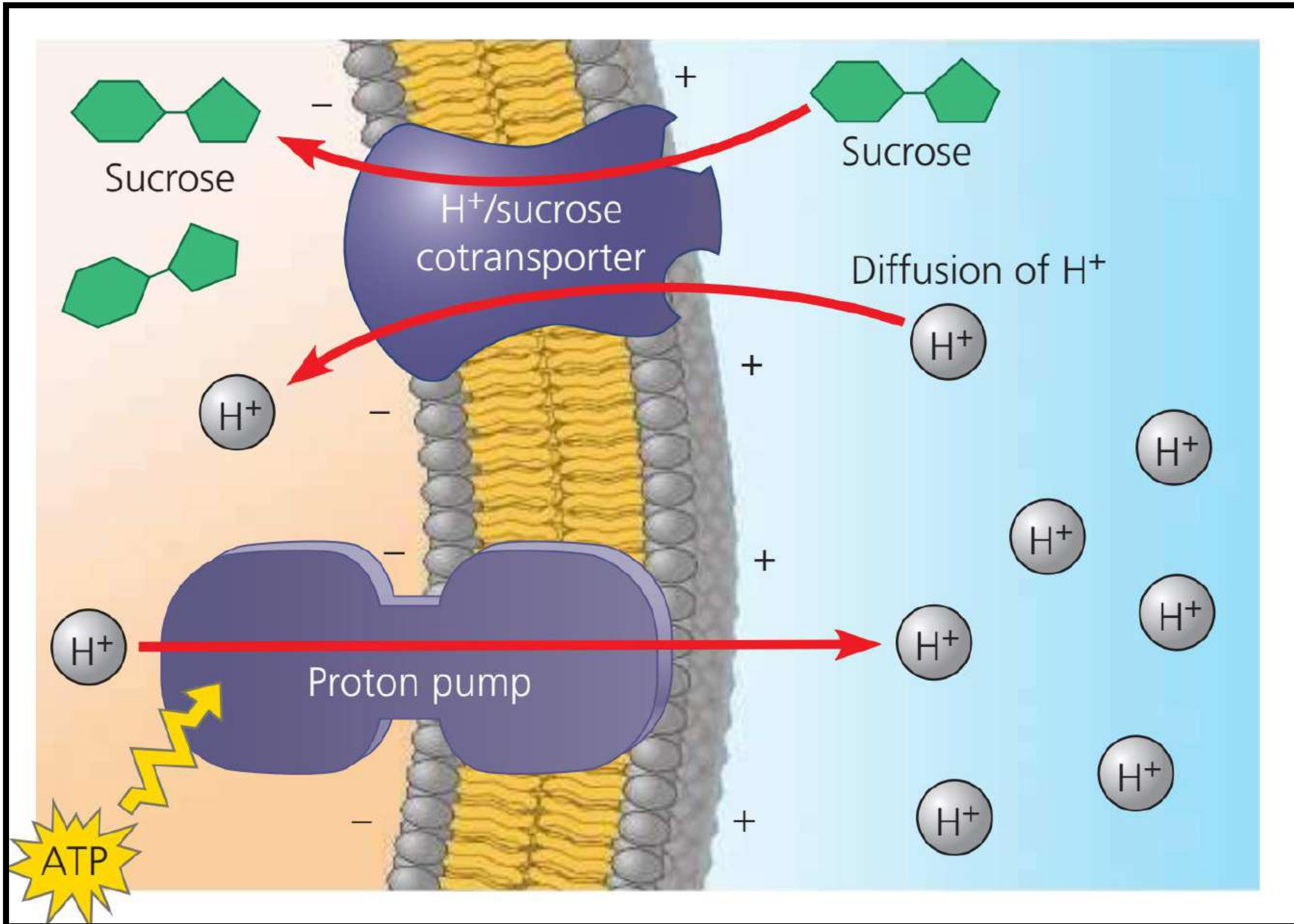


Na+
K+
Extracellular
Intracellular
ATP
1
P
ADP
ATP
2
3
P
4
P
P
5
ATP
6

Coupled transport: active transport uses ATP indirectly

- Some molecules are **moved against their concentration gradient** by using the **potential energy stored** in a gradient of a different molecule, this process, called ***coupled transport (cotransport and countertransport)***
- In a mechanism called **cotransport**, a transport protein (a **cotransporter**) can **couple** the “downhill” transport of the solute to the “uphill” transport of a second substance against its own concentration gradient.
- e.g a plant cell **uses the gradient of H+** generated by its ATP-powered proton pumps to drive an uphill transport of amino acids, sugars, and several other nutrients into the cell.
- A cotransporter couples the return of H+ to the transport of sucrose into the cell. This protein can t**ranslocate sucrose into the cell against its concentration gradient,** but only if the sucrose molecule travels in the company of an H+.(H+/sucrose cotransport)

