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Chaudhary Moazzam

Introduction to the Study of Cell Biology

The discovery of cells

- Because of their small size, cells can only be observed with the aid of a **microscope**.
- Spectacles were first made in Europe in the thirteenth century.
- The first compound (double-lens) light microscopes were constructed by the end of the sixteenth century.
- By the mid-1600s, a handful of pioneering scientists had used their handmade microscopes to uncover a world that would never have been revealed to the naked eye.

- Robert Hooke, an English microscopist discovered the cell at age 27, and he was awarded the position of curator of the Royal Society of London.
- He took a dead piece of cork and observed empty compartments in it under the microscope, and named them cell.
- Anton van Leeuwenhoek examined a drop of pond water under the microscope and he observed the crawling microscopic entities which he named as “animalcules”.

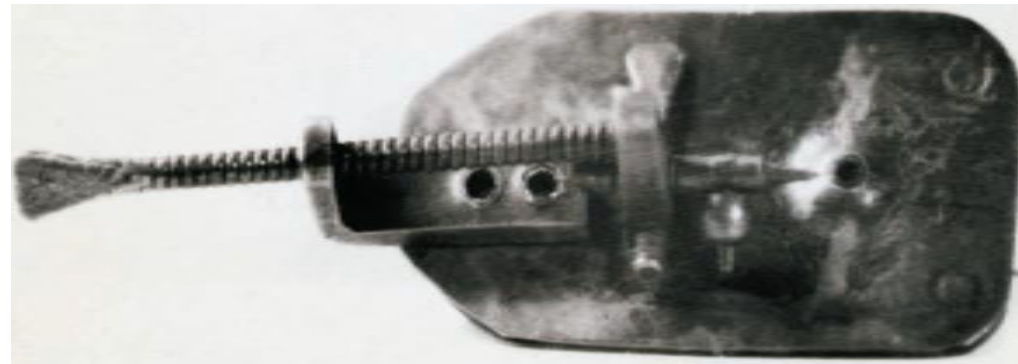
- He was also the first to describe various forms of bacteria, which he obtained from water in which pepper had been soaked and from scrapings of his teeth.
- In 1838, Matthias Schleiden, a German botanist, concluded that, plants were made of cells and that the plant embryo arose from a single cell.
- In 1839, Theodor Schwann, a German zoologist and colleague of Schleiden's, published a comprehensive report on the cellular basis of animal life.

■ Schwann concluded that the cells of plants and animals are similar structures and proposed these two views of the cell theory:

1. All organisms are composed of one or more cells.
2. The cell is the structural unit of life.



(a)



(b)

(a) One of Robert Hooke's more ornate compound (double-lens) microscopes. (Inset) Hooke's drawing of a thin slice of cork, showing the honeycomb-like network of "cells."

(b) Single-lens microscope used by Anton van Leeuwenhoek to observe bacteria and other microorganisms. The biconvex lens, which was capable of magnifying an object approximately 270 times and providing a resolution of approximately 1.35 μ m, was held between two metal plates.

Basic properties of cells

- Cells Are Highly Complex and Organized
- Cells Possess a Genetic Program and the Means to Use It
- Cells Are Capable of Producing More of Themselves
- Cells Acquire and Utilize Energy
- Cells Carry Out a Variety of Chemical Reactions
- Cells Engage in Mechanical Activities
- Cells Are Able to Respond to Stimuli
- Cells Are Capable of Self-Regulation

Introduction to Molecular Biology

- Molecular Biology
- (BIO-302)
- In the broader terms, definition of molecular biology includes all aspects of the study of life from a molecular perspective.

Introduction to Molecular Biology

- More precisely, the term “Molecular Biology” refers to the biology of the molecules related to genes, gene products and heredity.
- In other words, the term molecular biology is often substituted for a more appropriate term, **Molecular Genetics.**

Introduction to Molecular Biology

- So molecular biology grew out of the disciplines of genetics and biochemistry.
- In the present age, world is in the midst of two scientific revolutions. One is information technology and the other is Molecular Biology.

Introduction to Molecular Biology

- Both deal with the handling of large amounts of information.
- Molecular Biology has revolutionized the biological sciences as well especially in the fields of Health Sciences and Agricultural Sciences.

Introduction to Prokaryotic and Eukaryotic Cells

Two fundamentally different classes of cells

On the base of their size and the types of internal structures, or organelles, cells are divided into two classes.

1. The structurally simpler, **prokaryotic cells** include bacteria
2. The structurally more complex **eukaryotic cells** include protists, fungi, plants, and animals.

A Comparison of Prokaryotic and Eukaryotic Cells

Features held in common by the two types of cells:

1. Plasma membrane of similar construction
2. Genetic information encoded in DNA using identical genetic code
3. Similar mechanisms for transcription and translation of genetic information, including similar ribosomes
4. Shared metabolic pathways (e.g., glycolysis and TCA cycle)

5. Similar apparatus for conservation of chemical energy as ATP (located in the plasma membrane of prokaryotes and the mitochondrial membrane of eukaryotes)
6. Similar mechanism of photosynthesis (between cyanobacteria and green plants)
7. Similar mechanism for synthesizing and inserting membrane Proteins
8. Proteasomes (protein digesting structures) of similar construction (between archaebacteria and eukaryotes)

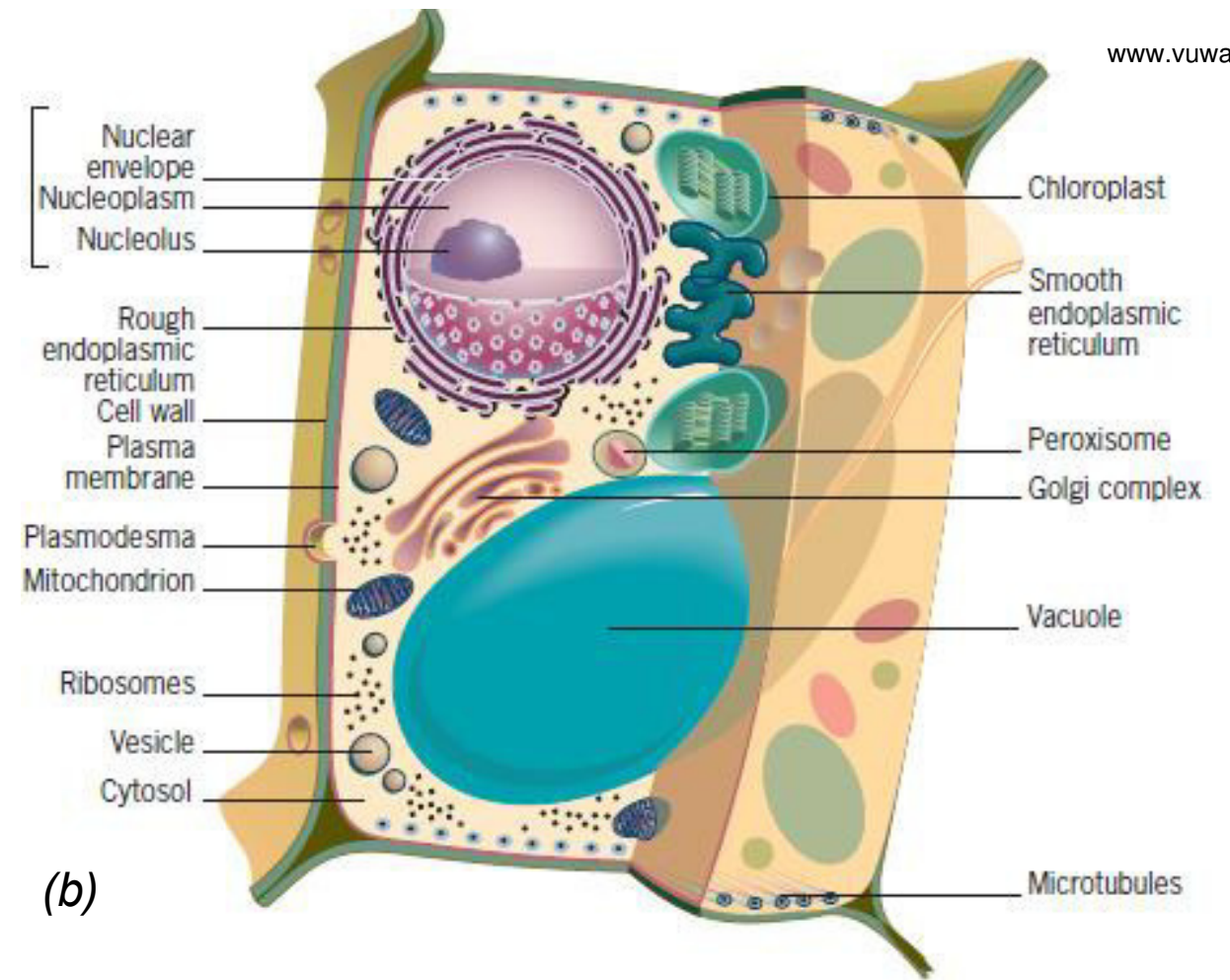
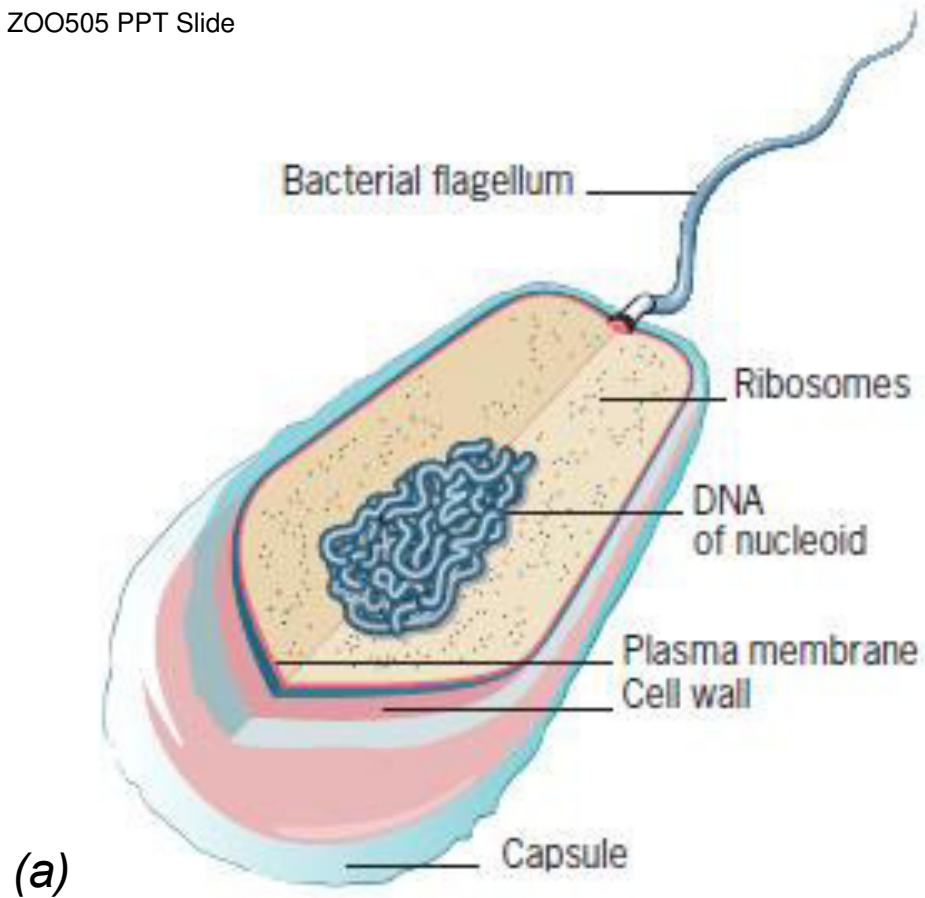
A Comparison of Prokaryotic and Eukaryotic Cells

Features of eukaryotic cells not found in prokaryotes:

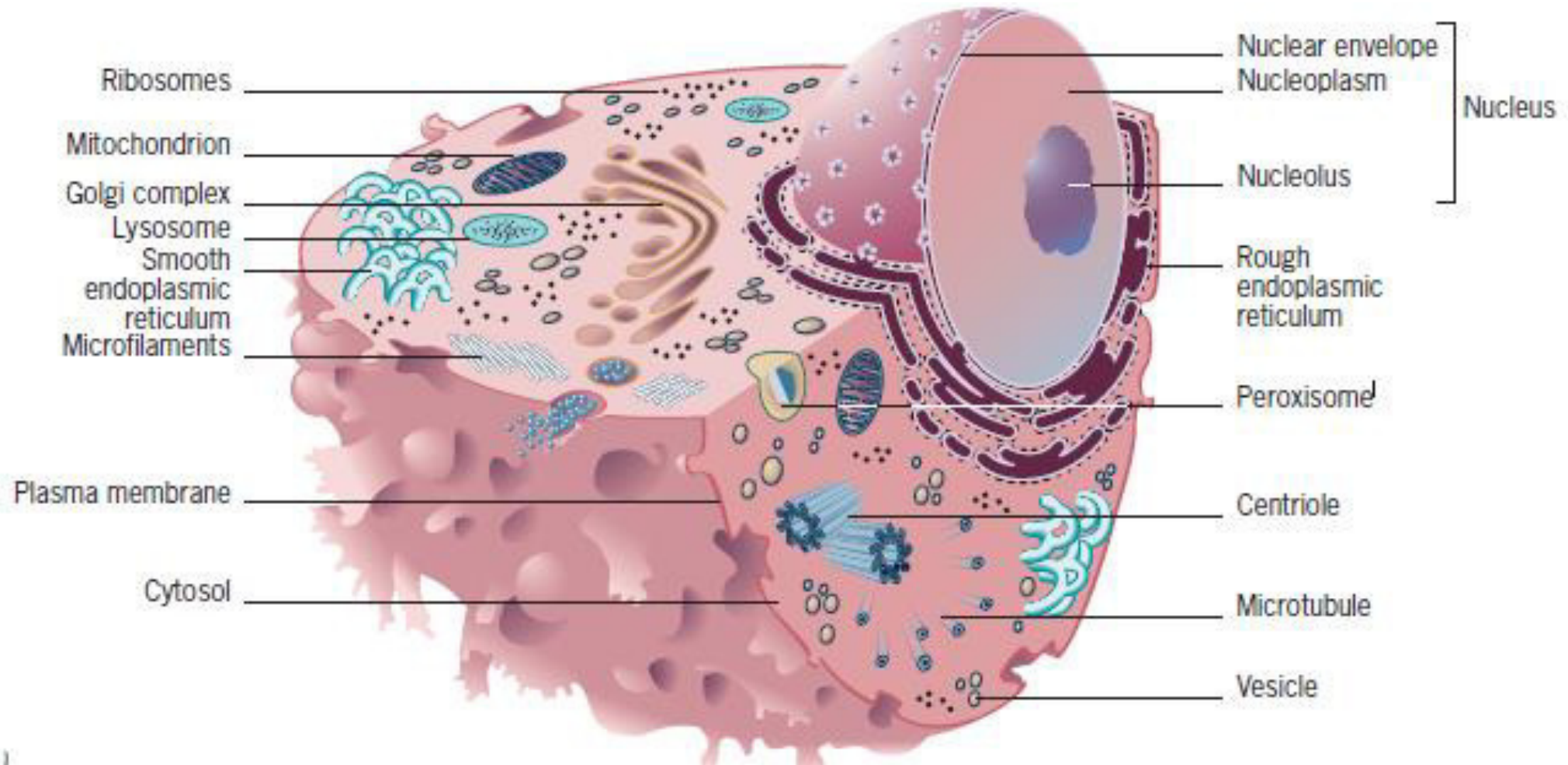
1. Division of cells into nucleus and cytoplasm, separated by a nuclear envelope containing complex pore structures
2. Complex chromosomes composed of DNA and associated proteins that are capable of compacting into mitotic structures
3. Complex membranous cytoplasmic organelles (includes endoplasmic reticulum, Golgi complex, lysosomes, endosomes, peroxisomes, and glyoxisomes)

4. Specialized cytoplasmic organelles for aerobic respiration (mitochondria) and photosynthesis (chloroplasts)
5. Complex cytoskeletal system (including microfilaments, intermediate filaments, and microtubules) and associated motor proteins
6. Complex flagella and cilia
7. Ability to ingest fluid and particulate material by enclosure within plasma membrane vesicles (endocytosis and phagocytosis)

8. Cellulose-containing cell walls (in plants)
9. Cell division using a microtubule-containing mitotic spindle that separates chromosomes
10. Presence of two copies of genes per cell (diploidy), one from each parent
11. Presence of three different RNA synthesizing enzymes (RNA polymerases)
12. Sexual reproduction requiring meiosis and fertilization



Schematic diagrams of a “generalized” bacterial (a), plant (b) cells



Schematic diagrams of a “generalized” animal cell

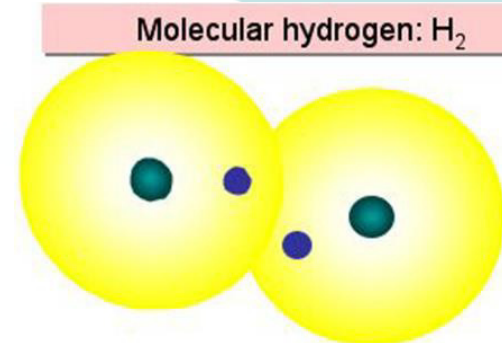
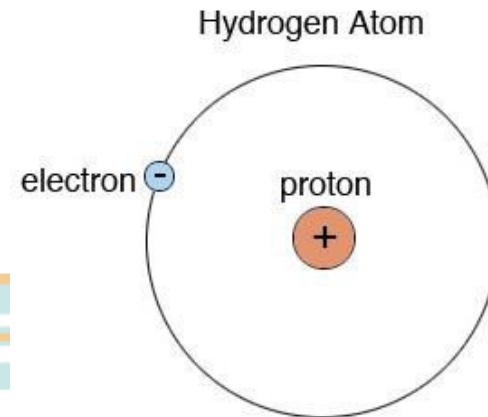
CELL BIOLOGY



Composition of Matter

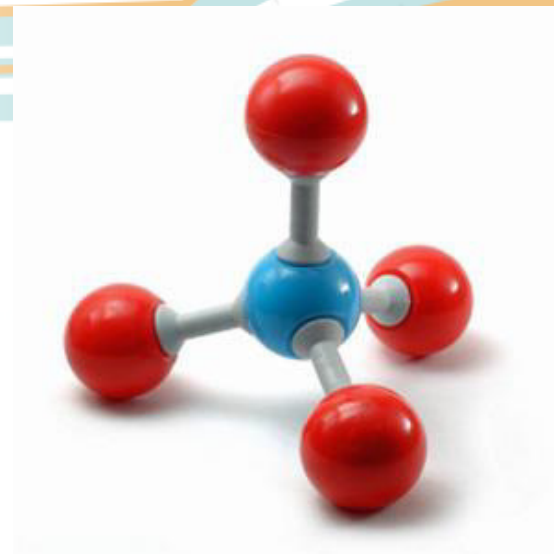
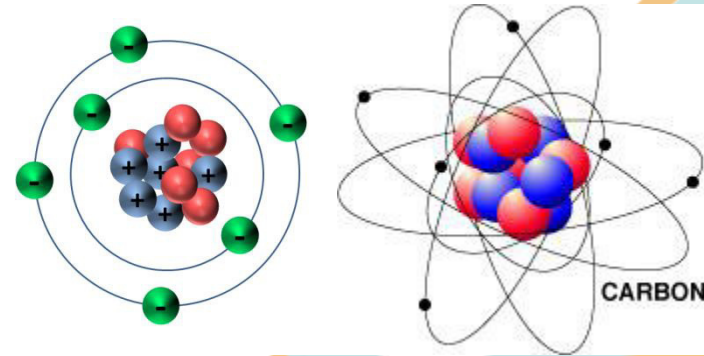
Composition of Matter

Atomic Structure



Composition of Matter

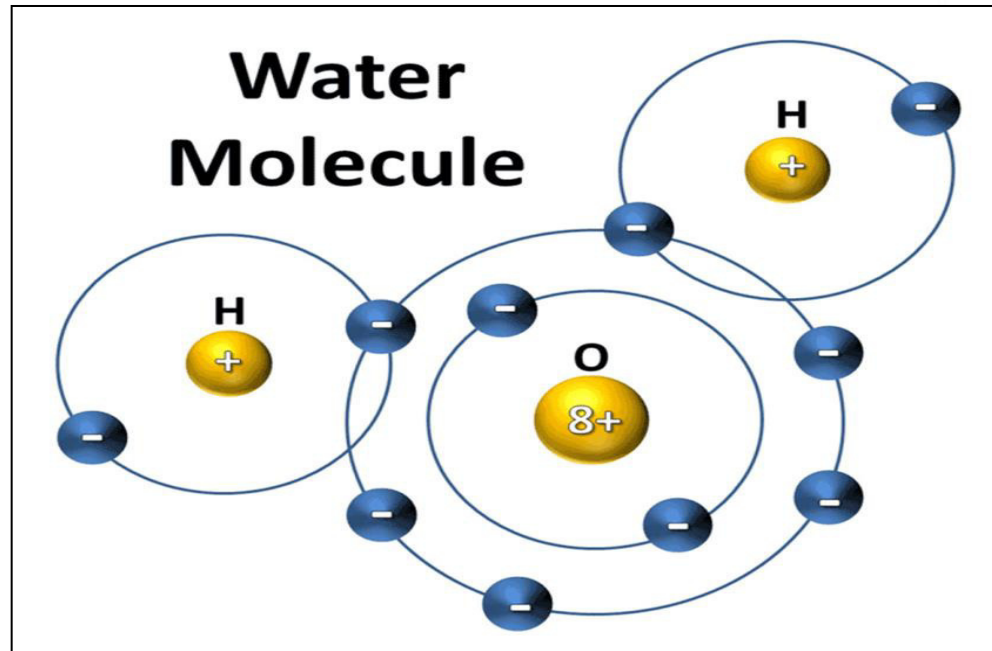
Carbon Atom



Composition of Matter

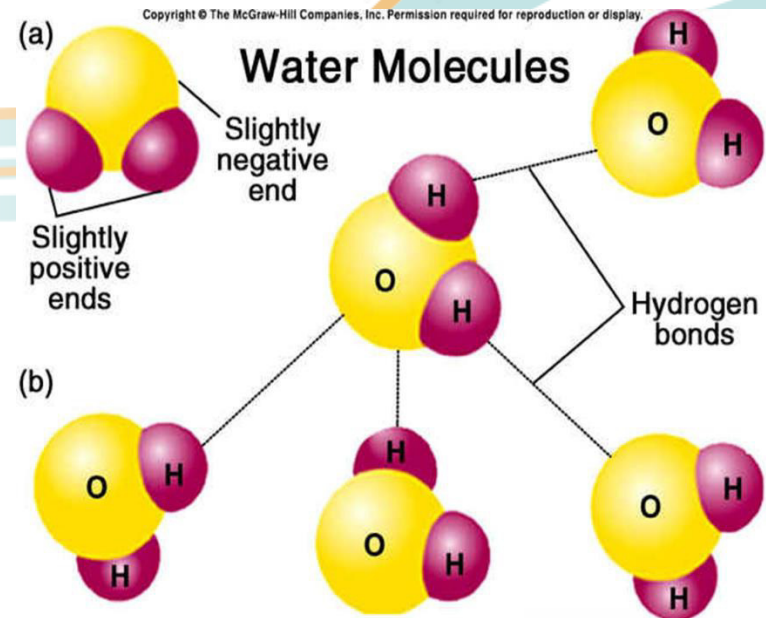
Electronegativity

The tendency of an atom to attract electrons towards itself.



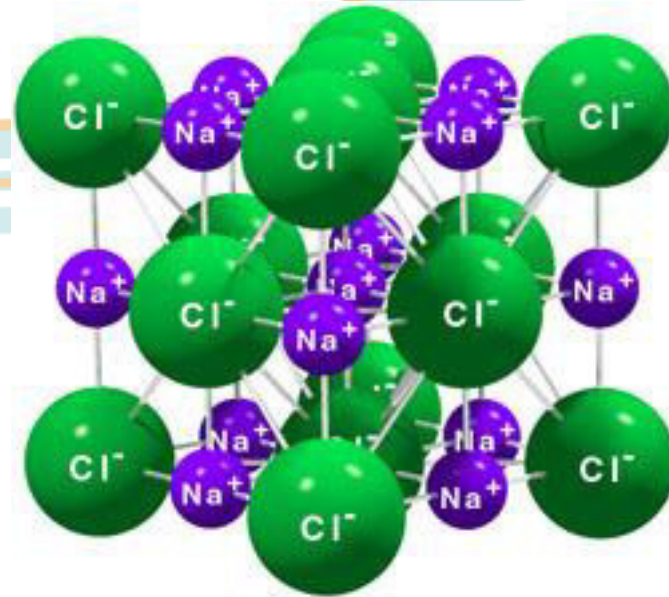
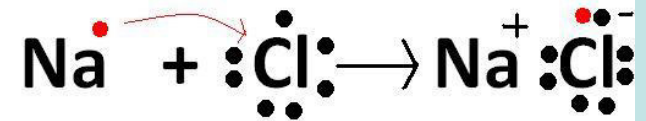
Composition of Matter

Polarity of H₂O Results in Hydrogen Bonding

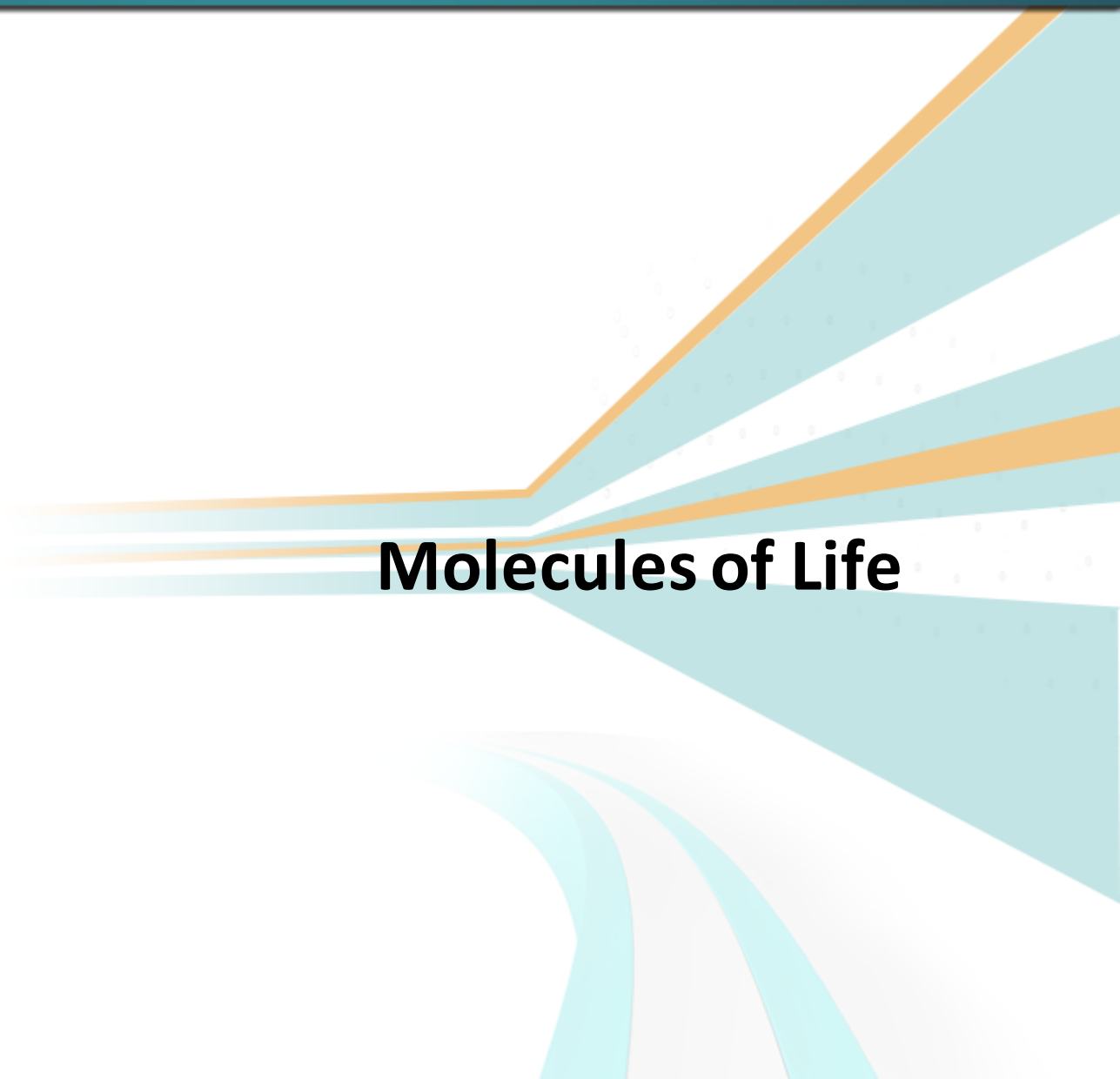


Composition of Matter

Ionic Bond



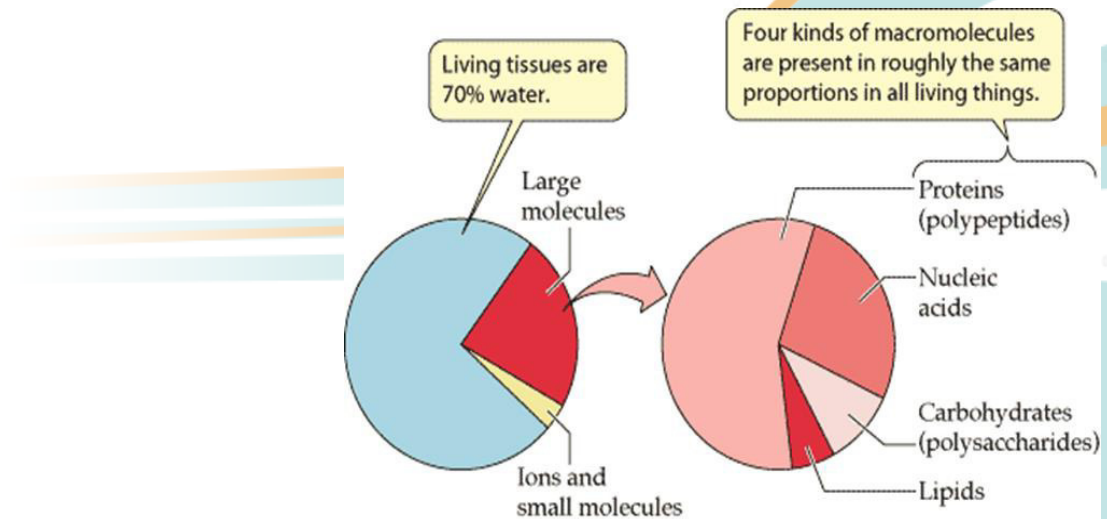
CELL BIOLOGY



Molecules of Life

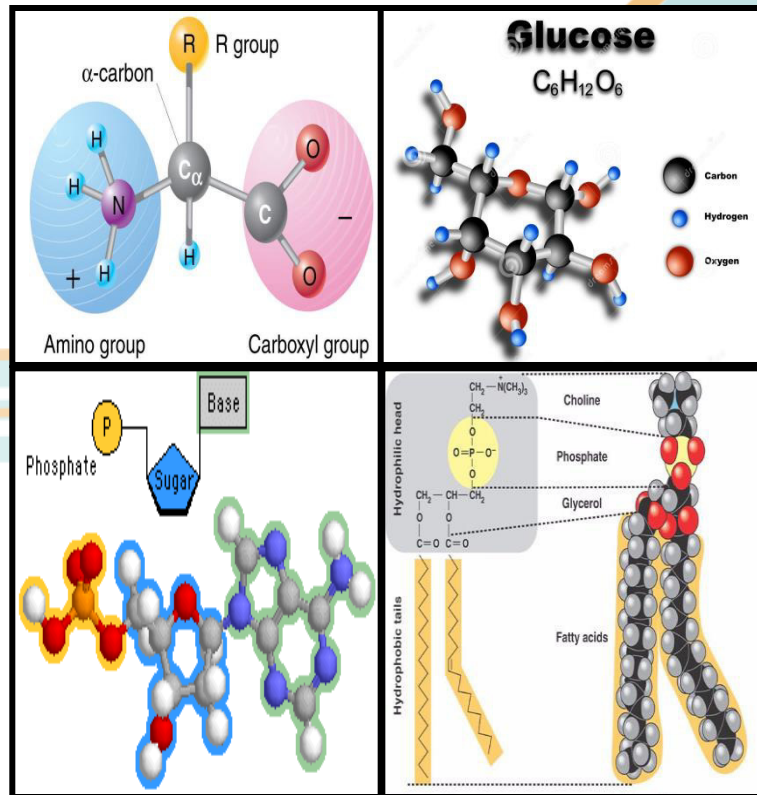
Molecules of Life

Composition of Life



Molecules of Life

Building Blocks of Life



Molecules of Life

Polymers & Monomers

Macromolecules are polymers of smaller monomers molecules

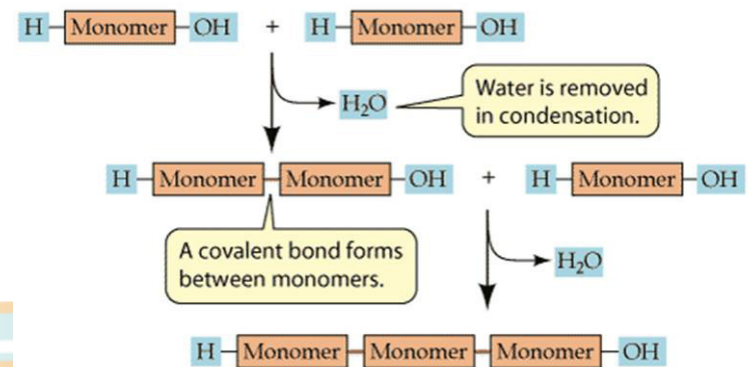
Condensation reactions: Monomers join H_2O Removal

Hydrolysis reactions: Use water to break polymers into monomers.

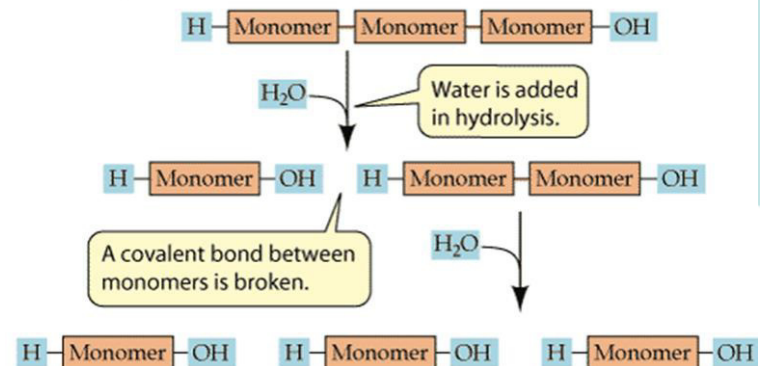
Molecules of Life

Condensation & Hydrolysis

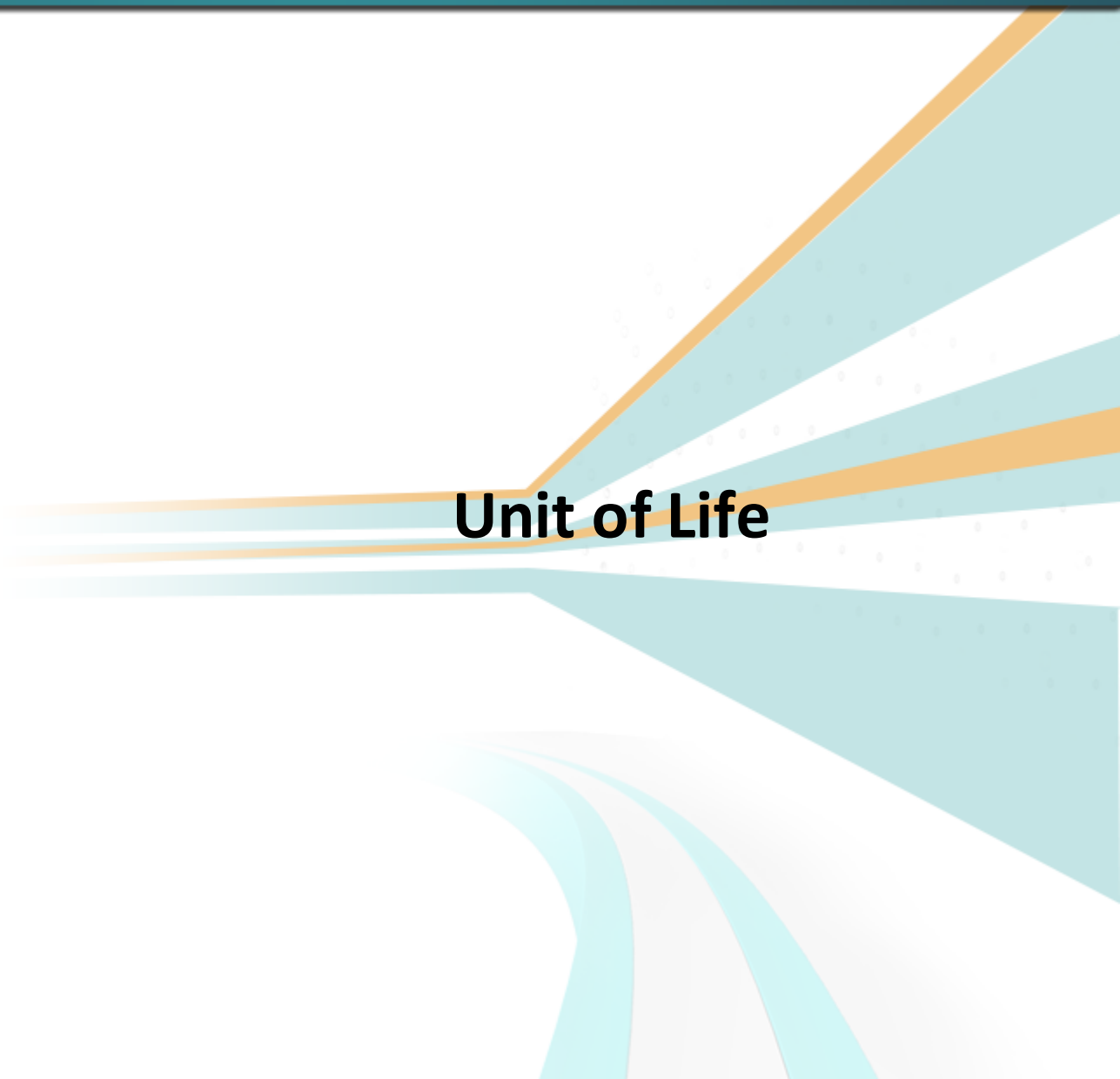
(a) Condensation



(b) Hydrolysis



CELL BIOLOGY



Unit of Life

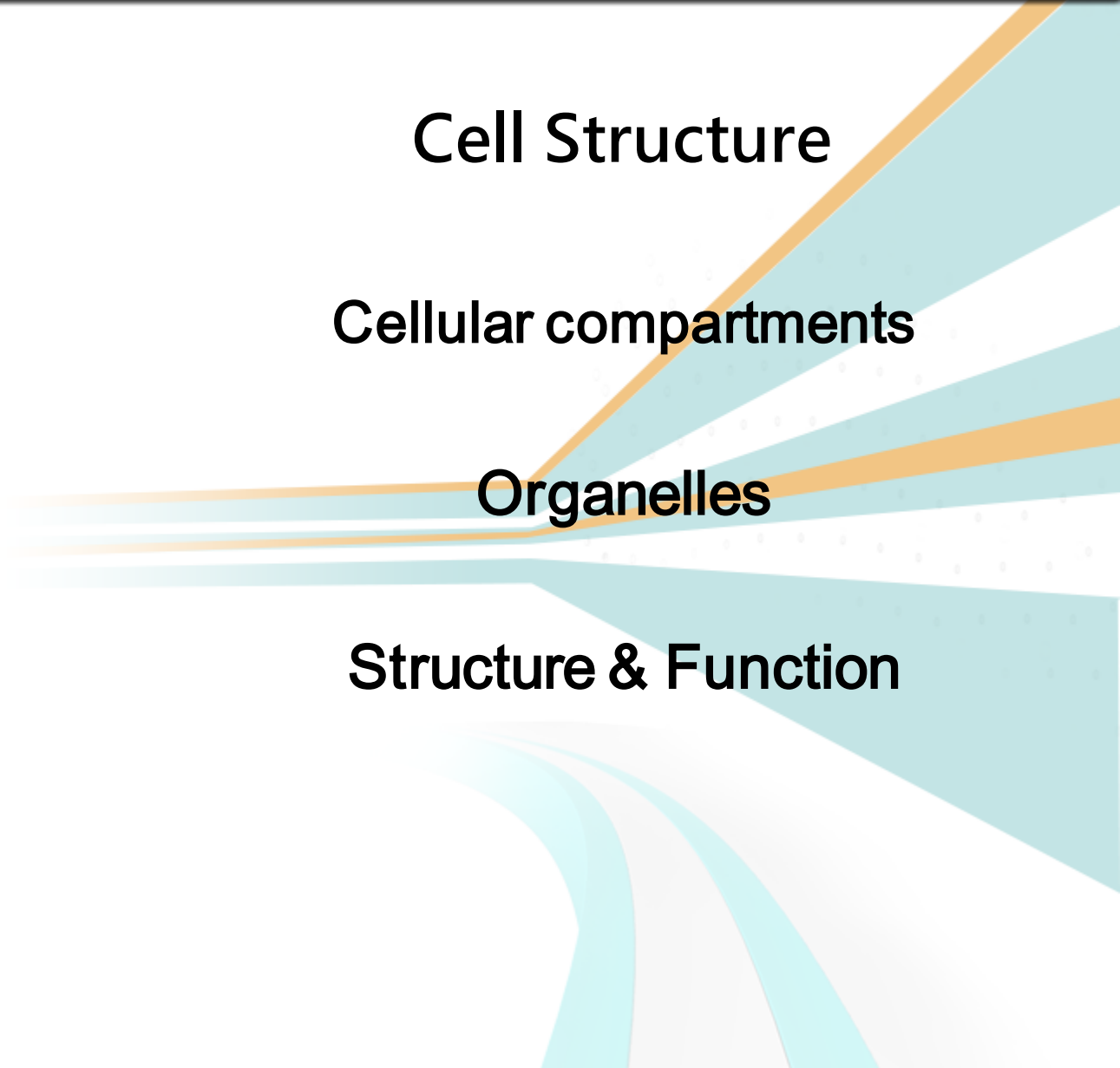
Unit of Life

Cell Structure

Cellular compartments

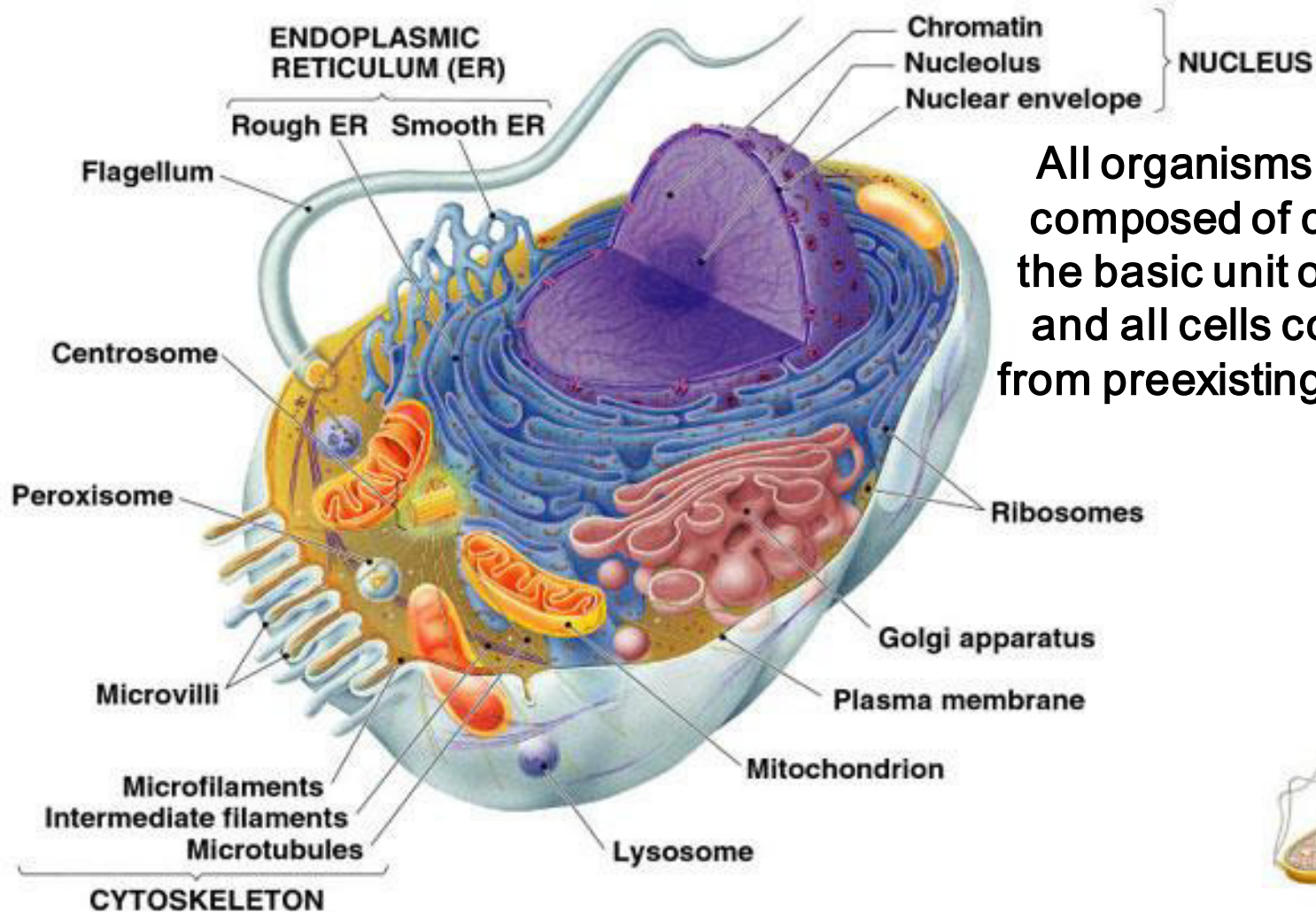
Organelles

Structure & Function



Unit of Life

All organisms are composed of cells the basic unit of life and all cells come from preexisting cells

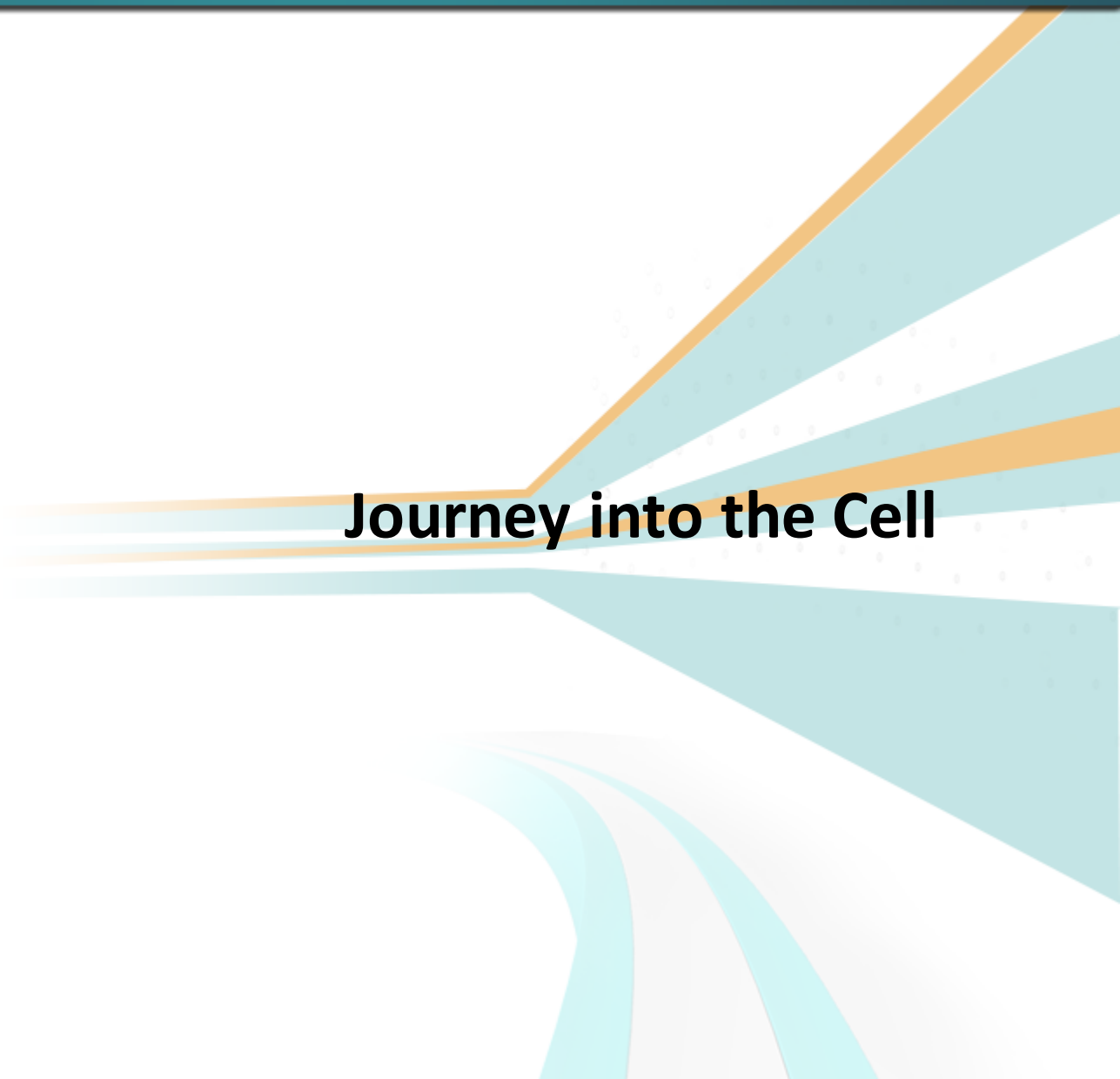


Not a random collection of molecules

Life

**collection of
macromolecules that
can perform unique
functions because the
are enclosed in
structural
compartment that
provides consistency
(homeostasis).**

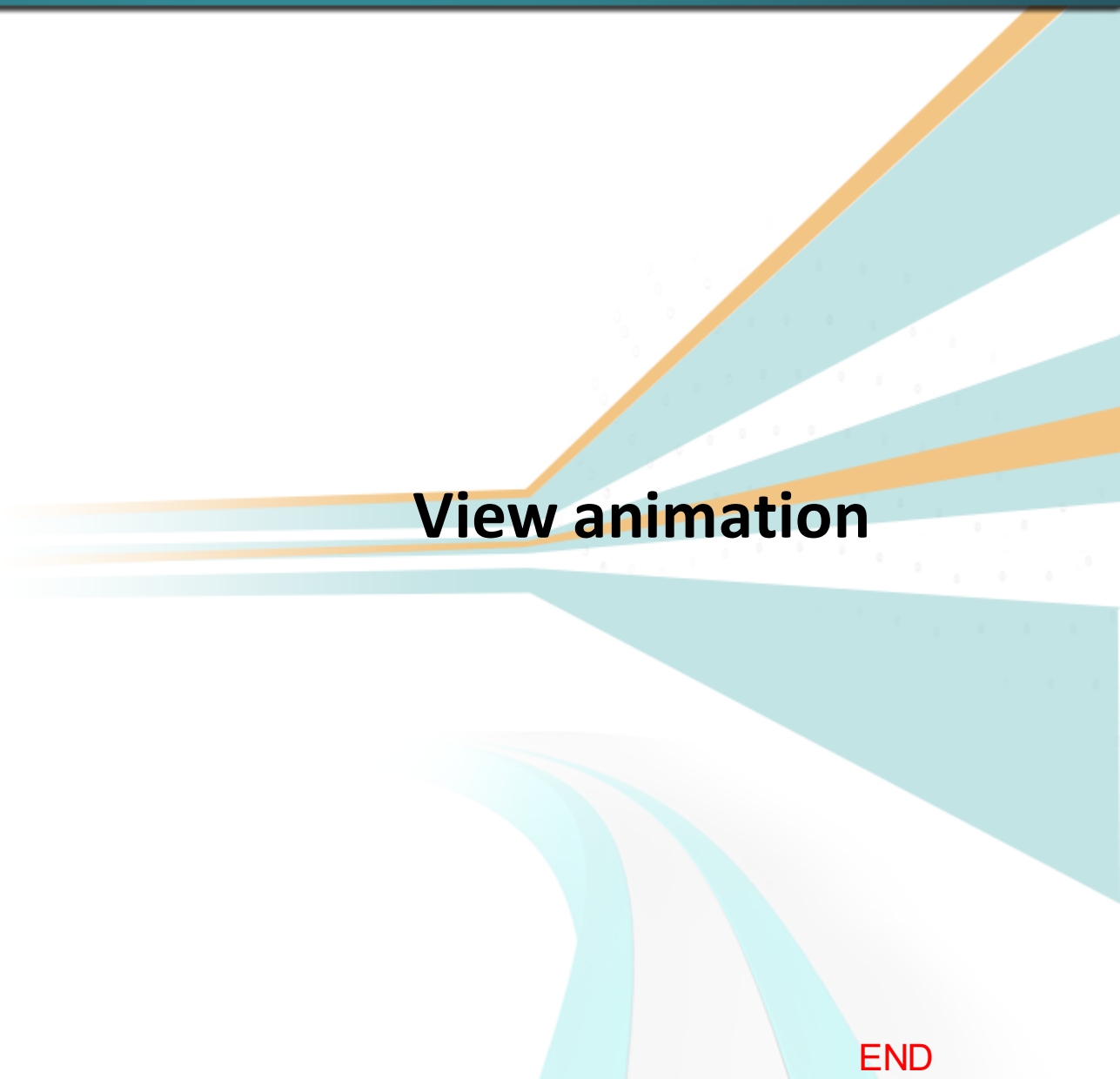
CELL BIOLOGY



Journey into the Cell

Unit of Life

View animation

The background features a series of overlapping, semi-transparent geometric shapes in shades of teal and orange. These shapes radiate from a central point on the right side of the slide, creating a sense of movement and depth. A pattern of small, light-colored dots is scattered across the right side, adding texture to the design.