Cotransport: Plant H+/sucrose cotransport



النقل المشترك والنقل المضاد

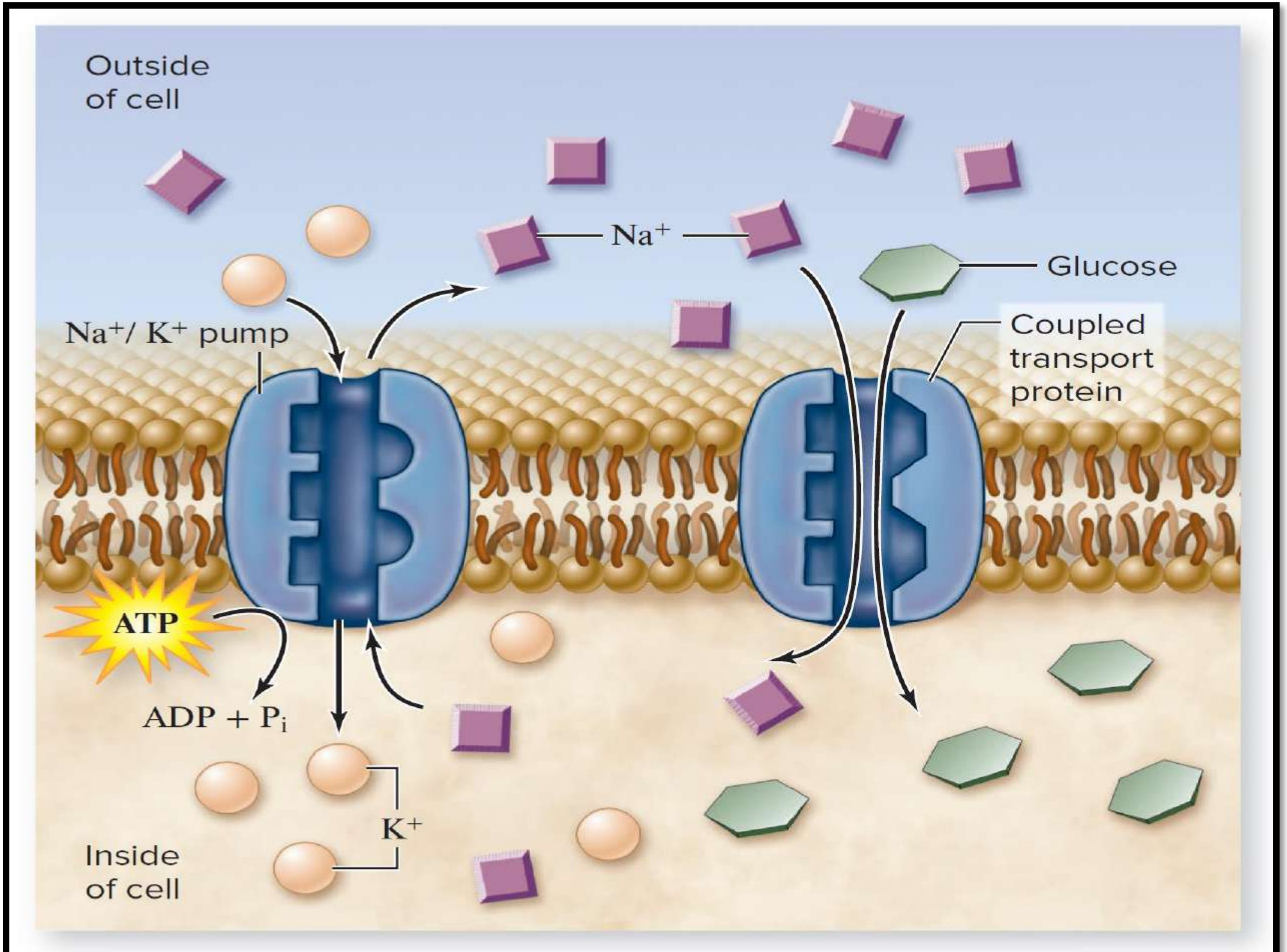
Cotransport and countertransport

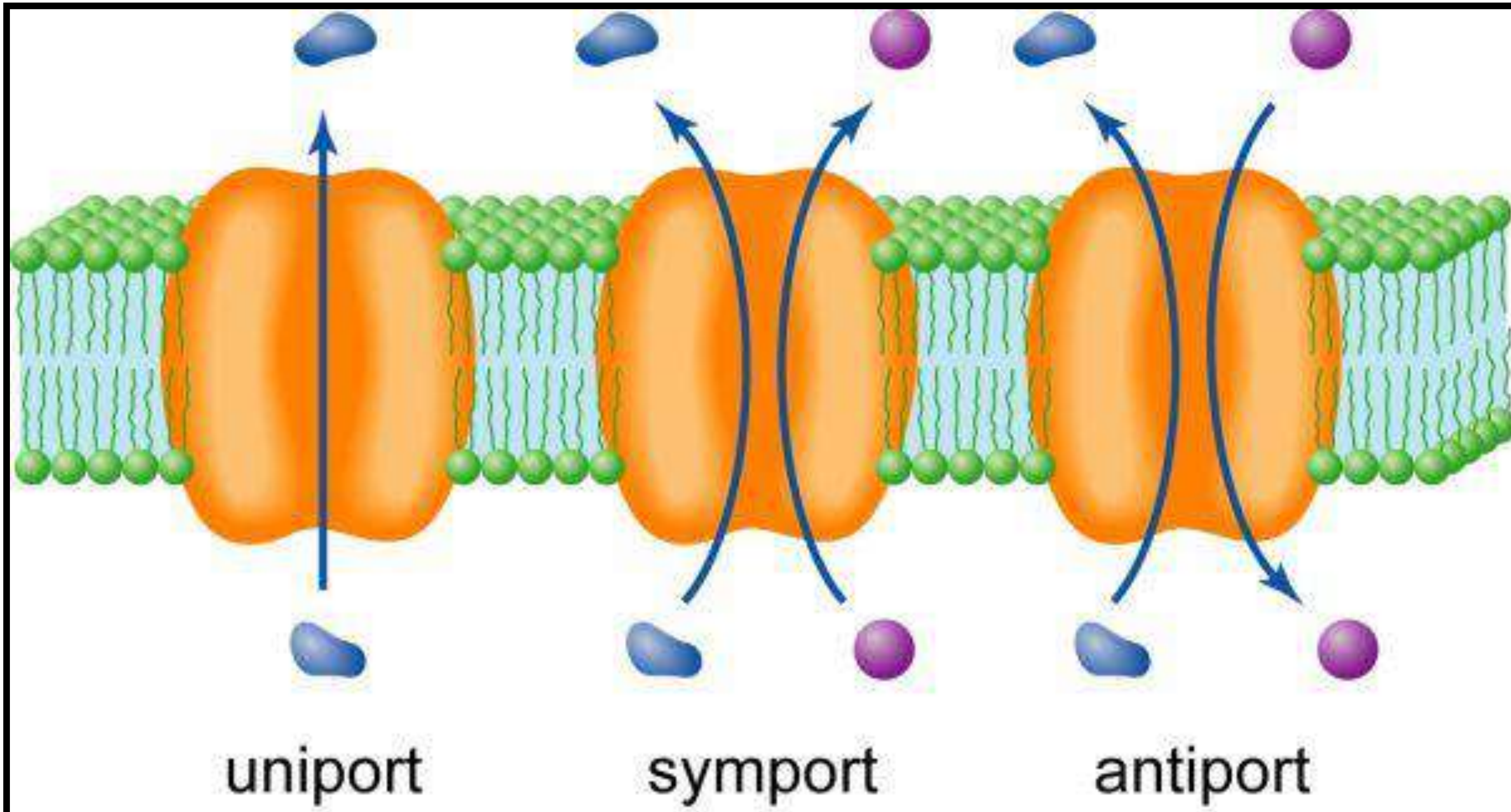
الناقل المشارك في الحيوانات هو نقل الصوديوم/الجلوكوز في الخلايا المعوية. يتحرك الصوديوم إلى أسفل تدرج تركيزه داخل الخلية