END

CELL BIOLOGY

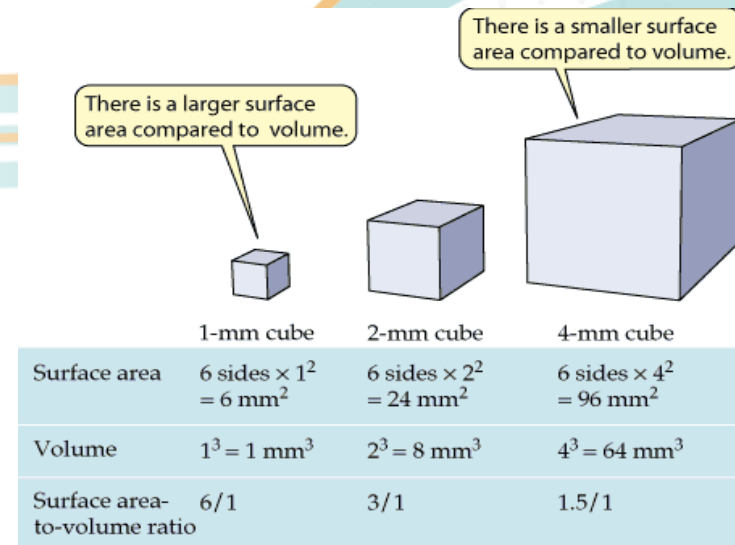


Size Matters

Size Matters

Cell Structure

Cells are small to maintain large surface area to volume ratio



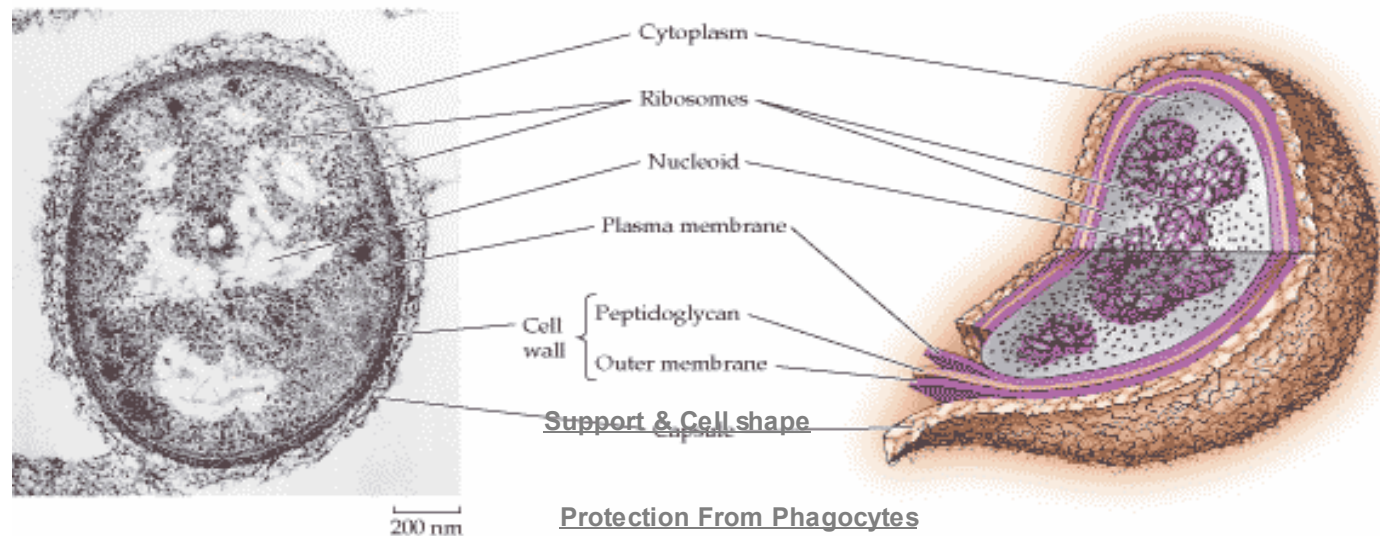
Prokaryotic Cells

No membrane enclosed internal compartments.

Plasma membrane regulates traffic (barrier).

Nucleoid region contains DNA.

Most have cell wall.



Prokaryotic Cells

Special Features

Cyanobacteria

Chlorophyll containing
have folds of plasma
membrane, other have
mesosomes (energy).

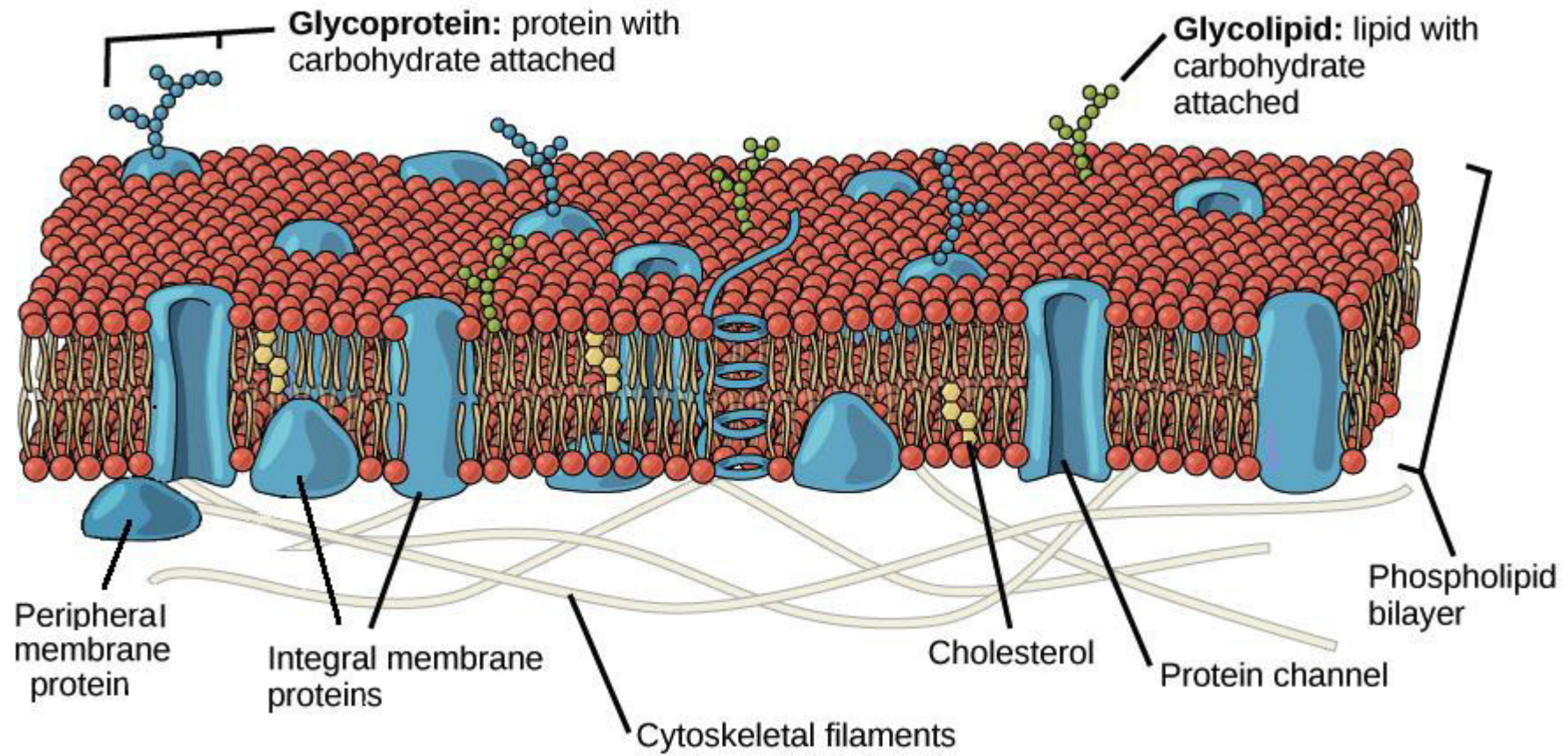
Some have actin like
filaments and other
have Flagella made-up
of Flagellin.

Plasma Membrane

Introduction

- The cells are separated from the external world by a thin, fragile structure called the **plasma membrane**.
- It consists of a lipid bilayer with embedded proteins.
- It is only 5 to 10 nm wide.
- The basic function of the cell membrane is to protect the cell from its surroundings.
- The cell membrane controls the movement of substances in and out of cells and organelles. In this way, it is selectively permeable to ions and organic molecules

- The cell membrane controls the movement of substances in and out of cells and organelles. In this way, it is selectively permeable to ions and organic molecules.
- In addition, cell membranes are involved in a variety of cellular processes such as;
 1. Cell adhesion
 2. Ion conductivity
 3. Cell signalling
 4. Serve as the attachment surface for several structures, including the cell wall, glycocalyx, and cytoskeleton.



plasma membrane

An overview of membrane functions

An overview of membrane functions

- 1. *Compartmentalization*

It allows specialized activities to proceed without external interference and also enables cellular activities to be regulated independently of one another.

- 2. *Scaffold for biochemical activities*

Membranes provide the cell with an extensive framework or scaffolding for effective interactions between reactants of a reaction.

3. Providing a selectively permeable barrier

Membranes prevent the unrestricted exchange of molecules from one side to the other.

- ***4. Transporting solutes***

The membrane's transport machinery allows the transport of specific ions, thereby establishing ionic gradients across itself. This capability is especially critical for nerve and muscle cells.

- *5. Responding to external signals*

The plasma membrane plays a critical role in the response of a cell to external stimuli, a process known as **signal transduction**.

- *6. Intercellular interaction*

The plasma membrane allows cells to recognize and signal one another, to adhere when appropriate, and to exchange materials and information.

- *7. Energy transduction*

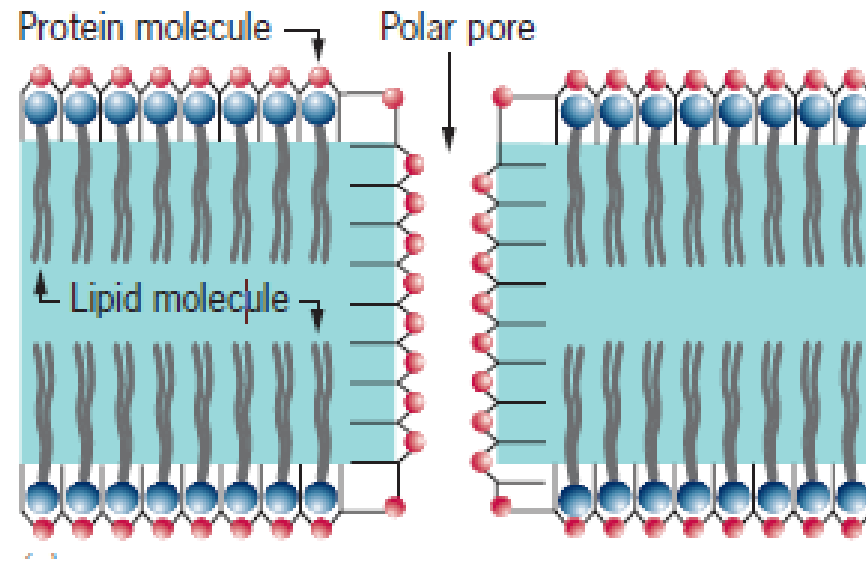
Membranes are intimately involved in the processes by which one type of energy is converted to another type through chloroplasts and mitochondria.

A brief history of studies on plasma membrane structure

A brief history of studies on plasma membrane structure

- The first insights into the chemical nature of the outer boundary layer of a cell were obtained by Ernst Overton of the University of Zürich during the 1890s.
- The first proposal that cellular membranes might contain a lipid bilayer was made in 1925 by two Dutch scientists, E. Gorter and F. Grendel.
- In the 1920s and 1930s, cell physiologists obtained evidence that there must be more to the structure of membranes than simply a lipid bilayer.

- In 1935, Hugh Davson and James Danielli proposed that the plasma membrane was composed of a lipid bilayer that was lined on both its inner and outer surface by a layer of globular proteins.
- Davson and Danielli revised their model in the early 1950s to account for the selective permeability of the membranes they had studied. In the revised version.
- They suggested that, in addition to the outer and inner protein layers, the lipid bilayer was also penetrated by protein-lined pores, which could provide conduits for polar solutes and ions to enter and exit the cell.



A revised 1954 version of the Davson-Danielli model showing the lipid bilayer.

- Fluidmosaic model proposed in 1972 by S. Jonathan Singer and Garth Nicolson of the University of California, San Diego.
- In the **fluid-mosaic model**, which has served as the “central dogma” of membrane biology for more than three decades, the lipid bilayer remains the core of the membrane, but attention is focused on the physical state of the lipid.

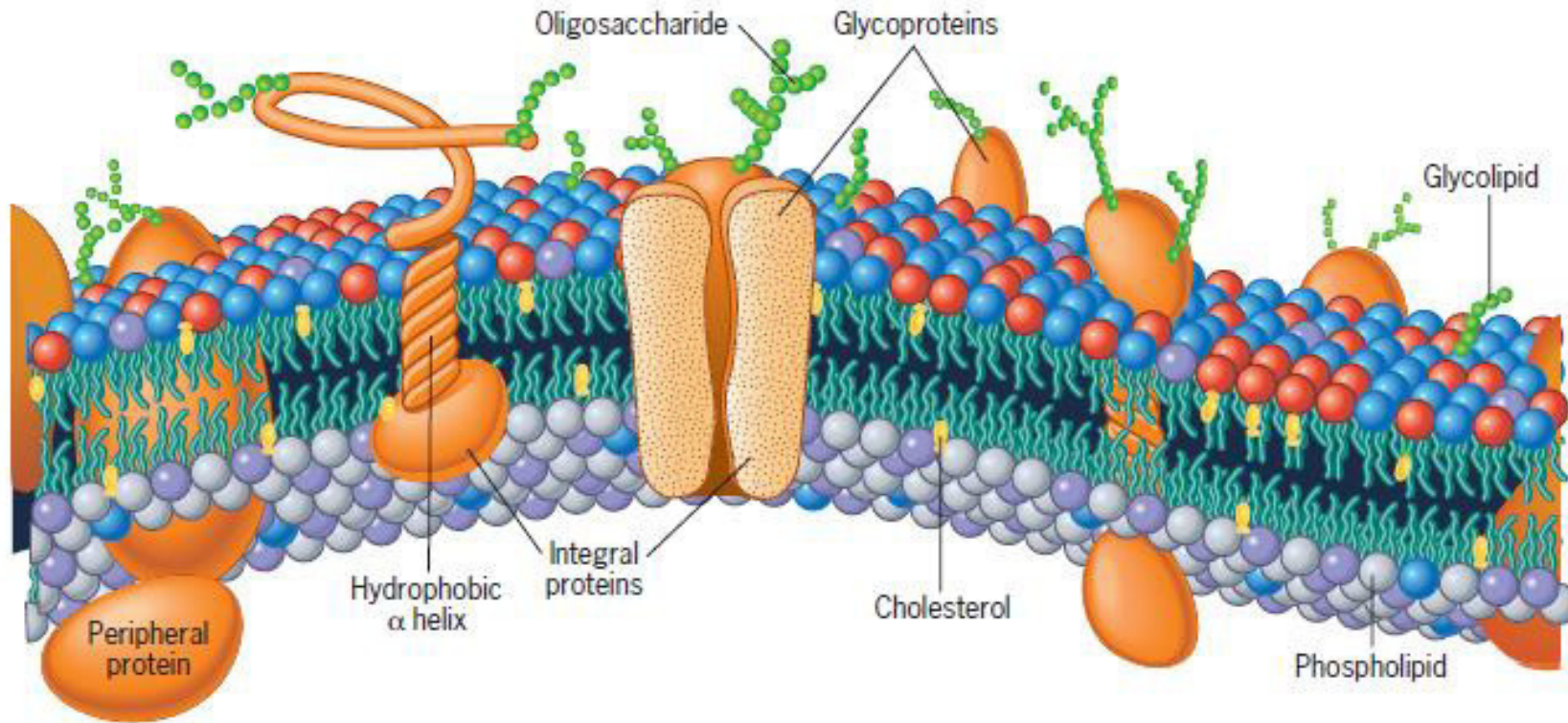
Chemical composition of membranes

Chemical composition of membranes

- Membranes are lipid–protein assemblies in which the components are held together in a thin sheet by non-covalent bonds.
- The core of the membrane consists of a sheet of lipids arranged in a bimolecular layer.
- The lipid bilayer serves primarily as a structural backbone of the membrane and provides the barrier that prevents random movements of water-soluble materials into and out of the cell.

- Each type of differentiated cell contains a unique complement of membrane proteins, which contributes to the specialized activities of that cell type.

- The ratio of lipid to protein in a membrane varies, depending on;
 1. The type of cellular membrane (plasma vs. endoplasmic reticulum vs. Golgi).
 2. The type of organism (bacterium vs. plant vs. animal).
 3. The type of cell (cartilage vs. muscle vs. liver).



A current representation of the **plasma membrane** showing the same basic organization as that proposed by Singer and Nicolson. The external surface of most membrane proteins, as well as a small percentage of the phospholipids, contain short chains of sugars, making them **glycoproteins** and **glycolipids**. Those portions of the polypeptide chains that extend through the lipid bilayer typically occur as helices composed of hydrophobic amino acids. The two leaflets of the bilayer contain different types of lipids as indicated by the differently colored head groups.

Membrane Lipids (Phosphoglycerides)

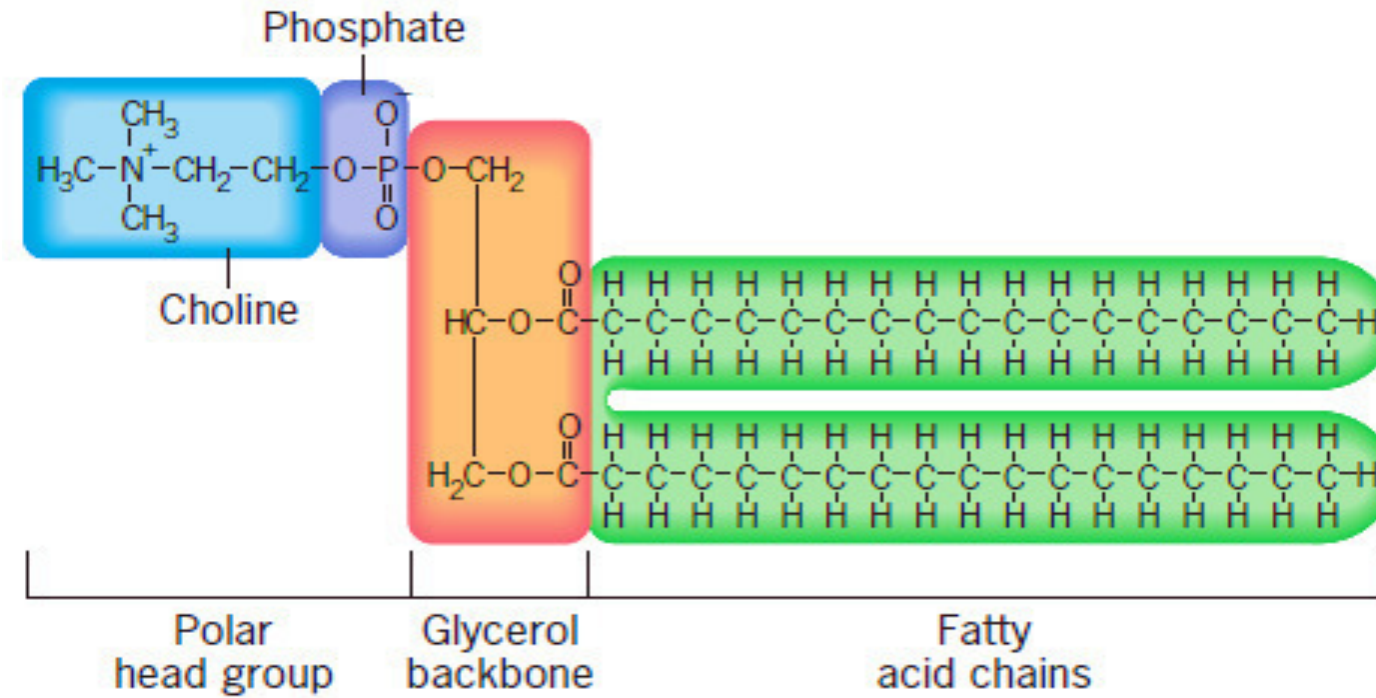
Membrane Lipids

- Membranes contain a wide diversity of lipids, all of which are **amphipathic**; that is, they contain both hydrophilic and hydrophobic regions.

- There are three main types of membrane lipids:
 1. Phosphoglycerides
 2. Sphingolipids
 3. Cholesterol.

Phosphoglycerides

- Most membrane lipids contain a phosphate group, which makes them **phospholipids**.
- And most membrane phospholipids are built on a glycerol backbone, they are called **phosphoglycerides**.
- Membrane glycerides are *diglycerides*—only two of the hydroxyl groups of the glycerol are esterified to fatty acids; the third is esterified to a hydrophilic phosphate group.



Phospholipid phosphatidylcholine

*The molecule consists of a **glycerol backbone** whose hydroxyl groups are covalently bonded to two fatty acids and a phosphate group. The negatively charged **phosphate** is also bonded to a small, positively charged choline group. The end of the molecule that contains the phosphorylcholine is **hydrophilic**, whereas the opposite end, consisting of the fatty acid tail, is **hydrophobic**.*

Membrane Lipids (Sphingolipids)

Sphingolipids

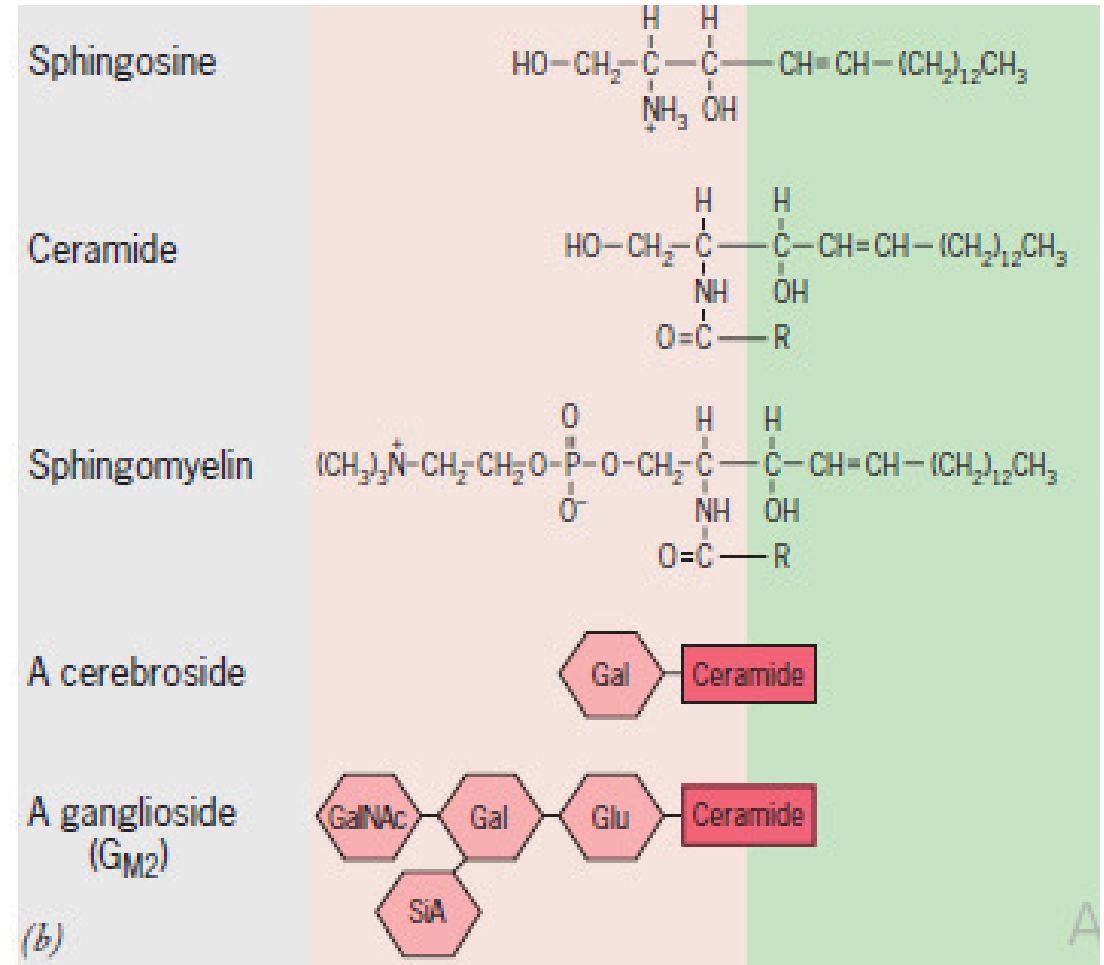
- A less abundant class of membrane lipids, called **sphingolipids**.
- These are derivatives of **sphingosine**, an amino alcohol that contains a long hydrocarbon chain.
- Sphingolipids consist of sphingosine linked to a fatty acid by its amino group. This molecule is a ***ceramide***.

- Various sphingosine-based lipids have additional groups esterified to the terminal alcohol of the sphingosine moiety.
 - If the substitution is phosphorylcholine, the molecule is *sphingomyelin*, which is the only phospholipid of the membrane that is not built with a glycerol backbone.
 - If the substitution is a carbohydrate, the molecule is a **glycolipid**.
 - a. If the carbohydrate is a simple sugar, the glycolipid is called a *cerebroside*;
 - b. If it is a small cluster of sugars, the glycolipid is called a *ganglioside*.

- Since all sphingolipids have two long, hydrophobic hydrocarbon chains at one end and a hydrophilic region at the other, they are also **amphipathic**
- These are basically similar in overall structure to the phosphoglycerides.

The structures of sphingolipids

*Sphingomyelin is a phospholipid; **cerebrosides** and **gangliosides** are glycolipids. The green portion of each lipid, which represents the hydrophobic tail(s) of the molecule, is actually much longer than the hydrophilic head group*

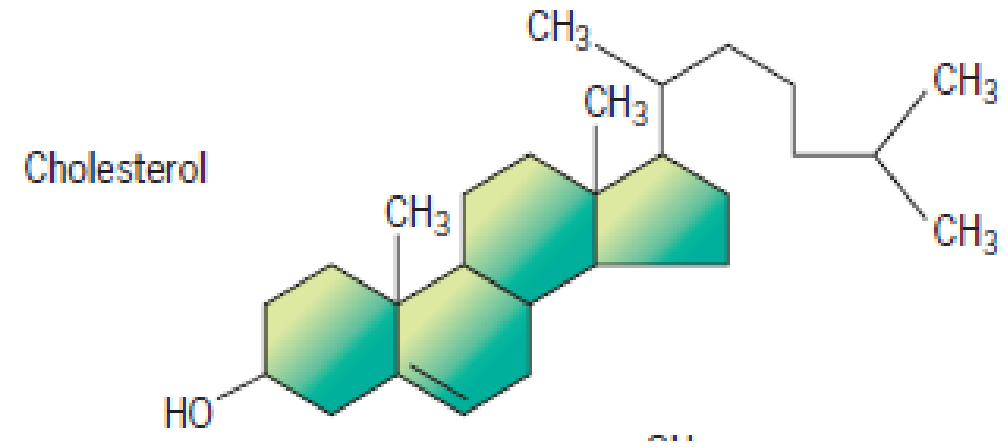


Membrane Lipids (Cholesterol)

Cholesterol

- Lipid component of certain membranes is the sterol **cholesterol**.
- In certain animal cells cholesterol may constitute up to 50 percent of the lipid molecules in the plasma membrane.
- Cholesterol is absent from the plasma membranes of most plant and all bacterial cells.

- Cholesterol molecules are oriented with their small **hydrophilic hydroxyl** group toward the membrane surface and the remainder of the molecule embedded in the lipid bilayer.
- The **hydrophobic rings** of a cholesterol molecule are flat and rigid, and they interfere with the movements of the fatty acid tails of the phospholipids



Cholesterol molecule

Membrane Carbohydrates

Membrane Carbohydrates

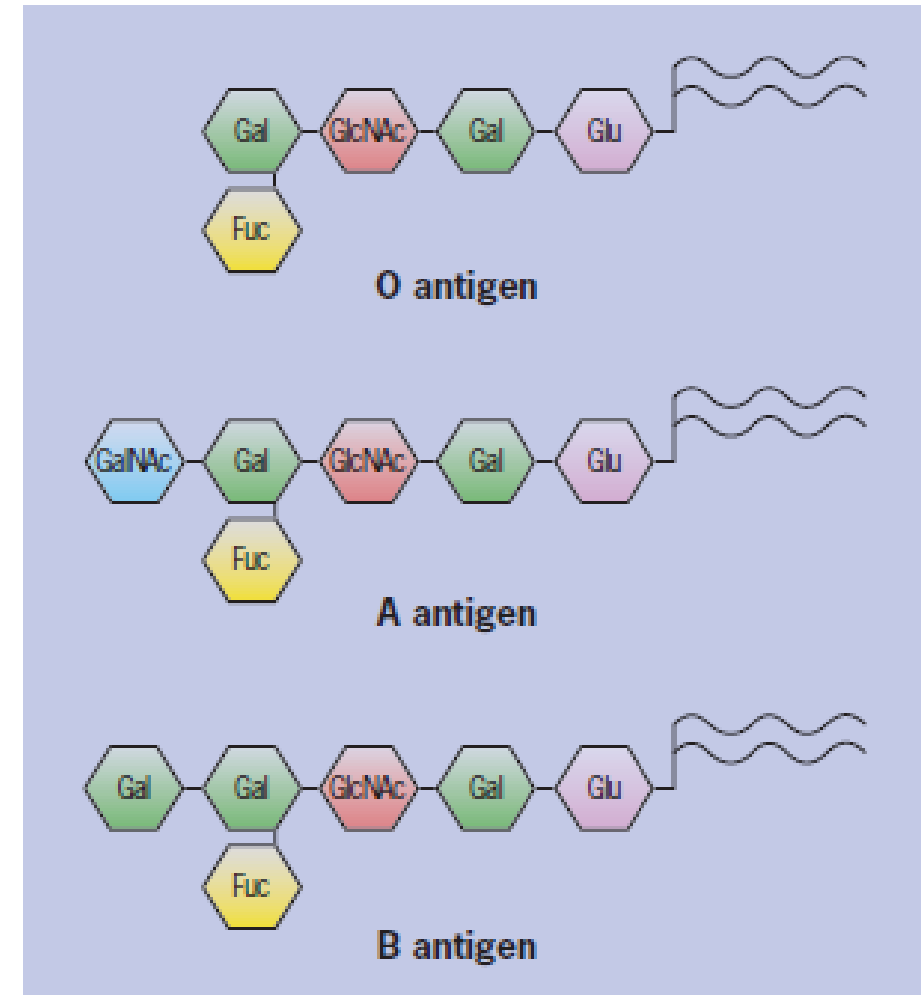
- Depending on the species and cell type, the carbohydrate content of the plasma membrane ranges between 2 and 10 percent by weight.
- More than 90 percent of the membrane's carbohydrate is covalently linked to proteins to form glycoproteins
- Remaining 10 percent carbohydrate is covalently linked to lipids to form glycolipids.

- All of the carbohydrate of the plasma membrane faces outward into the extracellular space.
- The addition of carbohydrate, or **glycosylation**, is the most complex of all types of protein modifications.
- The carbohydrate of glycoproteins is present as short, branched hydrophilic oligosaccharides, typically having fewer than about 15 sugars per chain.
- In contrast to most high-molecular-weight carbohydrates (such as glycogen, starch, or cellulose), the oligosaccharides attached to membrane proteins and lipids can display considerable variability in composition and structure.

- The carbohydrates of the **glycolipids** of the red blood cell plasma membrane determine whether a person's blood type is A, B, AB, or O.
- A person having blood type A has an enzyme that adds an *N*-acetylgalactosamine to the end of the chain, whereas a person with type B blood has an enzyme that adds galactose to the chain terminus. People with AB blood type possess both enzymes, whereas people with O blood type lack enzymes capable of attaching either terminal sugar.

Blood-group antigens. Whether a person has type A, B, AB, or O blood is determined by a short chain of sugars covalently attached to membrane lipids and proteins of the red blood cell membrane. The oligosaccharides attached to membrane lipids (forming a ganglioside) that produce the A, B, and O blood types are shown here. A person with type AB blood has gangliosides with both the A and B structure.

(Gal, galactose; GlcNAc, N-acetylglucosamine; Glu, glucose; Fuc, fucose; GalNAc, N-acetylgalactosamine.)



Membrane proteins

The structure and functions of membrane proteins

- Depending on the cell type and the particular organelle within that cell, a membrane may contain hundreds of different proteins.
- Each membrane protein has a defined orientation relative to the cytoplasm, so that the properties of one surface of a membrane are very different from those of the other surface.
- The asymmetry of membrane proteins is referred to as membrane “**sidedness.**”

- In the plasma membrane, for example, those parts of membrane proteins that interact with other cells or with extracellular substances project outward into the extracellular space, whereas those parts of membrane proteins that interact with cytoplasmic molecules project into the cytosol.
- Membrane proteins can be grouped into three distinct classes distinguished by the intimacy of their relationship to the lipid bilayer; These are
 1. Integral Protein
 2. Peripheral protein
 3. Lipid-Anchored Protein

Integral proteins

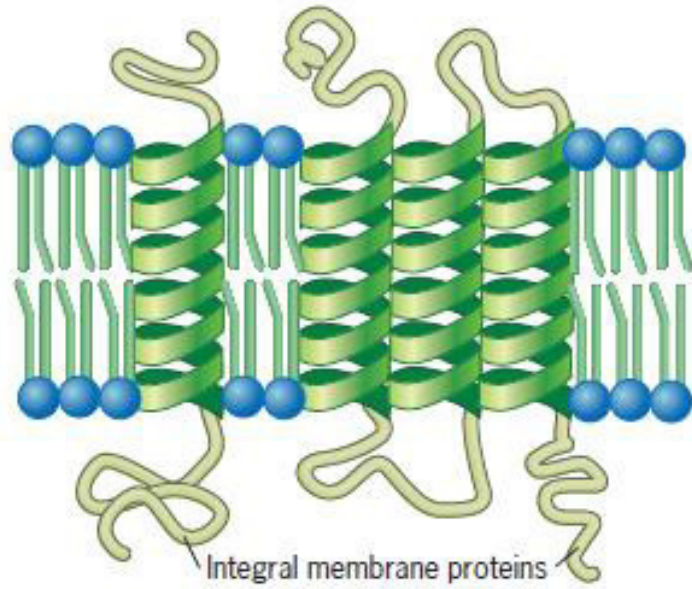
- Integral proteins are **transmembrane proteins**; that is, they pass entirely through the lipid bilayer and thus have domains that protrude from both the extracellular and cytoplasmic sides of the membrane.
- Some integral proteins have only one membrane-spanning segment, whereas others are multispanning.
- Genome-sequencing studies suggest that integral proteins constitute 20–30 percent of all encoded proteins.

Peripheral proteins

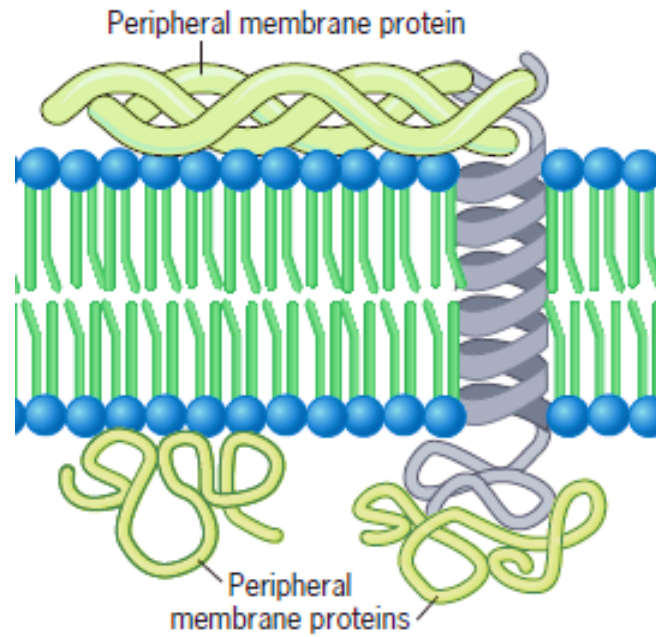
- Peripheral proteins that are located entirely outside of the lipid bilayer, on either the cytoplasmic or extracellular side, yet are associated with the surface of the membrane by noncovalent bonds.

Lipid-anchored proteins

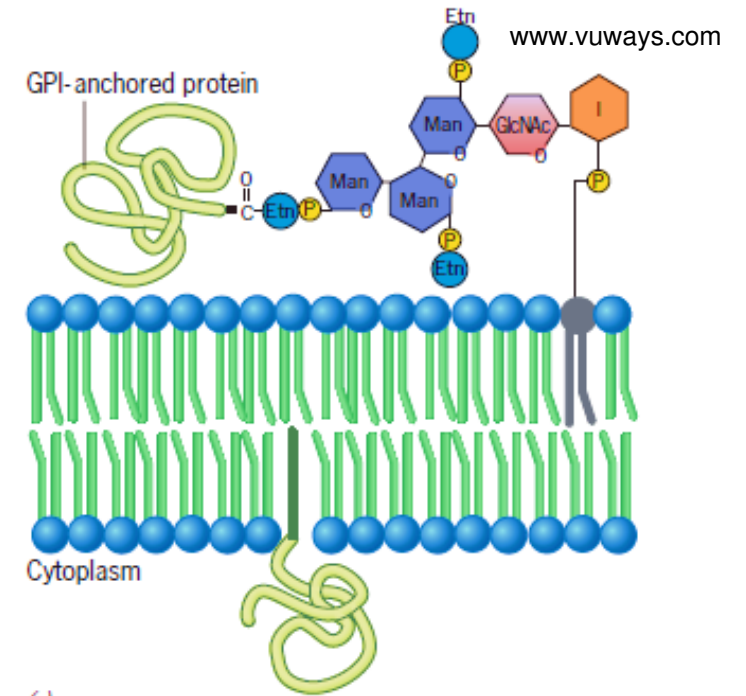
- Lipid-anchored proteins that are located outside the lipid bilayer, on either the extracellular or cytoplasmic surface, but are covalently linked to a lipid molecule that is situated within the bilayer.



(a)



(b)



(c)

(a) **Integral proteins** typically contain one or more transmembrane helices.

(b) **Peripheral proteins** are noncovalently bonded to the polar head groups of the lipid bilayer and/or to an integral membrane protein.

(c) **Lipid-anchored proteins** are covalently bonded to a lipid group that resides within the membrane. The lipid can be phosphatidylinositol, a fatty acid, or a prenyl group (a long-chain hydrocarbon built from five carbon isoprenoid units).

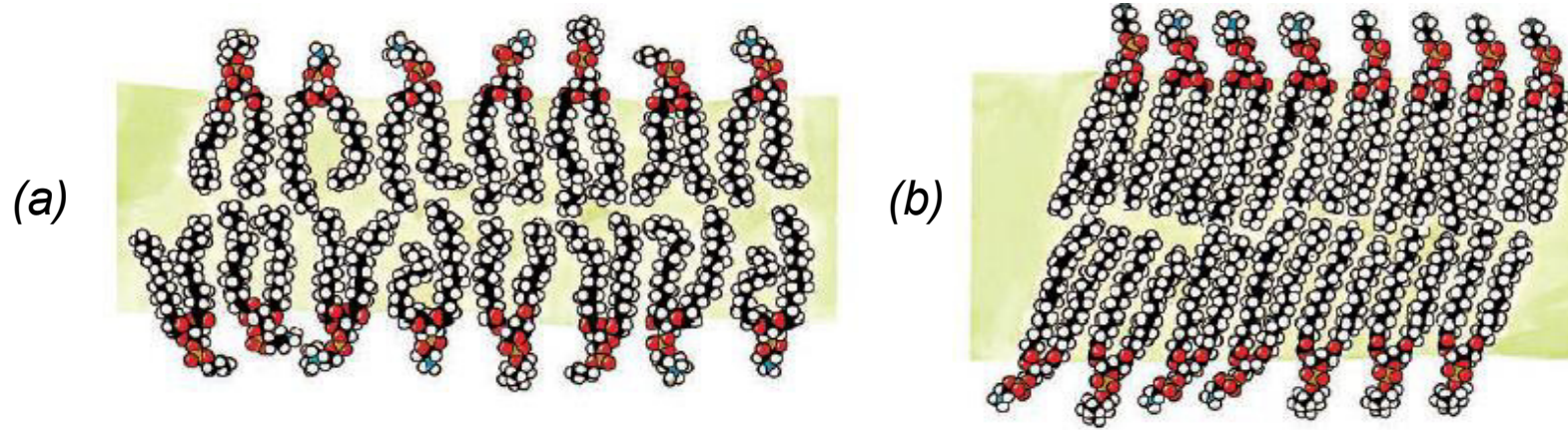
I, inositol; **GlcNAc**, N-acetylglucosamine; **Man**, mannose; **Etn**, ethanolamine; **GPI**, glycosylphosphatidylinositol.

Membrane lipids and membrane fluidity

Membrane lipids and membrane fluidity

- The physical state of the lipid of a membrane is described by its fluidity (or viscosity).
- If the temperature of the bilayer is kept relatively warm (e.g., 37C), the lipid exists in a relatively fluid state.
- If the temperature is slowly lowered, a point is reached where the bilayer distinctly changes .

- The lipid is converted from a liquid crystalline phase to a frozen crystalline gel in which the movement of the phospholipid fatty acid chains is greatly restricted. The temperature at which this change occurs is called the **transition temperature**.



The structure of the lipid bilayer depends on the temperature.

- (a) Above the transition temperature, the lipid molecules and their hydrophobic tails are free to move in certain directions, even though they retain a considerable degree (a) (b) of order.*
- (b) Below the transition temperature, the movement of the molecules is greatly restricted, and the entire bilayer can be described as a crystalline gel.*

Importance of Membrane Fluidity

1. Membrane fluidity provides a perfect compromise between a rigid, ordered structure in which mobility would be absent and a completely fluid, nonviscous liquid in which the components of the membrane could not be oriented and structural organization and mechanical support would be lacking.
2. Fluidity allows for interactions to take place within the membrane.
3. Fluidity also plays a key role in membrane assembly.

Following cellular processes depends upon movement of membrane components;

1. Cell movement
2. Cell growth
3. Cell division
4. Formation of intercellular junctions
5. Secretion
6. Endocytosis

Diffusion

The movement of substances across cell membranes

- In a sense, the plasma membrane has a dual function.
 1. On one hand, it must retain the dissolved materials of the cell so that they do not simply leak out into the environment,
 2. while on the other hand, it must allow the necessary exchange of materials into and out of the cell.
- The lipid bilayer of the membrane is ideally suited to prevent the loss of charged and polar solutes from a cell.

- There are basically two means for the movement of substances through a membrane:
 1. Passively by diffusion
 2. Actively by an energy-coupled transport process.
- Both types of movements lead to the net flux of a particular ion or compound.
- The term **net flux** indicates that the movement of the substance into the cell (influx) and out of the cell (efflux) is not balanced, but that one exceeds the other.

Diffusion

Diffusion is a spontaneous process in which a substance moves from a region of high concentration to a region of low concentration, eventually eliminating the concentration difference between the two regions.

- A membrane may be permeable to a given solute either
 - (1) because that solute can pass directly through the lipid bilayer
 - (2) because that solute can traverse an aqueous pore that spans the membrane.

- It is evident that the greater the lipid solubility, the faster the penetration.
- Measure of the polarity (or nonpolarity) of a substance is its **partition coefficient**, which is the ratio of its solubility in a nonpolar solvent.
- Another factor determining the rate of penetration of a compound through a membrane is its size. If two molecules have approximately equivalent partition coefficients, the smaller molecule tends to penetrate the lipid bilayer of a membrane more rapidly than the larger one.

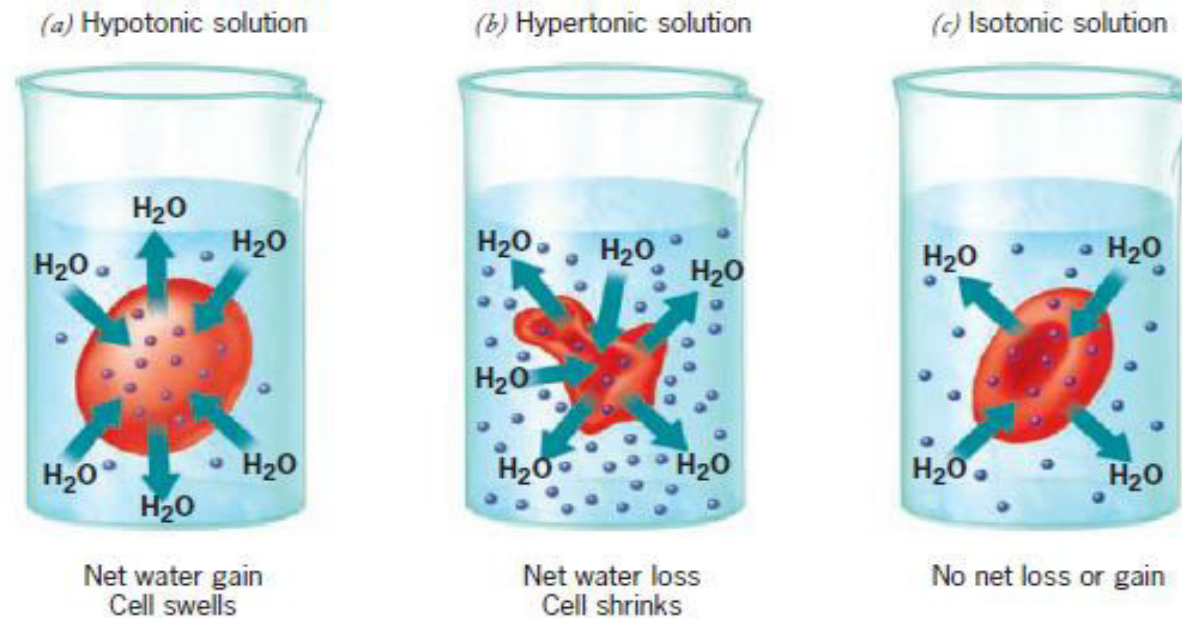
Diffusion of Water through Membranes

Diffusion of Water through Membranes

- Water molecules move much more rapidly through a cell membrane than do dissolved ions or small polar organic solutes, which are essentially non penetrating.
- Because of this difference in the penetrability of water versus solutes, membranes are said to be **semipermeable**.
- Water moves readily through a semipermeable membrane from a region of lower *solute* concentration to a region of higher *solute* concentration. This process is called **osmosis**.

- The compartment of higher solute concentration is said to be **hypertonic** (or **hyperosmotic**) relative to the compartment of lower solute concentration, which is described as being **hypotonic** (or **hypoosmotic**).
- When a cell is placed into a hypotonic solution, the cell rapidly gains water by osmosis and swells.
- Conversely, a cell placed into a hypertonic solution rapidly loses water by osmosis and shrinks.
- Once the internal solute concentration (which includes a high concentration of dissolved proteins) equals the external solute concentration, the internal and external fluids are **isotonic** (or **isosmotic**).

The effects of differences in the concentration of solutes on opposite sides of the plasma membrane.



- (a) A cell placed in a hypotonic solution (one having a lower solute concentration than the cell) swells because of a net gain of water by osmosis.
- (b) A cell in a hypertonic solution shrinks because of a net loss of water by osmosis.
- (c) A cell placed in an isotonic solution maintains a constant volume because the inward flux of water is equal to the outward flux.

The Diffusion of Ions through Membranes

The Diffusion of Ions through Membranes

- The lipid bilayer of biological membranes is highly impermeable to charged substances, including small ions such as Na, K, Ca²⁺, and Cl.
- In 1955, Alan Hodgkin and Richard Keynes of Cambridge University first proposed that cell membranes contain **ion channels**.
- Ion channels are openings in the membrane that are permeable to specific ions.

■ Three major categories of gated channels are distinguished:

- 1. Voltage-gated channels
- 2. Ligand-gated channels
- 3. Mechano-gated channels

1. Voltage-gated channels whose conformational state depends on the difference in ionic charge on the two sides of the membrane.

2. **Ligand-gated channels** whose conformational state depends on the binding of a specific molecule (the ligand), which is usually not the solute that passes through the channel.

For example, neurotransmitters, such as acetylcholine, act on the outer surface of certain cation channels, while cyclic nucleotides, such as cAMP, act on the inner surface of certain calcium ion channels.

3. **Mechano-gated channels** whose conformational state depends on mechanical forces (e.g., stretch tension) that are applied to the membrane. Members of one family of cation channels, for example, are opened by the movements of stereocilia on the hair cells of the inner ear in response to sound or motions of the head.

Facilitated Diffusion

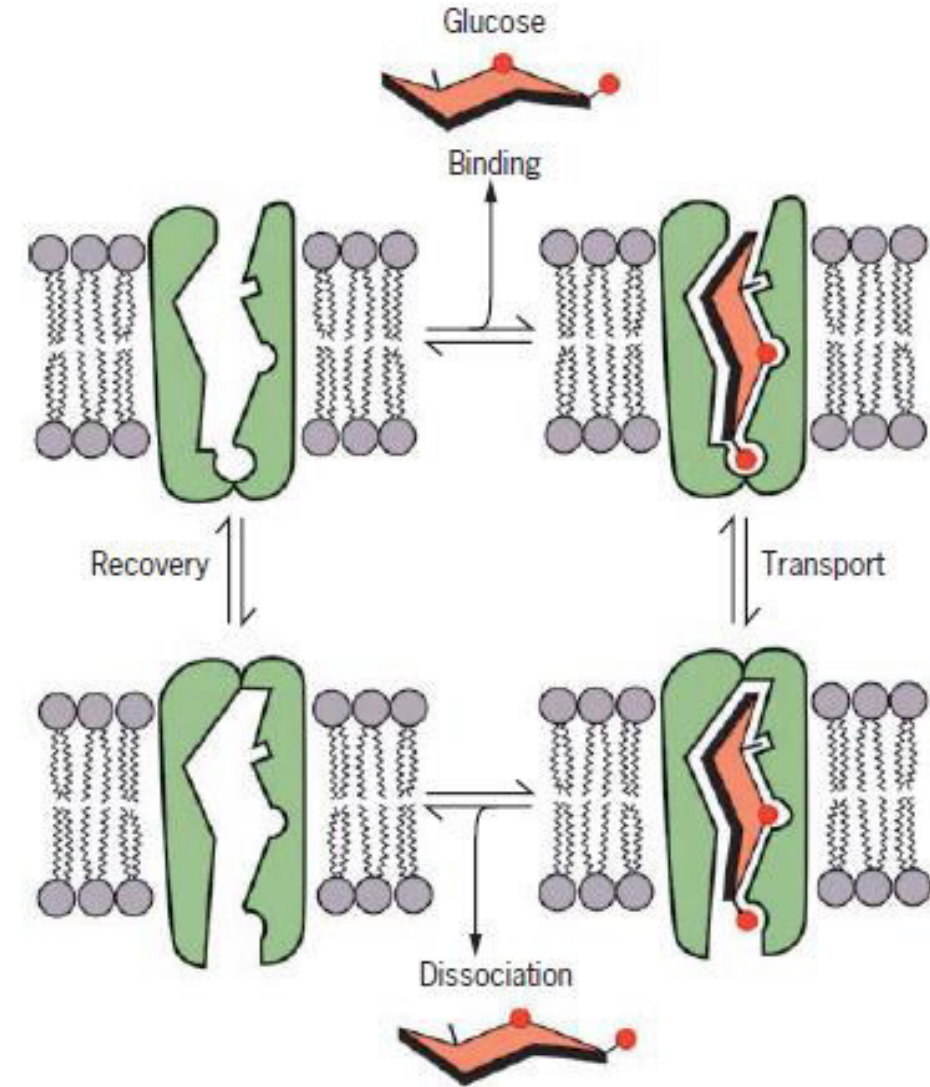
Facilitated Diffusion

- Substances always diffuse across a membrane from a region of higher concentration on one side to a region of lower concentration, but they do not always diffuse through the lipid bilayer or through a channel.
- In many cases, the diffusing substance first binds selectively to a membrane-spanning protein, called a **facilitative transporter**, that facilitates the diffusion process.

- Because they operate passively, that is, without being coupled to an energy-releasing system, facilitated transporters can mediate the movement of solutes equally well in both directions.
- The direction of net flux depends on the relative concentration of the substance on the two sides of the membrane.

Facilitated diffusion

A schematic model for the facilitated diffusion of glucose depicts the alternating conformation of a carrier that exposes the glucose binding site to either the inside or outside of the membrane.



Active Transport

Active Transport

The endergonic movement of ions or other solutes across the membrane against a concentration gradient is coupled to an exergonic process, such as the hydrolysis of ATP, the absorbance of light, the transport of electrons, or the flow of other substances down their gradients.

- Like facilitated diffusion, active transport depends on integral membrane proteins.
- Proteins that carry out active transport are often referred to as “pumps.”

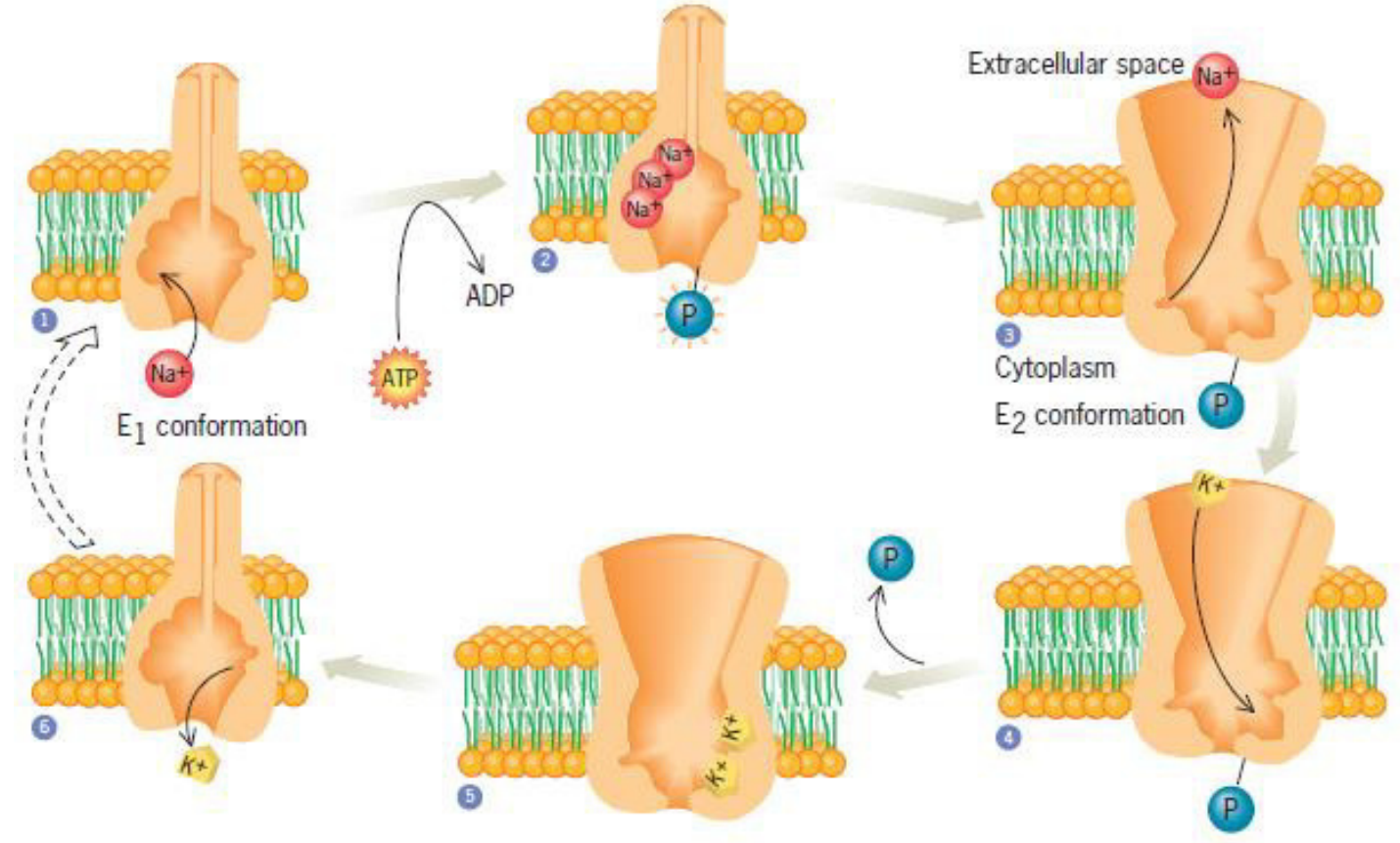
Coupling Active Transport to ATP Hydrolysis

- In 1957, Jens Skou, a Danish physiologist, discovered an ATP-hydrolyzing enzyme in the nerve cells of a crab that was only active in the presence of both Na and K ions.
- Skou proposed, that this enzyme, which was responsible for ATP hydrolysis, was the same protein that was active in transporting the two ions; the enzyme was called the Na/K-ATPase, or the *sodium–potassium pump*.
- The ratio of NaK pumped by the Na/K-ATPase is not 1:1.
- For each ATP hydrolyzed, three sodium ions are pumped out as two potassium ions are pumped in.

The Na/K-ATPase.

Simplified schematic model of the transport cycle. Sodium ions

(1) bind to the protein on the inside of the membrane. ATP is hydrolyzed, and the phosphate is transferred to the protein (2), changing its conformation (3) and allowing sodium ions to be expelled to the external space. Potassium ions then bind to the protein (4), and the phosphate group is subsequently lost (5), which causes the protein to snap back to its original conformation, allowing the potassium ions to diffuse into the cell (6). The cation binding sites are located deep within the transmembrane domain, which consists of 10 membrane-spanning helices.



Cell Biology



Endocytosis

Endocytosis

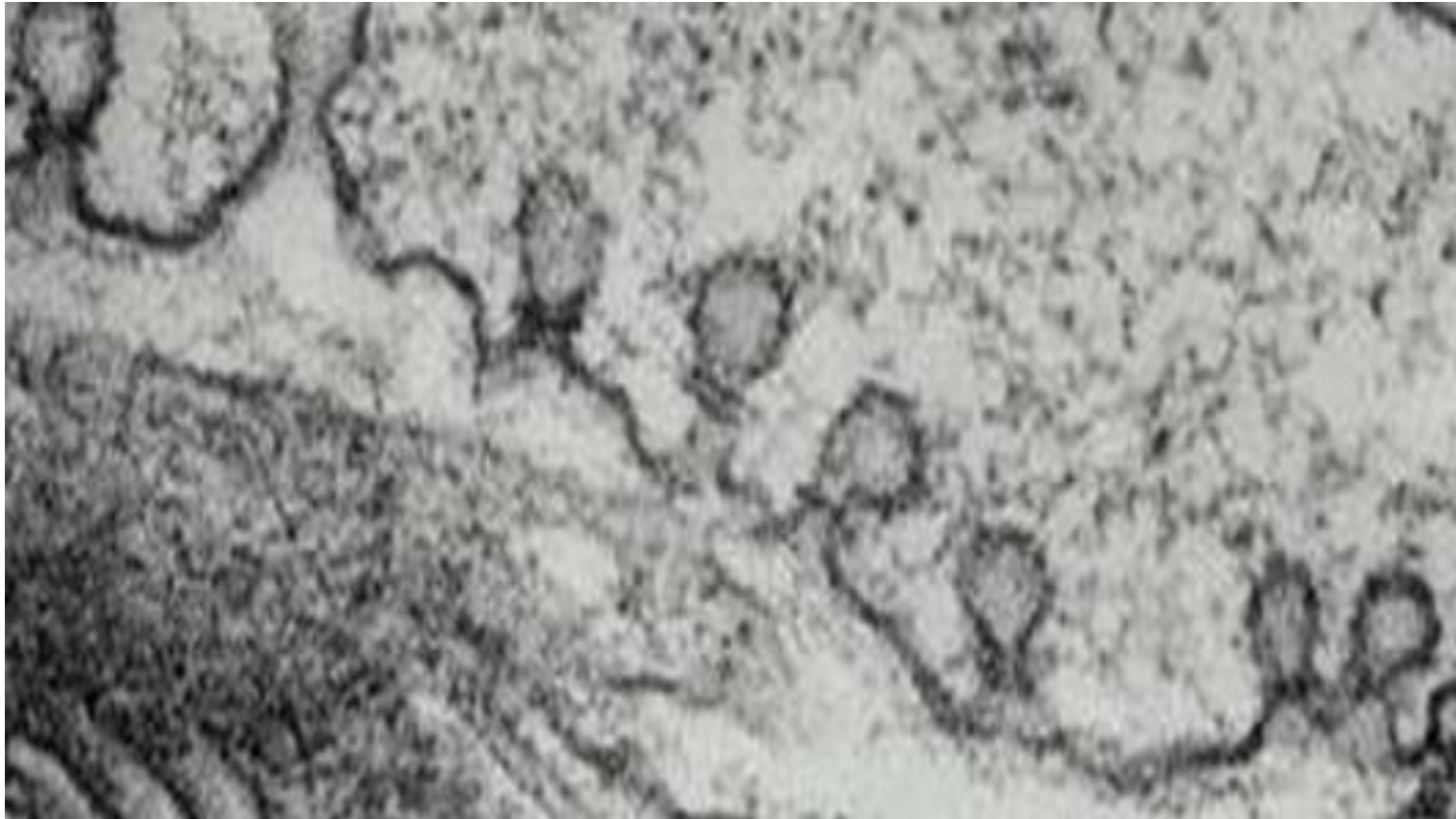
The material to be ingested is **progressively enclosed** by a small portion of the **plasma** membrane, which first **invaginates** and then **pinches** off to form an **endocytic vesicle** containing the ingested substance or particle

Phagocytosis involves the **ingestion** of **large** particles microorganisms or dead cells via large vesicles called phagosomes (**>250 nm** in diameter)

Pinocytosis involves ingestion of fluid & solutes via small pinocytic vesicles (about **100 nm** in diameter)

Most eucaryotic cells are **continually ingesting fluid** and solutes by pinocytosis; large particles are most efficiently ingested by specialized

Endocytosis



Endocytosis

In mammals, three classes of white blood cells act as **professional phagocytes** macrophages, neutrophils, and dendritic cells

These cells develop from hemopoietic stem cells and they **defend** us against infection by **ingesting invading microorganisms**.

Macrophages also **scavenge senescent cells** and cells that have died by apoptosis.

In quantitative terms, the latter function is by far the most important: our macrophages **phagocytose more than 10^{11} senescent red blood cells every day**.

Endocytosis

Particles first bind to the surface of the phagocyte.

Phagocytes have a variety of specialized surface receptors that are functionally linked to the phagocytic machinery of the cell.

Phagocytosis is a triggered process, requiring that receptors be activated that signal the cell interior and initiate the response

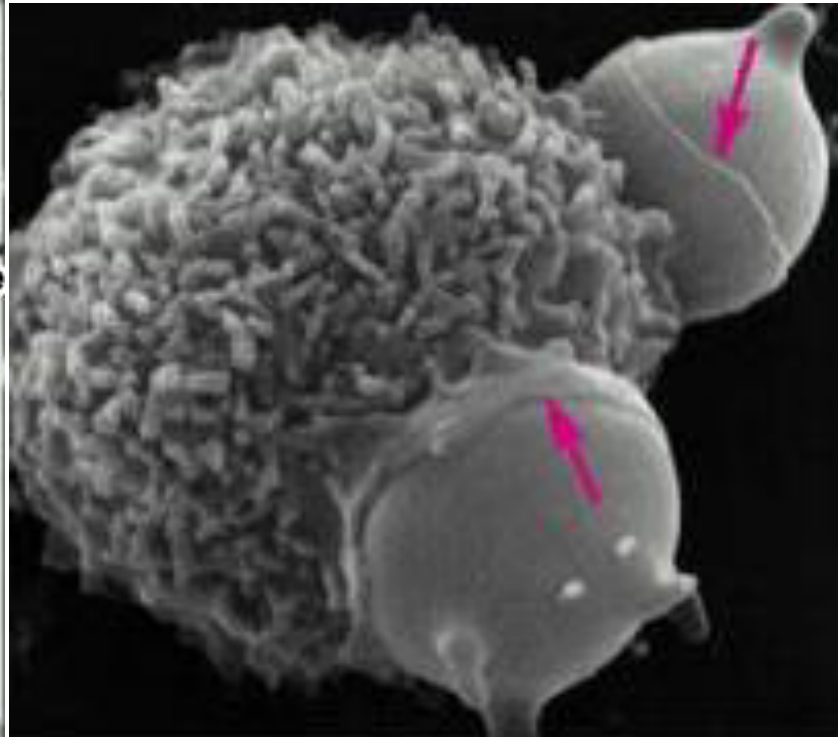
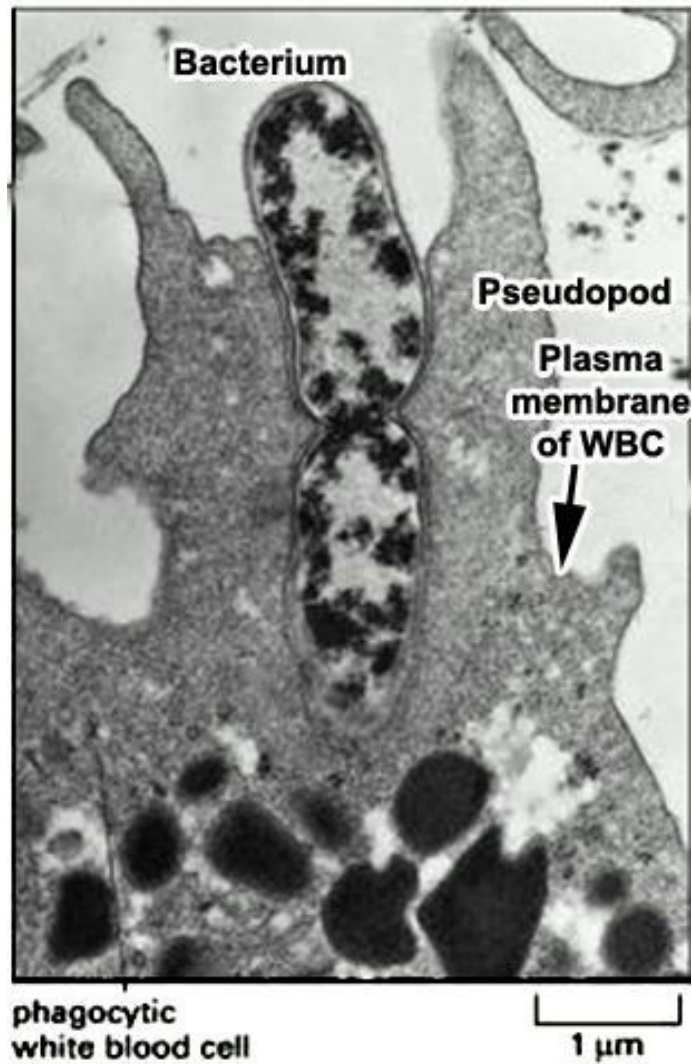
Best-characterized triggers are antibodies, which protect us by binding to the surface of infectious microorganisms to form a coat in which the tail region of each antibody molecule, called the Fc region, is exposed on the exterior

Endocytosis

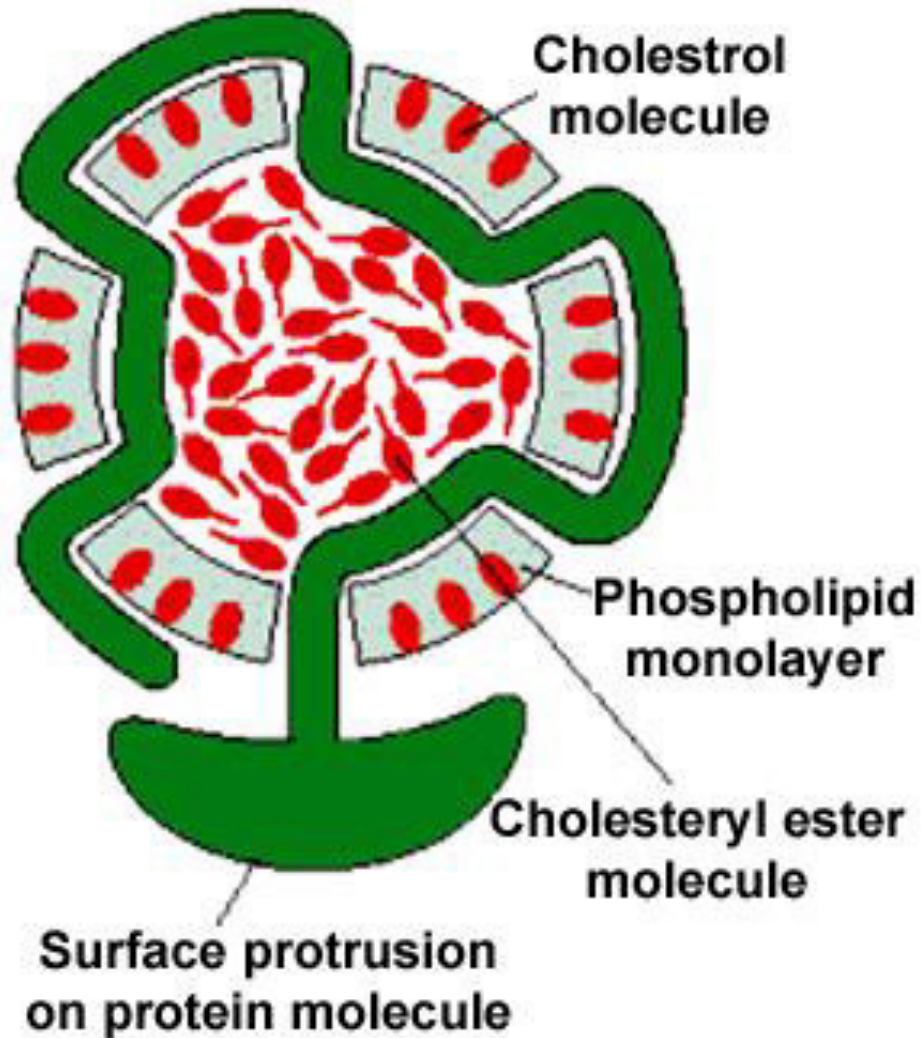
This antibody coat is recognized by specific **Fc receptors** on the surface of macrophages and neutrophils, whose **binding induces** the phagocytic cell to extend pseudopods that engulf the particle and fuse at their tips to form a phagosome.

Apoptotic cells lose the **asymmetric distribution** of phospholipids in their plasma membrane as a consequence, negatively charged **phosphatidylserine**, which is normally confined to the cytosolic leaflet of the lipid bilayer, is now exposed on the **outside of the cell**, where it triggers the phagocytosis of the dead cell

Endocytosis

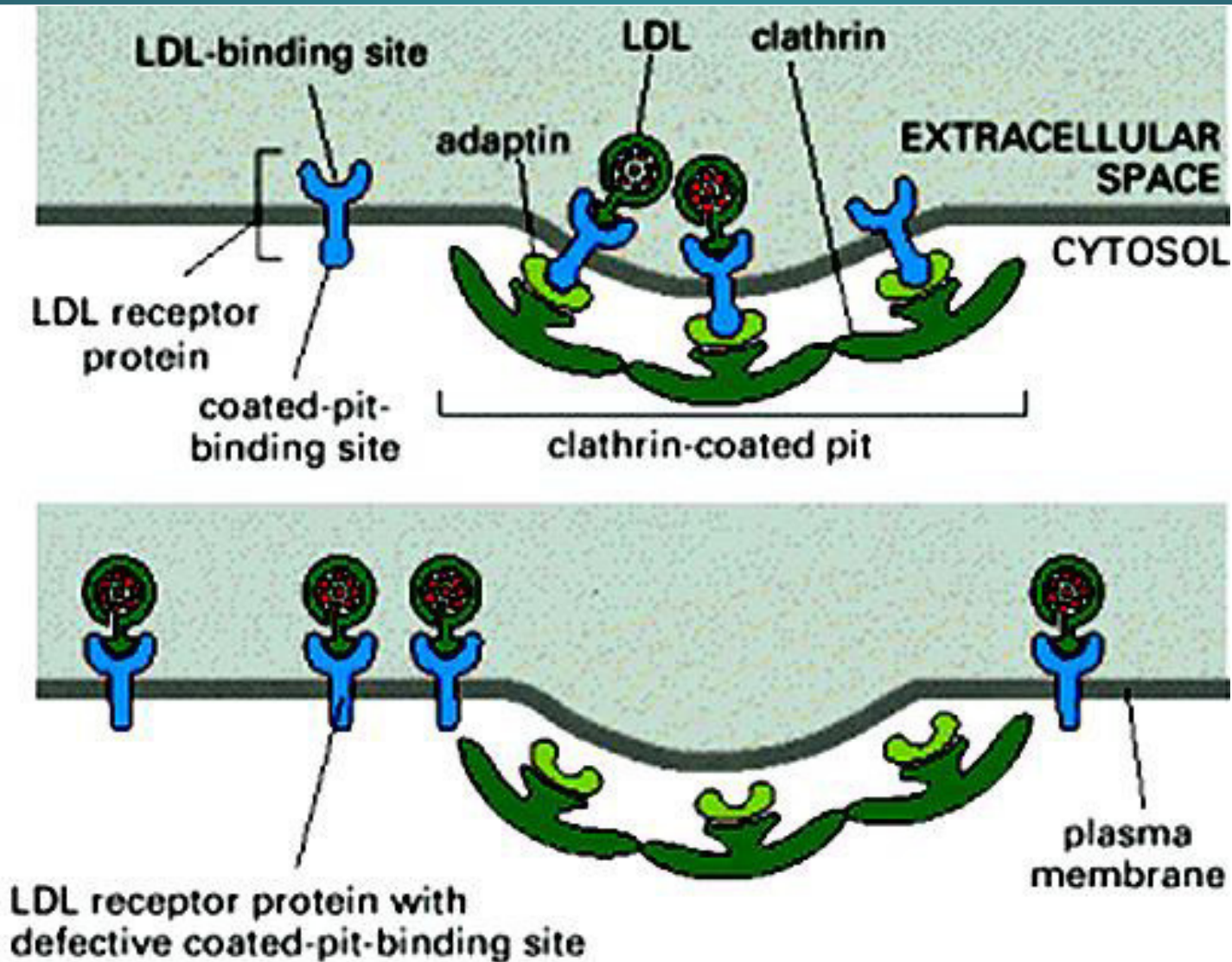


Low-density lipoprotein (LDL) particle



Each particle contains a core of about **1500** cholesterol molecules esterified to long-chain fatty acids

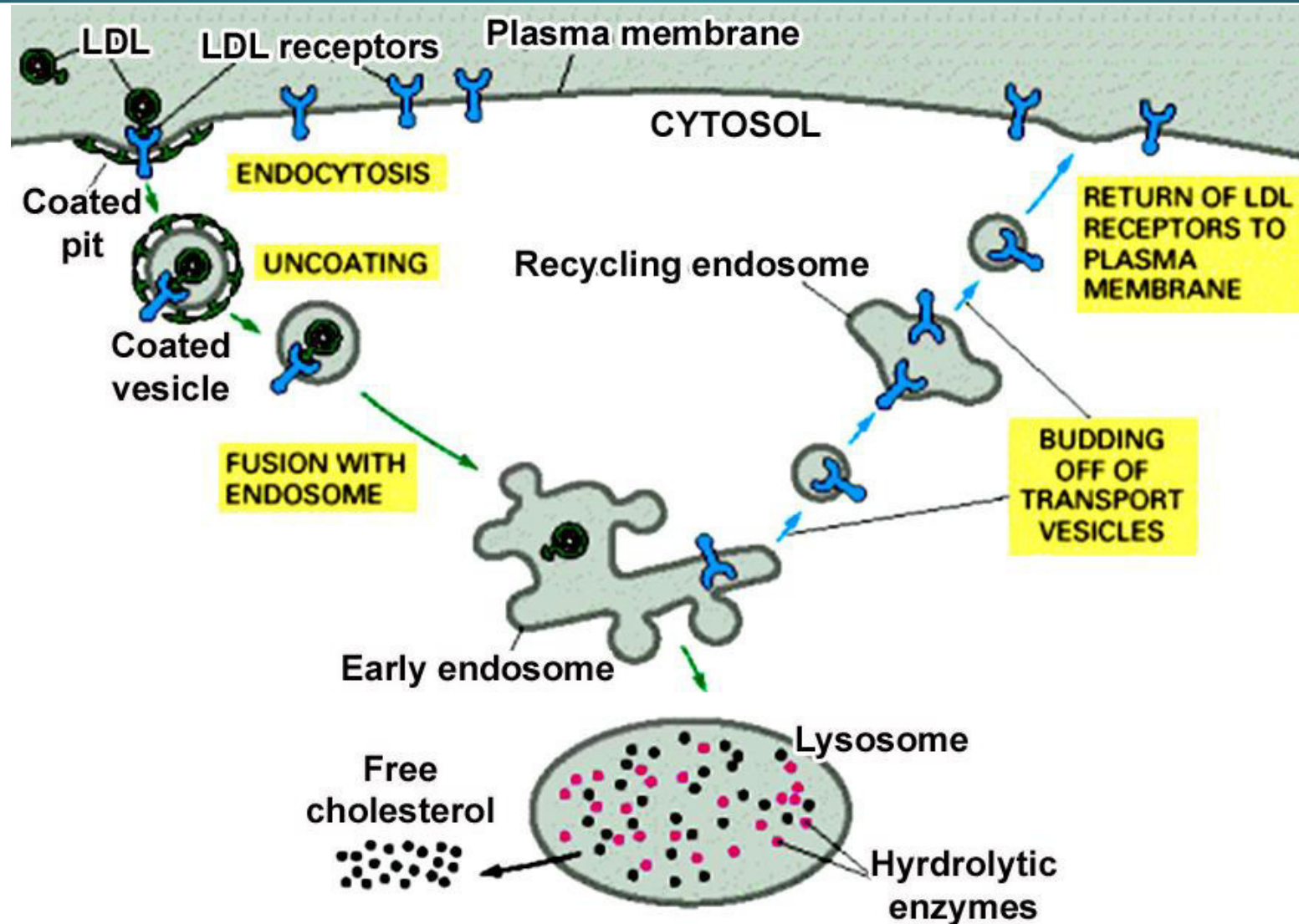
Low-density lipoprotein (LDL) particle



Low-density lipoprotein (LDL) particle



Low-density lipoprotein (LDL) particle



Phagocytosis

Phagocytosis

- Phagocytosis (“cell eating”) is carried out extensively by a few types of cells.
- Uptake of relatively large particles (0.5 μ m diameter) from the environment.
- Many single-celled protists, such as amoebas and ciliates, trap food particles and smaller organisms and enclosing them within folds of the plasma membrane.
- The folds fuse to produce a vacuole (or *phagosome*) that pinches off inwardly from the plasma membrane.

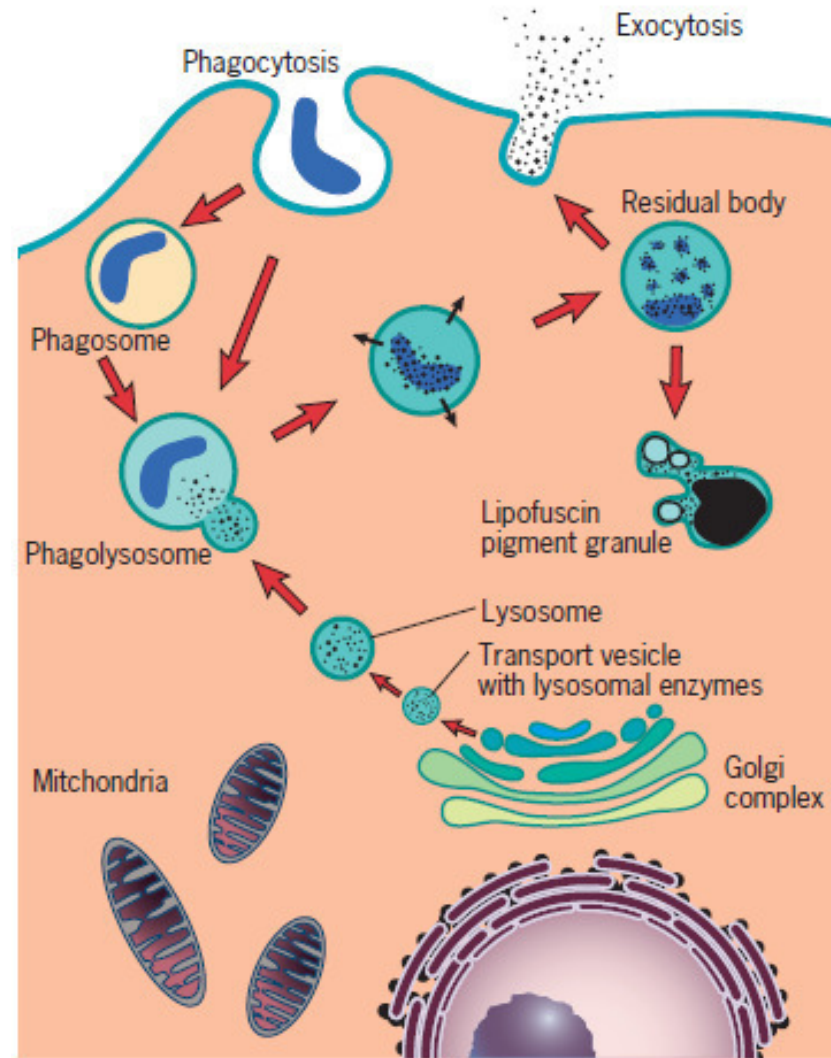
- The phagosome fuses with a lysosome, and the material is digested within the resulting *phagolysosome*.
- In most animals, phagocytosis is a protective mechanism rather than a mode of feeding.
- Mammals possess a variety of “professional” phagocytes, including macrophages and neutrophils.
- Once inside the phagocyte, microorganisms may be killed by lysosomal enzymes or by oxygen free radicals.

- The engulfment of particulate material is driven by contractile activities of the actin-containing microfilaments
- Some bacterial species hijack the phagocytic machinery to promote their own survival in the body.
- If the phagosome does become highly acidic, the bacterium is able to maintain its own physiological pH despite the lowered pH of its surrounding medium.

Examples

1. The bacterium responsible for Q fever, *Coxiella burnetii*, becomes enclosed in a phagosome that does fuse with a lysosome, but neither the acidic environment nor the lysosomal enzymes can destroy the pathogen.
2. *Listeria monocytogenes*, a bacterium that causes meningitis, produces proteins that destroy the integrity of the lysosomal membrane, allowing the bacterium to escape into the cell's cytosol.

A summary of the phagocytic pathway.



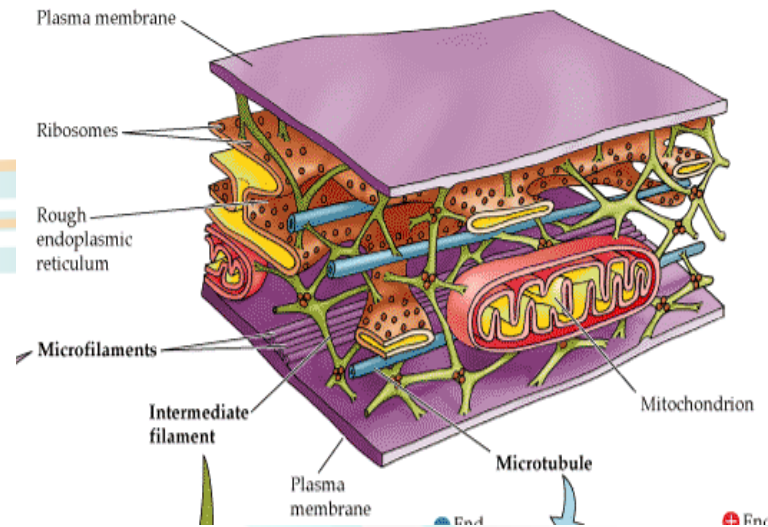
CELL BIOLOGY



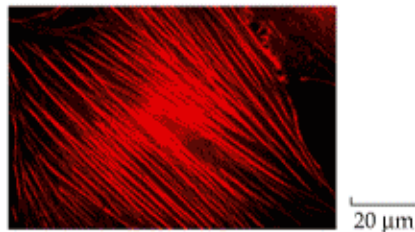
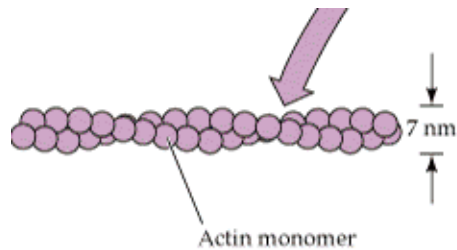
Cytoskeleton

Cytoskeleton

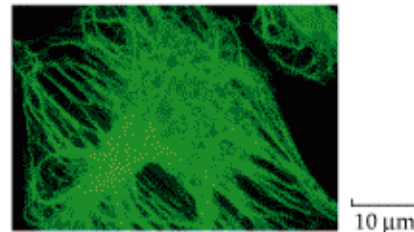
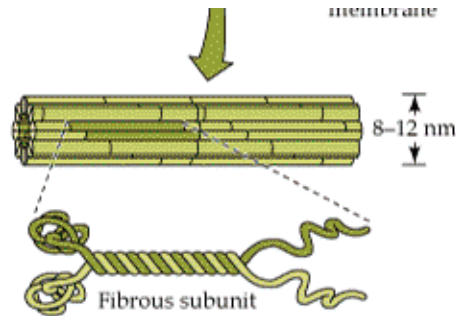
Shape & Function



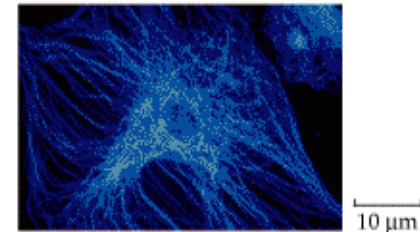
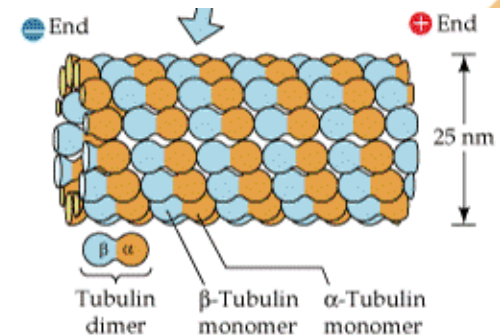
Cytoskeleton



Microfilaments are made up of strands of the protein actin and often interact with strands of other proteins. They change cell shape and drive cellular motion, including contraction, cytoplasmic streaming, and the “pinched” shape changes that occur during cell division. Microfilaments and myosin strands together drive muscle action.



Intermediate filaments are made up of fibrous proteins organized into tough, ropelike assemblages that stabilize a cell's structure and help maintain its shape. Some intermediate filaments help to hold neighboring cells together. Others make up the nuclear lamina.



Microtubules are long, hollow cylinders made up of many molecules of the protein tubulin. Tubulin consists of two subunits, α-tubulin and β-tubulin. Microtubules lengthen or shorten by adding or subtracting tubulin dimers. Microtubule shortening moves chromosomes. Interactions between microtubules drive the movement of cells. Microtubules serve as “tracks” for the movement of vesicles.

Cytoskeleton

Actin

Actin (cortical)

Stabilizes cell shape.

**Generates movement
local.**

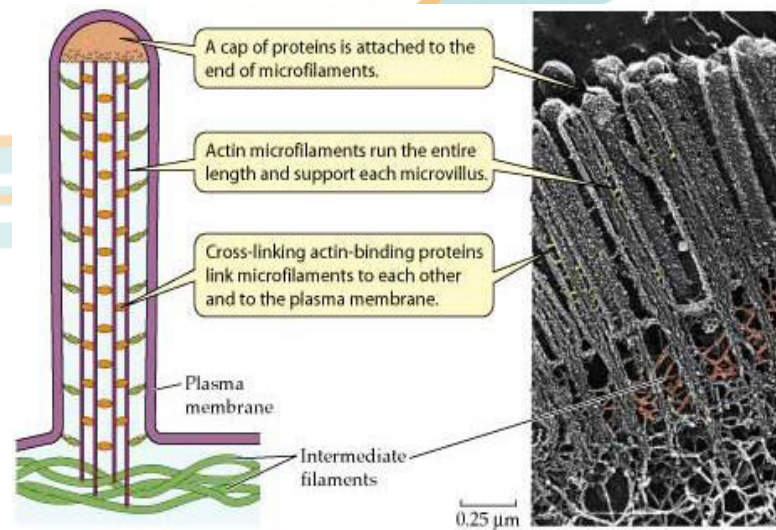
Muscle contraction.

**Constriction ring in cell
divission (Cytokinesis).**

**Cytoplasmic
streaming.**

Cytoskeleton

Actin for Support



CELL BIOLOGY

Cytoskeleton 2



Cytoskeleton

IF

IF stabilize cell structure (hold organelles).

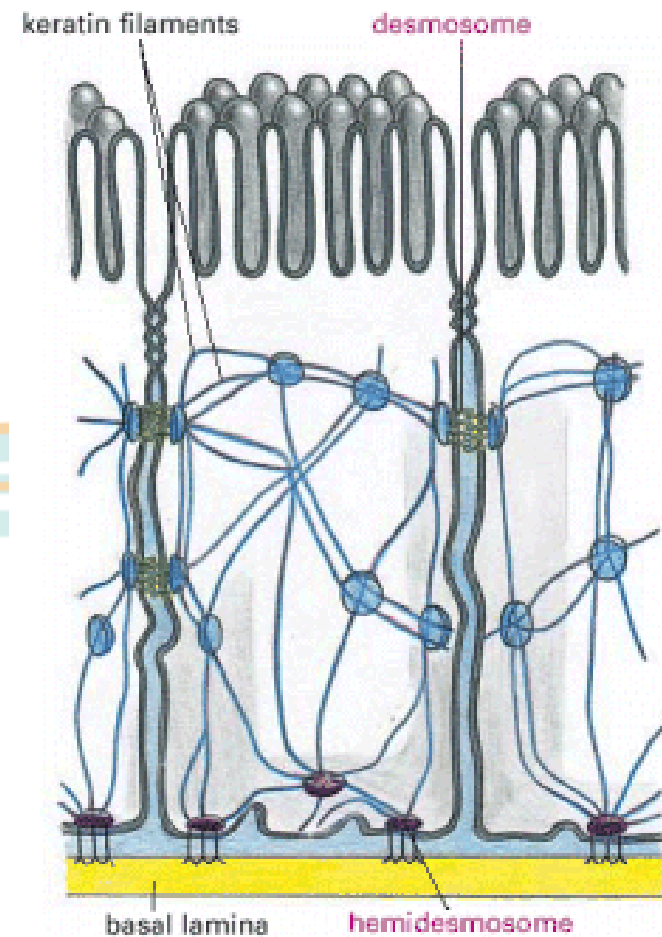
Stabilize and maintain tissue rigidity (desmosomes).

Lamins in nucleus.

Resist tension.

Cytoskeleton

IF



Cytoskeleton

Microtubules

Rigid internal skeleton
resist compression.

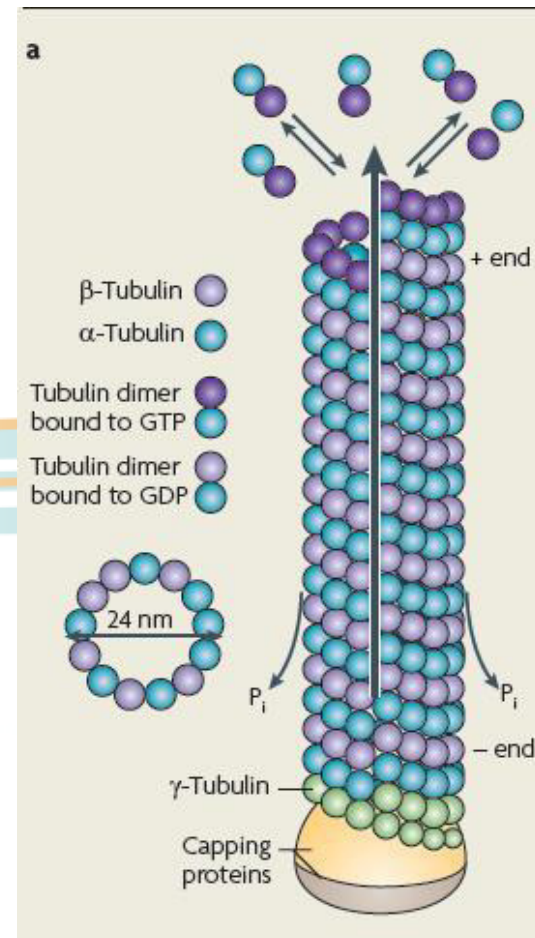
Tracks along for motor
proteins.

Tubulin is a dimer of
 α -tubulin and β -tubulin.

The two ends different
plus (+) end & minus
(-) end (cat Tail &
dynamic).

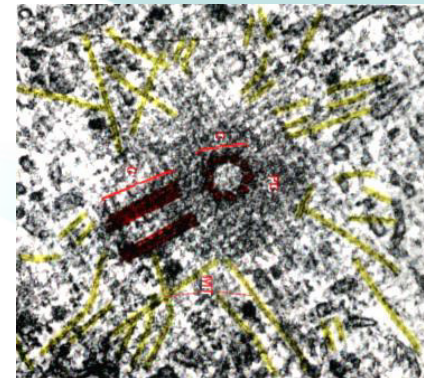
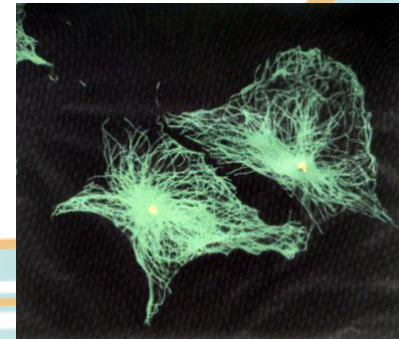
Cytoskeleton

Microtubules 13



Cytoskeleton

Centrosome Microtubule organizing center



END

Types of cytoskeleton

Types of cytoskeleton

- The cytoskeleton is composed of three well-defined filamentous structures
 1. **Microtubules** are long, hollow, unbranched tubes composed of subunits of the protein tubulin.
 2. **Microfilaments** are solid, thinner structures, often organized into a branching network and composed of the protein actin.
 3. **Intermediate filaments** are tough, ropelike fibers composed of a variety of related proteins.
- Each of the three types of cytoskeletal filaments is a polymer of protein subunits held together by weak, noncovalent bonds.

Properties of Microtubules, Intermediate Filaments, and Actin Filaments

	Microtubules	Intermediate filaments	Actin filaments
Subunits incorporated into polymer	GTP- $\alpha\beta$ -tubulin heterodimer	~70 different proteins	ATP-actin monomers
Preferential site of incorporation	+ End (β -tubulin)	Internal	+ End (barbed)
Polarity	Yes	No	Yes
Enzymatic activity	GTPase	None	ATPase
Motor proteins	Kinesins, dyneins	None	Myosins
Major group of associated proteins	MAPs	Plakins	Actin-binding proteins
Structure	Stiff, hollow, inextensible tube	Tough, flexible, extensible filament	Flexible, inextensible helical filament
Dimensions	25 nm outer diam.	10-12 nm diam.	8 nm diam.
Distribution	All eukaryotes	Animals	All eukaryotes
Primary functions	Support, intracellular transport, cell organization	Structural support	Motility, contractility
Subcellular distribution	Cytoplasm	Cytoplasm + nucleus	Cytoplasm

Overview of the major functions of the cytoskeleton

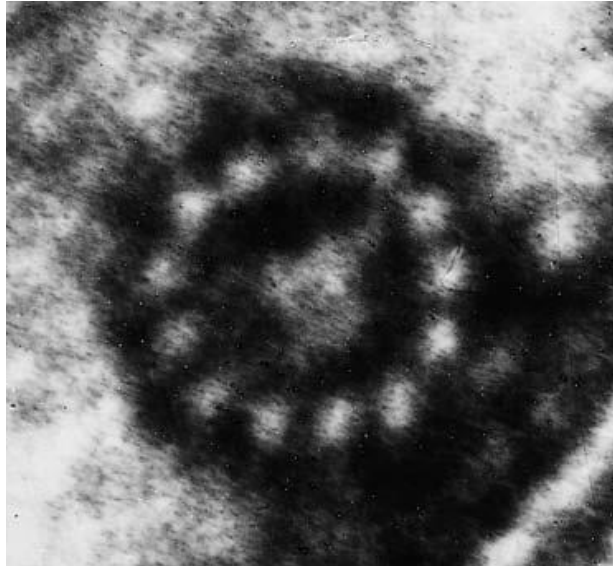
1. It provides structural support that can determine the shape of the cell and resist forces that tend to deform.
2. It is responsible for positioning the various organelles within the interior of the cell.
3. It direct the movement of materials and organelles within cells.
4. It helps in movement of cells from one place to another. Single-celled organisms move with the aid of specialized, microtubule-containing locomotor organelles (cilia and flagella).
5. It serves as an essential component of the cell's division machinery.

MICROTUBULES

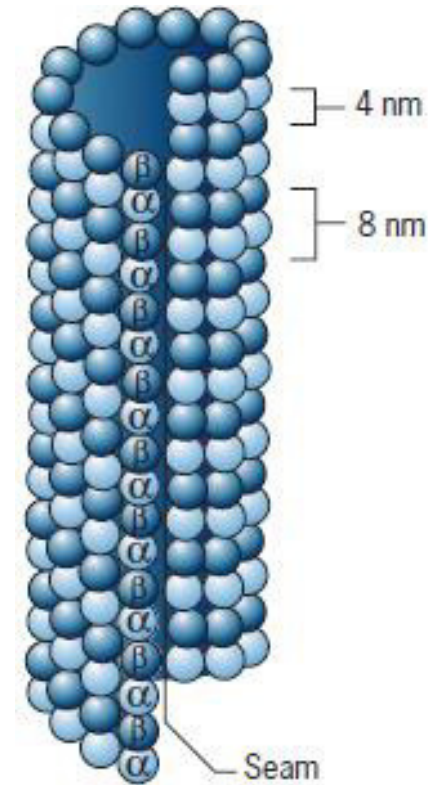
Structure and Composition

- Microtubules are hollow, relatively rigid, tubular structures.
- They occur in nearly every eukaryotic cell.
- They have an outer diameter of 25 nm and a wall thickness of approximately 4 nm.
- The wall of a microtubule is composed of globular proteins arranged in longitudinal rows, termed **protofilaments**.
- .

- Microtubules are consist of 13 protofilaments.
- Each protofilament is assembled from dimeric building blocks consisting of one α -tubulin and one β -tubulin subunit.
- The two types of globular tubulin subunits have a similar three-dimensional structure and fit tightly together.
- All of the protofilaments of a microtubule have the same polarity. Consequently, the entire polymer has polarity.



Electron micrograph of a cross section through a microtubule of a Juniperus root tip cell revealing the 13 subunits arranged within the wall of the tubule.



Longitudinal section of a microtubule

Functions

- In animal cells, microtubules extend in a radial array outward around the nucleus, giving these cells their round, flattened shape.
- Microtubules serves as skeletal elements which is obvious from its role in cilia and flagella and the axons of nerve cells.
- In plant cells, microtubules play role in maintaining cell shape.
- They help in maintaining the internal organization of cells.

Intermediate Filaments

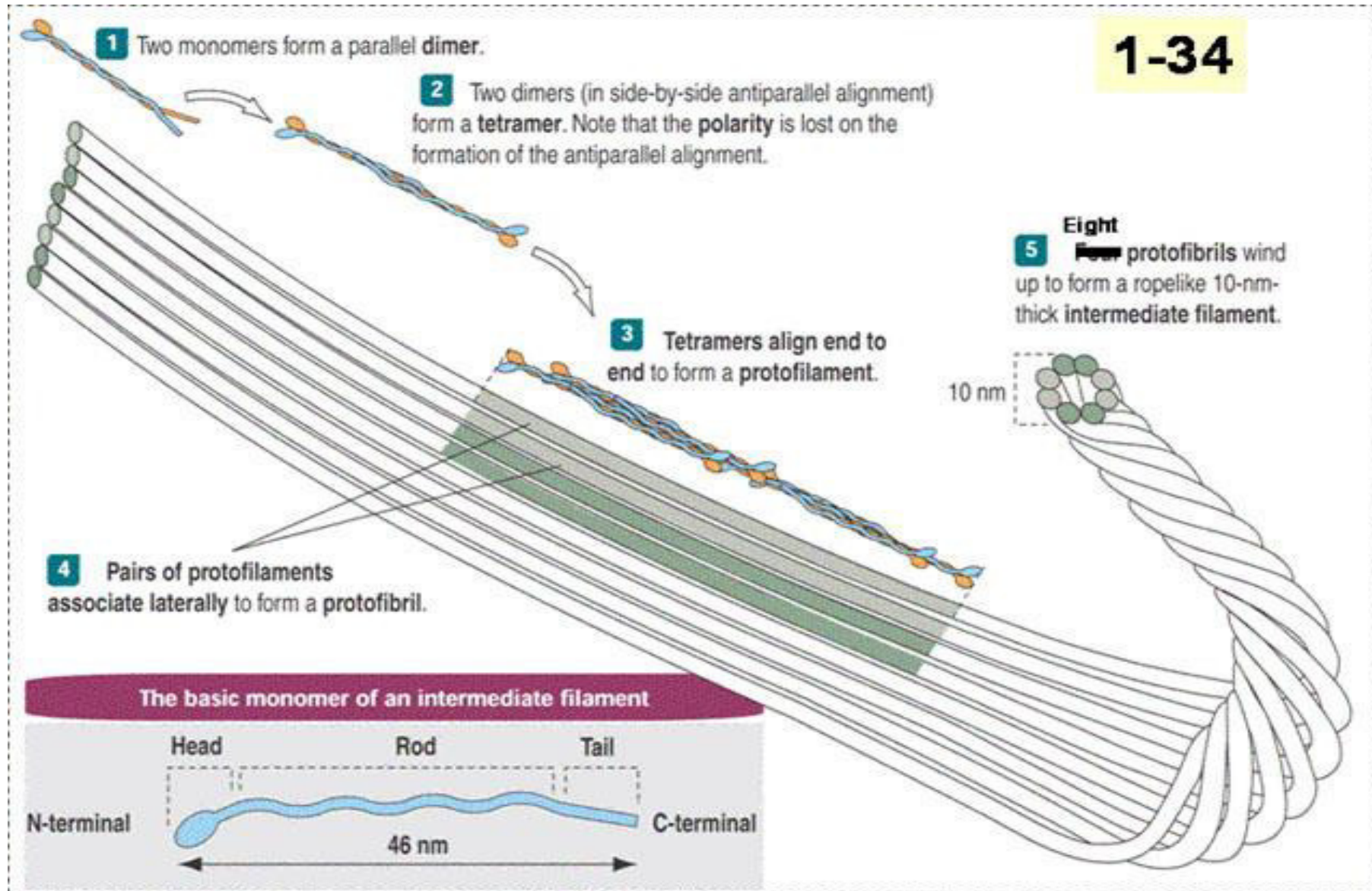
Introduction

- The term "intermediate filaments" refers only to the diameter of the fibers, and bears no relationship to position or function.
- Intermediate filaments are about 11 nm in diameter.
- Intermediate filaments are strong, flexible ropelike fibers that provide mechanical strength to cells.
- IFs are a chemically heterogeneous group of structures that, in humans, are encoded by approximately 70 different genes.