- **A cotransporter in animals** is the intestinal cells **Na^+/glucose transport**. Na^+ is moving down its concentration gradient into the cell.
- The active glucose transporter uses the **Na^+ gradient produced by the Na^+/K^+ pump** as a source of potential energy to power the movement of glucose into the cell. In this system, both glucose and Na^+ bind to the transport protein, which allows Na^+ to pass into the cell down its concentration gradient, and move glucose into the cell. In this kind of cotransport, both molecules **are moving in the same direction** across the membrane; therefore the transporter is a **symporter**.
- Sometimes, the **inward movement of Na^+** is coupled with the **outward movement** of another substance, such as Ca^{2+} or H^+, this is called **countertransport** where both Na^+ and the other substance (e.g Ca^{2+}) bind to the same transport protein (**antiporter**) because the two substances bind on **opposite sides** of the membrane and are moved in **opposite directions**.
- In **countertransport**, the cell uses the potential energy in the concentration gradient of Na^+ while moves downhill into the cell to **eject/expel** another substance (Ca^{2+}) against its concentration gradient. ضد تدرج تركيزها (Ca2+) أثناء التحرك إلى أسفل الخلية لإخراج/إخراج مادة أخرى Na+ في النقل المضاد، تستخدم الخلية الطاقة الكامنة في تدرج تركيز
- In both **cotransport and countertransport**, the potential energy in the concentration gradient of one molecule is used to transport another molecule against its concentration gradient. **They differ only** in the **direction** in which the second molecule moves relative to the first.

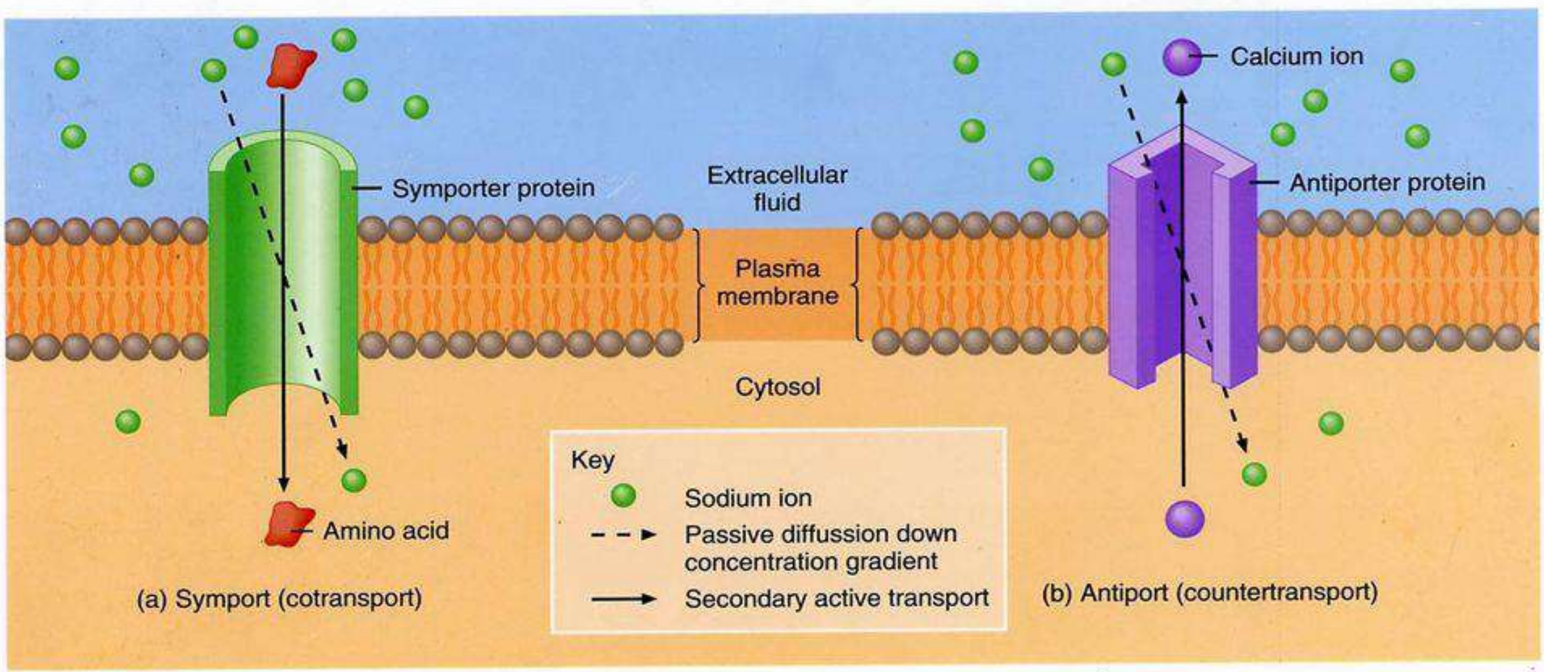
في كل من النقل المشترك والنقل المضاد، تُستخدم الطاقة الكامنة في تدرج تركيز جزيء واحد لنقل جزيء آخر ضد تدرج تركيزه. ويختلفان فقط في الاتجاه الذي يتحرك فيه الجزيء الثاني بالنسبة للجزيء الأول