Structure

- The structural subunit of an intermediate filament is a dimeric fibrous protein which makes it fairly rigid.
- These are *non-polarized*, in contrast to the polarized nature of microfilaments and microtubules. Thus intermediate filaments do not possess (+) or (-) ends, but are symmetrical.
- To make an intermediate filament, these tetramers lengthen, and eight join laterally to form the 11 nm intermediate filament. The length may be very great.

Structure of intermediate filament



Functions

1. The tight association between protofilaments provide intermediate filaments with a high tensile strength, therefore found in particularly durable structures such as hair, scales and fingernails.
2. Intermediate filaments is to create cell cohesion and prevent the acute fracture of epithelial cell sheets under tension.

Microfilaments

Introduction

- **Microfilaments** are approximately 8 nm in diameter and composed of globular subunits of the protein **actin**.
- In the presence of ATP, actin monomers polymerize to form a flexible, helical filament.
- An actin filament is essentially a two-stranded structure with two helical grooves running along its length.
- The terms *actin filament*, *F-actin*, and *microfilament* are basically synonyms for this type of filament.

Functions

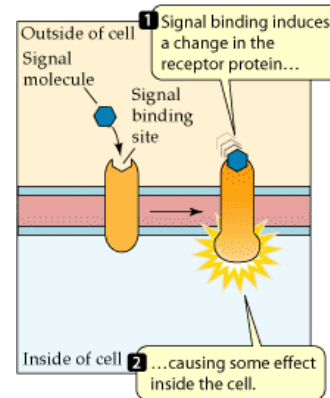
Microfilament functions include;

1. Cytokinesis
2. Amoeboid movement
3. Cell motility in general
4. Changes in cell shape
5. Endocytosis and exocytosis
6. Cell contractility and mechanical stability.

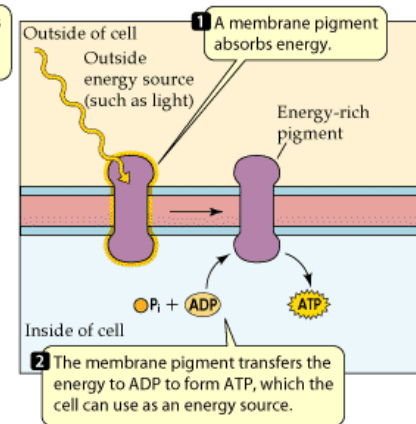
Membranes

More Than Barriers

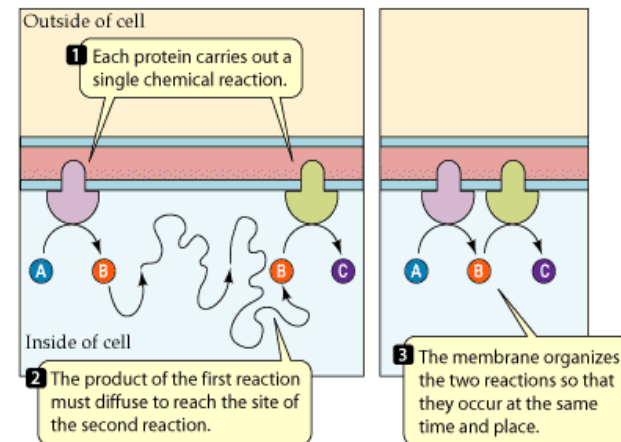
(a) Information processing

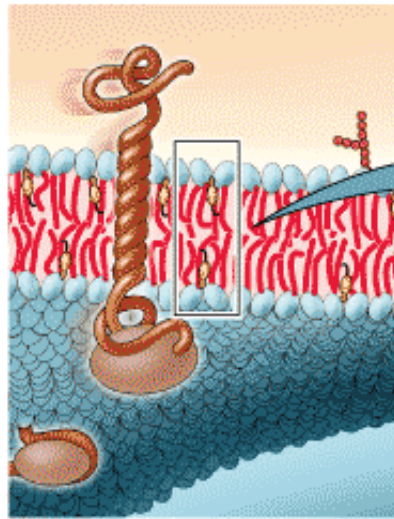


(b) Energy transformation



(c) Organizing chemical reactions

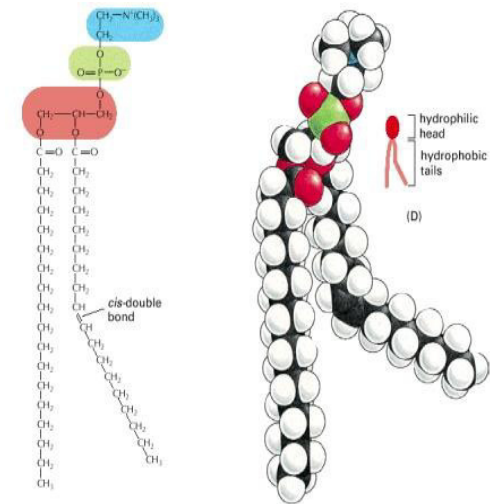
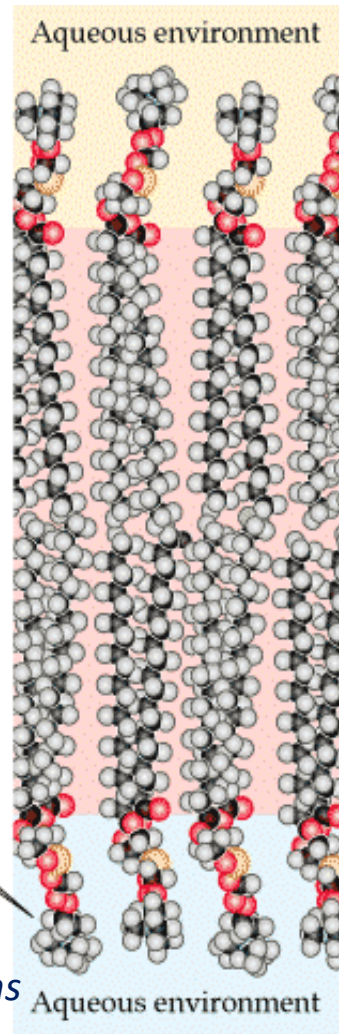




The nonpolar, hydrophobic fatty acid "tails" interact with one another in the interior of the bilayer.

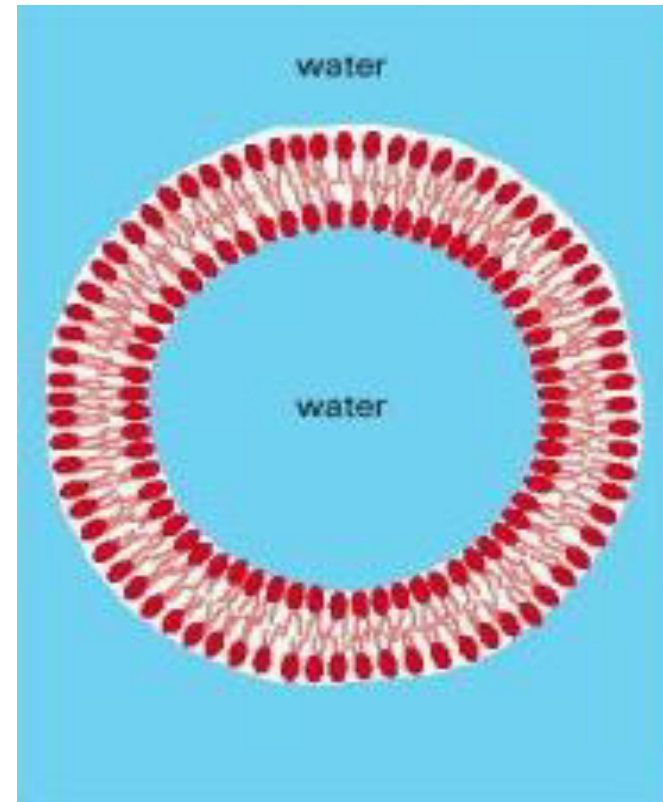
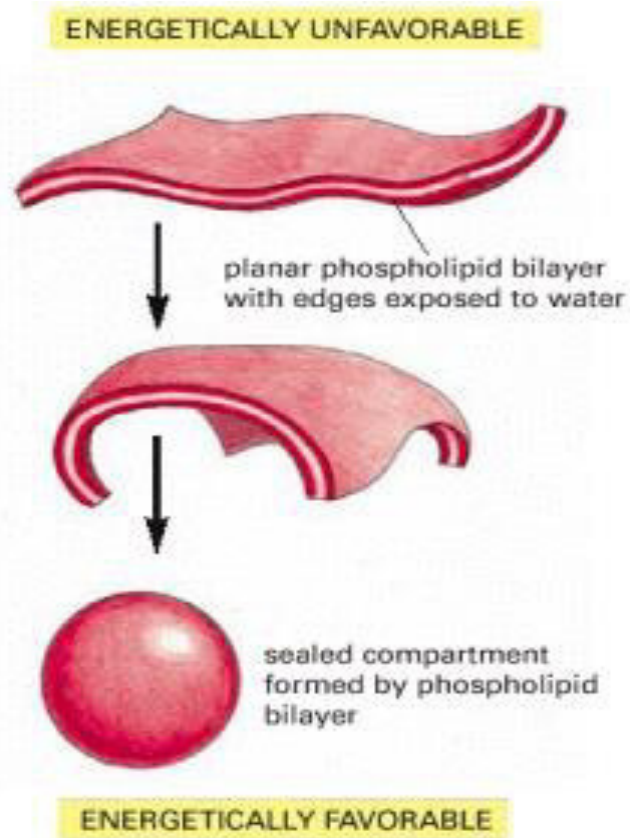
The charged, or polar, hydrophilic "head" portions interact with polar water.

Amphipathic: *Hydrophilic regions*
+ *Hydrophobic regions*



Fatty Acid
Length: 14-24 Cs
One Tail
Unsaturated Cis
Spontaneous
Assembly

Free Energy Dictates



Features

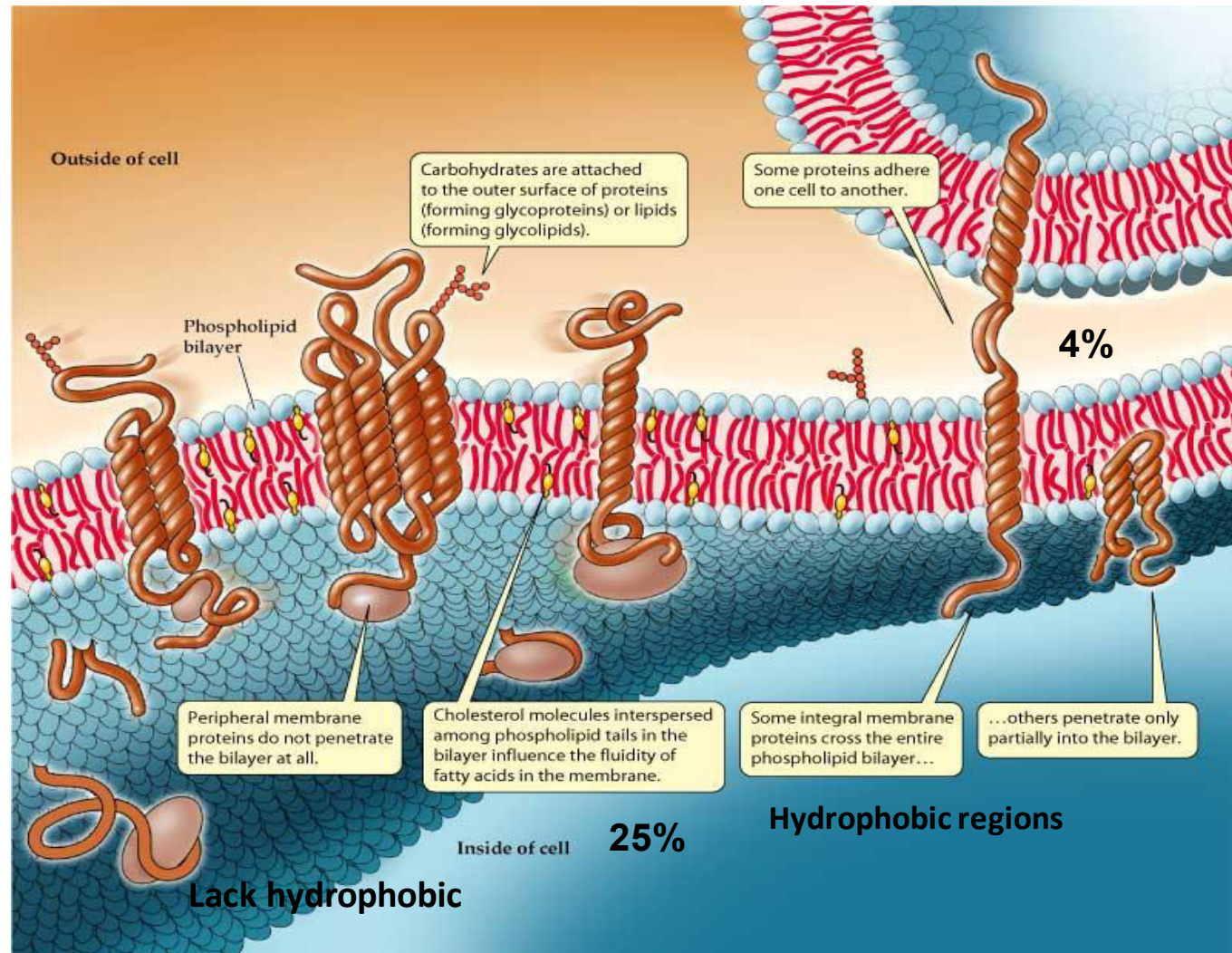
Phospholipids coexist with water form a bilayer

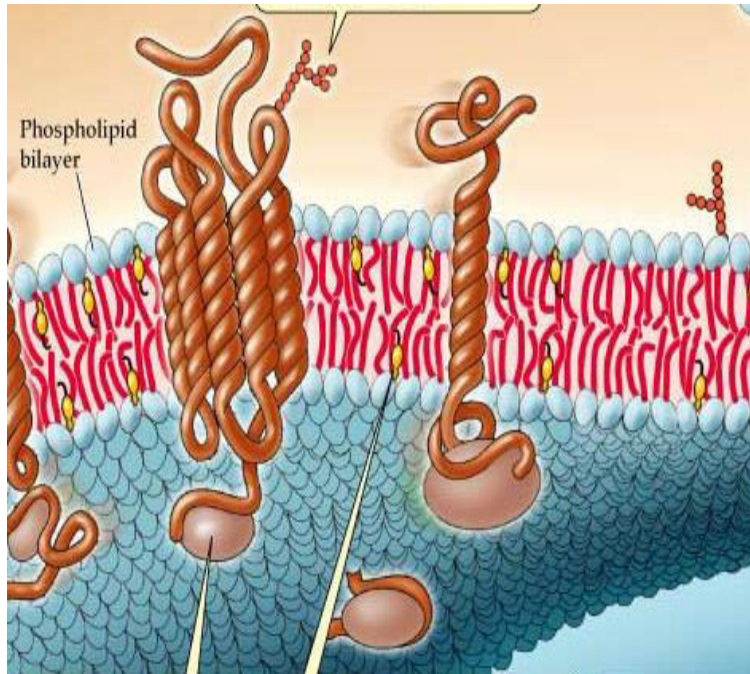
Dynamic structures: parts move & change.

Vital physiological roles: cell cell & cell interaction with environmental

Physical integrity: lipids, create a barrier to hydrophilic materials such as water and ions

Membranes Components





Fatty acids interact with each other & the polar regions face aqueous environment outside

Lipid “lake” in which a variety of proteins “float”

Each membrane has a set of proteins suitable to the specialized function of the cell or organelle it surrounds.

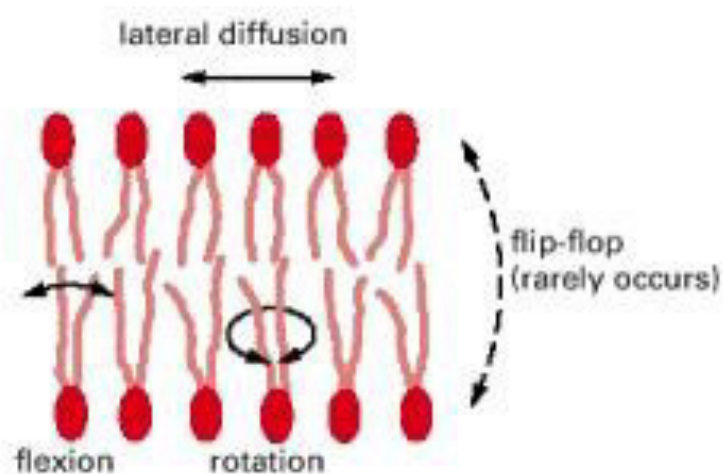
Carbohydrates attached either to lipids/protein molecules

Movement

A phospholipid molecule travels from one end the other in about 1 second

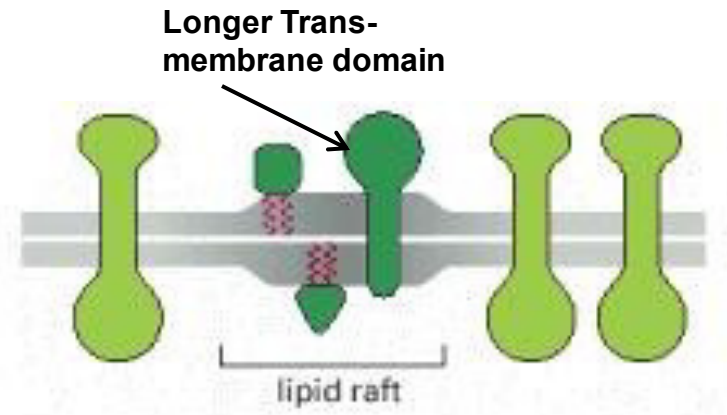
Phospholipid molecule flip overs seldom (polar part of molecule hardly ever moves through the hydrophobic interior

Inner and outer halves of the bilayer have different phospholipids



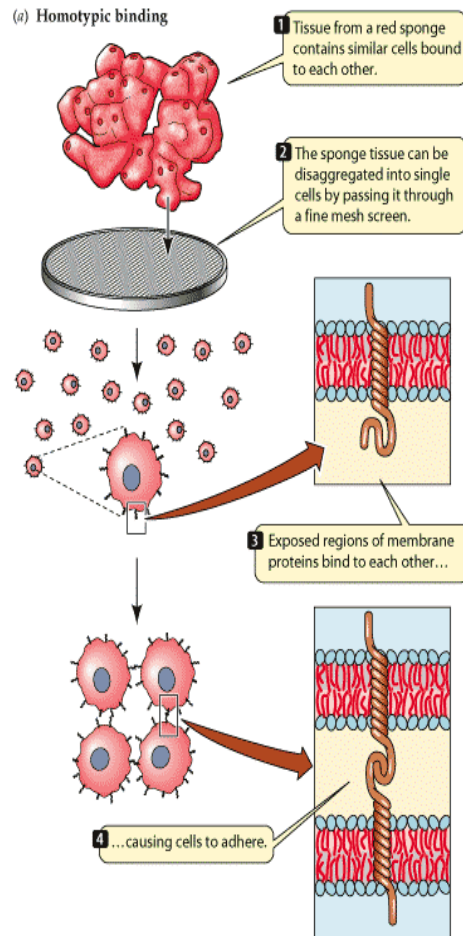
Lipid Rafts

Some proteins migrate freely others “anchored” to specific semisolid region different lipid composition (very long fatty acid chains)

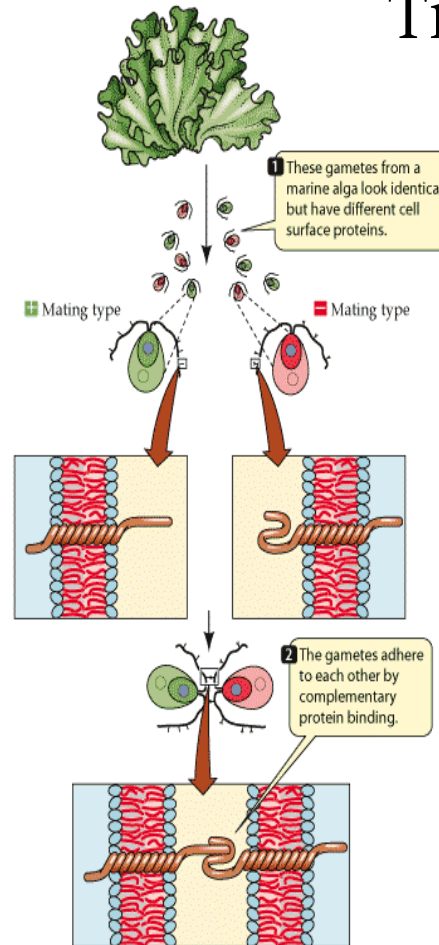


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Recognition & Adhesion



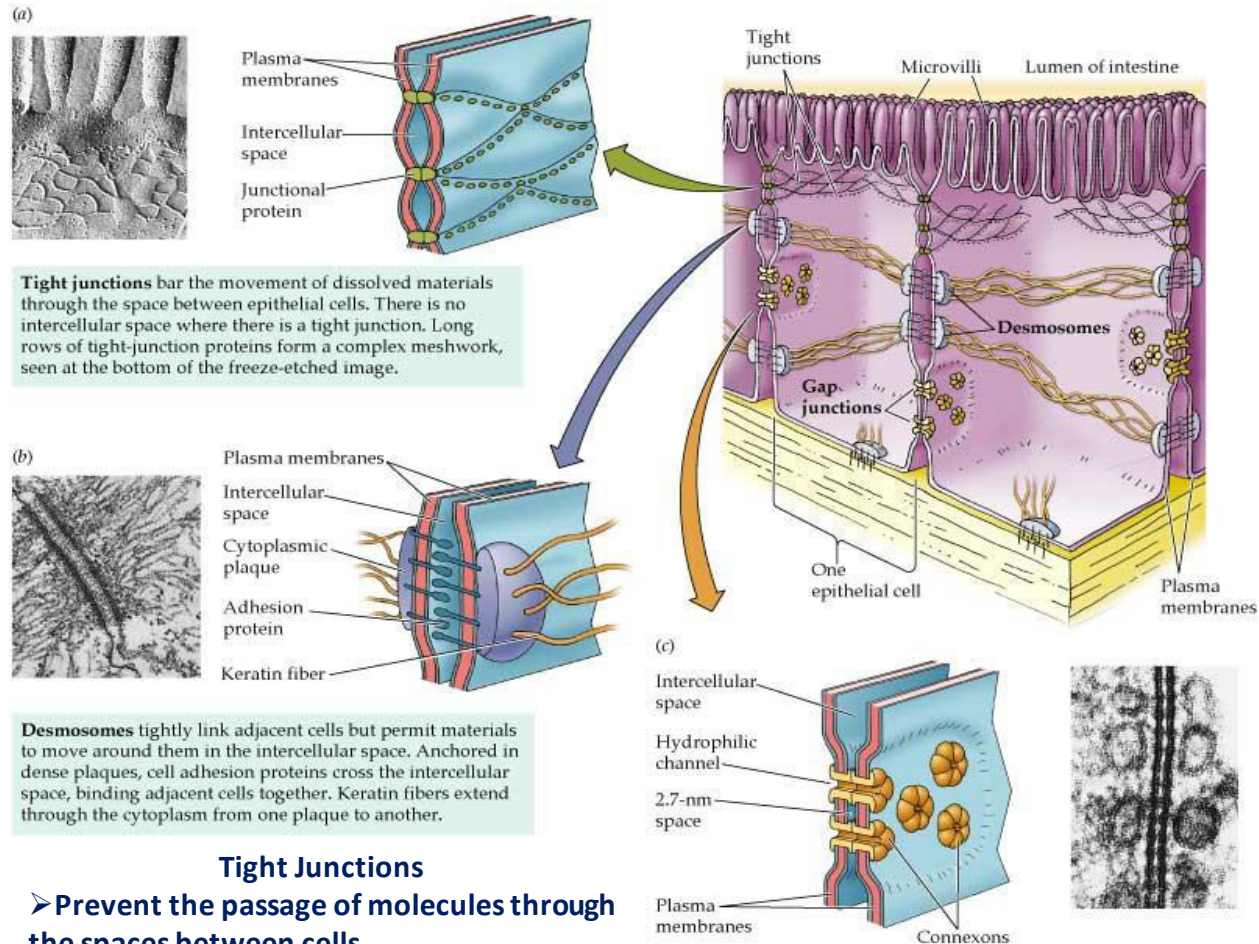
(b) Heterotypic binding



Tissue Formation

**Cell recognition:
One cell
specifically
binds to another
cell**

**Cell adhesion:
relationship
between the
two cells is
"cemented"**



Tight Junctions

- Prevent the passage of molecules through the spaces between cells
- Restricting the migration of lipid molecules & membrane proteins

Passive Transport

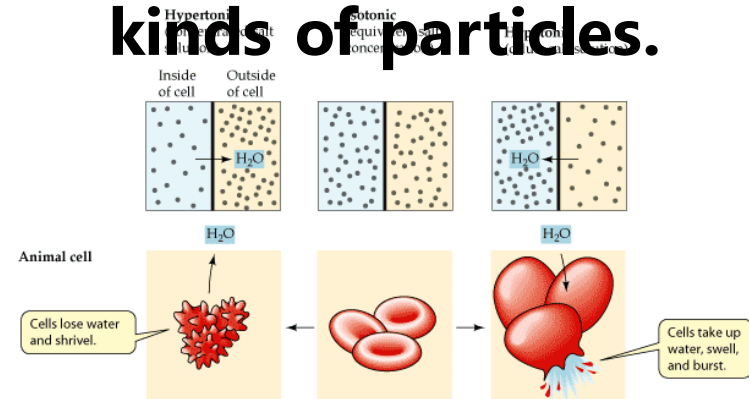
**Does not require any
input of energy to
drive the process**

Active Transport

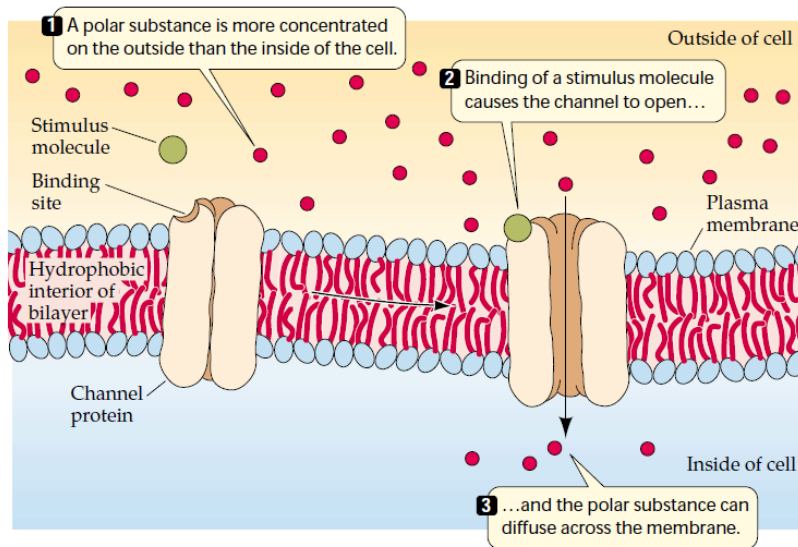
**Requires input of
energy to drive the
process**

Transport Across Membrane

Aqua-porins:
Water molecules move
through membranes
by
Osmosis (diffusion).
Number of solute
particles not on the
kinds of particles.



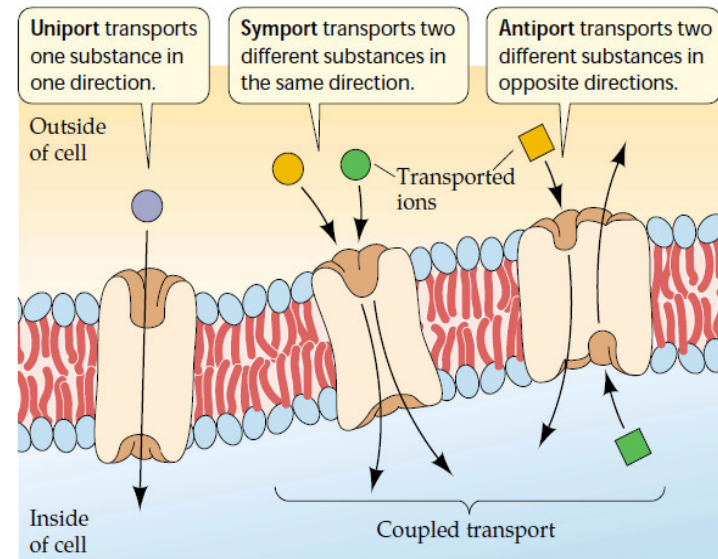
The Two Domains



Polar amino acids and water on the inside of the channel pore (to bind to the polar or charged substance and allow it to pass through)

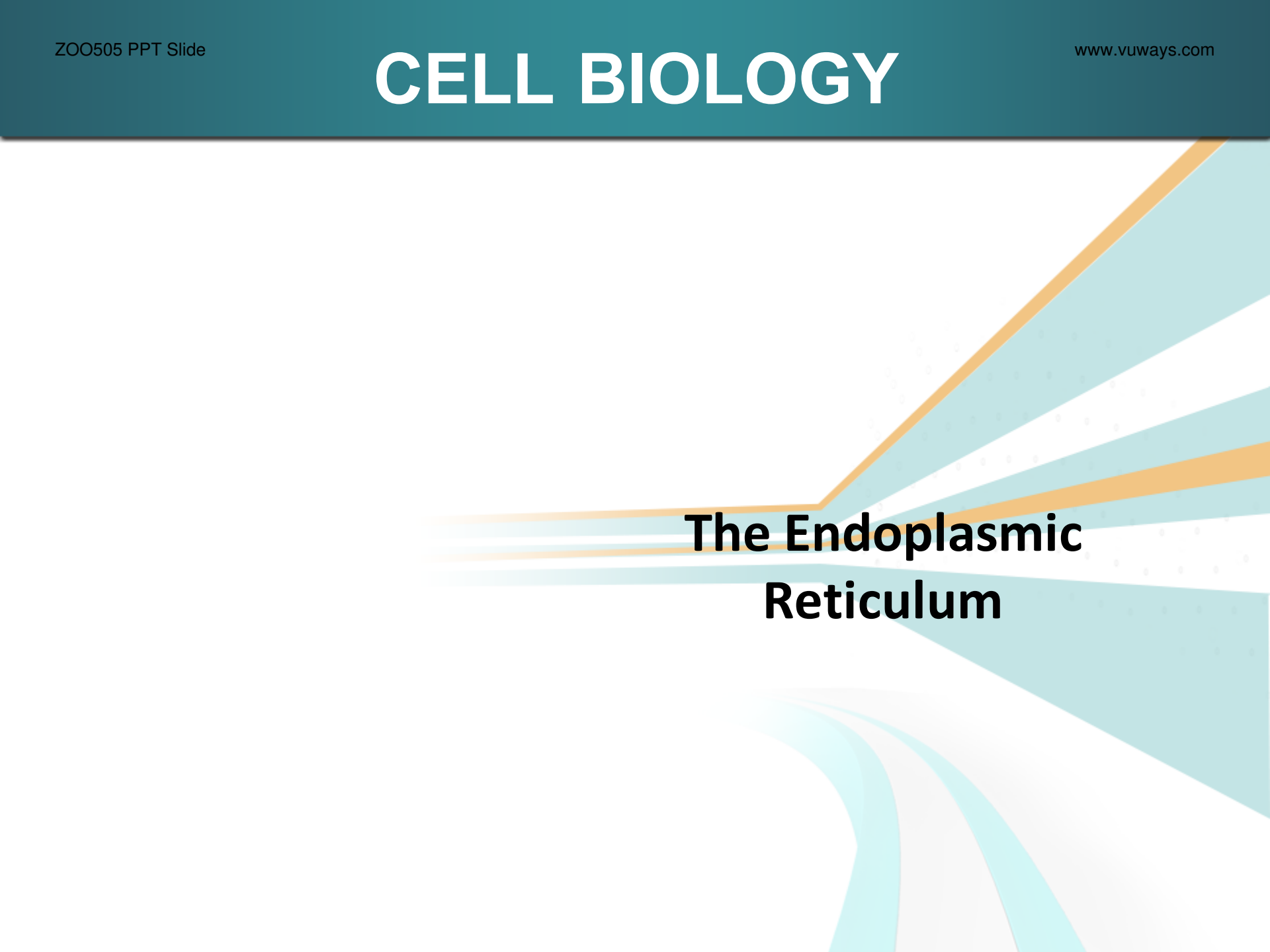
Nonpolar amino acids on the outside of the macromolecule (to allow the channel protein to insert itself into the lipid bilayer)

Primary active transport: ATP required directly.
Secondary active transport: ATP not used directly; ion conc



END

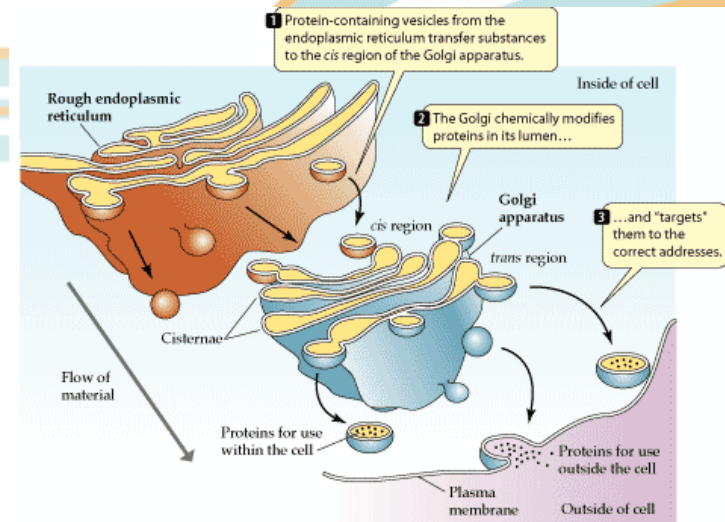
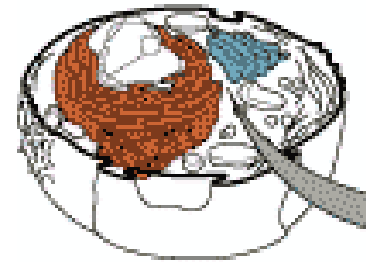
CELL BIOLOGY



The Endoplasmic Reticulum

The Endoplasmic Reticulum

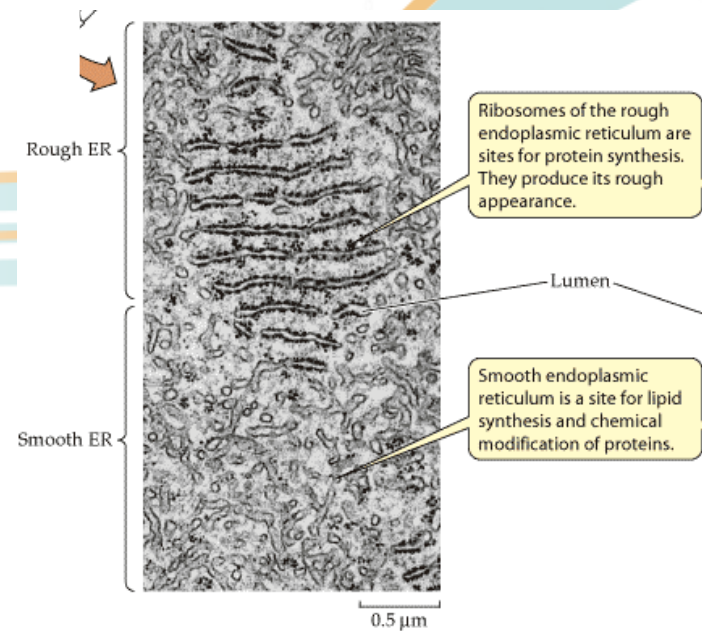
RER + SER



The Endoplasmic Reticulum

RER

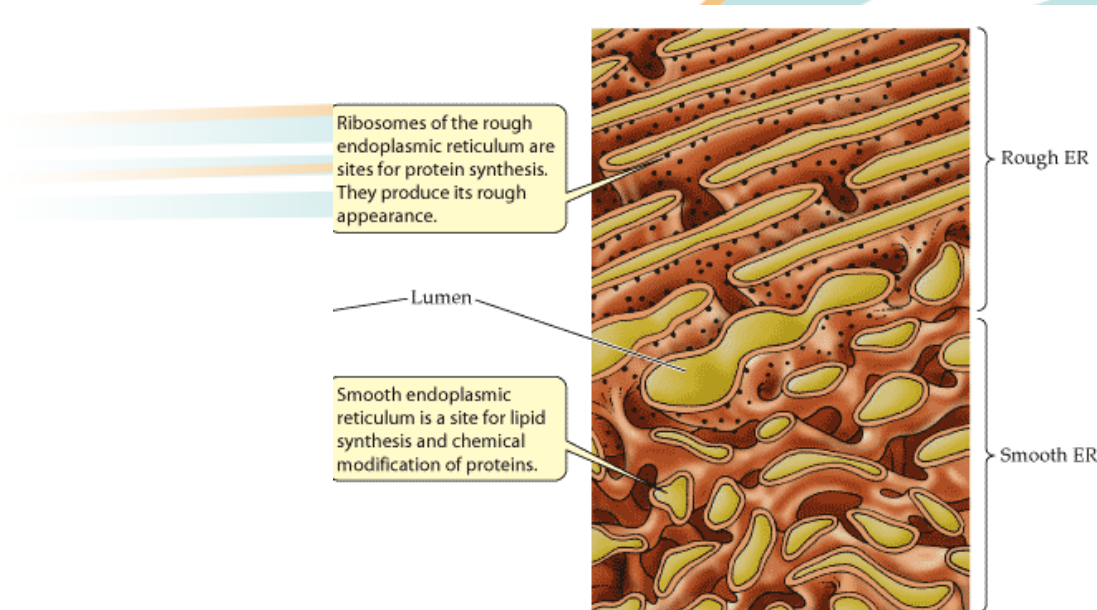
Segregates newly synthesized Proteins



The Endoplasmic Reticulum

RER

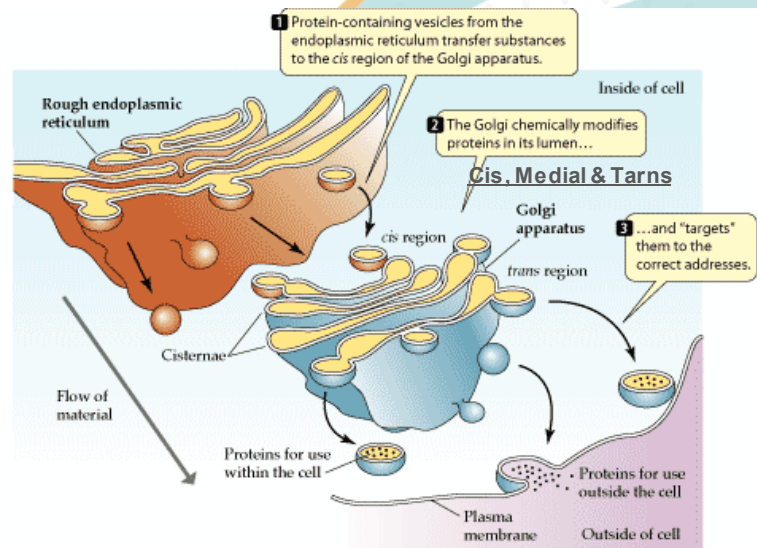
Chemically modifies
proteins (Glycosylation
address)



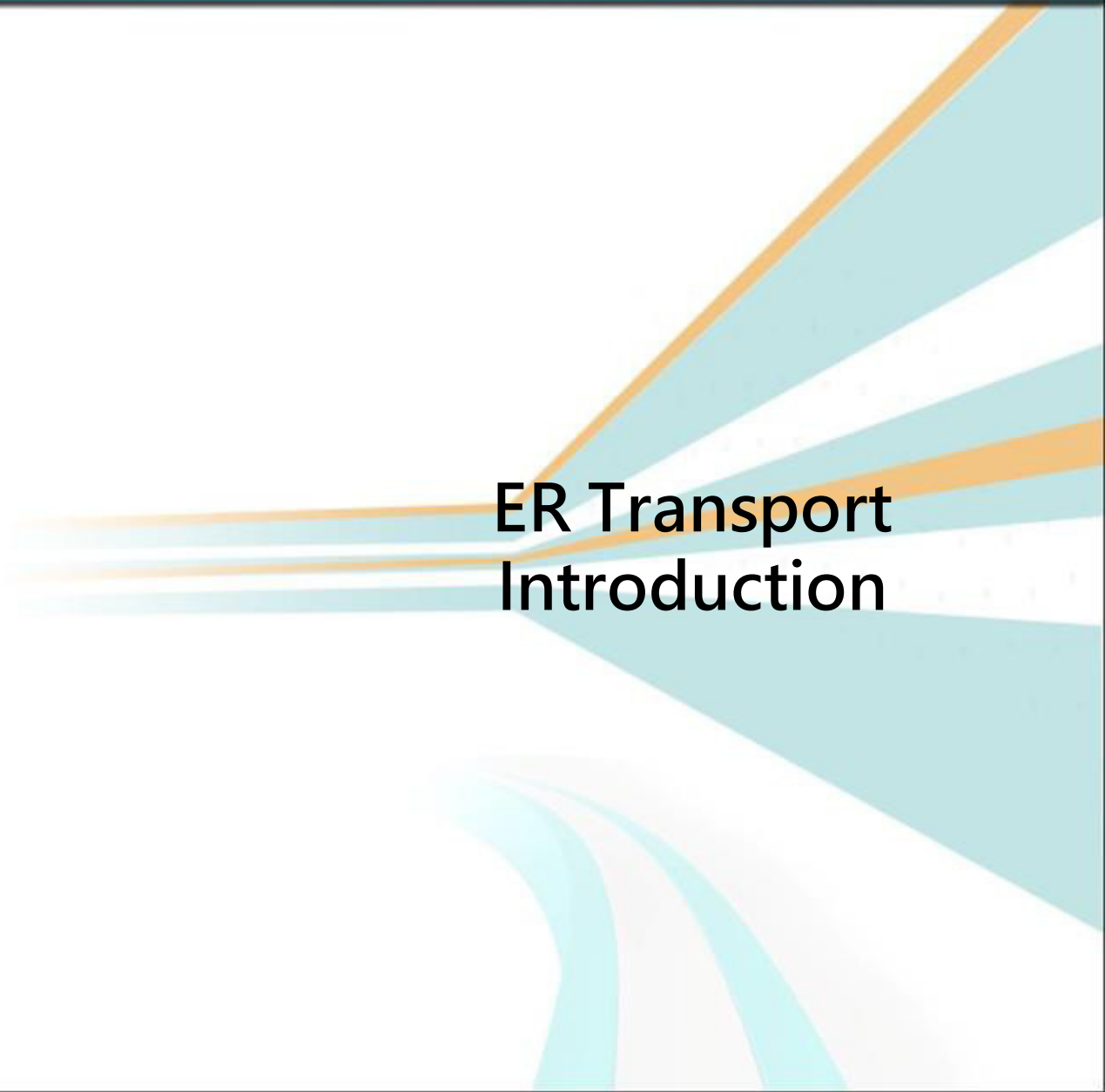
The Endoplasmic Reticulum

SER

Glycogen hydrolysis
Secreting cells have
abundant SER

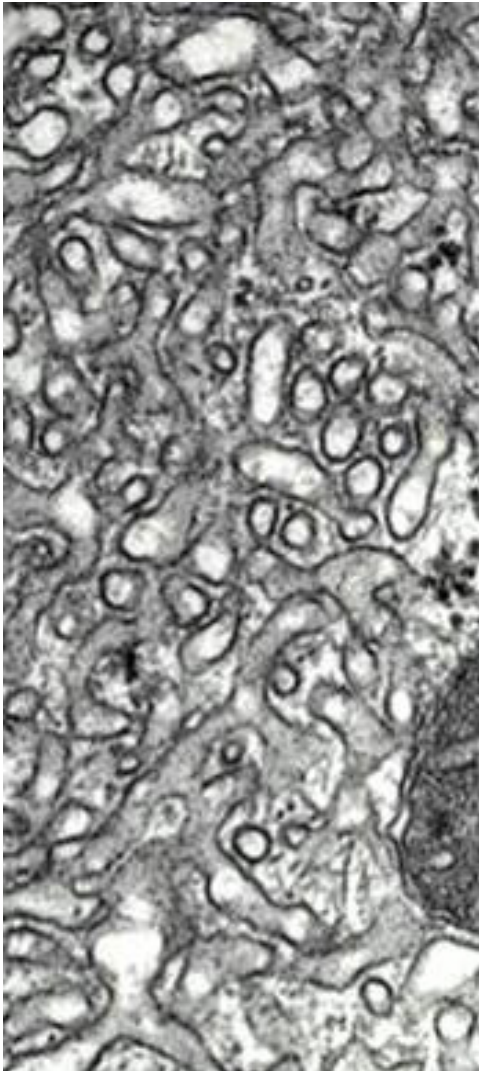


Cell Biology



ER Transport Introduction

The Endoplasmic Reticulum

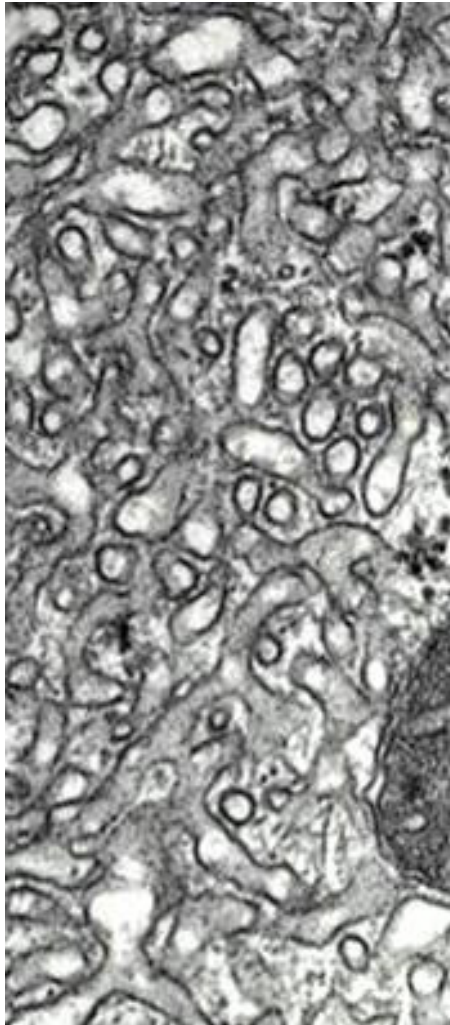


Smooth ER

Regions of ER that **lack** bound **ribosomes** are called smooth endoplasmic reticulum, or **smooth ER** in the great majority of cells, such regions are scanty and are often partly smooth and partly rough

Smooth ER contains ER **exit sites** from which transport **vesicles** carrying newly synthesized proteins and lipids bud off for transport to the Golgi apparatus

The Endoplasmic Reticulum

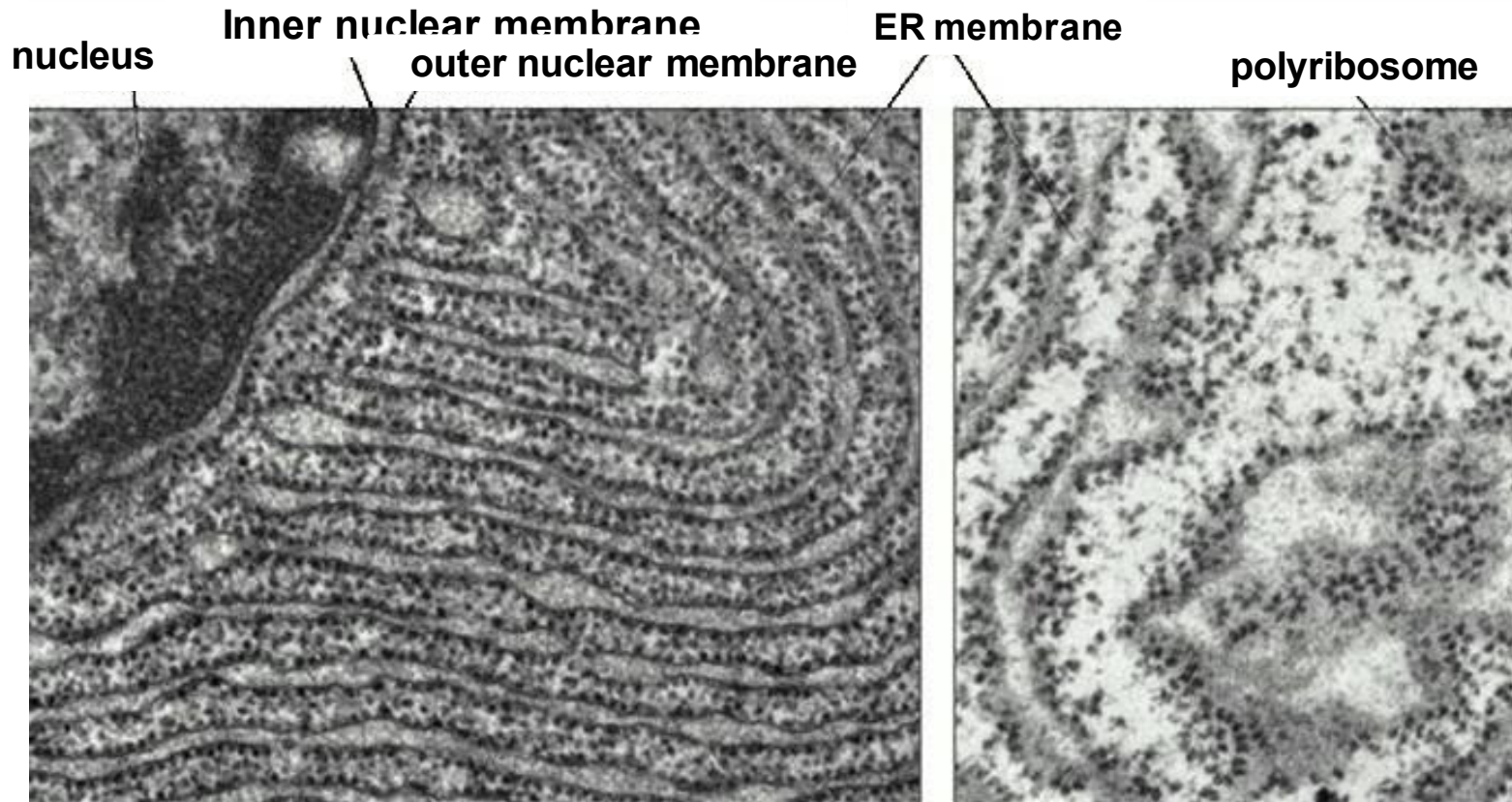


Smooth ER

In hepatocytes smooth ER **doubles** in surface area during **detoxification** of both lipid-soluble drugs and various harmful compounds produced by metabolism e.g. phenobarbital

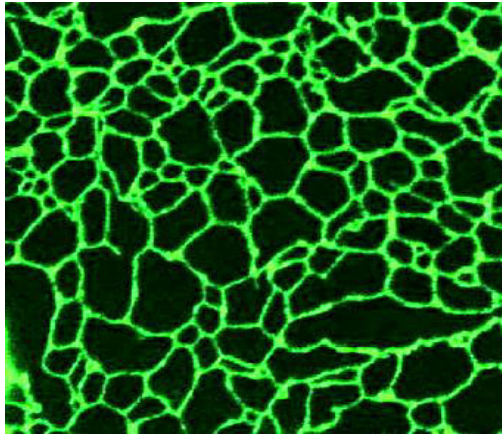
ER in most eucaryotic cells stores **Ca²⁺** e.g. Muscle cells, have an abundant specialized smooth ER, "**sarcoplasmic reticulum**", which sequesters Ca²⁺ from the cytosol

The Endoplasmic Reticulum



The ribosome that is synthesizing the protein is directly attached to the ER membrane creating regions termed rough endoplasmic reticulum

The Endoplasmic Reticulum



All eucaryotic cells have an endoplasmic reticulum (ER) which is organized into **a netlike branching tubules** and **flattened sacs** throughout the cytosol

The tubules and sacs are **interconnected** the ER membrane encloses a single internal space

This highly convoluted space is called the **ER lumen** or the ER cisternal space.