Cotransport: animal Na+/glucose cotransport




uniport
symport
antiport

Secondary Active Transport
-Co-transport
-Counter transport



النقل بالجملة: الإخراج الخلوي والبلعمة الخلوية

Bulk transport: exocytosis & endocytosis

- **Large molecules**, such as proteins and polysaccharides, generally **don't cross the membrane** by simple transport or transport proteins. Instead, they usually enter (**endocytosis**) and leave (**exocytosis**) the cell in bulk, packaged in vesicles.

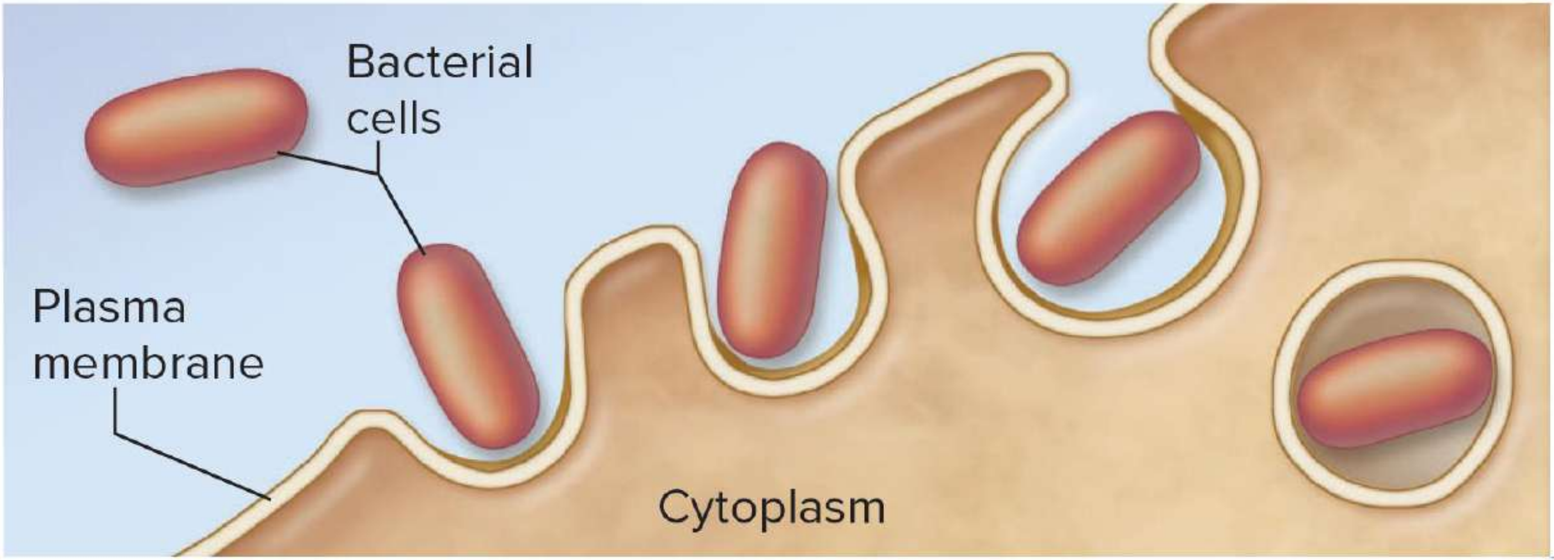
لا تعبر الجزيئات الكبيرة، مثل البروتينات والسكريات المتعددة، الغشاء عن طريق النقل البسيط أو بروتينات النقل. وبدلاً من ذلك، تدخل الخلية عادةً)البلعمة الخلوية) وتغادرها (الإخراج الخلوي) بكميات كبيرة، معبأة في حويصلات