The ER membrane separates the ER lumen from the cytosol, and it mediates the **selective transfer of molecules between these two compartments**

The Endoplasmic Reticulum

The ER captures selected proteins from the cytosol as they are being synthesized

Two types: 1)transmembrane proteins, partly translocated across the ER membrane and become embedded in it, 2)water-soluble proteins, which are fully translocated across the ER membrane and are released into the ER lumen

Some of the transmembrane proteins function in the ER, but many are destined to reside in the plasma membrane or the membrane of another organelle, water-soluble proteins are destined either for the lumen of an organelle or for secretion.

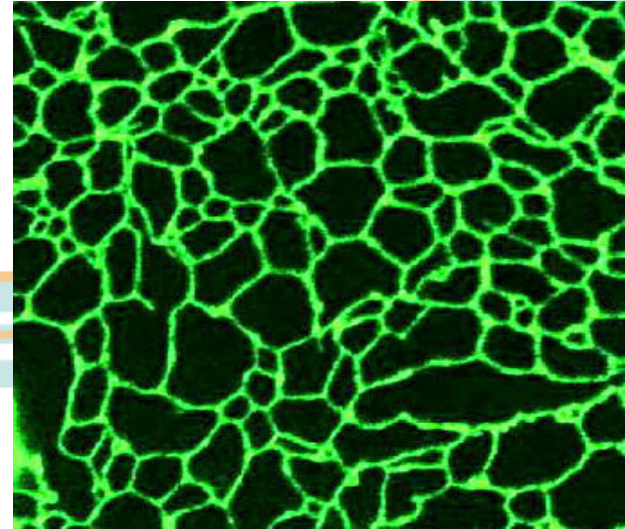
The Endoplasmic Reticulum

All of these **proteins**, have same kind of signal sequence & are translocated by **similar mechanisms**

ER protein import is a **co-translational** process
the import of proteins into mitochondria, chloroplasts, nuclei, and peroxisomes, is **posttranslational** processes

One end of the protein is usually translocated into the ER as the rest of the **polypeptide chain is being made**, the protein is never released into the cytosol and therefore is never in danger of folding up before reaching the translocator in the ER membrane

The Endoplasmic Reticulum



END

Cell Biology



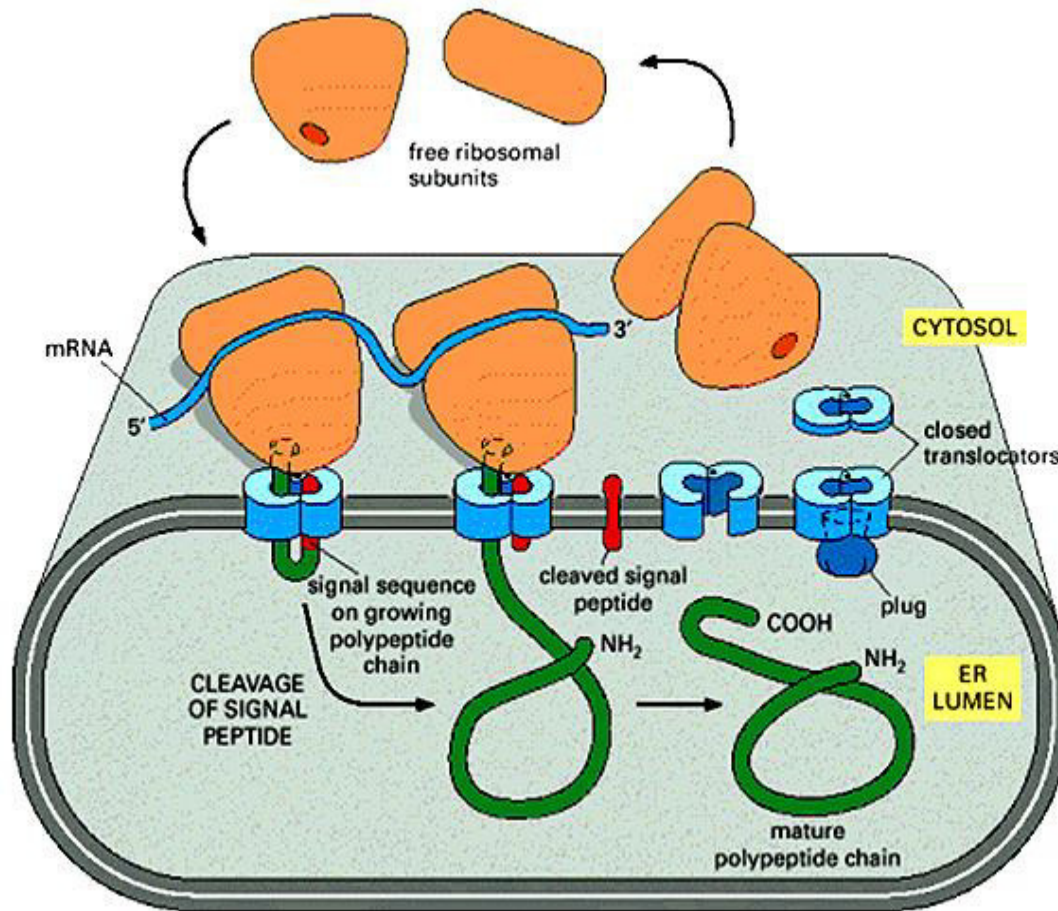
ER Transport

ER Transport

Import into ER

+H₃N-Met-Met-Ser-Phe-Val-Ser-Leu-Leu-Leu-Val-Gly-Ile-Leu-Phe-Trp-Ala-Thr-
 Glu-Ala-Glu-Gln-Leu-Thr-Lys-Cys-Glu-Val-Phe-Gln-
 -Lys-Asp-Glu-Leu-COO⁻

Return to ER

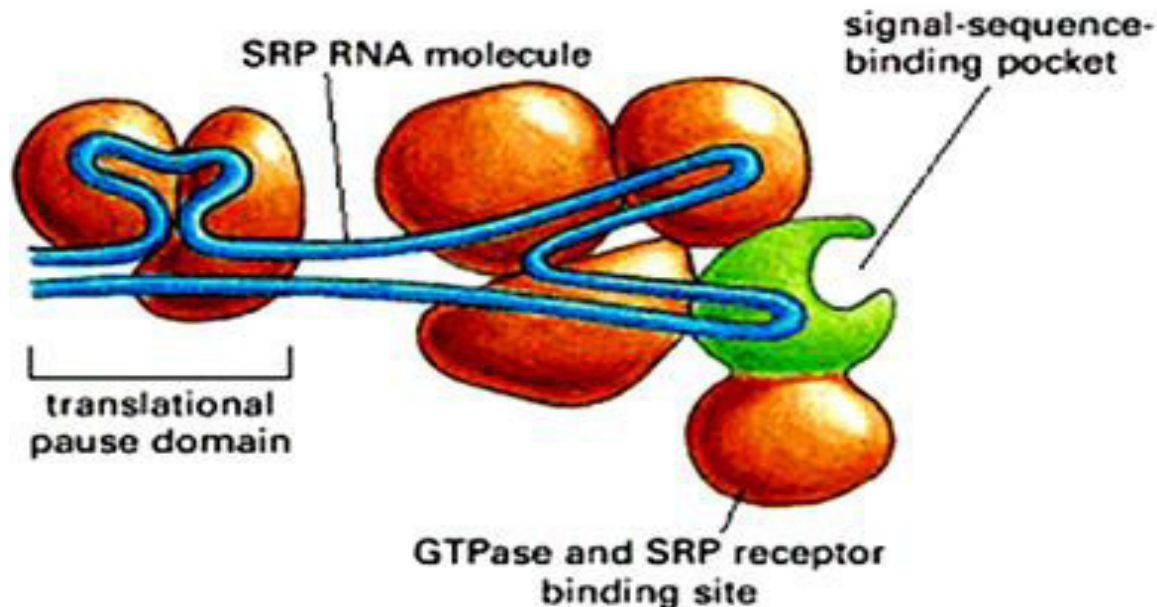


Signal
Sequences
Were First
Discovered
in Proteins
Imported
into the
Rough ER

Signal-Recognition Particle (SRP)

The ER signal sequence is guided to the ER by 2 components: **1) SRP which cycles between the ER membrane and the cytosol & binds to the signal sequence, & 2) SRP receptor in the ER membrane**

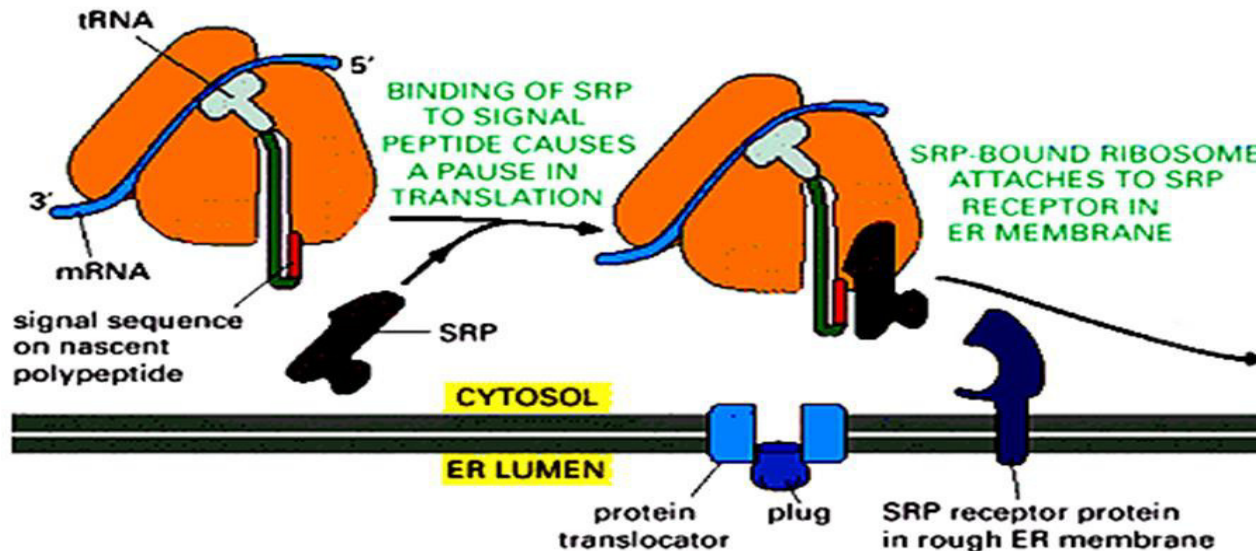
The SRP consisting of **six** different polypeptide chains bound to a single small **RNA** molecule



SRP

The SRP binds to the ER signal sequence **as soon as the peptide has emerged** from the ribosome causes a pause in protein synthesis, ensuring that the protein is **not released** into the **cytosol**

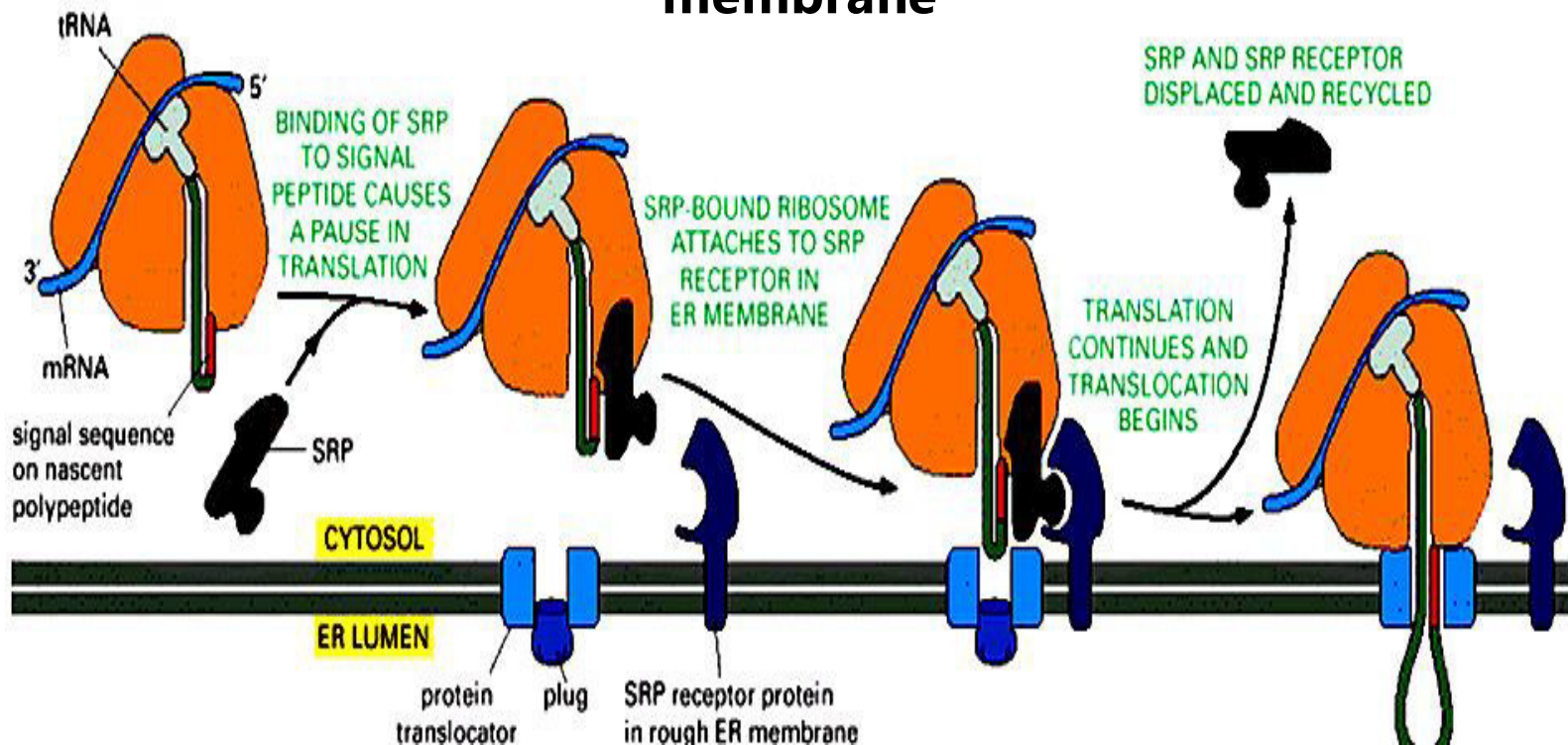
This is safety mechanism especially for **lysosomal** hydrolases that could wreak havoc in the cytosol



the pause presumably gives the ribosome enough time to bind to the ER

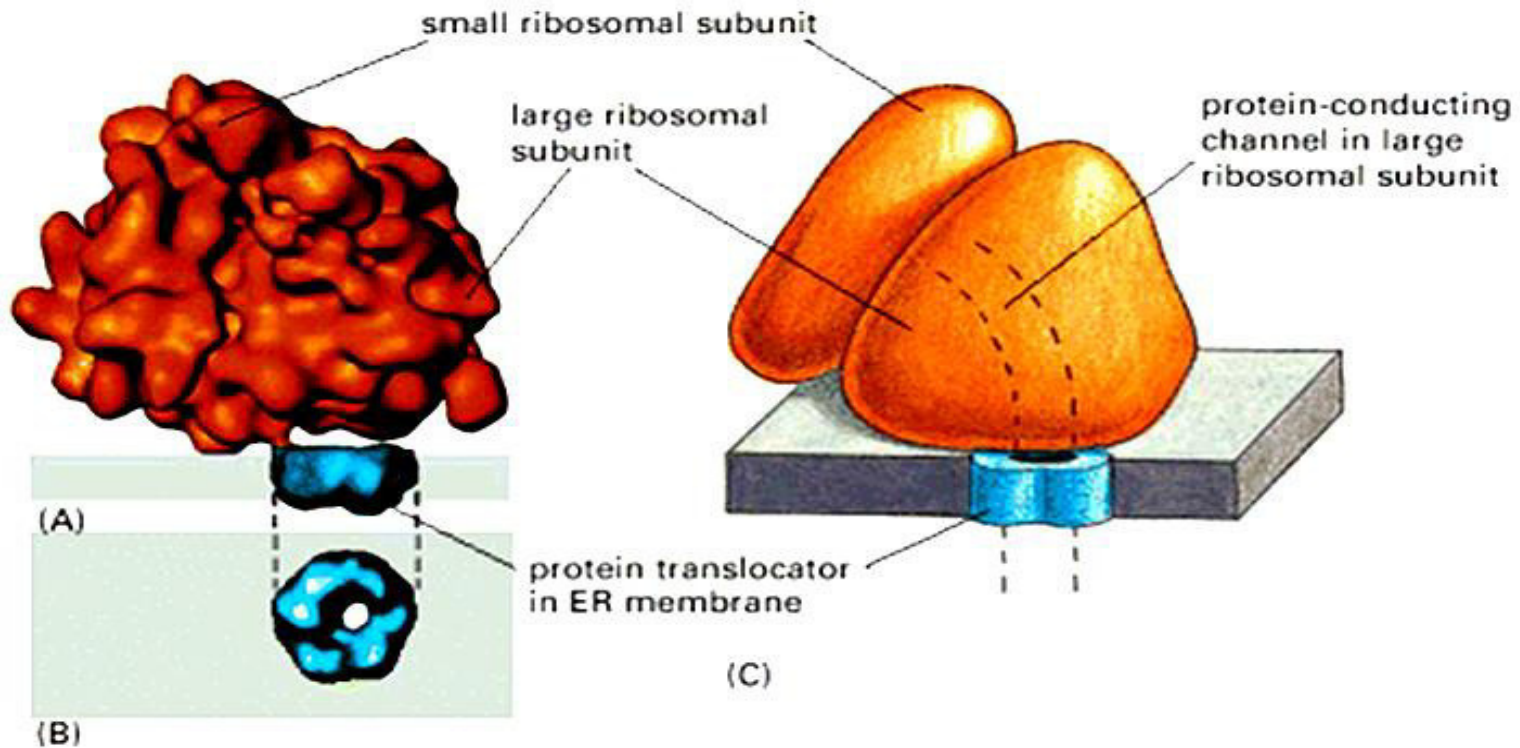
ER Transport

SRP-ribosome complex binds to the SRP receptor, this interaction brings the SRP-ribosome complex to a **protein translocator** SRP & SRP receptor are then **released**, and the growing **polypeptide** chain is **transferred** across the membrane



The Translocator

The translocator **Sec61** complex forms a water-filled pore in the membrane through which the polypeptide chain traverses the membrane, it consists of **4** protein which assemble into a **donut**



The Translocator

When a ribosome binds, the **central hole** in the translocator **lines up with a tunnel** in the large ribosomal subunit through which the growing polypeptide chain exits from the ribosome

The bound ribosome forms a **tight seal** with the translocator, such that the space inside the ribosome is continuous with the lumen of the ER and no molecules can **escape from the ER**

The pore in the translocator cannot be open permanently, however; if it were, **Ca²⁺ would leak** out of the ER when the ribosome detaches

The Translocator

A luminal ER protein serves as **a plug** or that the translocator itself can rearrange to **close the pore** when no ribosome is bound

Thus, the pore is a **dynamic structure** that **opens only transiently** when a ribosome with a growing polypeptide chain attaches to the ER membrane

The **signal sequence** in the growing polypeptide chain **triggers the opening** of the pore: after the signal sequence is released from the SRP and the growing chain has reached a sufficient length, the **signal sequence binds** to a specific site inside the **pore** itself, thereby opening the pore

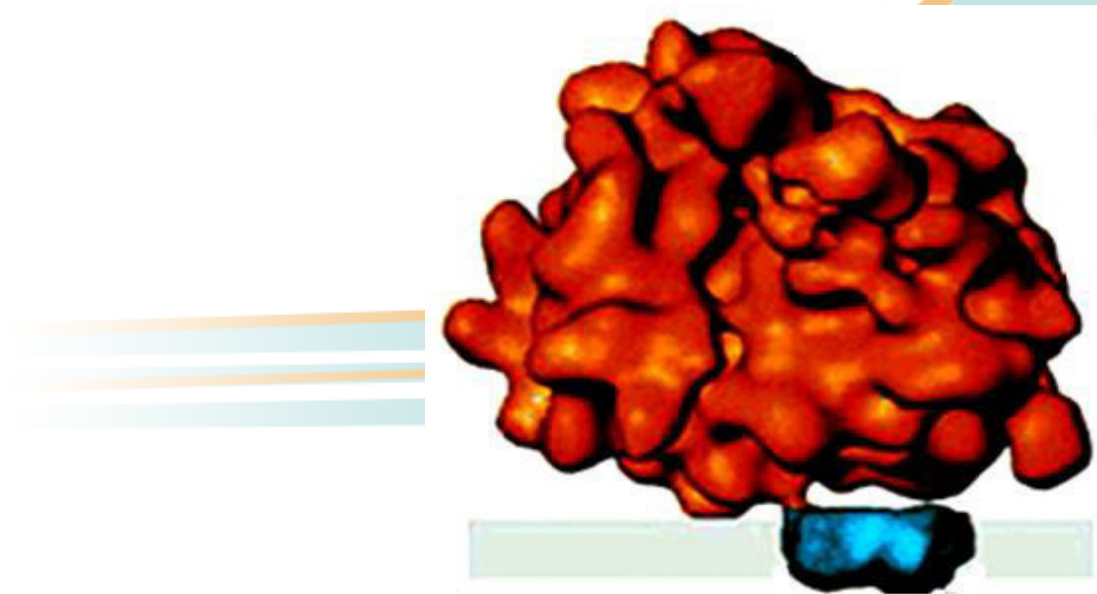
The Translocator

An ER signal sequence is therefore recognized twice: first, by an **SRP in the cytosol, and then by a binding site in the ER protein **translocator****

This may help to ensure that only appropriate proteins enter the lumen of the ER

Some proteins, however, are imported into the ER **after their synthesis has been completed, demonstrating that translocation does not always require ongoing translation**

The Translocator



END

CELL BIOLOGY

Golgi & Lysosomes



Golgi

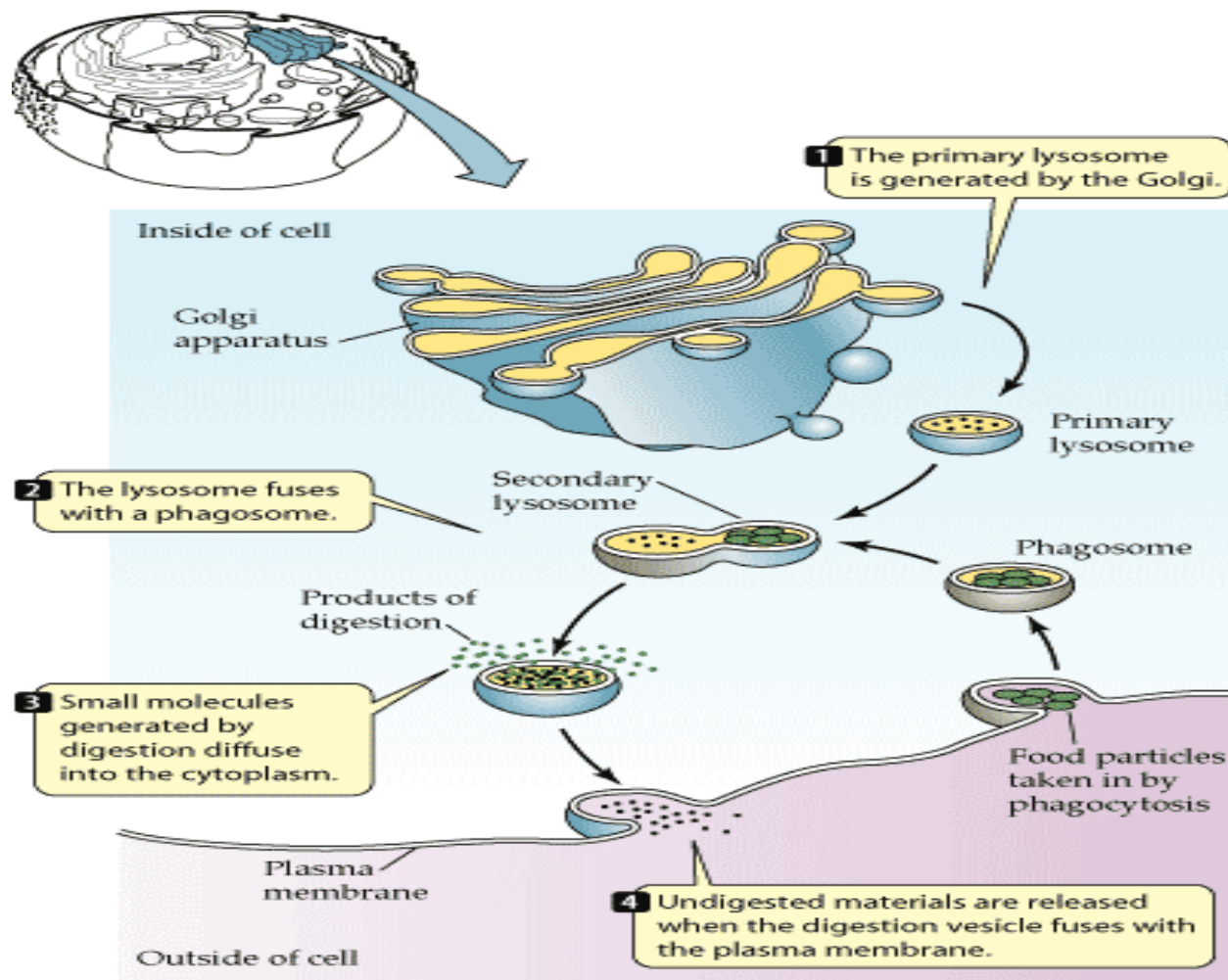
Golgi Apparatus

Receives materials from the rough ER and modifies them.

Concentrates sorts and packages proteins and sends them to other destinations.

Manufactures polysaccharides for the plant wall

Golgi



Lysosomes

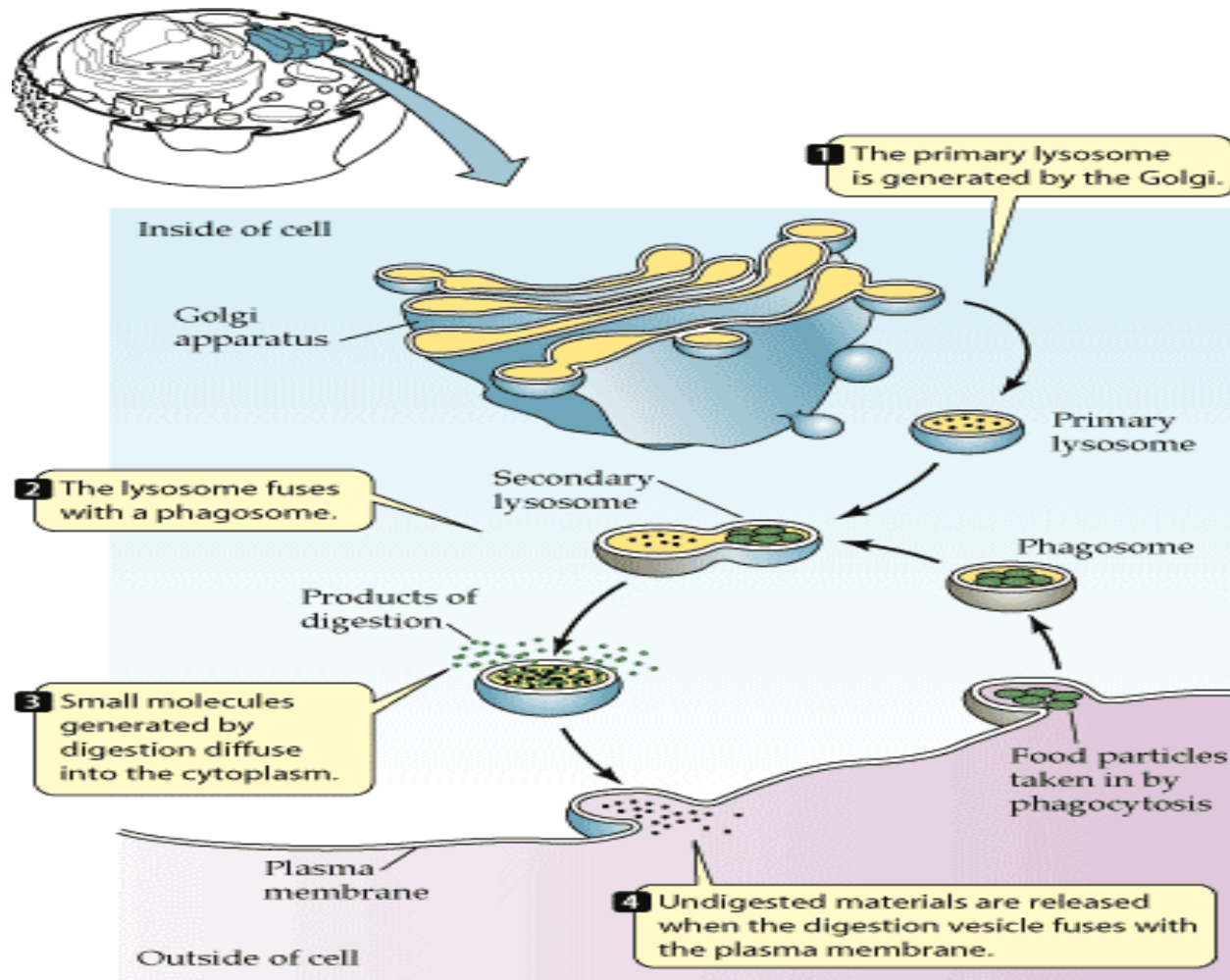
Garbage Disposal

Contain many digestive enzymes.

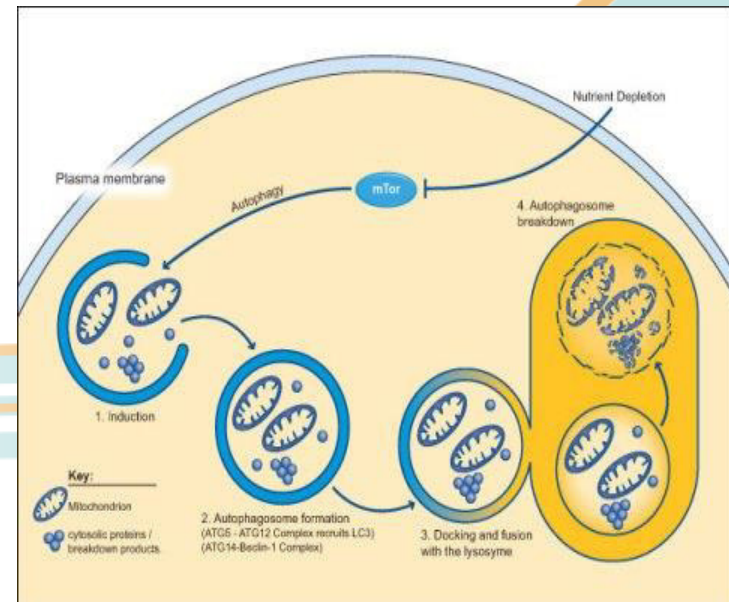
Fuse with phagosomes (autophagy).

Secondary lysosomes, where engulfed materials are digested phagocytosis.

Lysosomes



Lysosomes



Cell Biology

Vesicle Transport

An abstract graphic on the right side of the slide, featuring several overlapping geometric shapes in shades of teal and orange. The shapes include triangles and curved polygons, creating a dynamic, modern design.

Golgi Apparatus

The Golgi complex is a major site of **carbohydrate synthesis**, as well as a sorting and dispatching station for the products of the ER.

Many of the cell's **polysaccharides** are **made** in the **Golgi**, including the pectin and hemicellulose of the cell wall in plants and most of the glycosamino-glycans of the **extracellular matrix in animals**

Golgi apparatus also lies on the **exit route** from the **ER**, and a large proportion of the carbohydrates that it makes are attached as **oligosaccharide** side chains to the many **proteins & lipids** that ER sends

Golgi Apparatus

A subset of these oligosaccharide groups serve as tags to direct specific proteins into vesicles that then transport them to lysosomes

Most proteins and lipids, after acquiring their appropriate oligosaccharides in the Golgi, are recognized in other ways for targeting into the transport vesicles going to other destinations

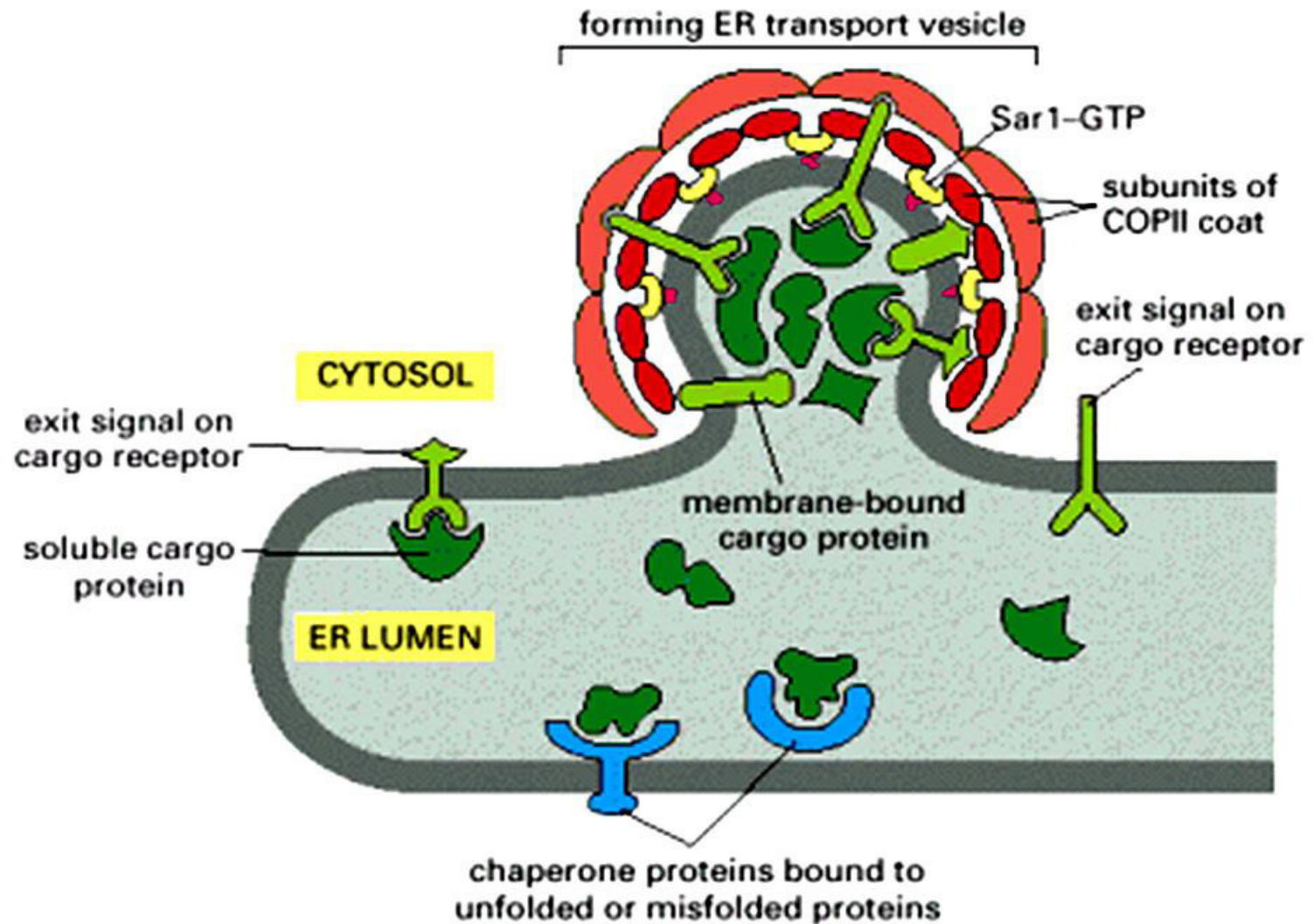
Proteins that enter the ER and are destined for the Golgi apparatus are packaged into small COPII-coated transport vesicles which, bud from specialized regions of the ER called ER exit sites whose membrane lacks bound ribosomes

Golgi Apparatus

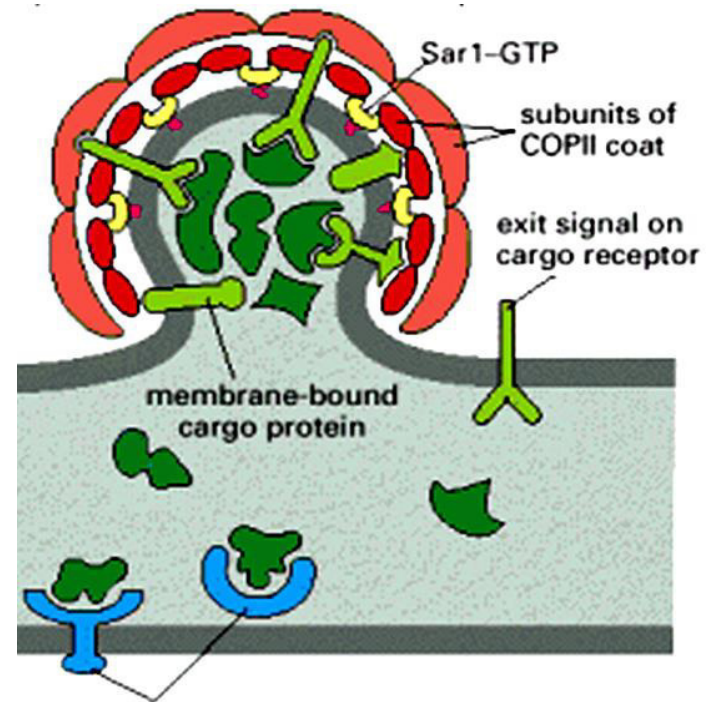
Some **cargo proteins** are actively **recruited** into such **vesicles**, where they become **concentrated**, these cargo proteins display **exit (transport) signals** on their surface that are **recognized by** complementary **receptor** proteins that become trapped in the budding vesicle by interacting with components of the COPII coat

Cargo proteins display exit (transport) signals on their surface that are recognized by complementary receptor proteins that become trapped in the budding vesicle by interacting with components of the COPII coat, some **ER resident proteins without such exit signals can also get packaged in vesicles** .

Golgi Apparatus



Golgi Apparatus



The ERGIC53 protein

To exit from the ER, proteins must be **properly folded** and completely assembled

Misfolded or incompletely assembled are **retained** in the ER, where they are bound to chaperone proteins

The **ERGIC53** protein serves as a **receptor** for packaging some secretory proteins into COPII-coated vesicles

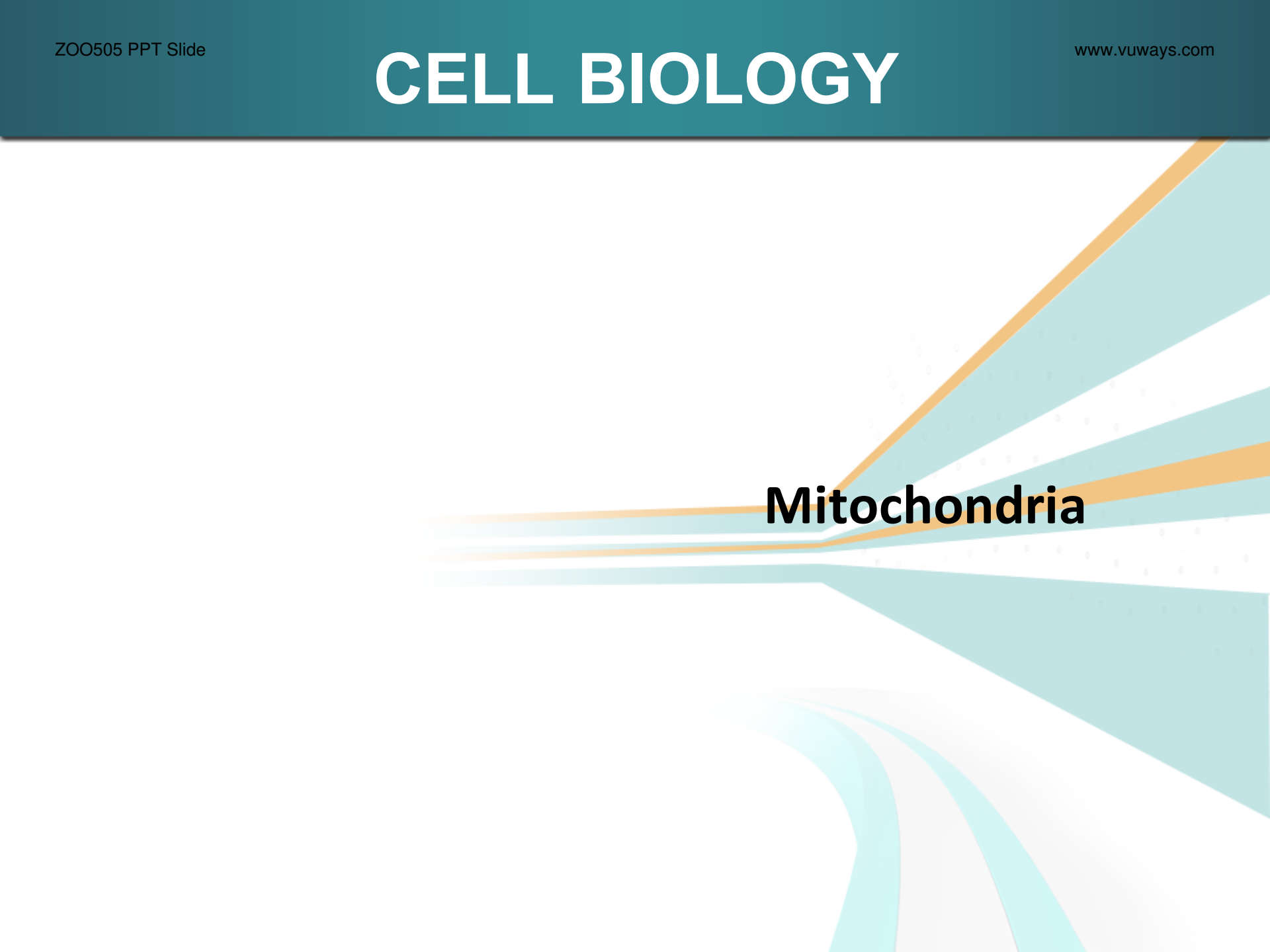
Its role in protein transport was identified because humans who lack it owing to an inherited mutation have lowered serum levels of two secreted blood-clotting factors (Factor V and Factor VIII) and therefore bleed excessively

The ERGIC53 protein

**The ERGIC53 protein is
a lectin that binds
mannose on Factor V
and Factor VIII
proteins, thereby
packaging the proteins
into transport vesicles
in the ER**

END

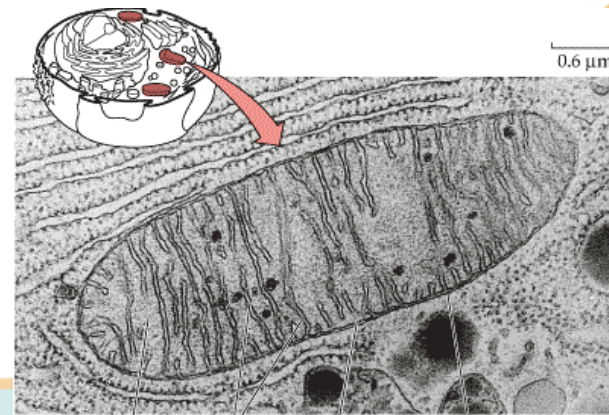
CELL BIOLOGY



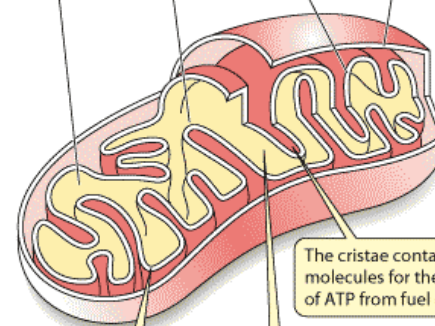
Mitochondria

Mitochondria

Make ATP
Breakdown fuel



Matrix Cristae Inner membrane Outer membrane



The cristae contain key molecules for the generation of ATP from fuel molecules.

The inner membrane is the primary barrier between the cytosol and mitochondrial enzymes.

The matrix contains ribosomes, DNA, and several of the enzymes used for cellular respiration.

Mitochondria

Make ATP

Breakdown fuel

Some protists have one, liver more than a thousand and egg a few hundred thousand MT.

Mitochondria and chloroplasts contain their own DNA and ribosomes for making some of their own proteins

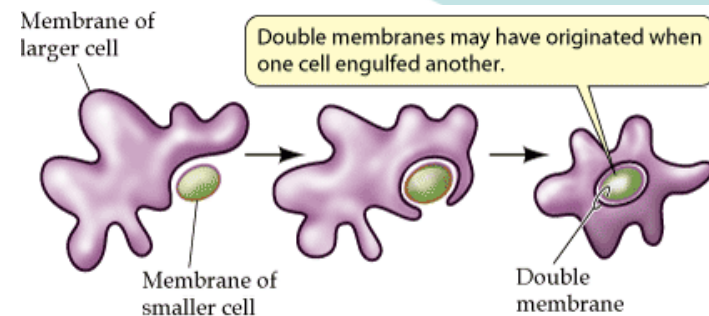
Mitochondria

Endosymbiosis

**Mutual benefits
permitted this symbiotic
relationship**

Photosynthesis

Detoxification of O₂



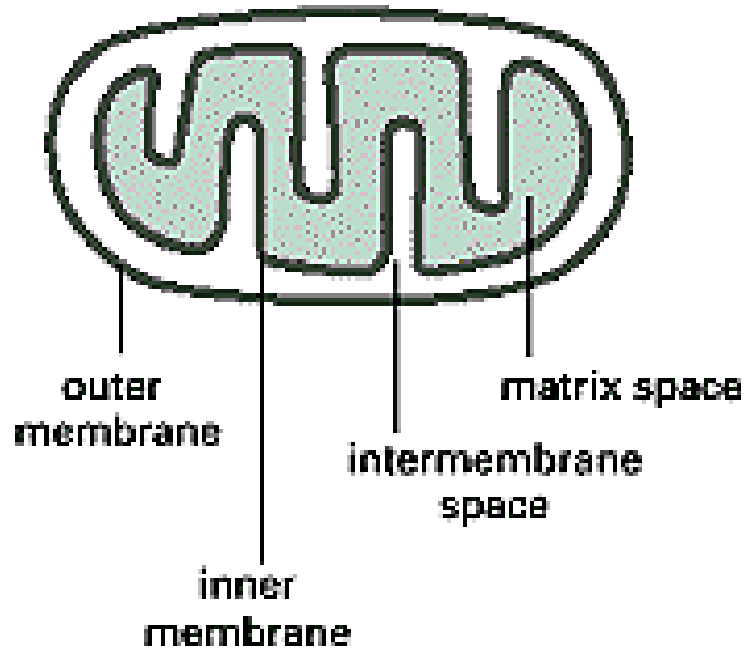
END

Cell Biology

Protein Transport into Mitochondria



Mitochondria Structure



Mitochondria is **double-membrane**-enclosed organelle

It contains its own **DNA, ribosomes**, and other components required for protein synthesis, most of its **proteins are encoded** in the **cell nucleus** and imported from the

There are two subcompartments in mitochondria: the **internal matrix space** and the **intermembrane space**

Mitochondrial Import

Proteins imported into the matrix of mitochondria are usually **taken up from the cytosol within seconds** or minutes of their **release from ribosomes**.

Mitochondrial proteins are first **fully synthesized** as **precursor proteins** in the **cytosol** & then **translocated into mitochondria** by a **posttranslational mechanism**

Mitochondrial precursor proteins have a **signal sequence at their N terminus** that is rapidly **removed after import** by a protease (the signal peptidase) in the mitochondrial matrix

The signal sequences are both **necessary and sufficient** for import of the proteins that contain **genetic engineering signals linked to cytosolic protein to direct the protein into the mitochondrial**

Targeting Sequence

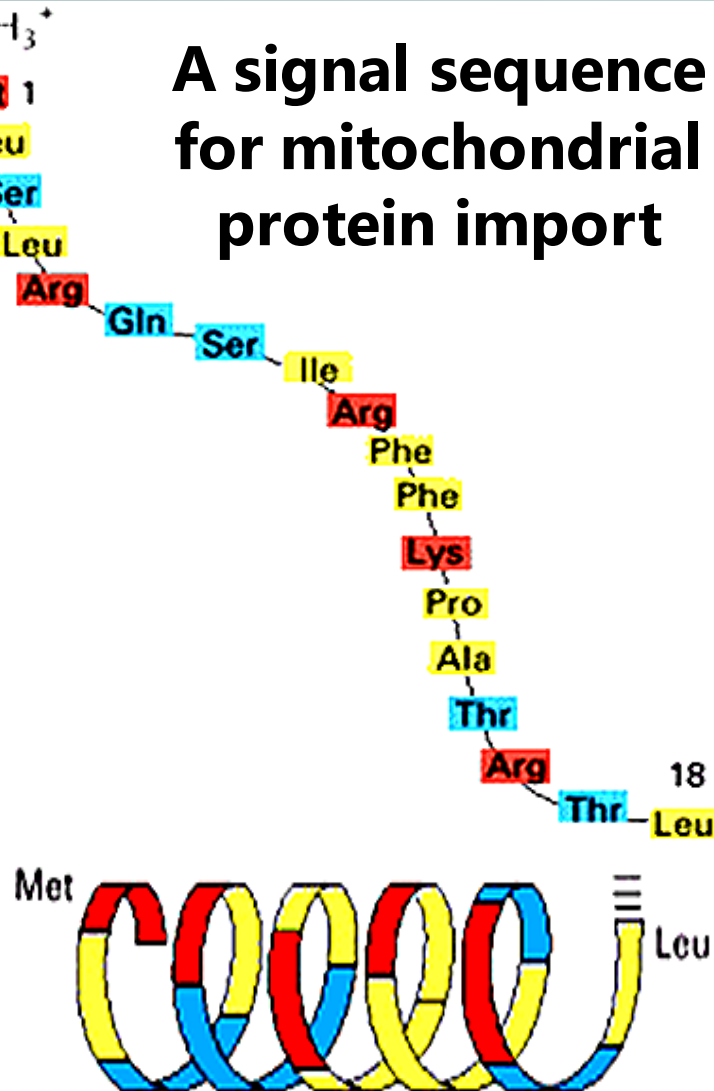
Matrix signal sequences have propensity to fold into an **amphipathic α helix**, in which **positively** charged residues are clustered on one side of the helix, while uncharged **hydrophobic residues** are clustered on the opposite side

This **configuration**—rather than a precise **amino acid sequence**—is **recognized** by specific receptor proteins that initiate protein translocation

Signal Sequence

**A signal sequence
for mitochondrial
protein import**

**When the signal
sequence is folded as an
 α helix, the positively
charged residues (red)
are seen clustered on
one face of helix, while
the nonpolar residues
(yellow) are clustered
on opposite face**



**amphipathic α helix, is
recognized by receptor
proteins on
mitochondrial surface**

Signal Sequence

Mitochondrial precursor proteins do not fold into their native structures after they are synthesized; instead, they remain unfolded through interactions with other proteins in the cytosol.