- **Exocytosis**
- The cell secretes certain molecules by the **fusion of vesicles with the plasma membrane**; this process is called exocytosis. A transport vesicle that has budded from the Golgi apparatus moves along a microtubule of the cytoskeleton to the plasma membrane. When the vesicle membrane and plasma membrane come into contact, specific proteins in both membranes rearrange the lipid molecules of the two bilayers so that the two membranes fuse. The contents of the vesicle spill out of the cell, and the vesicle membrane **becomes part** of the plasma membrane.
- Many secretory cells use exocytosis to export products. For example, cells in the pancreas that make insulin secrete it into the extracellular fluid by exocytosis. In another example, **nerve cells** use exocytosis to release **neurotransmitters** that signal other neurons or muscle cells.

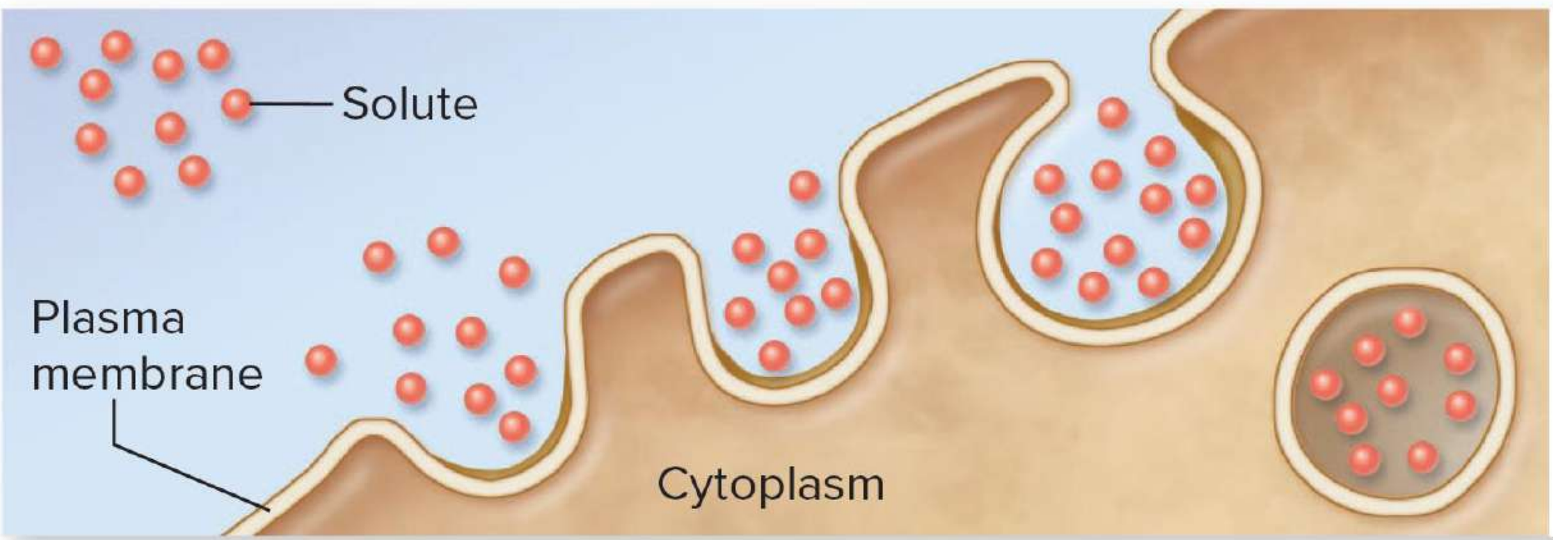
تستخدم العديد من الخلايا الإفرازية عملية الإخراج الخلوي لتصدير المنتجات. على سبيل المثال، تفرز الخلايا الموجودة في البنكرياس التي تنتج الأنسولين الأنسولين في السائل خارج الخلايا عن طريق عملية الإخراج الخلوي. وفي مثال آخر، تستخدم الخلايا العصبية عملية الإخراج الخلوي لإطلاق النواقل العصبية التي ترسل إشارات إلى الخلايا العصبية الأخرى أو خلايا العضلات.