Cell Biology



**Lysosomal
Transport**

Lysosomal Transport

Lysosomes are membrane-enclosed compartments filled with **hydrolytic enzymes that are used for the controlled intracellular digestion of macromolecules**

They contain **40 types of hydrolytic enzymes, including proteases, nucleases, glycosidases, lipases, phospholipases, phosphatases, and sulfatases they are all are acid hydrolases**

For **optimal activity they require an acid environment, and the lysosome provides this by maintaining a **pH of about 5.0** in its interior**

The contents of the cytosol are **doubly protected against attack by the cell's own digestive system**

Lysosomal Transport

Lysosomal hydrolases and membrane proteins are **synthesized in the rough ER** and transported through the Golgi apparatus to the lysosome.

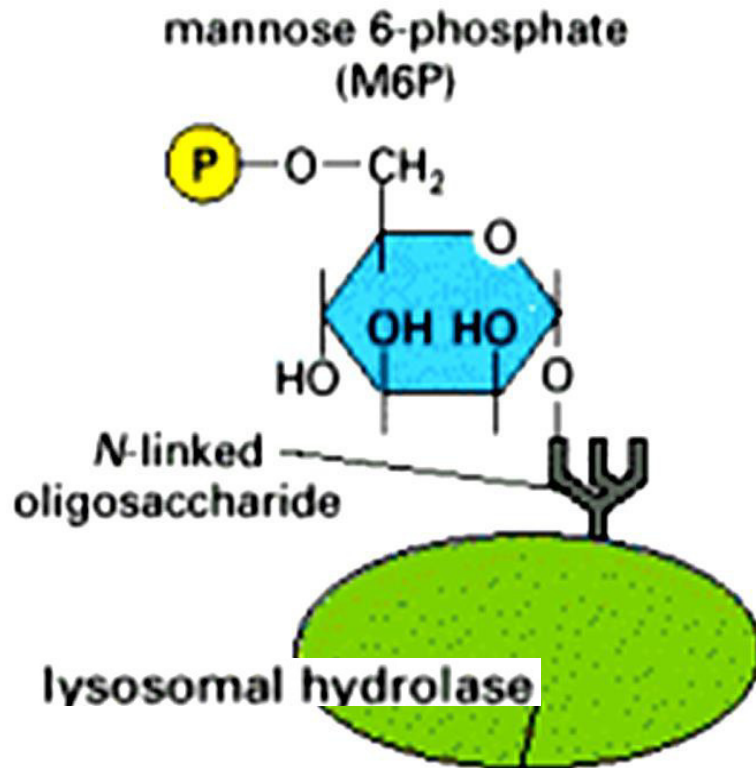
The transport vesicles that deliver these proteins to lysosomes bud from the trans Golgi network

These vesicles **incorporate the lysosomal proteins** & exclude other proteins being packaged into different transport vesicles for delivery elsewhere

Lysosomal proteins are recognized and selected in the trans Golgi network with the required accuracy

Lysosomal hydrolases carry a **unique marker** in the form of mannose 6-phosphate (**M6P**) groups,.

Lysosomal Transport

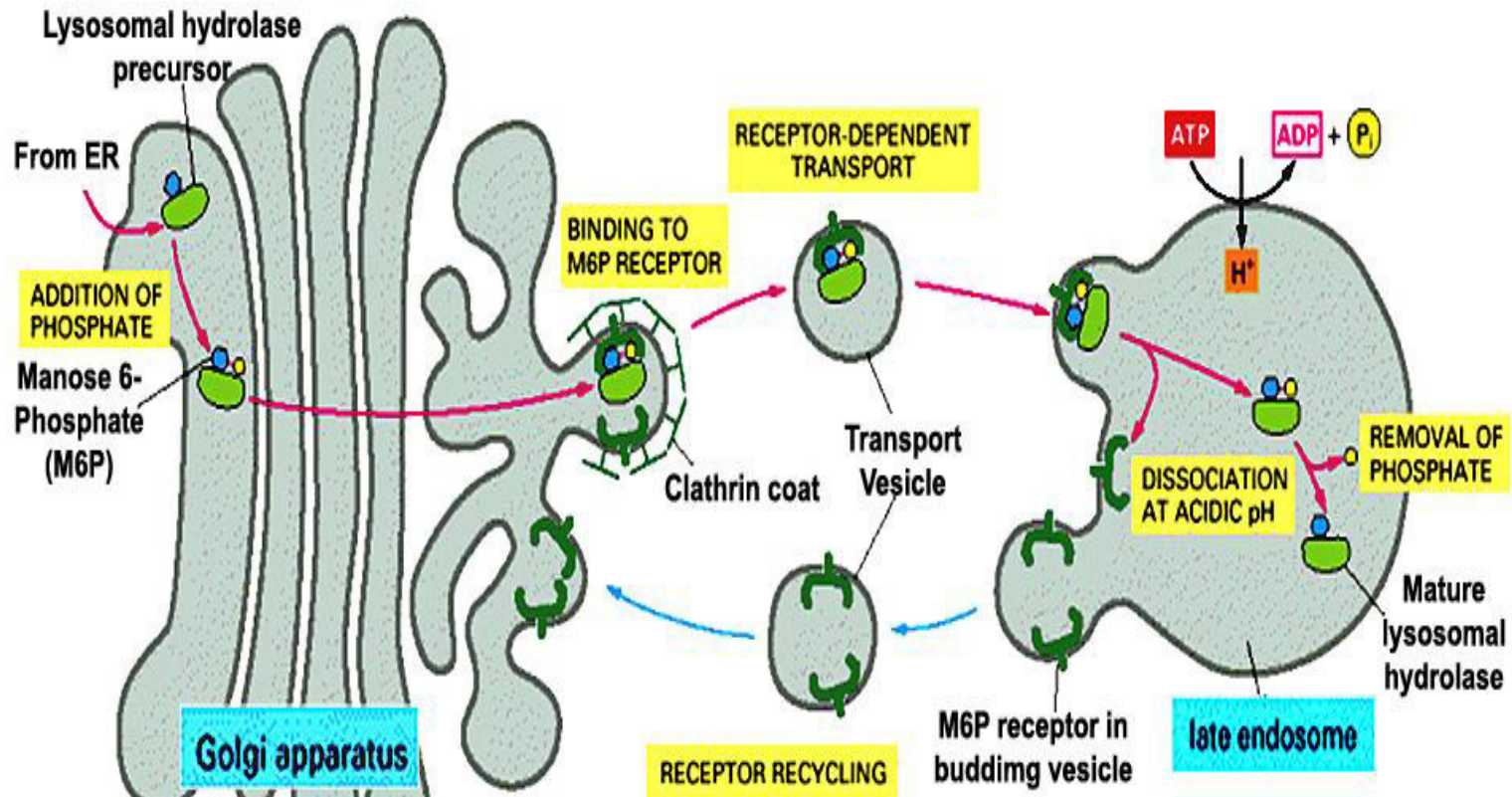


M6P is added to N-linked oligosaccharides of the soluble lysosomal enzymes in the lumen of the C-Golgi

The M6P groups are **recognized by trans-membrane M6P receptor** proteins, which are present in the **T-Golgi**

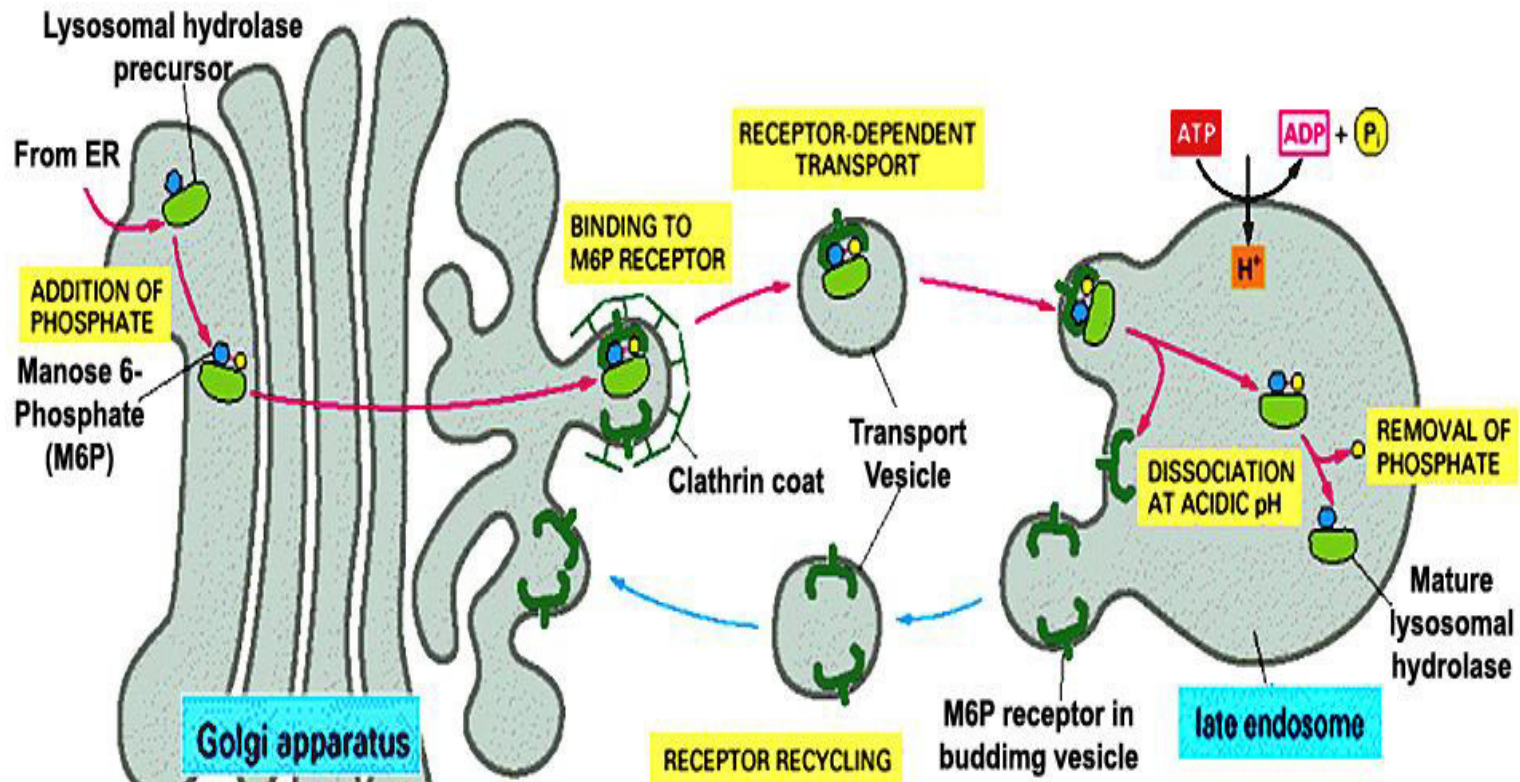
Receptors bind to lysosomal hydrolases on the **luminal side** of the membrane and to adaptins to assemble clathrin coats on the **cytosolic side**

Lysosomal Transport



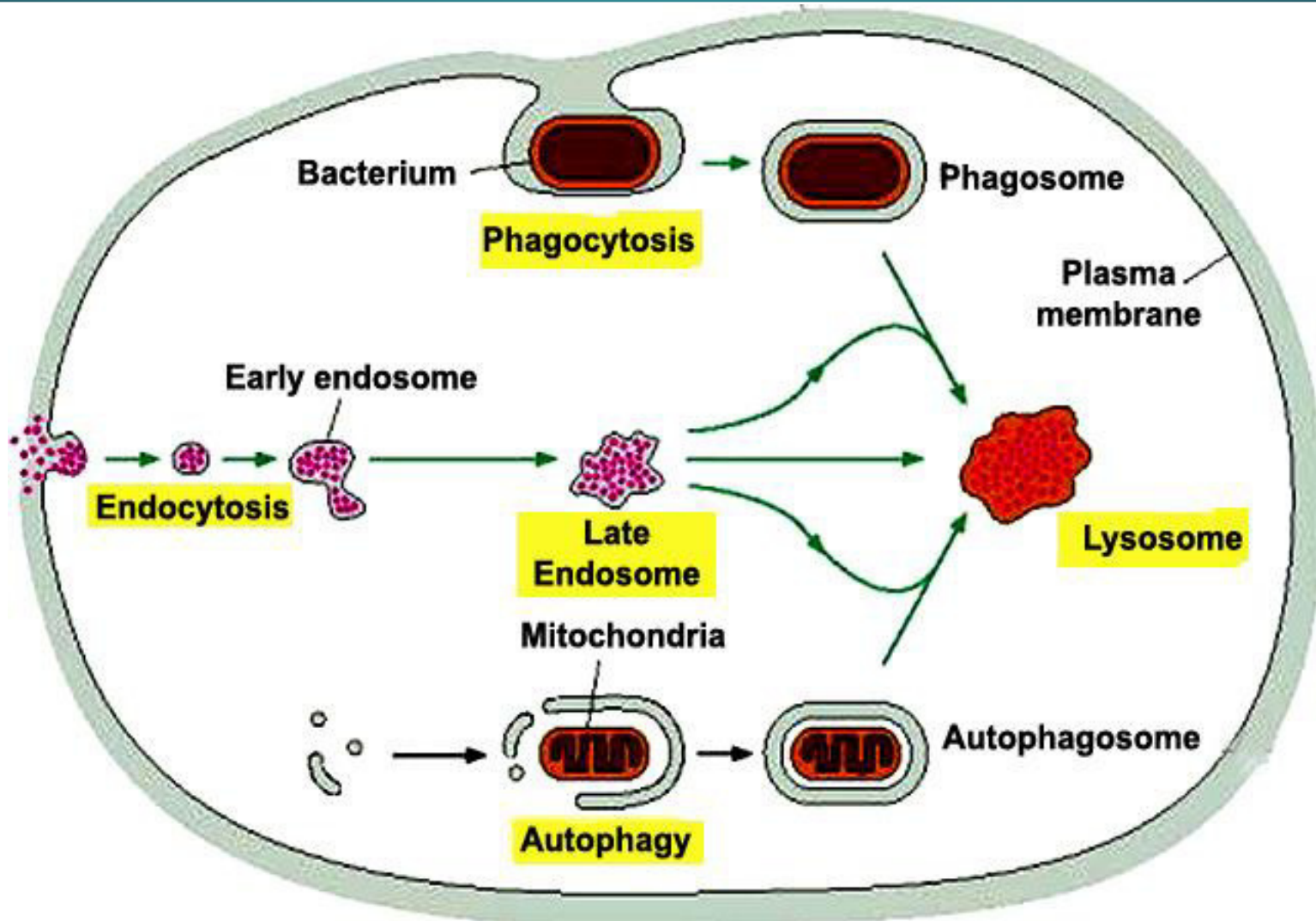
Receptors help package the **hydrolases into clathrin-coated vesicles** that bud from the T-Golgi network. Vesicles contents are subsequently delivered to **Lysosomes**.

Lysosomal Transport



M6P receptor binds its specific oligosaccharide at **pH 6.5** in the **T-Golgi** network & releases it at **pH 6**, **late endosomes**. M6P receptors are **retrieved** into transport vesicles from late endosomes the receptors are **returned to the T-Golgi for reuse**.

Lysosome Function



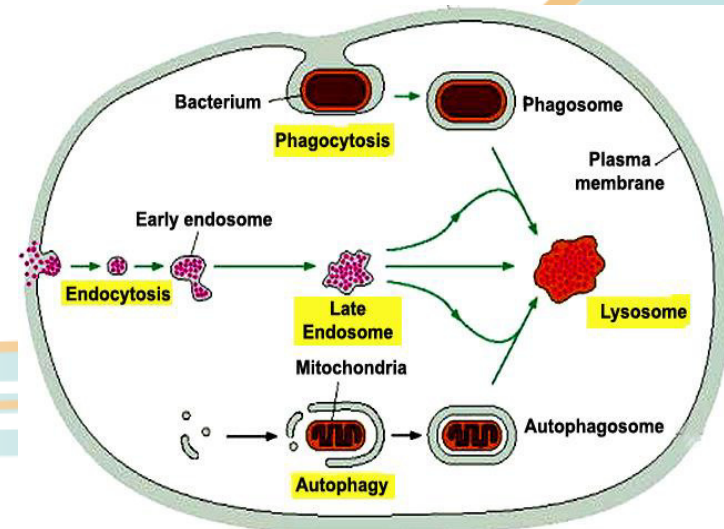
Inclusion-cell (I-cell) Disease

In this disease almost all of the **hydrolytic enzymes** are **missing** from the **lysosomes** of **fibroblasts**, and their **undigested** substrates **accumulate in lysosomes**, which consequently form large “**inclusions**” in the cells

In I-cell disease patients, all the hydrolases missing from lysosomes are **found** in the **blood**

Because they **fail to be sorted** properly in the Golgi apparatus, the hydrolases are **secreted** rather than transported to lysosomes.

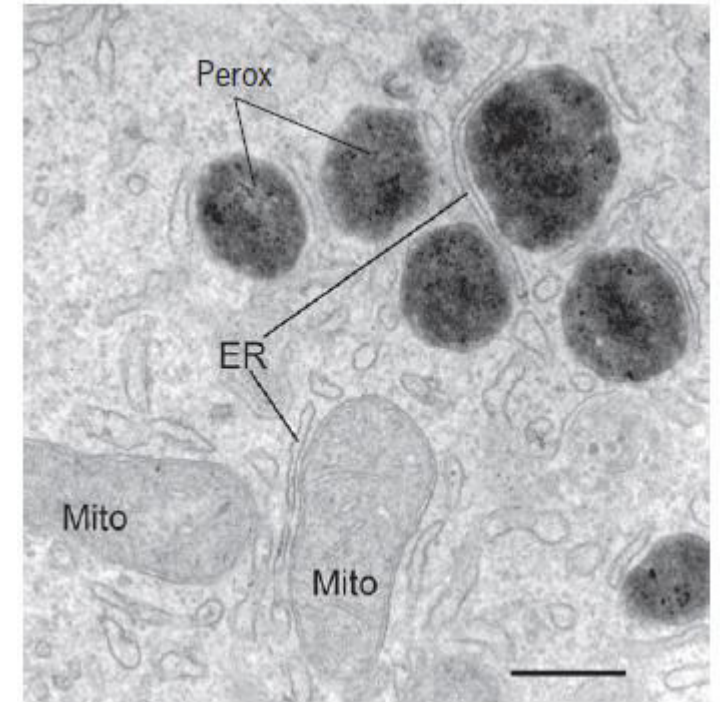
The Retrieval Process

**END**

Peroxisomes & Glyoxysome

Introduction

- **Peroxisomes** also called as **microbodies** are simple, membrane-bound vesicles.
- They have a diameter of 0.1 to 1.0 μ m.
- It may contain a dense, crystalline core of oxidative enzymes.
- Peroxisomes are multifunctional organelles containing more than 50 enzymes.
- These are involved in oxidation of very-long-chain fatty acids.

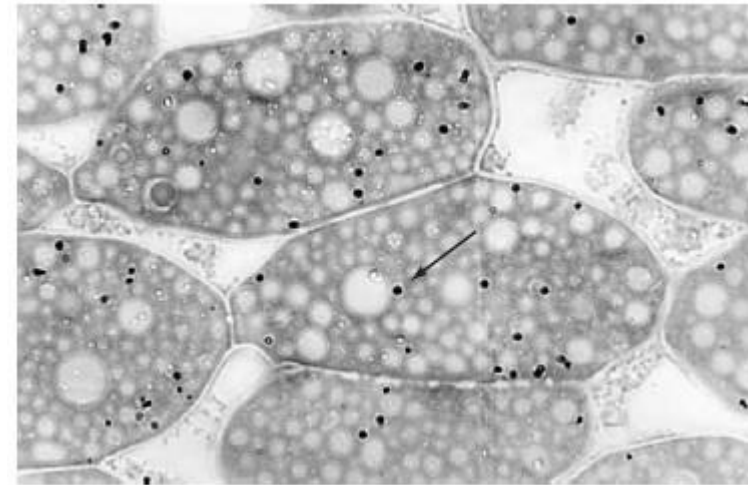


Electron micrograph of a section of a rat liver cell, showing peroxisomes.

- These organelles were named “peroxisomes” because they are the site of synthesis and degradation of hydrogen peroxide (H_2O_2), a highly reactive and toxic oxidizing agent.
- Hydrogen peroxide is produced by a number of peroxisomal enzymes, including *urate oxidase*, *glycolate oxidase*, and *amino acid oxidases*, that utilize molecular oxygen to oxidize their respective substrates.
- The H_2O_2 generated in these reactions is rapidly broken down by the enzyme catalase, which is present in high concentrations in these organelles.

Glyoxysome

- Plant seedlings contain a specialized type of peroxisome, called a **glyoxysome**.
- Plant seedlings rely on stored fatty acids to provide the energy and material to form a new plant.



Glyoxysome localization within plant seedlings

Functions

- One of the primary metabolic activities of glyoxisomes in germinating seedlings is the conversion of stored fatty acids to carbohydrate.

- Following steps are involved in this conversion;
 1. Disassembly of stored fatty acids generates acetyl CoA
 2. Acetyl CoA condenses with oxaloacetate (OAA) to form citrate
 3. Citrate is then converted into glucose by a series of enzymes of the glyoxylate cycle localized in the glyoxysome.

CELL BIOLOGY

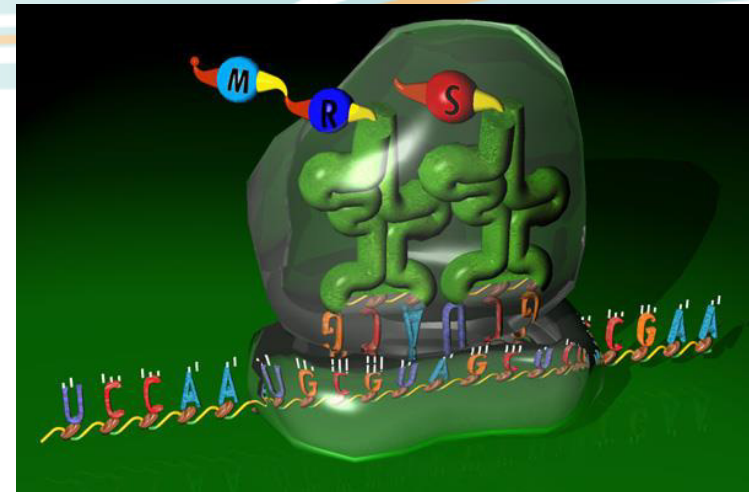


Ribosome

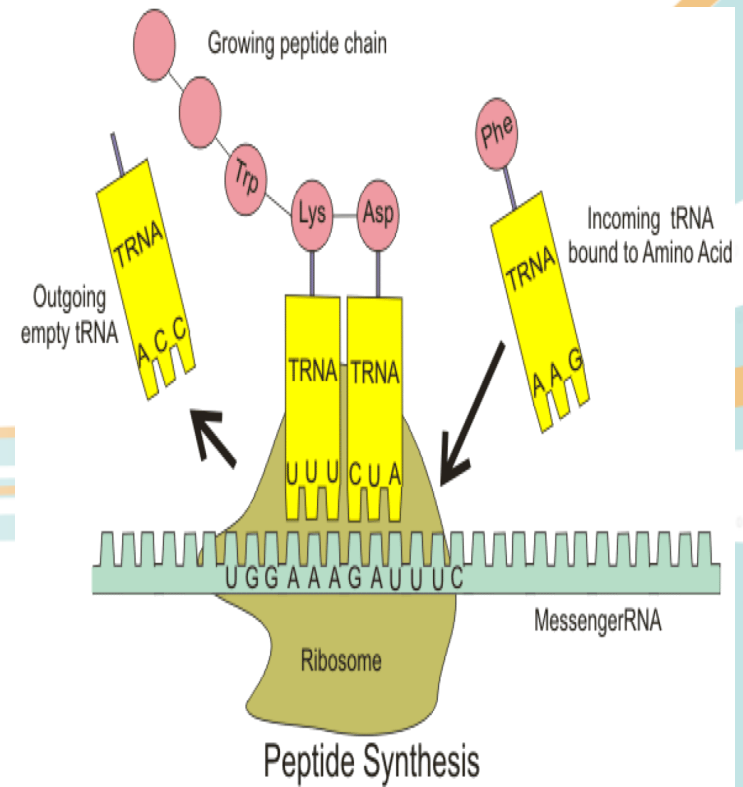
Ribosome

Protein & RNA
Free or attached to ER
involved in protein
synthesis.

Mitochondria &
Chloroplasts.

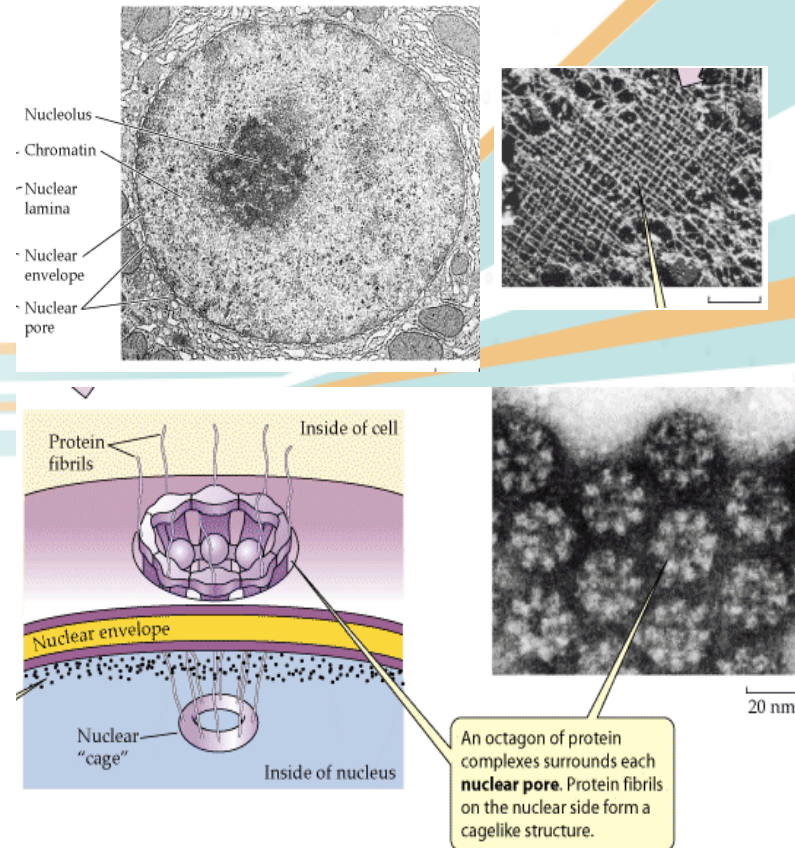


Ribosome



The Nucleus

Nuclear EMs



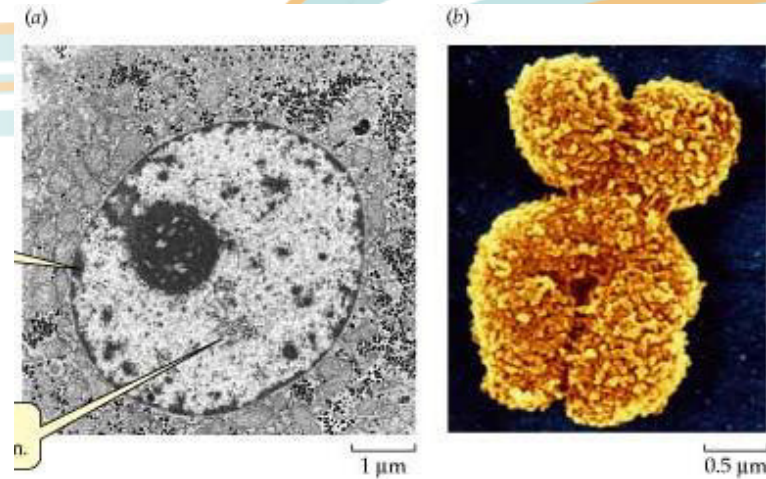
The Nucleus

Chromatin

Euchromatin

Hetrochromatin

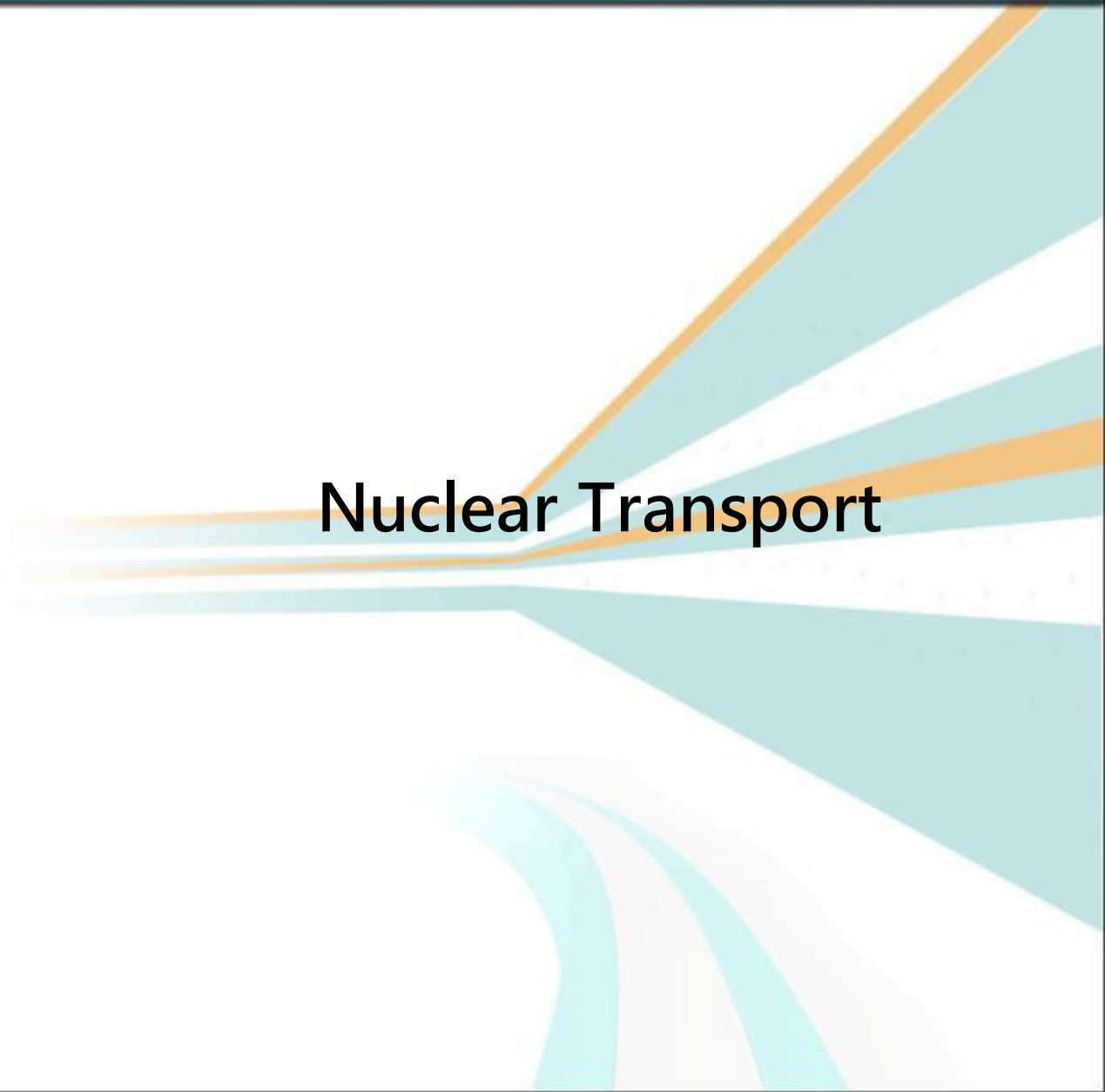
Chromosome



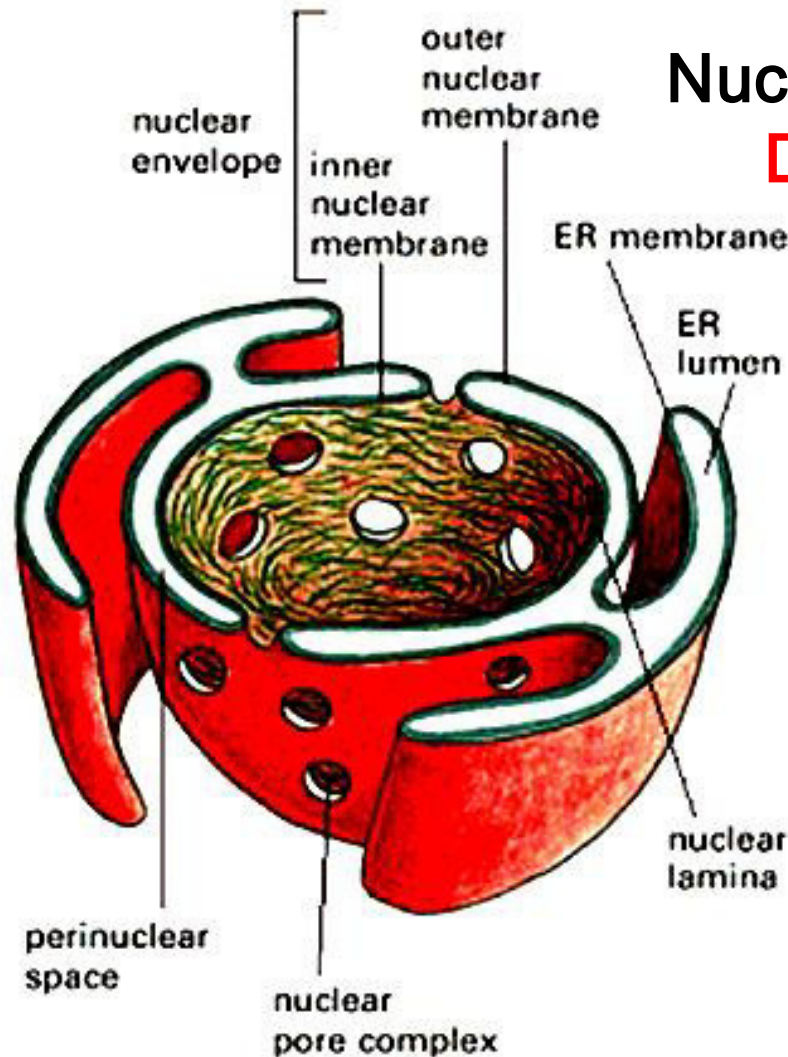
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Cell Biology

Nuclear Transport

The background of the slide features an abstract graphic on the right side. It consists of several overlapping, semi-transparent geometric shapes in shades of teal and orange. These shapes form a series of diagonal lines and triangular areas that create a sense of depth and movement, extending from the top right towards the center of the slide.

Nuclear Transport



Nuclear envelope **encloses**
DNA & defines nuclear
compartment

Envelope consists of **2**
concentric membranes
that are penetrated by
nuclear pore complexes

The inner & outer
membranes are
continuous & **maintain**
distinct protein
compositions.

Nuclear Transport



The **inner nuclear membrane** contains specific **proteins** that act **as binding sites** for **chromatin & protein** meshwork of the nuclear **lamina** that provides structural support.

The inner membrane is surrounded by the **outer nuclear membrane**, which is **continuous** with the membrane of the **ER**

The **outer nuclear membrane** is studded with **ribosomes** engaged in protein synthesis

Nuclear Transport



Bidirectional traffic
between the
cytosol and the
nucleus

Many proteins that function in nucleus—including histones, DNA and RNA polymerases, gene regulatory proteins, & RNA-processing proteins—are **selectively imported** into the nuclear compartment from the cytosol,

At the same time, **tRNAs and mRNAs** are synthesized in the nuclear compartment and then **exported** to cytosol

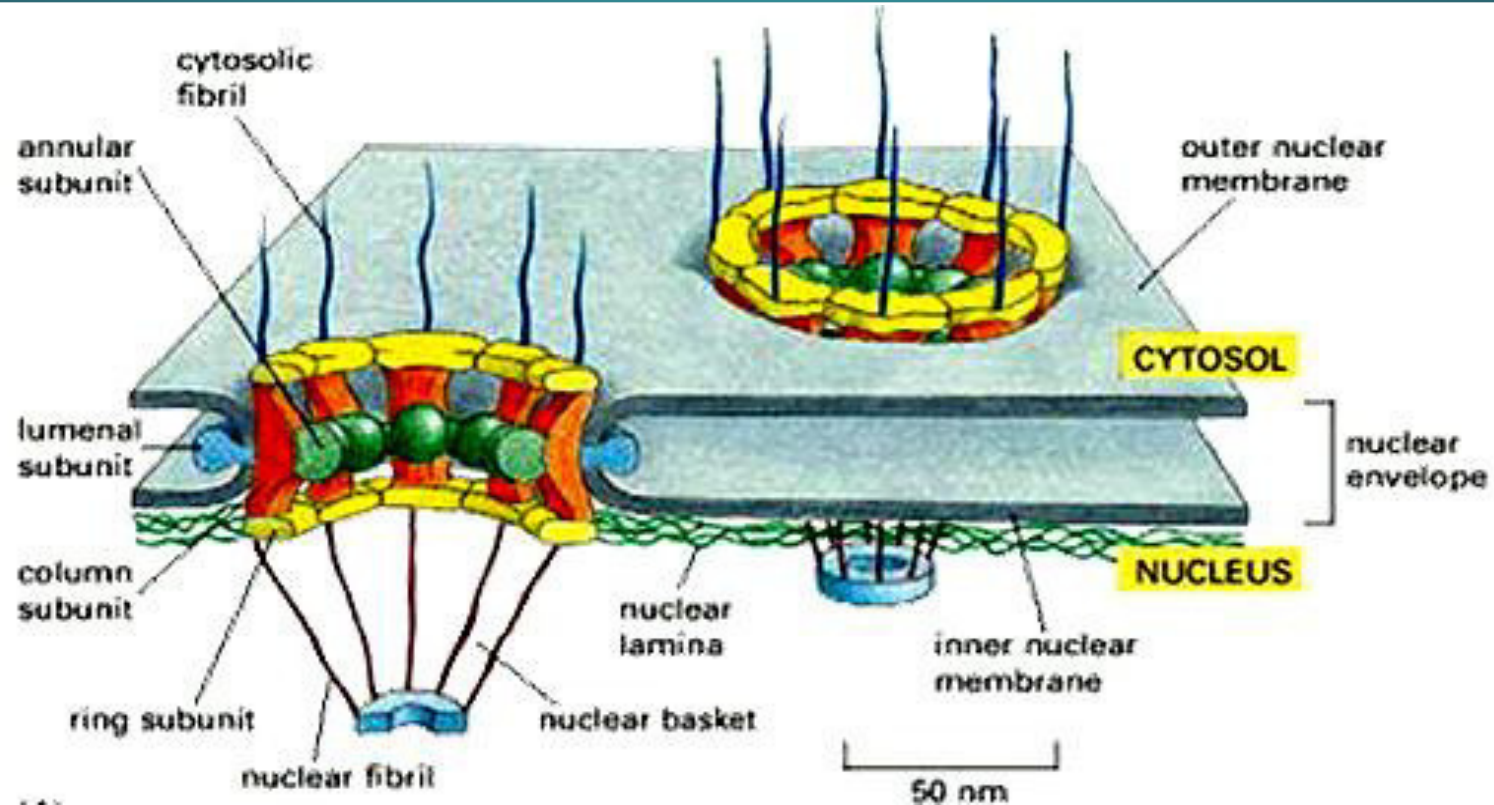
Nuclear Transport



Like the **import** process, the **export** process is **selective**; mRNAs, for example, are exported only after they have been properly modified by RNA-processing reactions in the nucleus

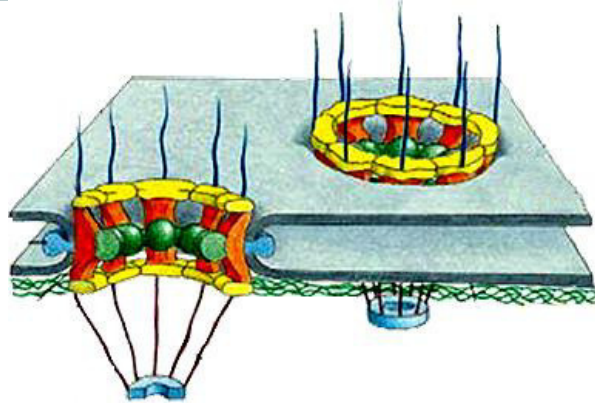
Ribosomal proteins, are made in the **cytosol**, imported into the nucleus—where they assemble with newly made ribosomal RNA into particles—and are then exported again to the cytosol as part of a ribosomal subunit

Nuclear Pore Complexes



Eukaryotic nuclear envelope is perforated by large, elaborate structures called nuclear pore complexes which **selectively facilitate nuclear transport**

Nuclear Pore Complexes



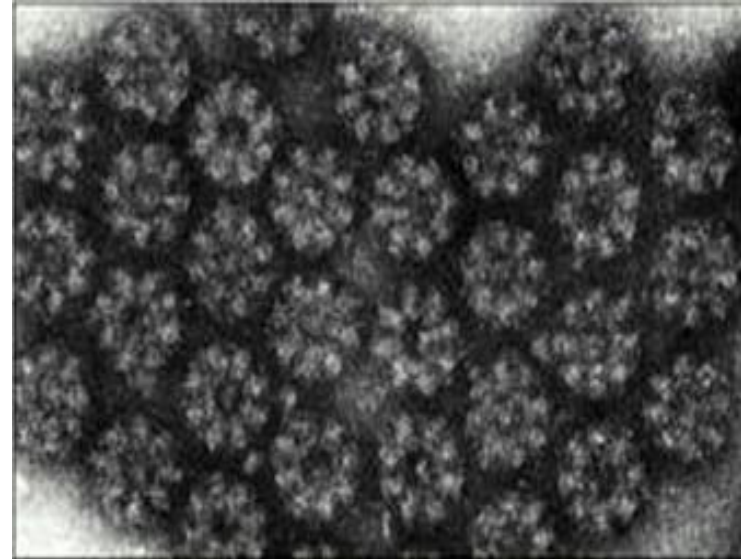
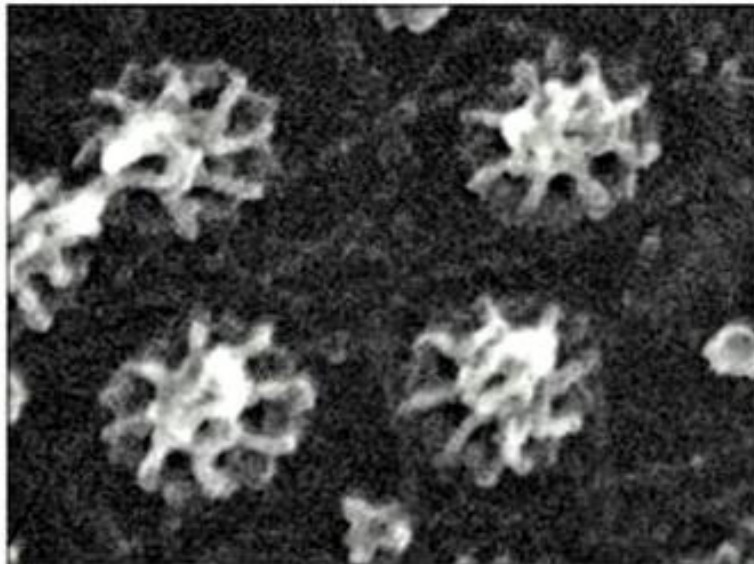
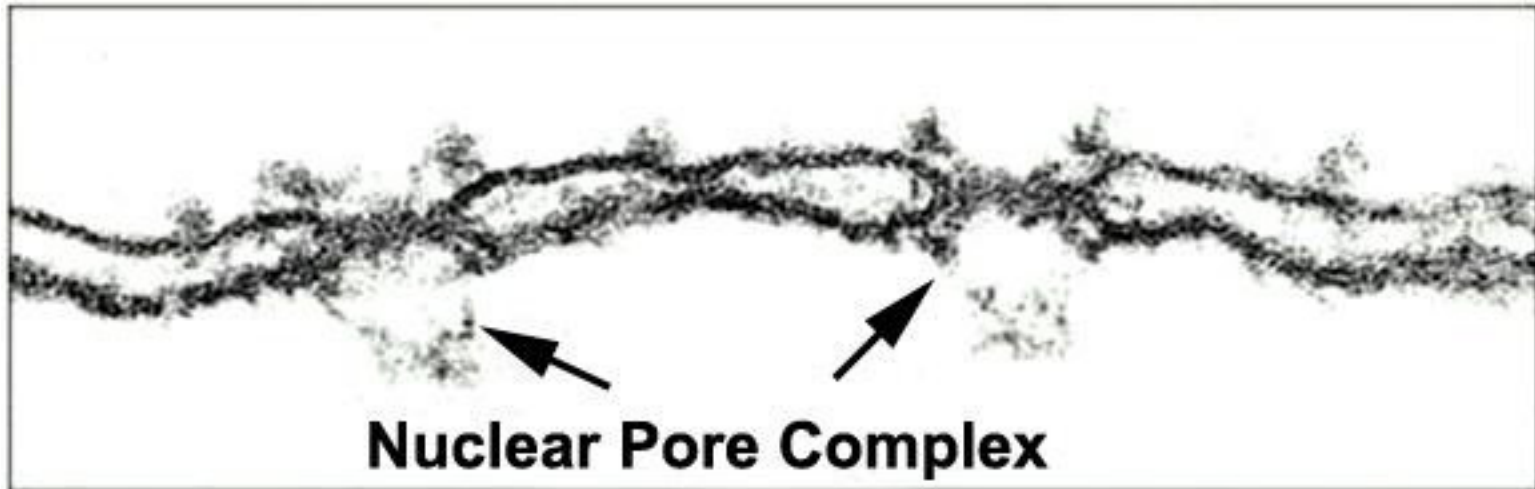
Each pore complex contains one or more open aqueous channels through which **small water-soluble molecules can passively diffuse**

Each complex has a molecular mass of about 125 million & is composed of aprox **50 different proteins**, called nucleoporins, arranged octagonal symmetry

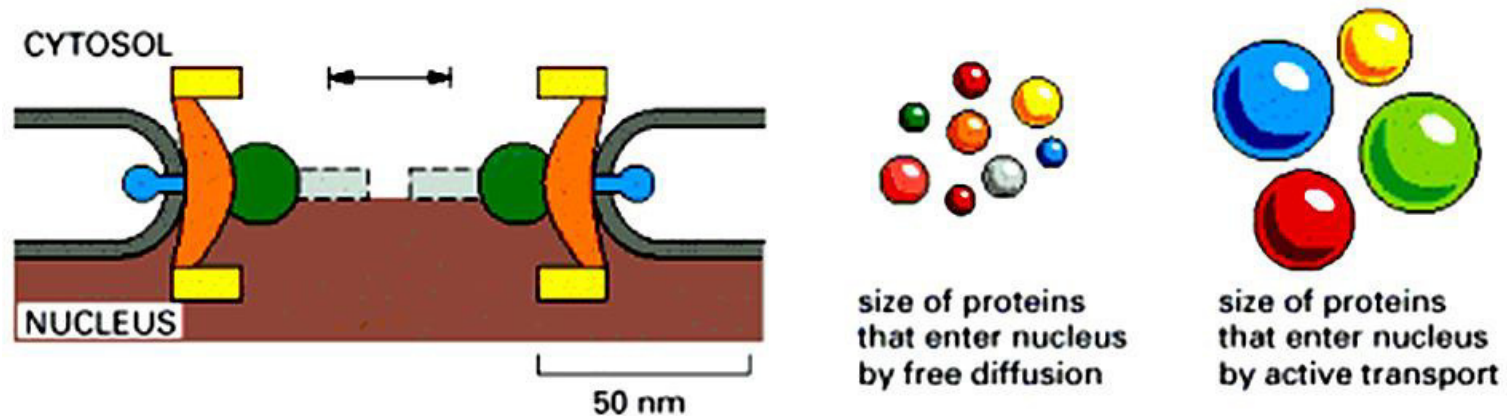
Small molecules (5000 daltons or less) diffuse in so fast that the nuclear envelope can be considered to be freely permeable to them, a protein of **17,000 daltons takes 2 minutes** to proteins larger than 60,000 daltons are unable to enter the nucleus.

(injecting labeled water-soluble molecules)

Nuclear Pore Complexes



Nuclear Pore Complexes



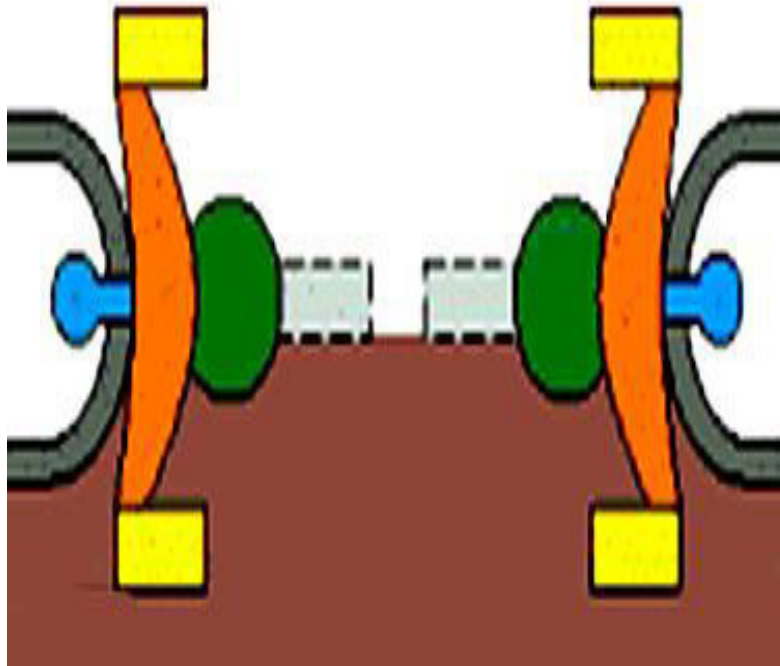
Nuclear pore contains a pathway for free diffusion **9 nm in diameter & 15 nm long**, this channel occupies a small fraction of total volume of the pore complex.

The more active the nucleus is in transcription, the greater the number of pore complexes

The nuclear envelope of a typical mammalian cell contains 3000–4000 pore complexes

equivalent to a water-filled cylindrical channel

Nuclear Pore Complexes



Cells **synthesizing DNA**, need to import about **10^6 histone molecules** from the cytosol **every 3 minutes** to package DNA into chromatin, ie **each pore** complex needs to transport about **100 histone molecules/minute**

Rapidly growing cell need to transport about **6 large & small ribosomal subunits/minute** from nucleus, where they are produced, to the cytosol.

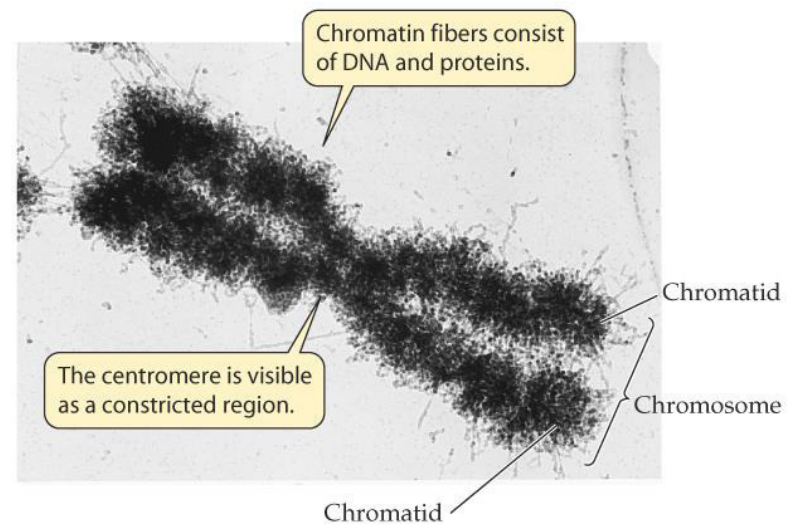
Nuclear Transport



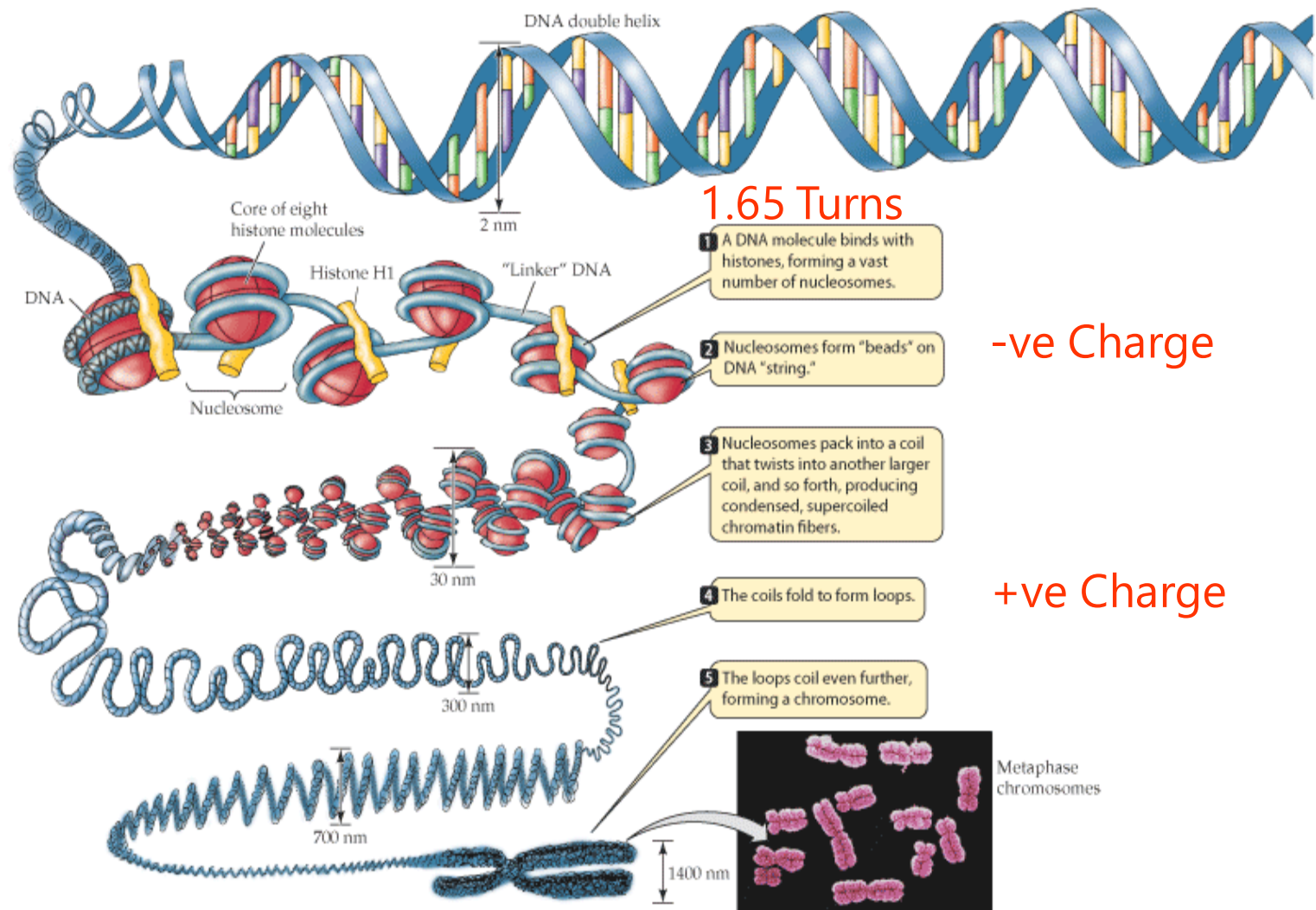
END

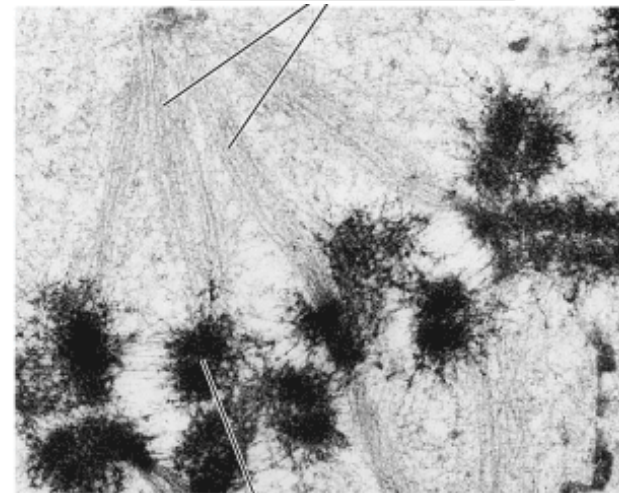
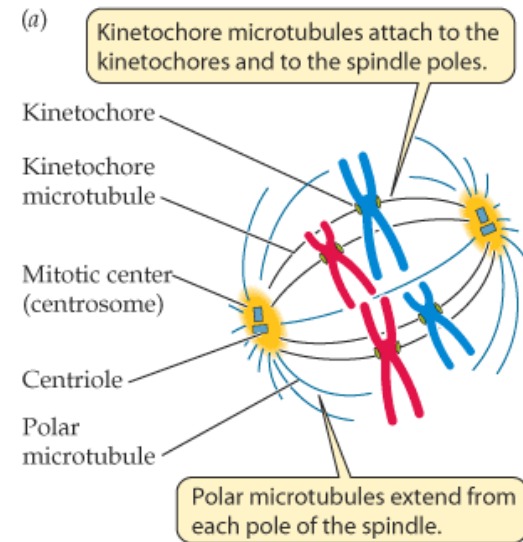
Chromosome

Anatomy

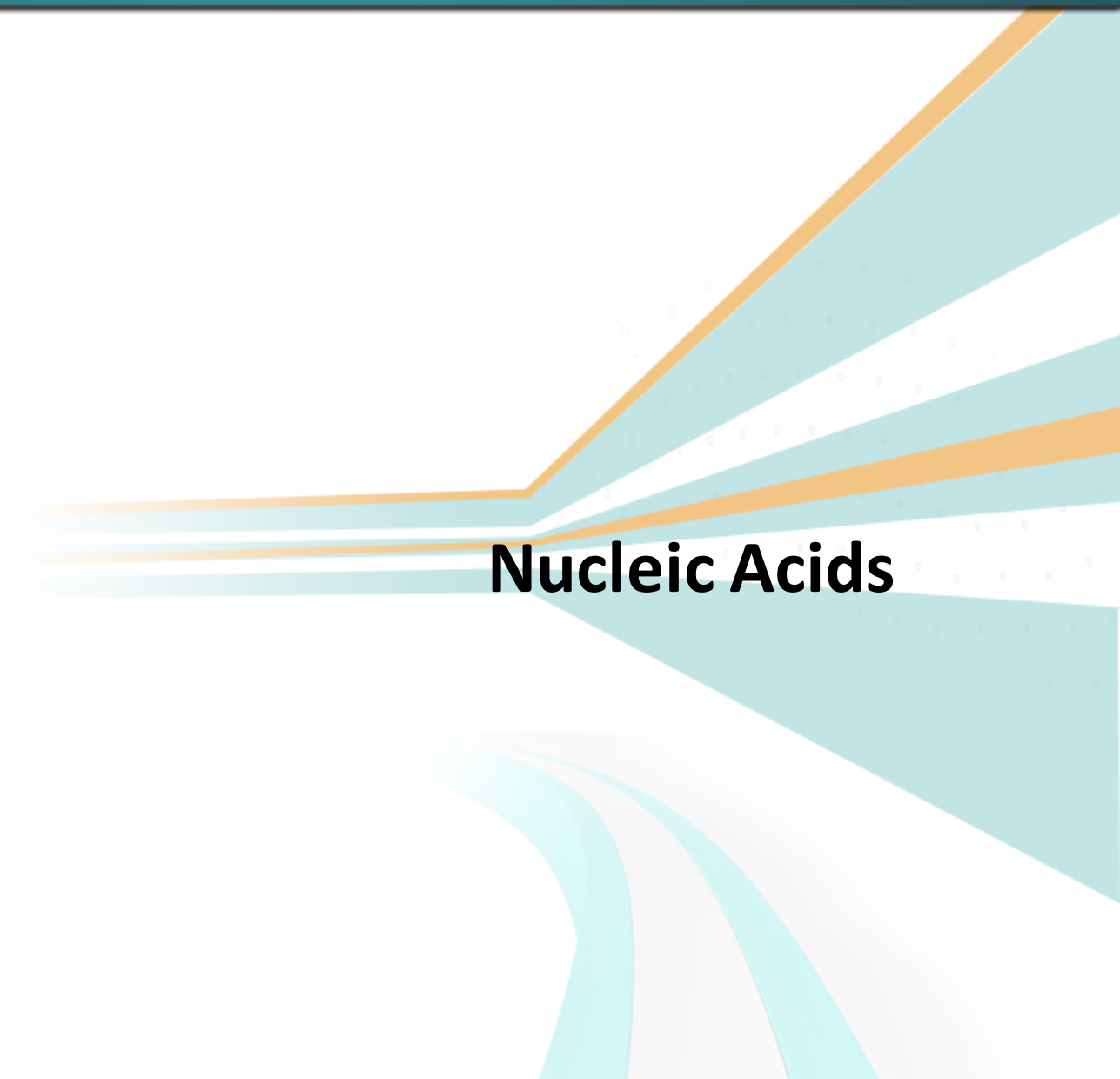


A chromosome is an organized structure of DNA and protein





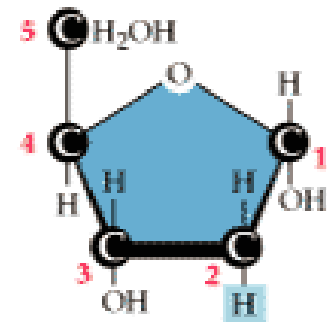
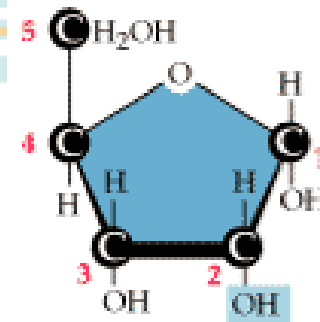
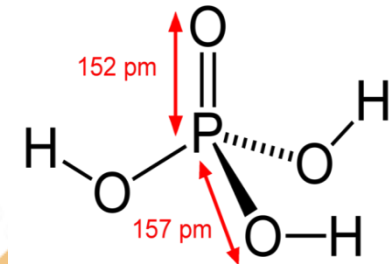
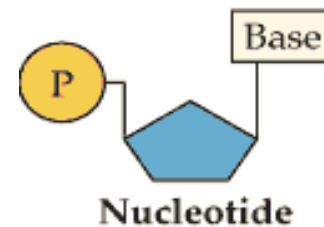
Kinetochores



Nucleic Acids

Nucleic Acids

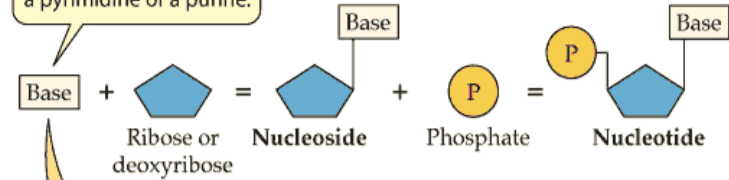
DNA & RNA



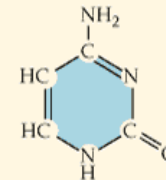
Nucleic Acids

The Bases

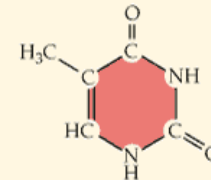
The base may be either a pyrimidine or a purine.



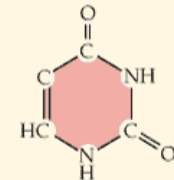
Pyrimidines



Cytosine (C)

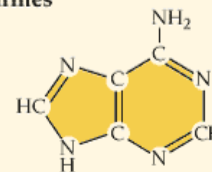


Thymine (T)

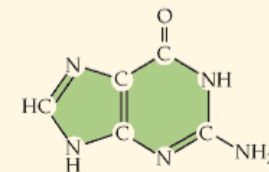


Uracil (U)

Purines



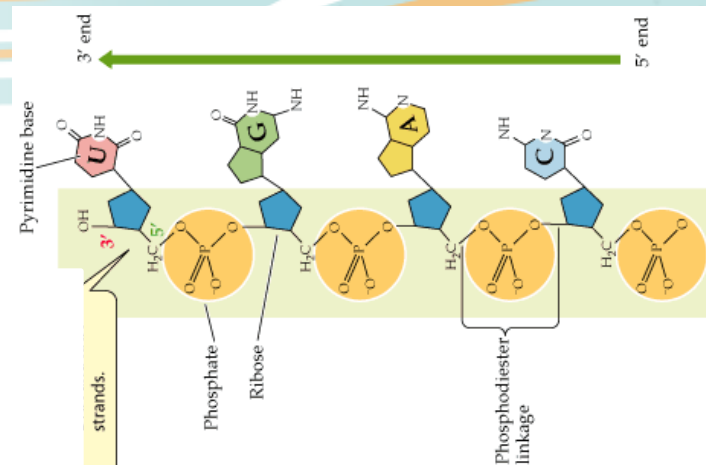
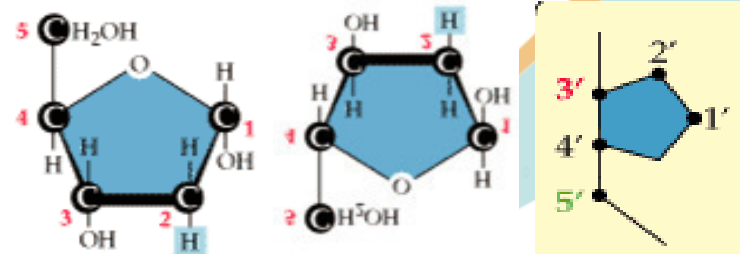
Adenine (A)



Guanine (G)

Nucleic Acids

Prime Ends (3' & 5')



END

CELL BIOLOGY



RNA & DNA

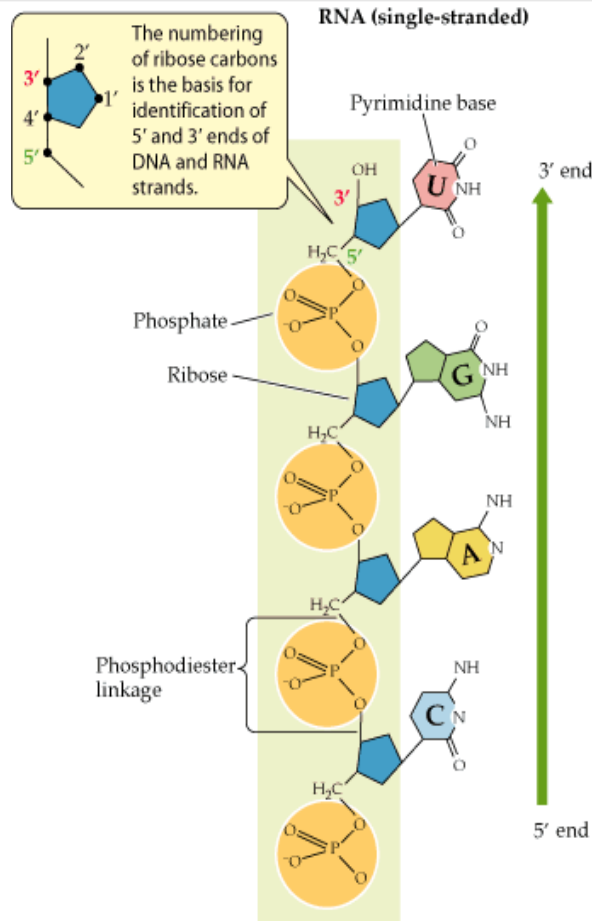
Nucleic Acids

RNA vs. DNA

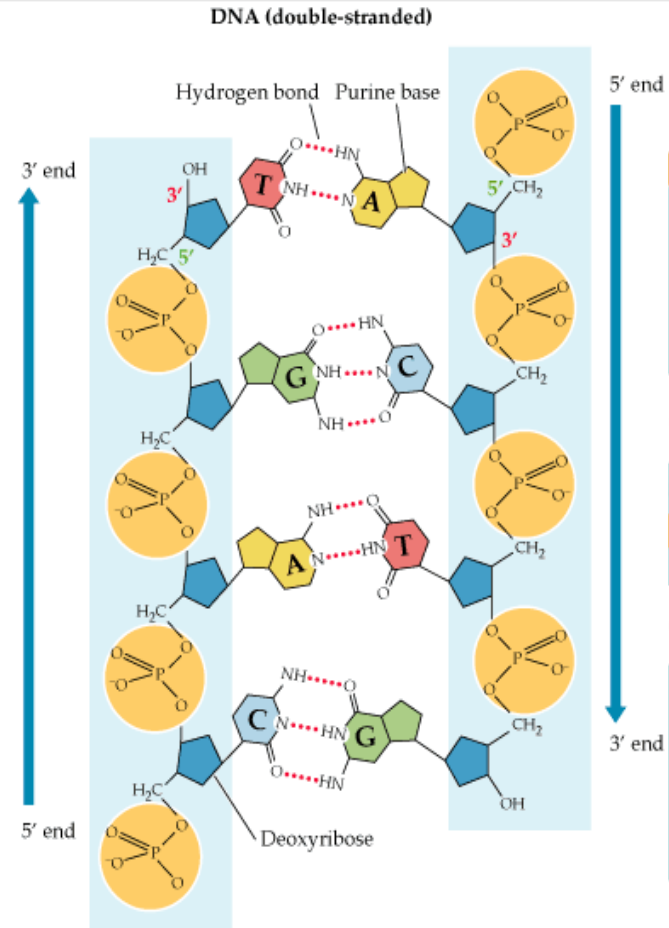
3.3 *Distinguishing RNA from DNA*

NUCLEIC ACID	SUGAR	BASES
RNA	Ribose	Adenine Cytosine Guanine Uracil
DNA	Deoxyribose	Adenine Cytosine Guanine Thymine

Nucleic Acids



In RNA, the bases are attached to ribose. The bases in RNA are the purines adenine (A) and guanine (G) and the pyrimidines cytosine (C) and uracil (U).

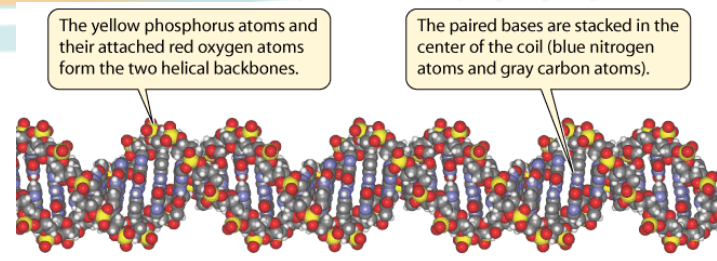


In DNA, the bases are attached to deoxyribose, and the base thymine (T) is found instead of uracil. Hydrogen bonds between purines and pyrimidines hold the two strands of DNA together.

Nucleic Acids

DNA Uniform
Width

Information in
Sequence not Shape



Chicken vs. Egg: What Came 1st

Protein or DNA

**Genetic information
codes for enzymes**

**Enzymes are required
to decipher genetic
information and
replicate it**

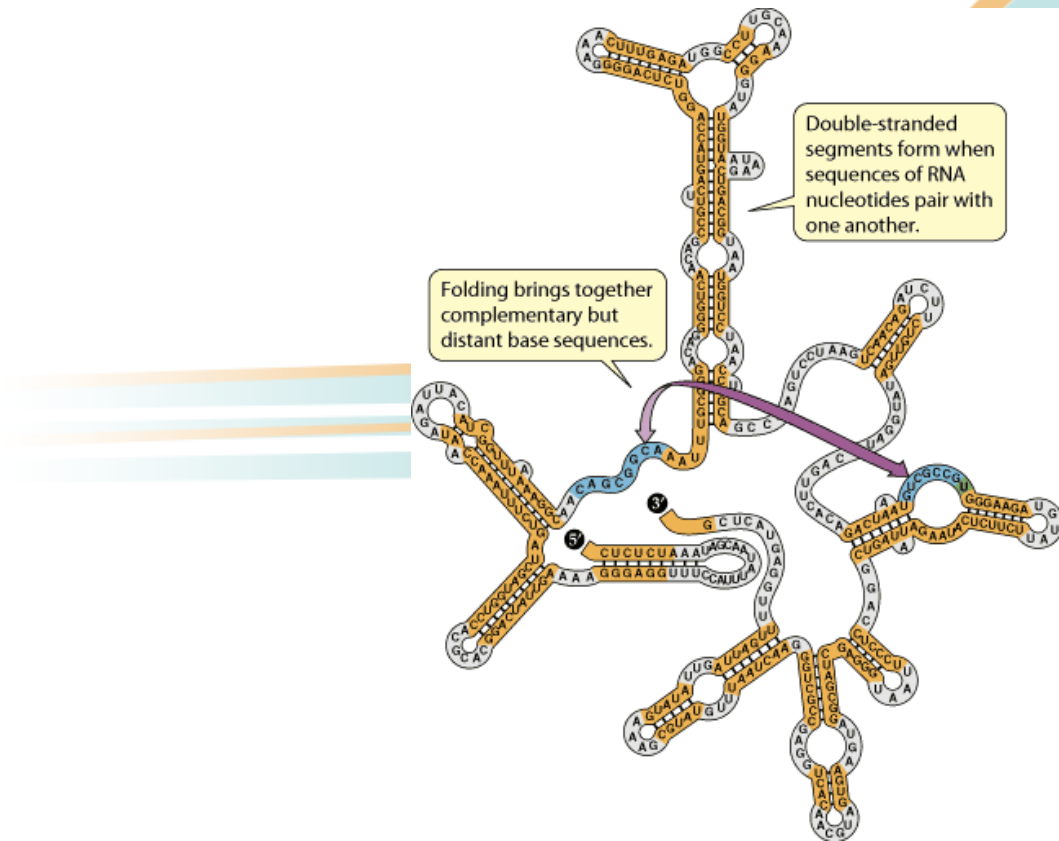
RNA Genetic Material & Enzyme

**Many viruses use RNA
as their hereditary
material**

**RNAs can achieve
chemical catalysis, like
enzymes: ribosome the
active site is composed
entirely of RNA
(peptide bond
formation)**

RNA: Information in Sequence and Shape

Why Then DNA?

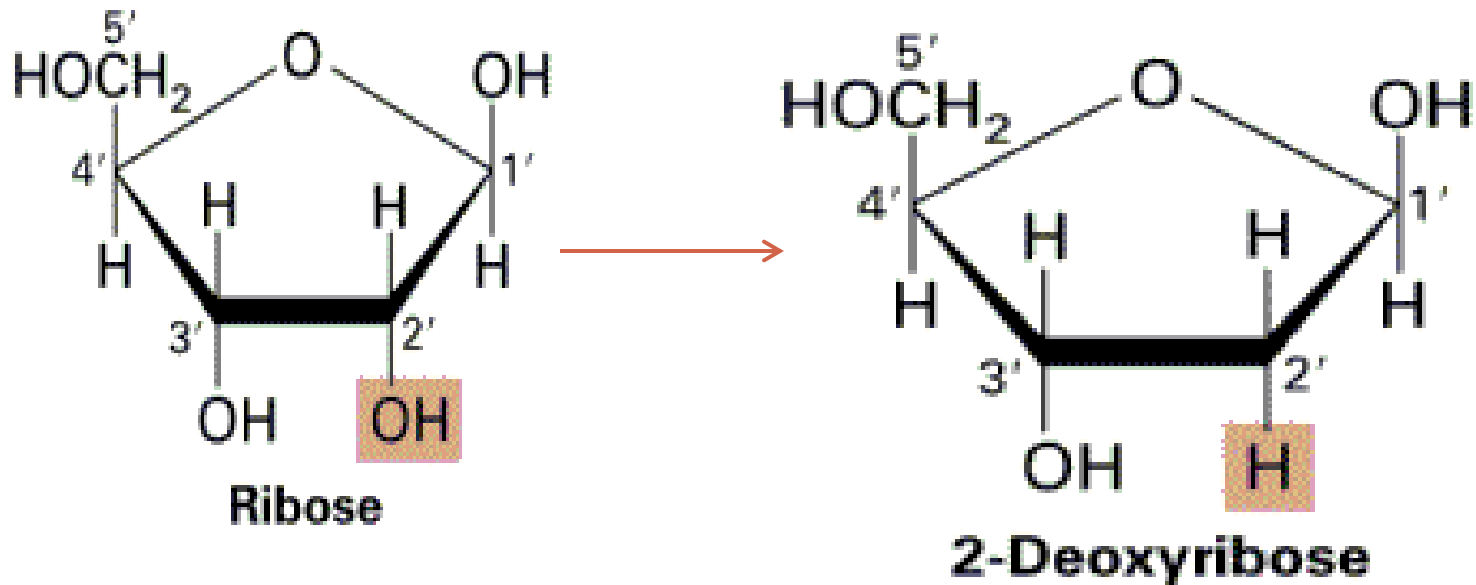


Chemical composition of DNA

- DNA is a polymer of Deoxyribonucleotides.
- Deoxyribonucleotide is composed of three components:
 - Deoxyribose
 - Nitrogenous Base
 - Phosphoric acid

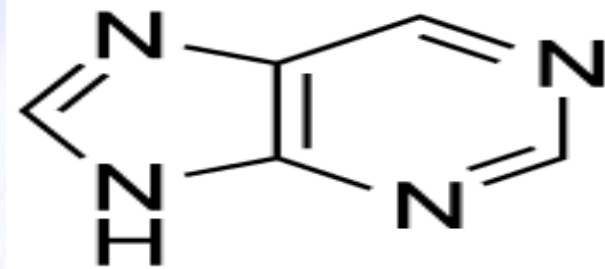
Chemical composition of DNA

Deoxyribose (a pentose sugar derivative)

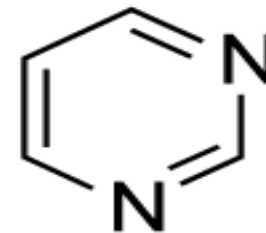


Chemical composition of DNA

Nitrogenous Bases



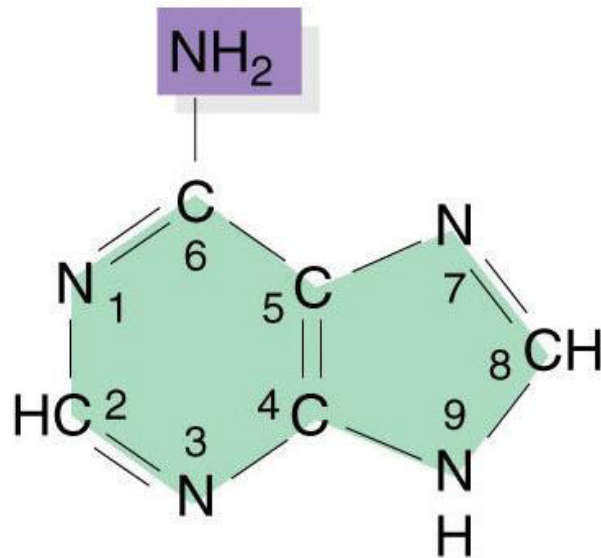
purine



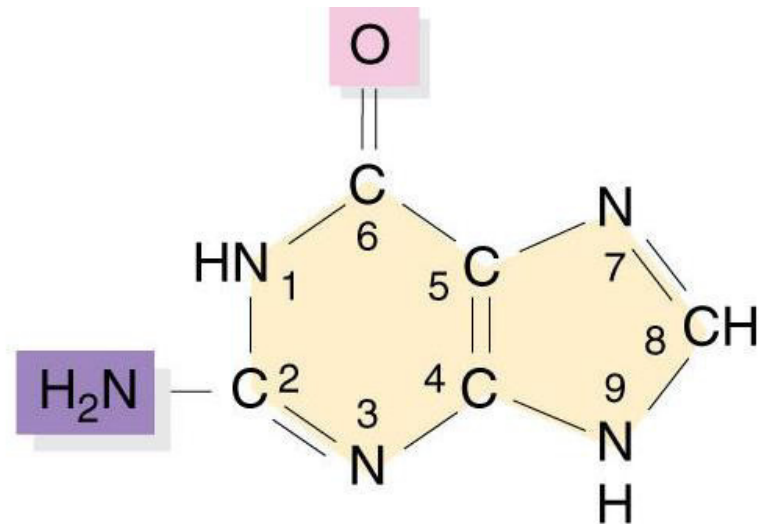
pyrimidine

Chemical composition of DNA

Purines



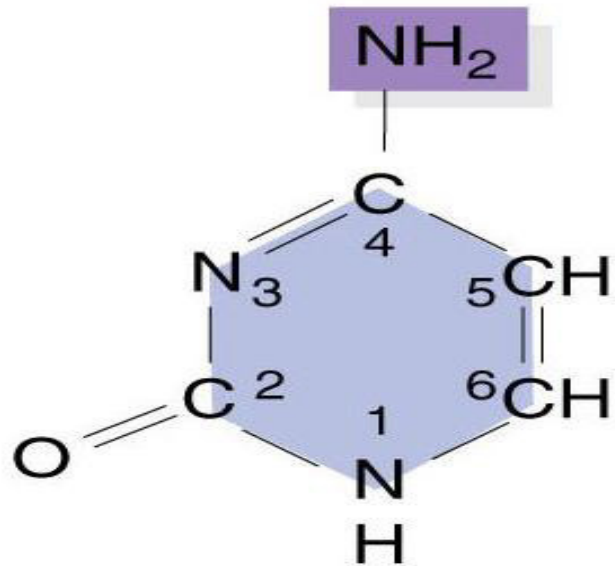
Adenine (A)



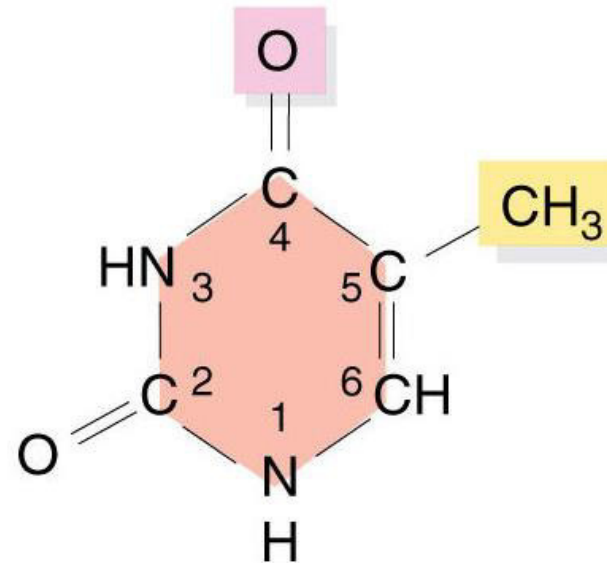
Guanine (G)

Chemical composition of DNA

Pyrimidines



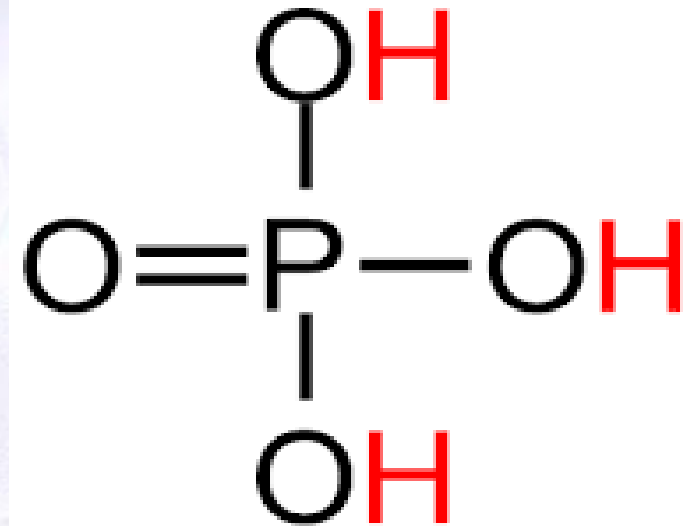
Cytosine (C)



Thymine (T)

Chemical composition of DNA

Phosphoric acid

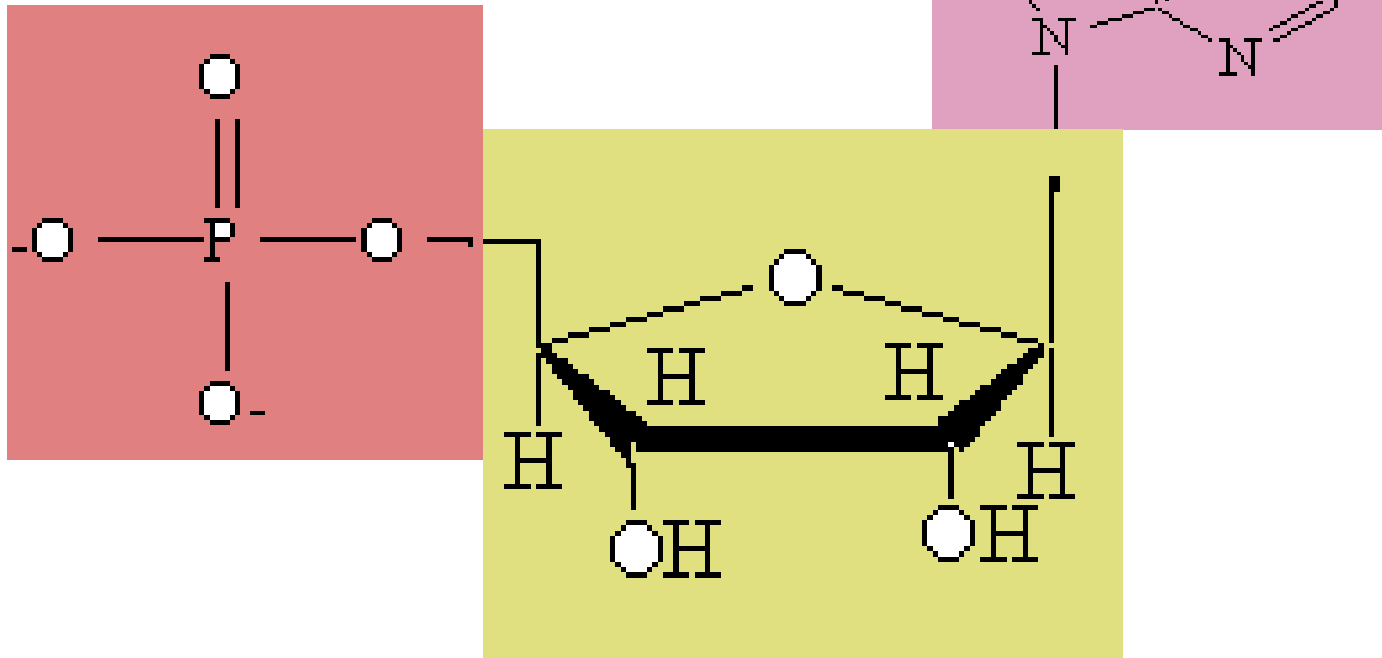


end

Nucleoside & Nucleotide

- A molecule containing all these three components is called a **nucleotide**.
- While a molecule without the phosphate group is called a **nucleoside**.

Nucleoside & Nucleotide



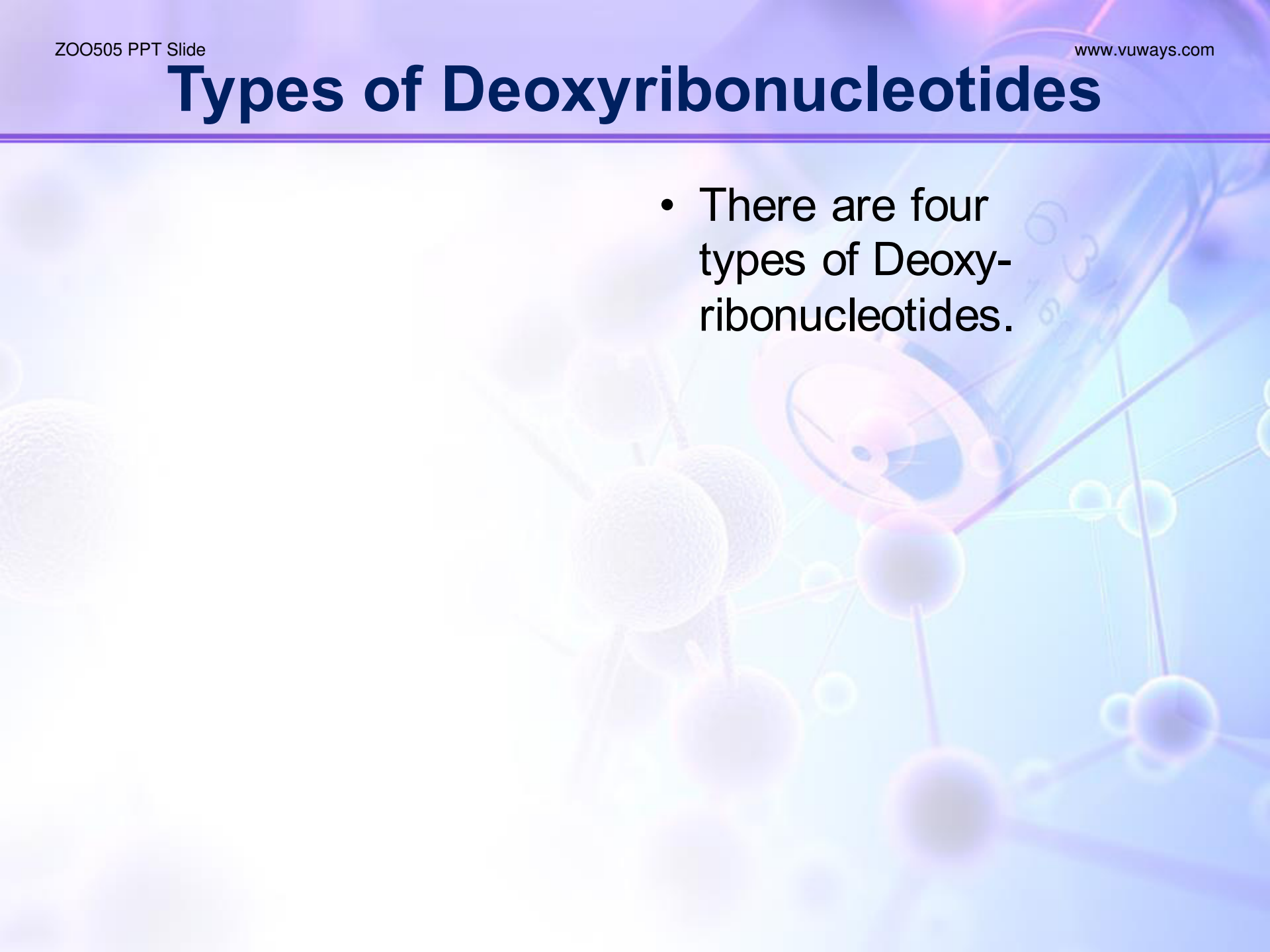
Nucleoside & Nucleotide

Nucleotide =
Nucleoside +
Phosphoric acid
&
Nucleoside =
Nucleotide –
Phosphoric acid

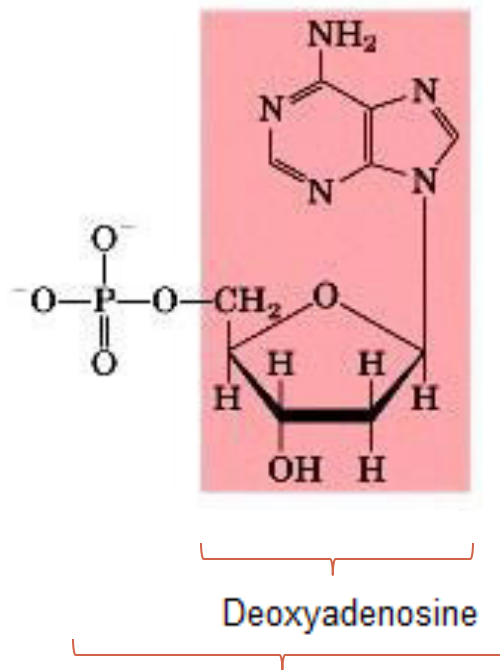
end

Types of Deoxyribonucleotides

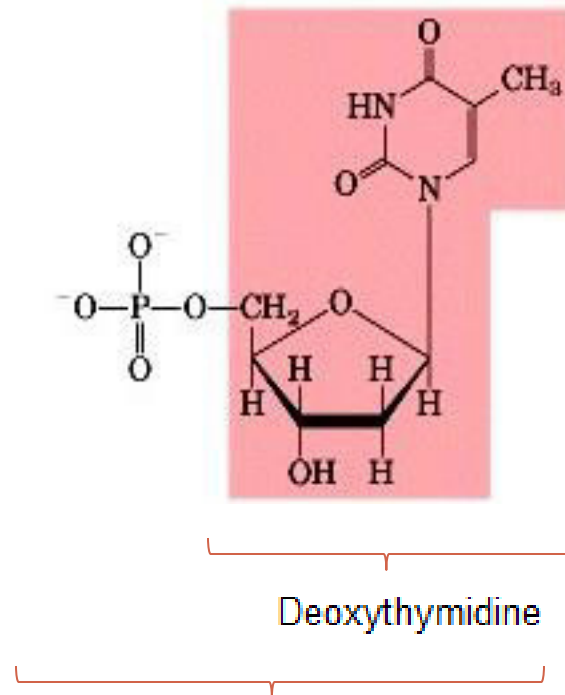
- There are four types of Deoxyribonucleotides.



Types of Deoxyribonucleotides

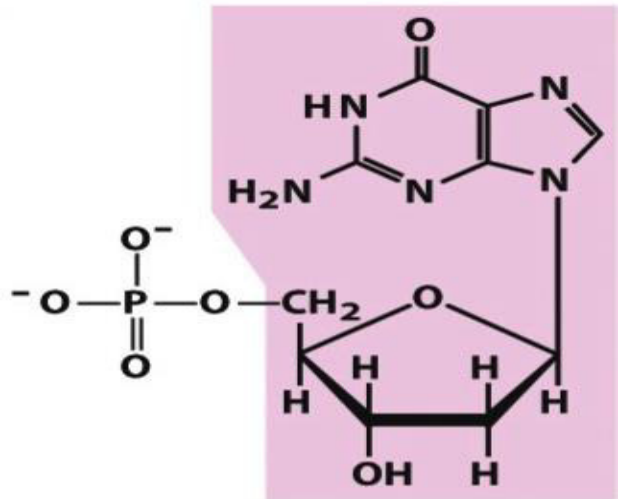


Deoxyadenylate



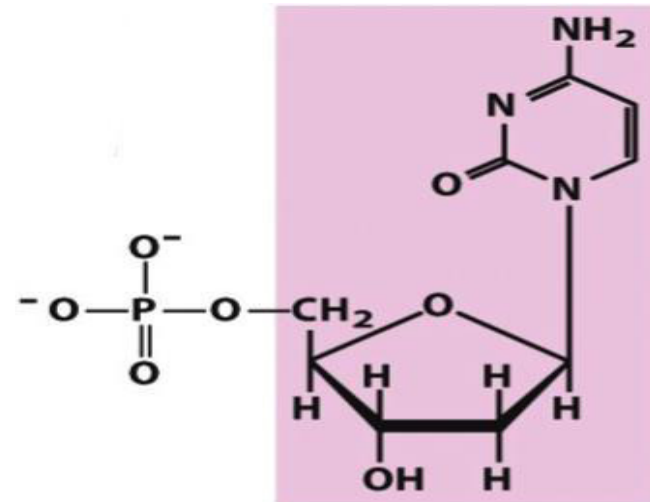
Deoxythymidylate

Types of Deoxyribonucleotides



Deoxyguanosine

Deoxyguanylate



Deoxycytidine

Deoxycytidylate

Types of Deoxyribonucleotides

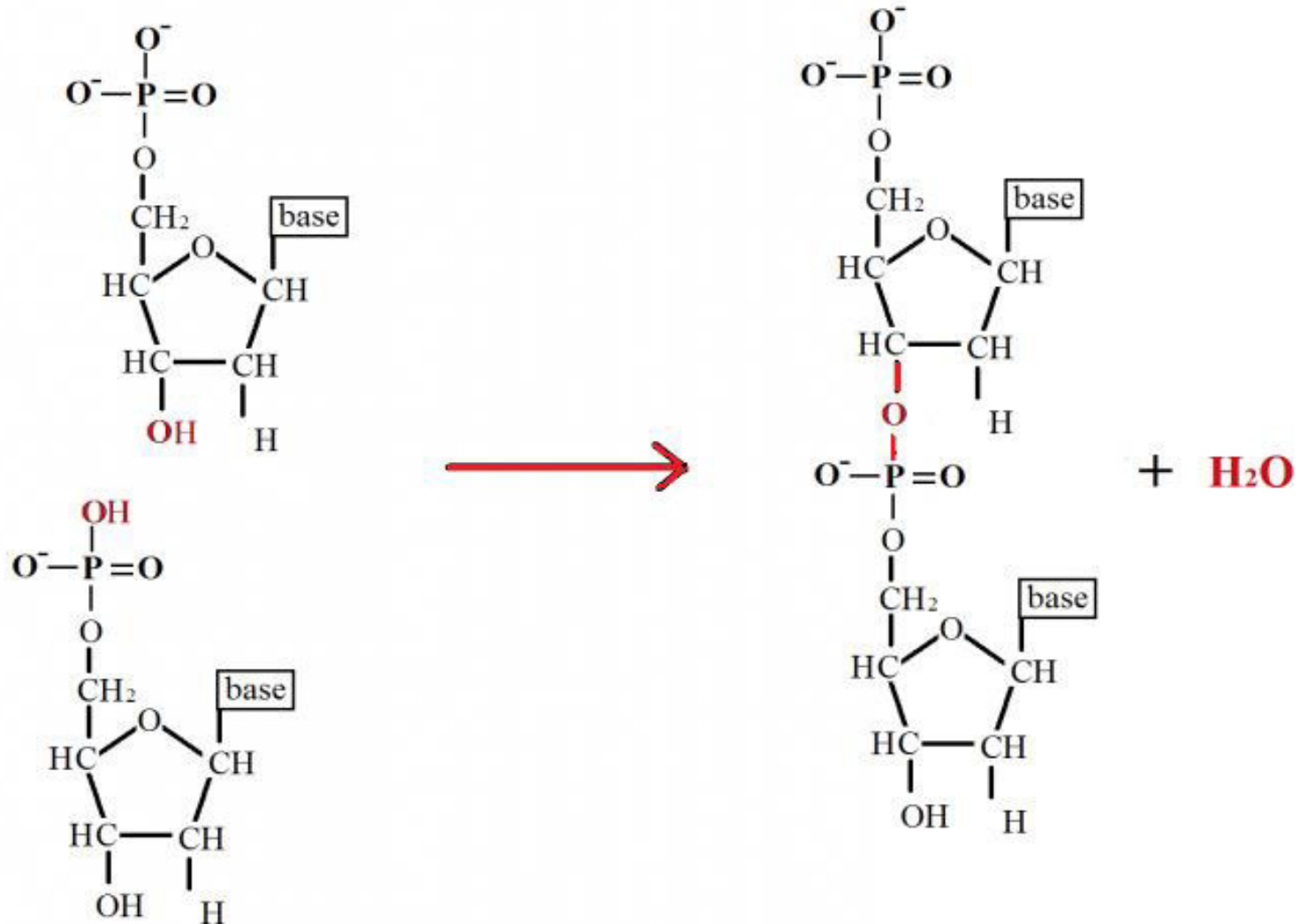
- These four deoxyribonucleotides make the structural units of DNA.

end

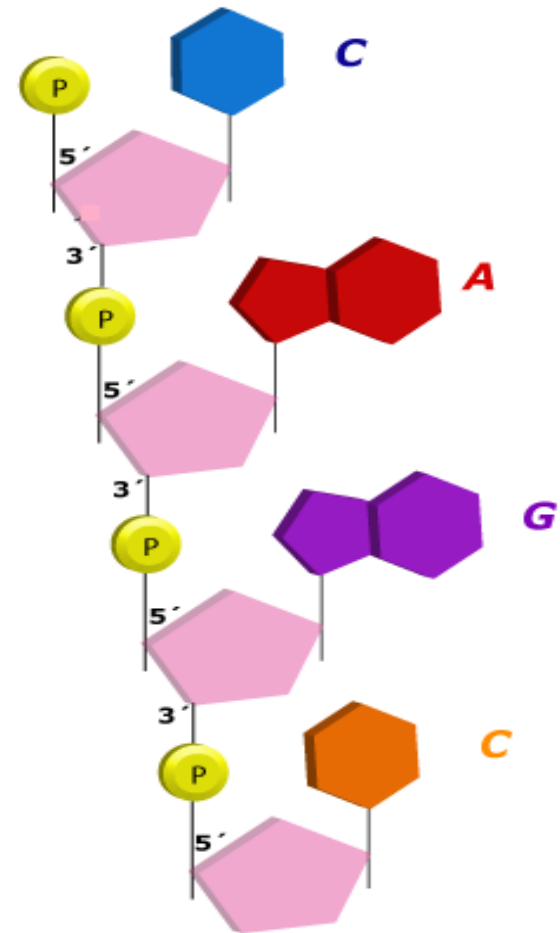
How do Deoxyribonucleotides Join?

- The successive nucleotides of DNA are joined together through phosphodiester linkages.

How do Deoxyribonucleotides Join?



How do Deoxyribonucleotides Join?



Structure of DNA

Work of Chargaff (Late 1940s)

- The discovery of the structure of DNA is one of the greatest events in the history of science.

Structure of DNA

Work of Chargaff (Late 1940s)

- Erwin Chargaff and his colleagues provided a most important clue to the structure of DNA.
- The work of Chargaff led him to following conclusions, also called “Chargaff Rules”:-

Structure of DNA

Work of Chargaff (Late 1940s)

1. Base composition of DNA varies from one species to another.

Structure of DNA

Work of Chargaff (Late 1940s)

2. The DNA isolated from different tissues of the same species have the same base composition.

Structure of DNA

Work of Chargaff (Late 1940s)

3. The base composition of DNA in a given species does not change with an organism's age, nutritional state, or changing environment.

Structure of DNA

Work of Chargaff (Late 1940s)

4. In DNA, the number of adenosine residues is equal to the number of thymidine ($A=T$) and the number of guanosine residues is equal to the number of cytidine ($G=C$).

Structure of DNA

Work of Chargaff (Late 1940s)

- It means that the sum of the purine residues equals the sum of the pyrimidine residues (AG=TC).

Structure of DNA

Work of Watson & Crick

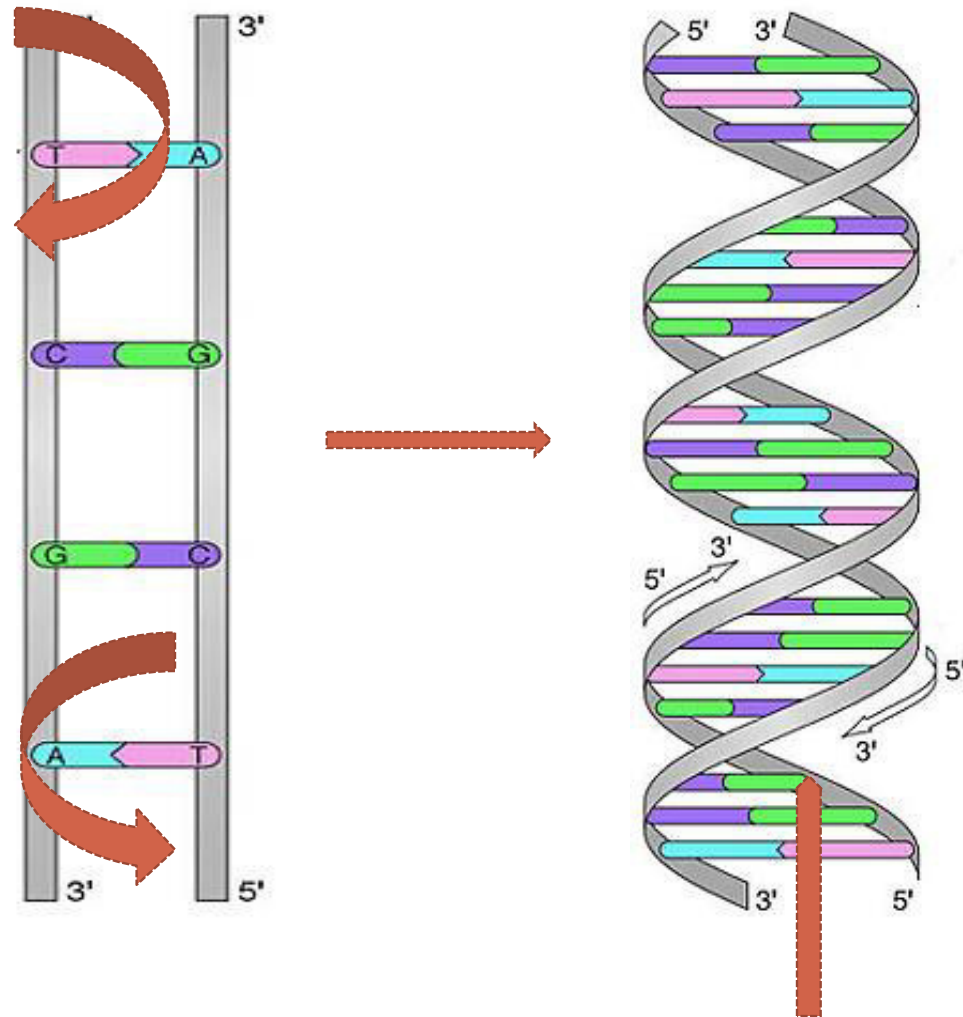
- James Watson and Francis Crick postulated a three dimensional model of DNA structure in 1953. The major features of this model are as follow:-

Structure of DNA

Work of Watson & Crick

1. DNA consists of two helical polynucleotide strands which are wound around the same axis to form a right handed double helix.