Endocytosis: phagocytosis and pinocytosis

- In **endocytosis, the cell takes** in molecules and particulate matter by forming new vesicles from the plasma membrane, something looks like the **reverse of exocytosis.**
- **First**, a small area of the **plasma membrane sinks inward** to form a deep pocket that pinches in, **forming a vesicle** containing material that had been outside the cell.
- According to the **nature to enclosed material**, three types of endocytosis can be described:
- **phagocytosis** ("cellular eating"): a cell engulfs a particle by extending pseudopodia around it and packaging it within a membranous sac called a food vacuole.
- **pinocytosis** ("cellular drinking"): n pinocytosis, a **cell continually "swallows**" droplets of extracellular fluid into tiny vesicles, formed by infoldings of the plasma membrane. In this way, the cell obtains molecules dissolved in the droplets. Because any and all solutes are taken into the cell, pinocytosis as shown here is **nonspecific** for the substances it transports.



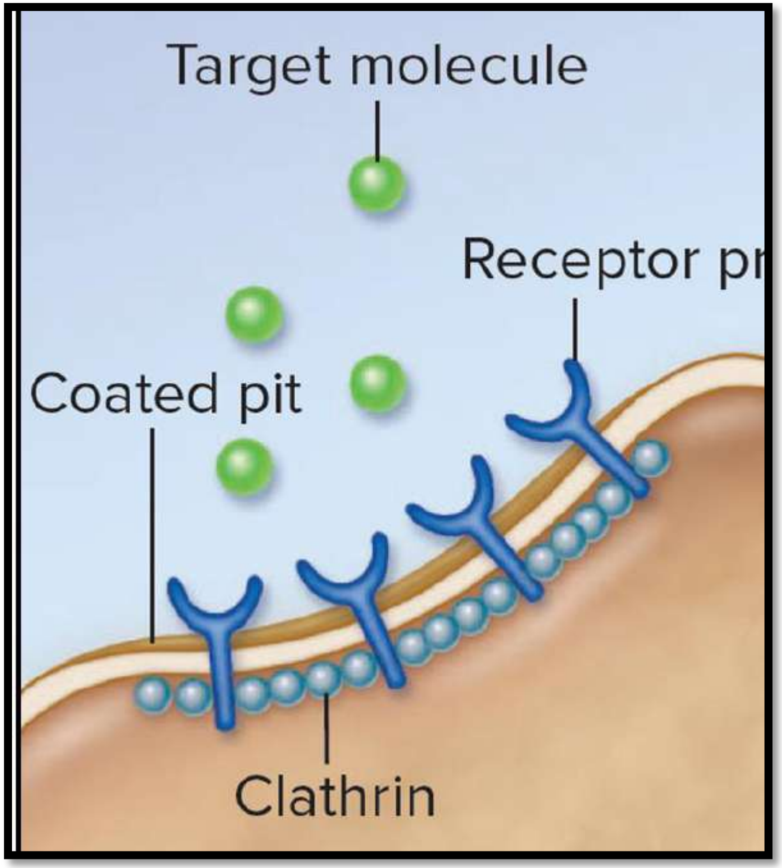
a. Phagocytosis

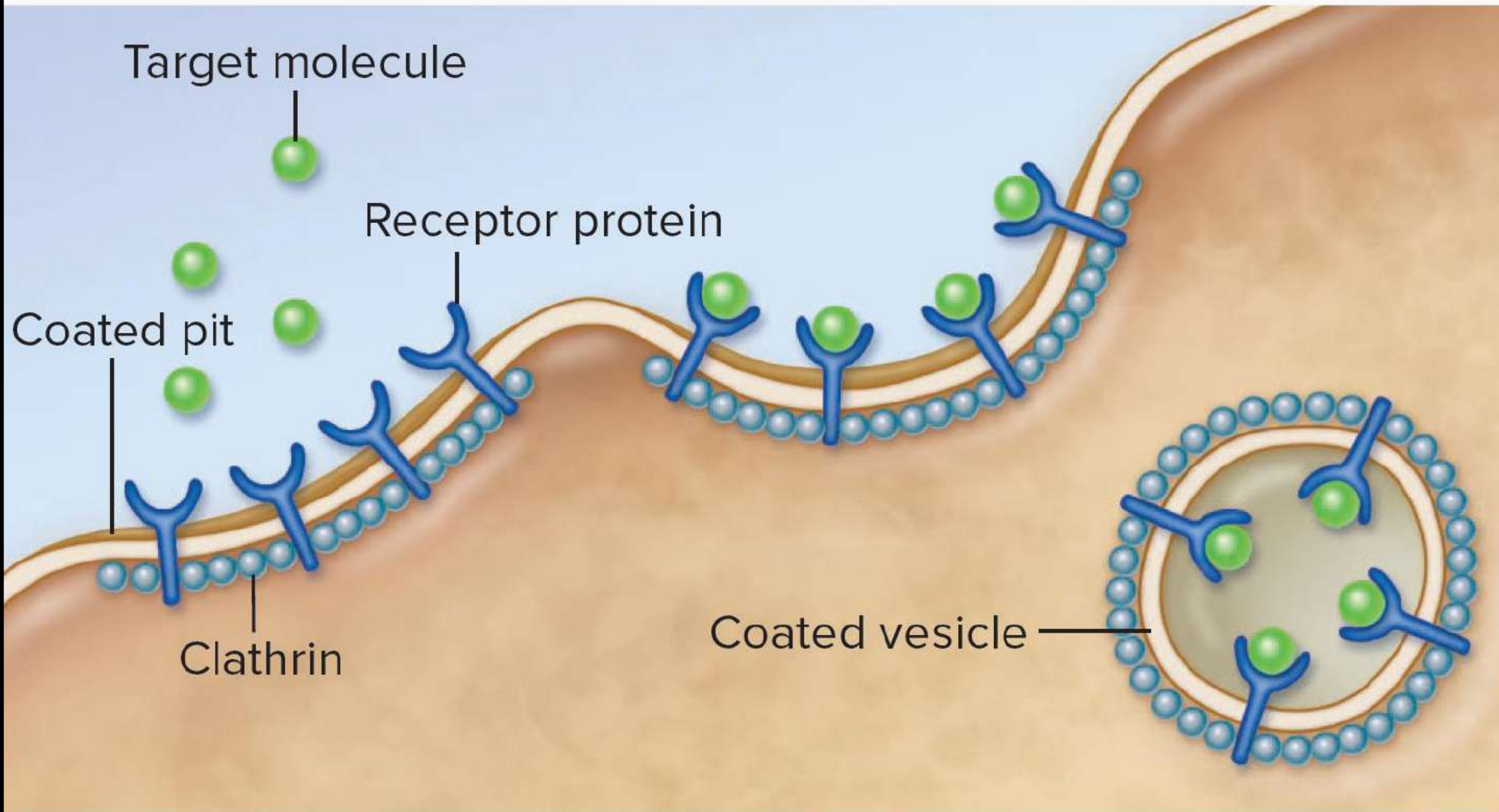


b. Pinocytosis

Receptor-mediated endocytosis

- Receptor-mediated endocytosis (e.g. **take in cholesterol**): large molecules are often transported into eukaryotic cells through receptor-mediated endocytosis.
- These large molecules **first bind to specific receptors** in the plasma membrane.
- Different cell types contain a characteristic set of receptor types, each for a different kind of molecule in their membranes. When **binding occurs**, the cell reacts **by initiating endocytosis**; the process is highly specific and very fast. The vesicle is now inside the cell carrying its cargo.
- The **portion of the receptor molecule** that lies inside the membrane is trapped in an **indented pit /cavity coated on the cytoplasmic** side with the protein **clathrin**.
- Each pit /cavity acts like a molecular mousetrap, **closing over** to form an internal vesicle when the right molecule enters the pit.





. Receptor-mediated endocytosis