Structure of DNA



Structure of DNA

Work of Watson & Crick

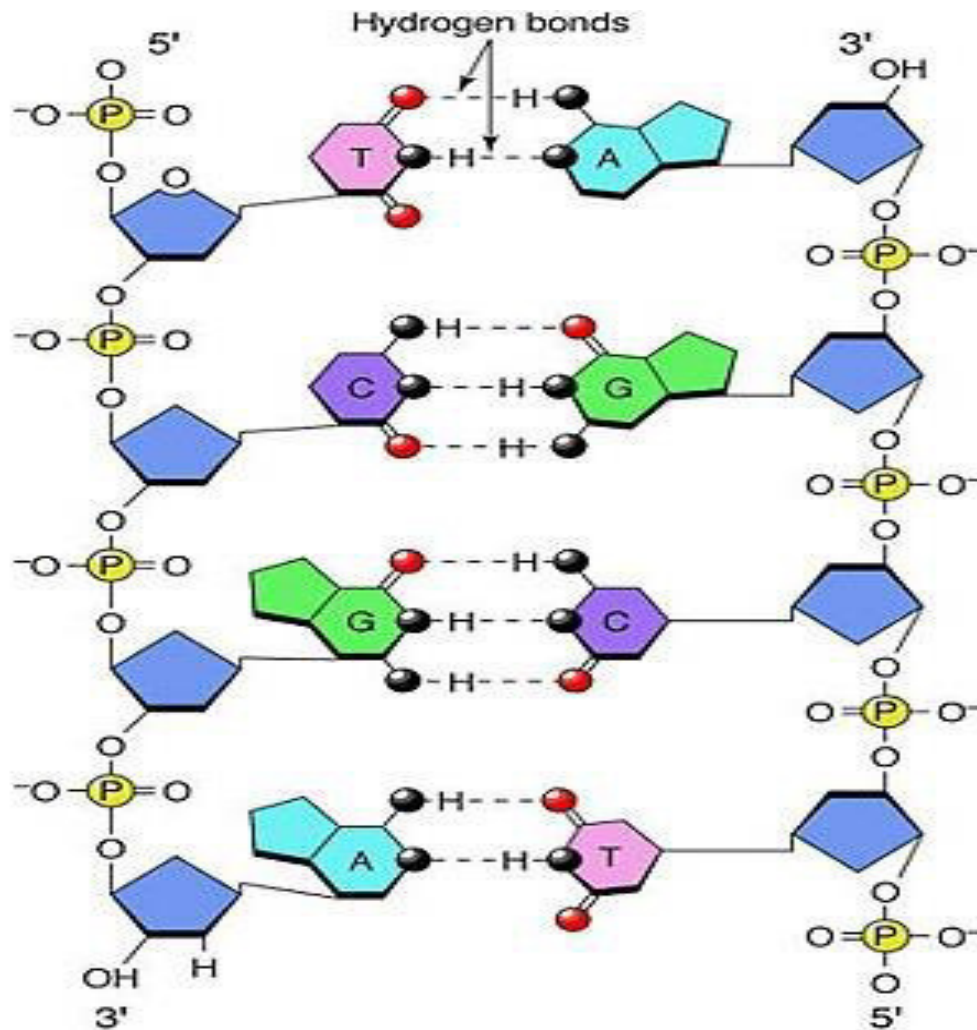
2. The hydrophilic backbones of alternating deoxyribose and phosphate groups are on the outside of the double helix, facing the surrounding water.

Structure of DNA

Work of Watson & Crick

3. The nitrogenous bases of both strands are stacked inside the double helix lying perpendicular to the long axis of the helix.

Structure of DNA

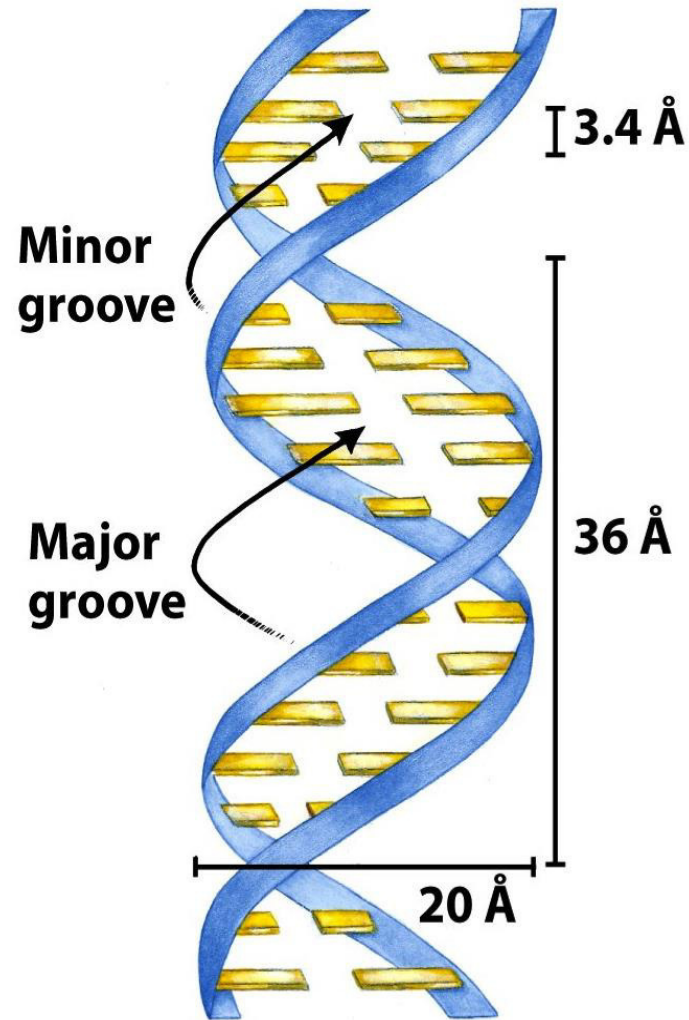


Structure of DNA

Work of Watson & Crick

4. The pairing and coiling of the two strands create a **major groove** and **minor groove** on the surface of the helix.

Structure of DNA

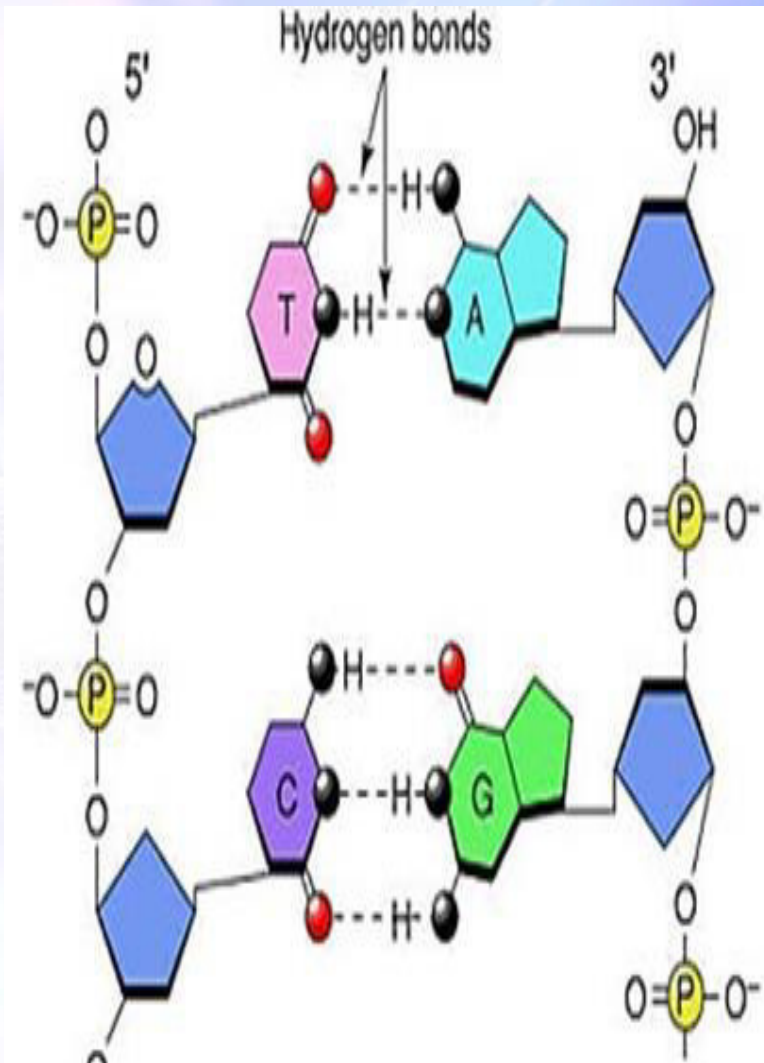


Structure of DNA

Work of Watson & Crick

5. Each nucleotide base of one strand is paired in the same plane with a base of the other strand.

Structure of DNA



Structure of DNA

Work of Watson & Crick

6. They also found that G pairs with C and A pairs with T due to the reason that they fit best within the structure.

Structure of DNA

Work of Watson & Crick

7. The two strands in DNA are present in **antiparallel orientation** i.e; their 5,3-phosphodiester bonds run in the opposite directions.

Structure of DNA

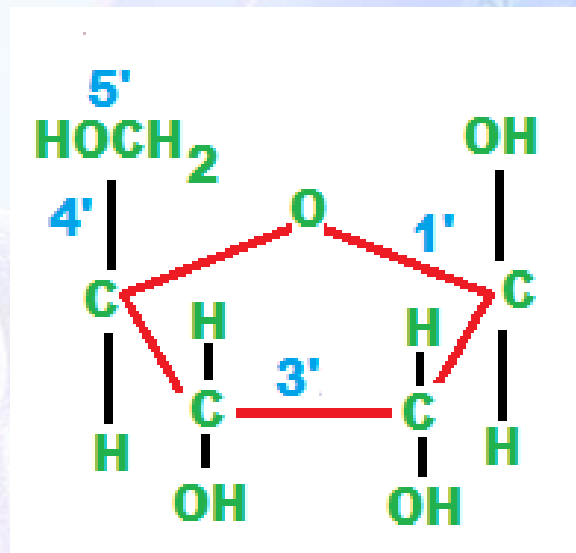
Work of Watson & Crick

8. The two antiparallel strands of double-helical DNA are **complementary** to each other.

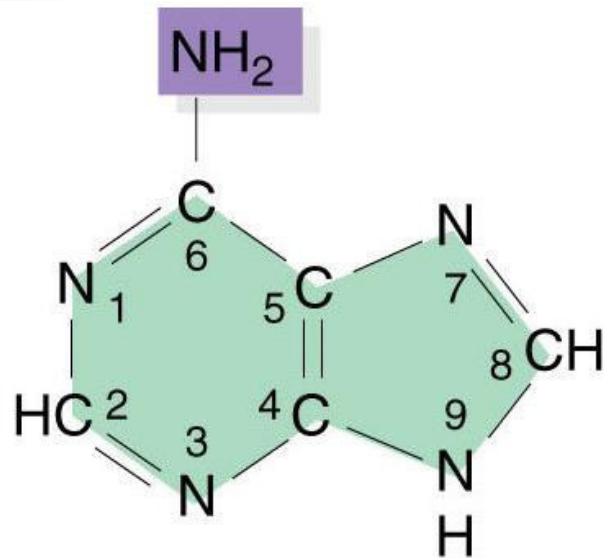
Chemical composition of RNA

- RNA (Ribonucleic acid) is a polymer of ribonucleotides.
- Each ribonucleotide is composed of three components:
 - A ribose sugar
 - A Nitrogenous Base
 - A Phosphoric acid

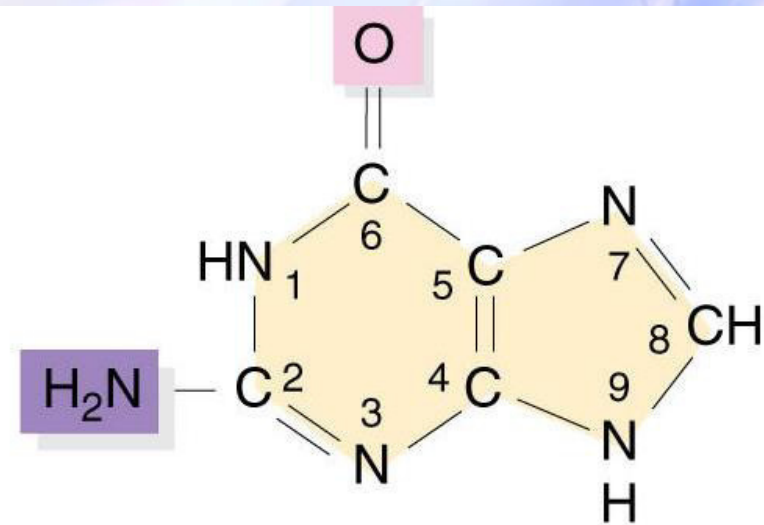
Ribose (a pentose sugar)



Nitrogenous Bases

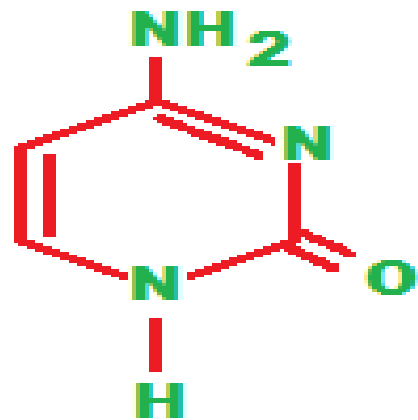


Adenine (A)

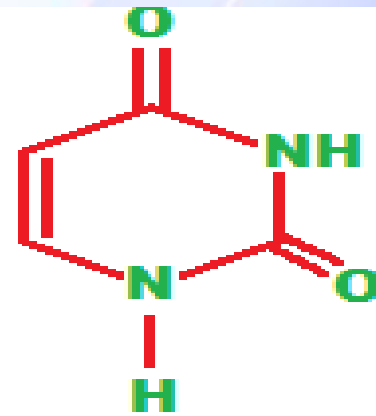


Guanine (G)

Nitrogenous Bases

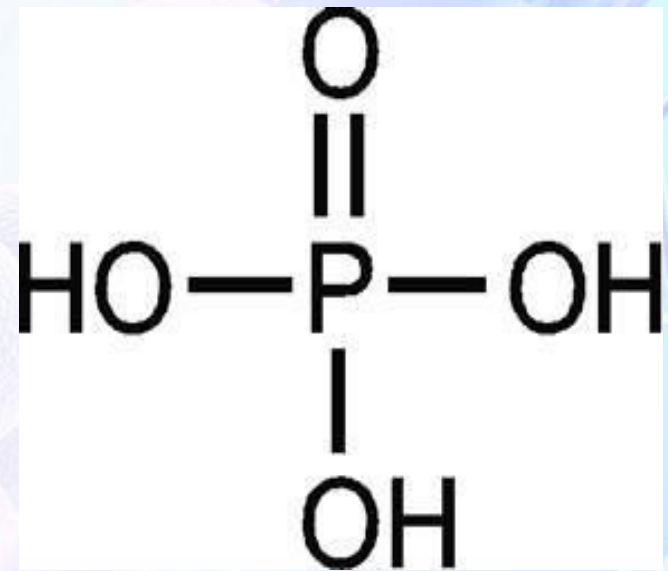


Cytosine (C)

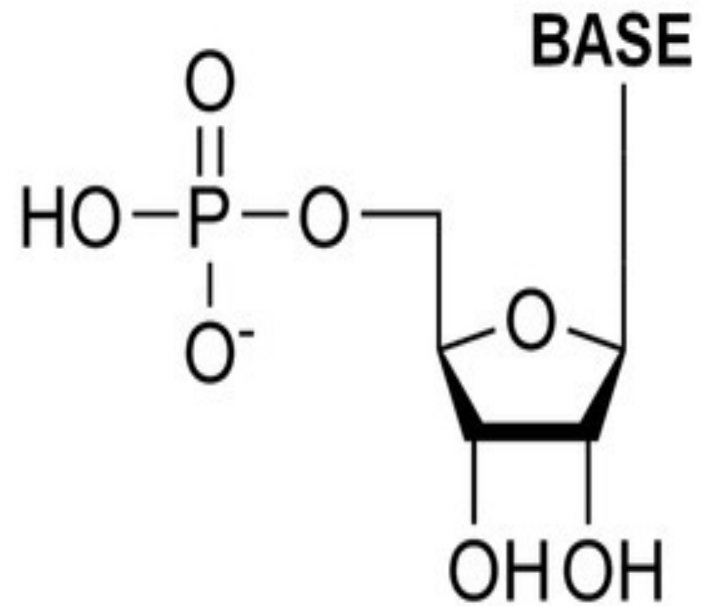


Uracil (U)

Phosphoric acid



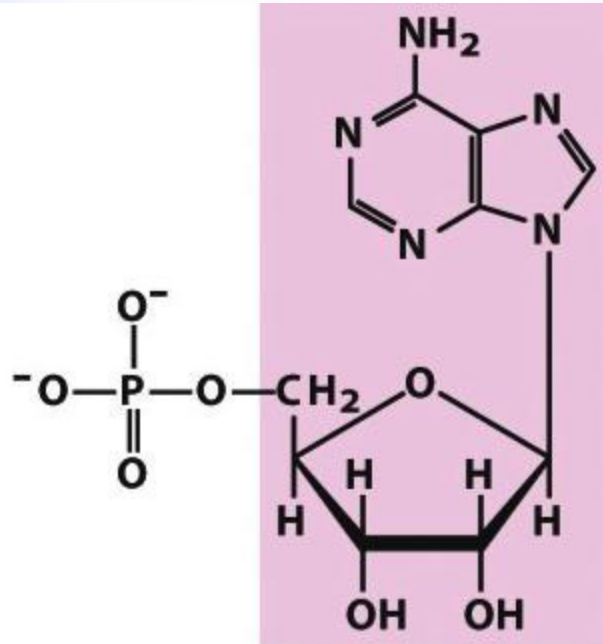
A Ribonucleotide



Types of Ribonucleotides

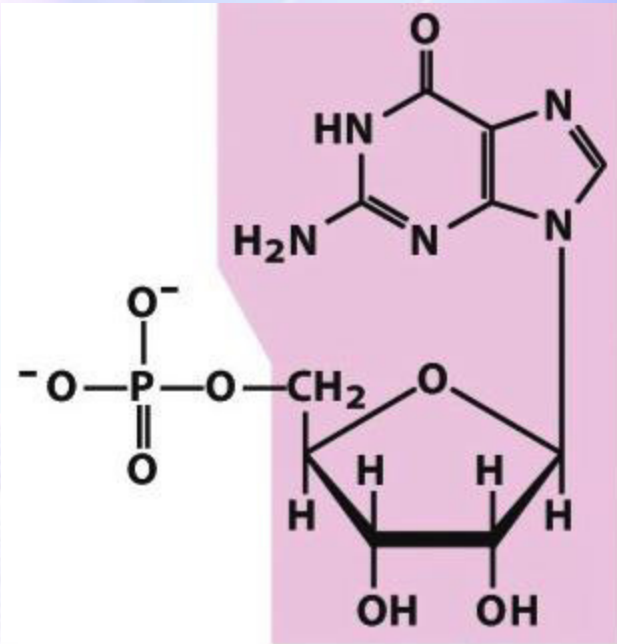
- There are mainly four types of ribonucleotides depending upon the types of nitrogenous bases present in RNA.

Types of Ribonucleotides



**Adenylate (adenosine
5'-monophosphate)**

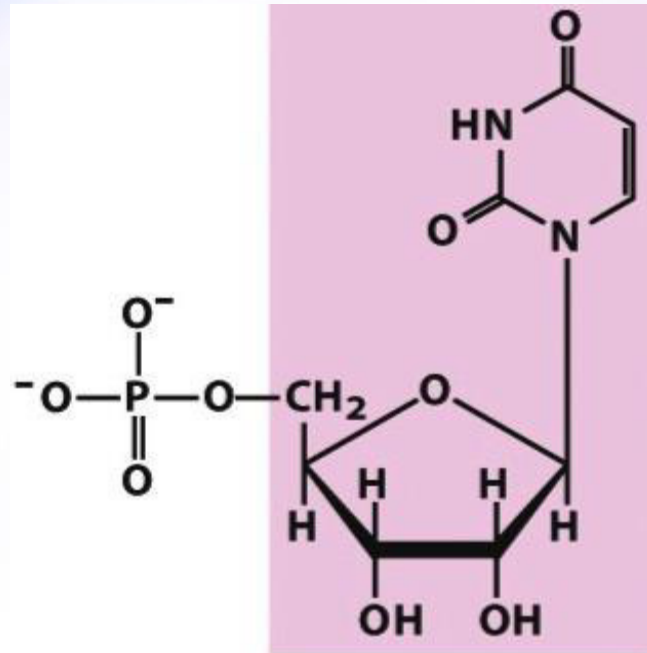
Adenosine



**Guanylate (guanosine
5'-monophosphate)**

Guanosine

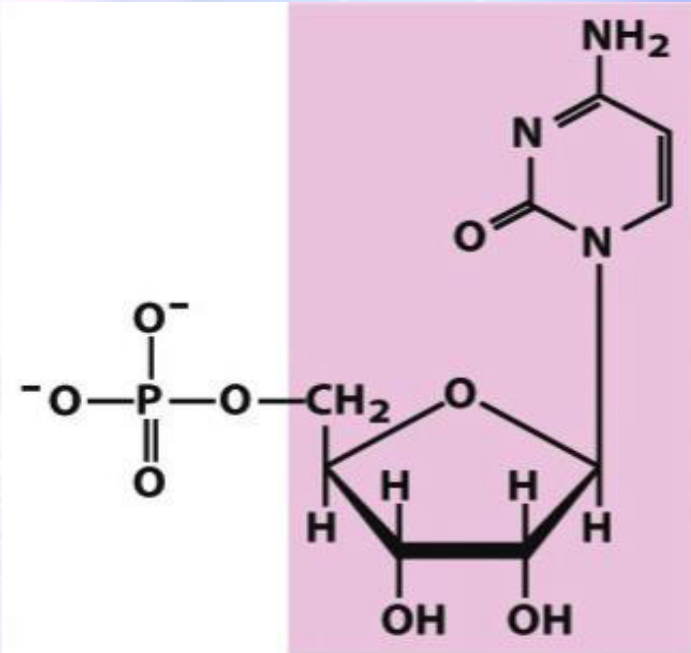
Types of Ribonucleotides



**Uridylate (uridine
5'-monophosphate)**

U, UMP

Uridine



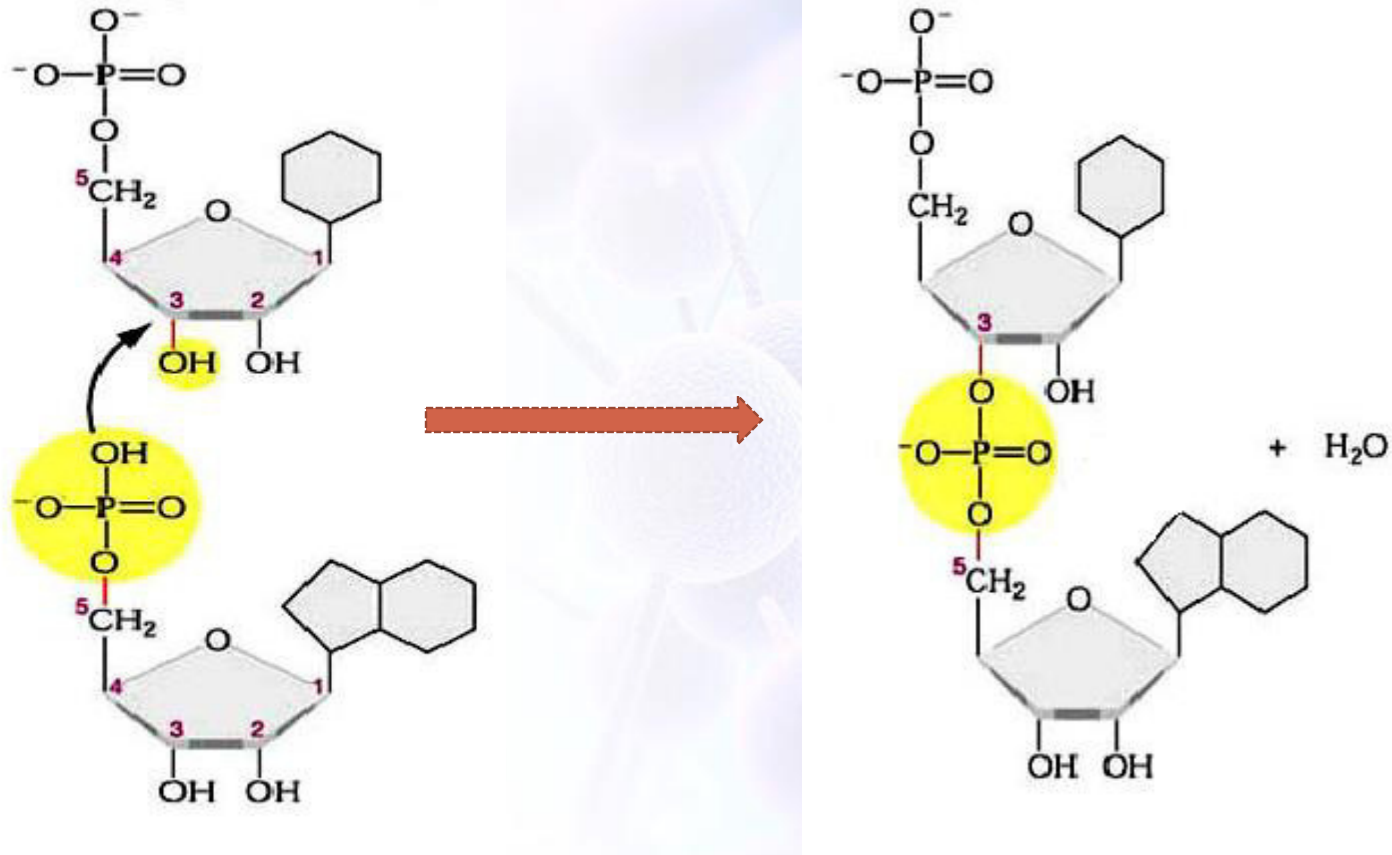
**Cytidylate (cytidine
5'-monophosphate)**

C, CMP

Cytidine

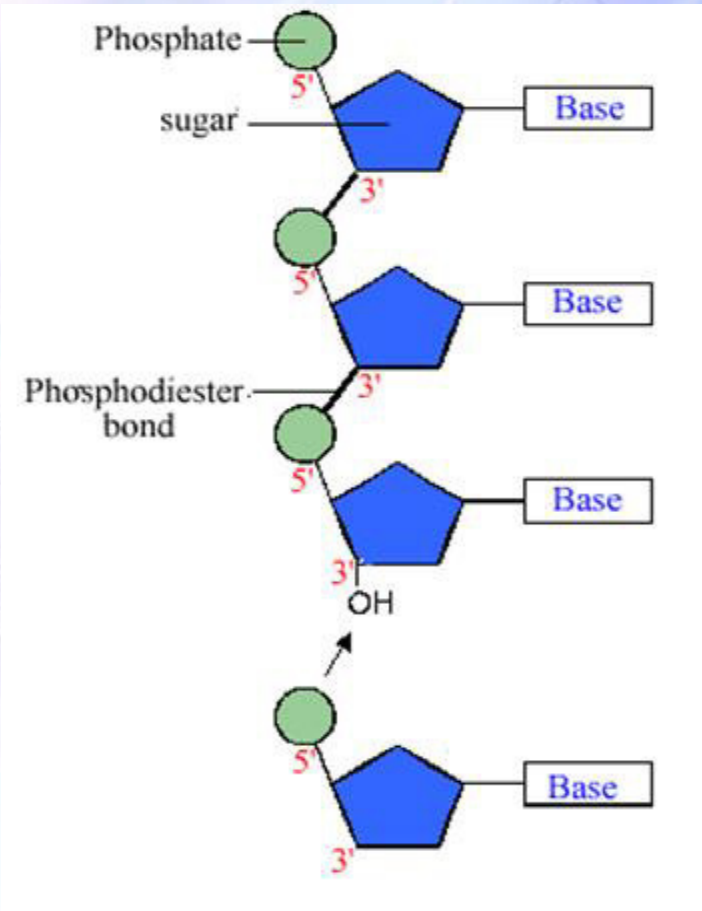
Types of Ribonucleotides

How do Ribonucleotides Join?



Types of Ribonucleotides

A Poly-Ribonucleotide



Types of RNAs

- There are mainly three types of Ribonucleic acids (RNAs) present in the cells of living organisms.
 - Messenger RNA (mRNA)
 - Transfer RNA (tRNA)
 - Ribosomal RNA (rRNA)

Types of RNAs

Messenger RNA (mRNA)

- It is the type of RNA that carries genetic information from DNA to the protein biosynthetic machinery of the ribosome.
- It provides the templates that specify amino acid sequences in polypeptide chains.
- The process of forming mRNA on a DNA template is known as **transcription**.

Types of RNAs

Messenger RNA (mRNA)

- It may be **monocistronic** or **polycistronic**.
- The length of mRNA molecules is variable and it depends on the length of gene.

Types of RNAs

Transfer RNA (tRNA)

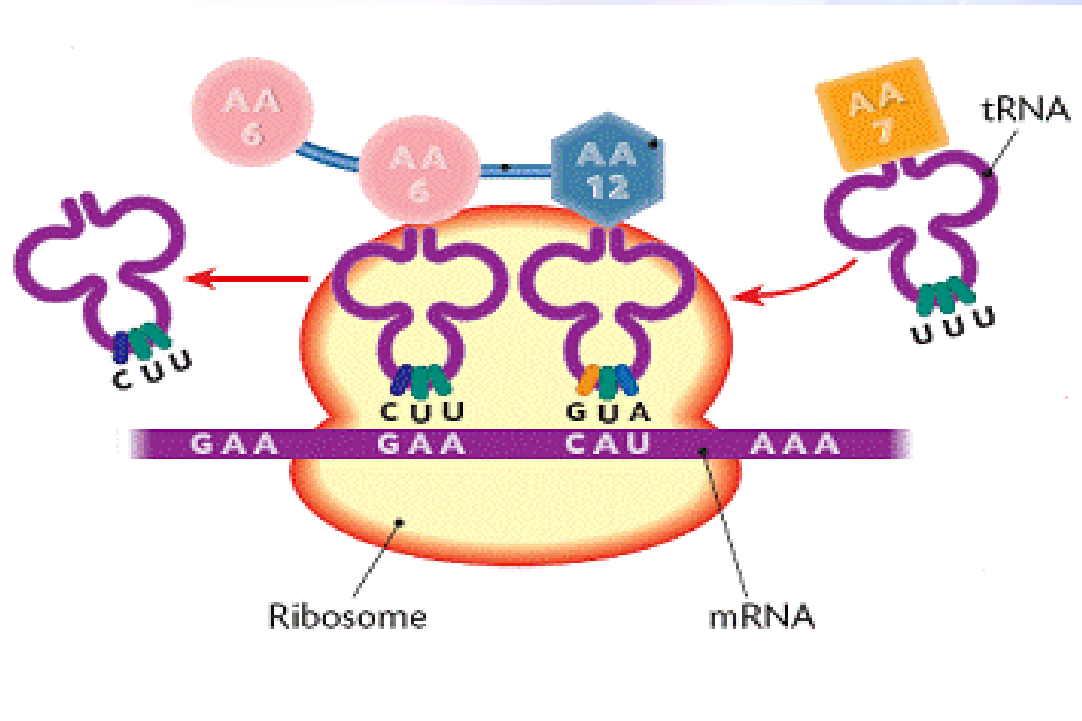
- Transfer RNAs serve as adapter molecules in the process of protein synthesis.
- They are covalently linked to an amino acid at one end.

Types of RNAs

Transfer RNA (tRNA)

- They pair with the mRNA in such a way that amino acids are joined to a growing polypeptide in the correct sequence.

Types of RNAs



Types of RNAs

Ribosomal RNA (rRNA)

- Ribosomal RNAs are components of ribosomes.
- rRNA is a predominant material in the ribosomes constituting about 60% of its weight.
- It has a number of functions to perform in the ribosomes.

Structures of RNAs

- mRNA is always single stranded when it is formed from DNA.
- But this single strand assumes a double helical conformation soon after its formation.
- This confirmation is achieved mainly due to base stacking interactions.

Structures of RNAs

Messenger RNA (mRNA)



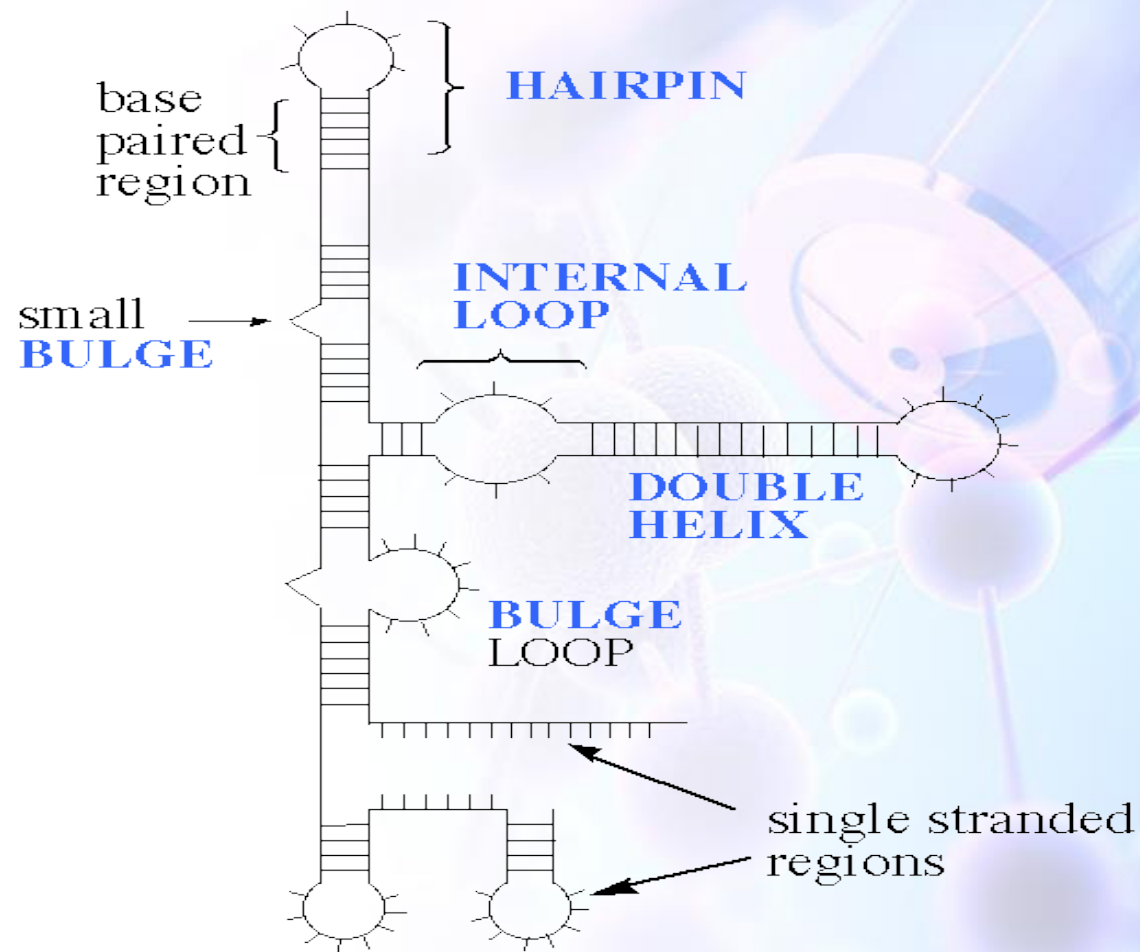
Structures of RNAs

- Self-complementary sequences may occur in the RNA molecules which produce more complex structures.
- So RNA can base-pair with complementary regions of either RNA or DNA.
- RNA has no any regular secondary structure that serves as a reference point. The three-dimensional structures of many RNAs are complex and unique.

Structures of RNAs

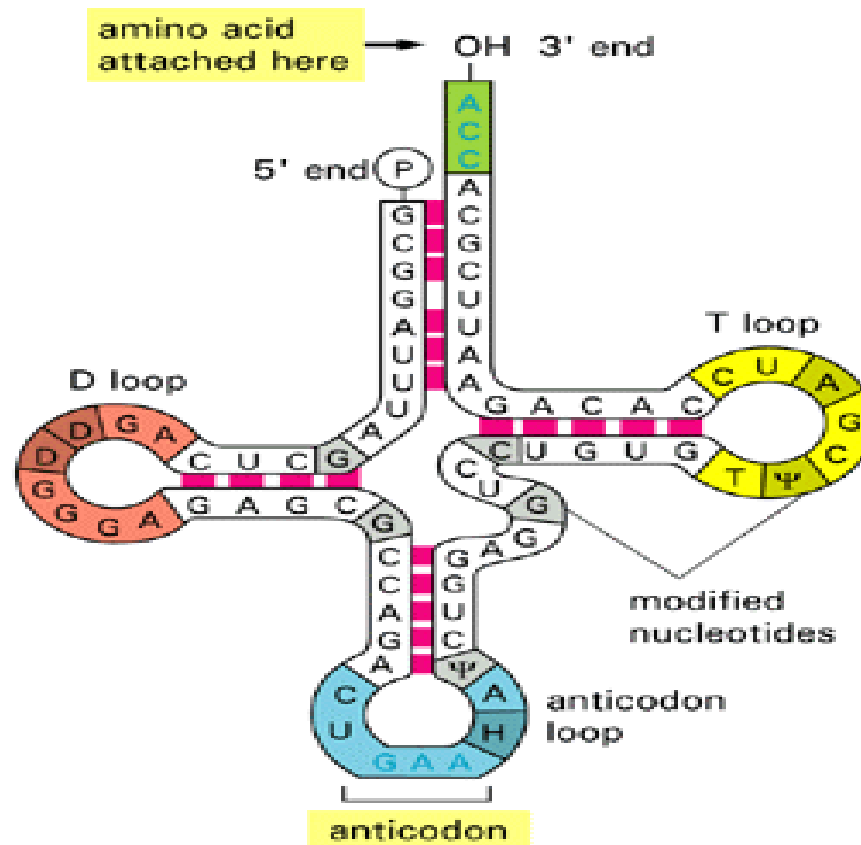
- Breaks in the helix caused by mismatched or unmatched bases in one or both strands are common and result in bulges or internal loops.
- Hairpin loops form between nearby self-complementary sequences.

Structures of RNAs



Structures of RNAs

Transfer RNA (tRNA)



Nature of Genetic Material

- After establishment of the fact that genes are the physical units located on the chromosomes. A major problem for the biologists was to find out the molecules responsible for carrying the hereditary information.

Nature of Genetic Material

Characteristics of Genetic Material

- Genetic material must contain complex information.
- Genetic material must replicate faithfully.
- Genetic material must encode phenotype.

Nature of Genetic Material

- Three sets of experiments provided a pivotal evidence that DNA rather than protein, is the hereditary material.
 - Griffith's Experiments (1928)
 - Avery's Experiments (1944)
 - Hershey-Chase experiments (1952)

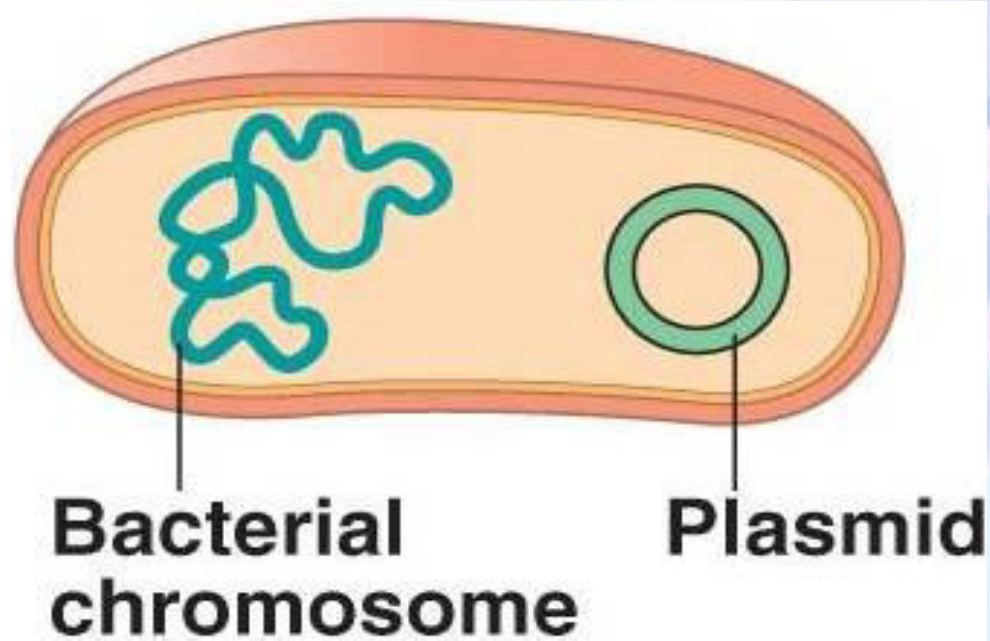
Organization of Genetic Material in Bacteria

- Bacteria typically have a single circular chromosome consisting of a single circular molecule of DNA with associated proteins.

Organization of Genetic Material in Bacteria

- The bacterial chromosome is a very long (up to 1mm).
- It is looped and folded and attached at one or several points to the plasma membrane.

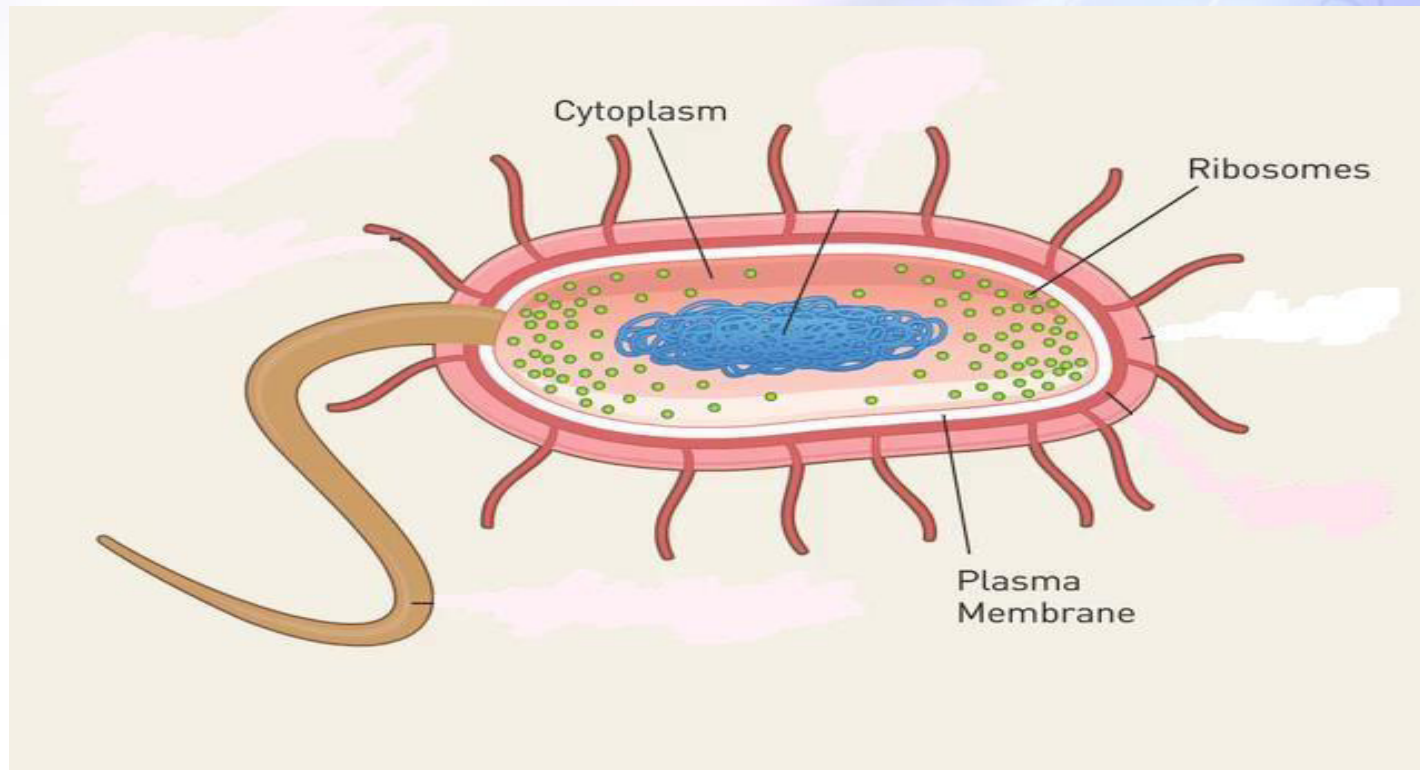
Organization of Genetic Material in Bacteria



Organization of Genetic Material in Bacteria

- Specific proteins interact with the bacterial DNA to form a highly condensed nucleoprotein complex called the **nucleoid**.

Organization of Genetic Material in Bacteria



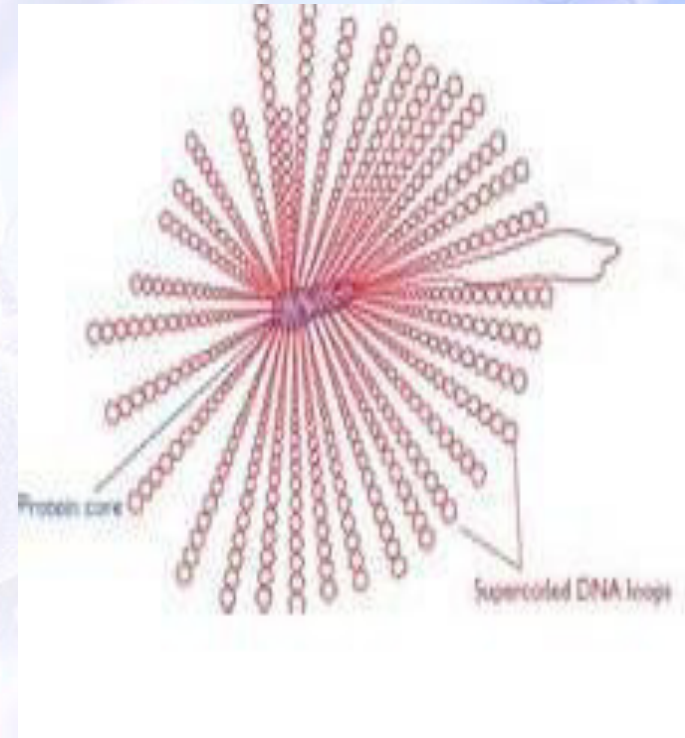
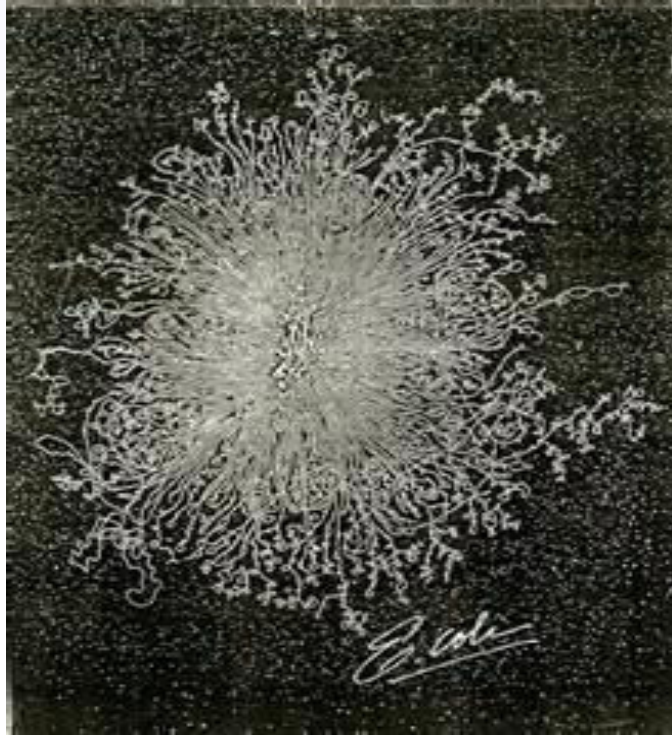
Organization of Genetic Material in Bacteria

- Bacterial chromatin can be released from the cell by gentle lysis of the cell.
- Electron micrograph of the chromatin reveals that it consists of multiple loops which emerge from a central region of the chromatin.

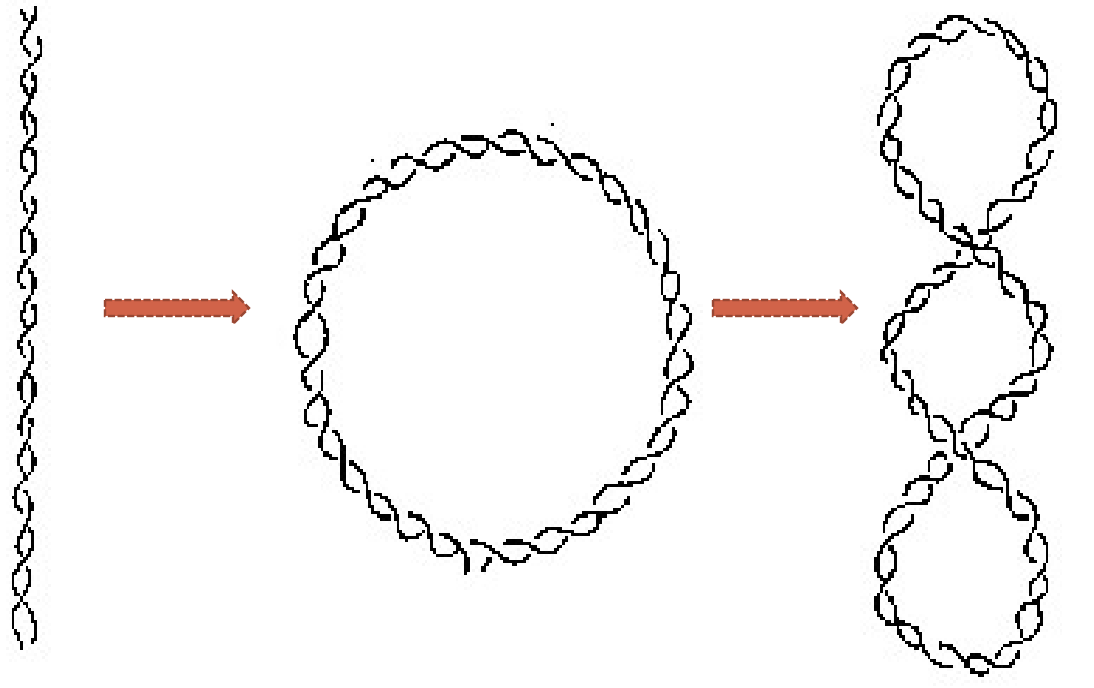
Organization of Genetic Material in Bacteria

- Some of the loops are super-coiled while some are relaxed.
- Relaxed loops are formed as a result of a nick introduced into super-coiled loops by a cellular DNase.

Organization of Genetic Material in Bacteria



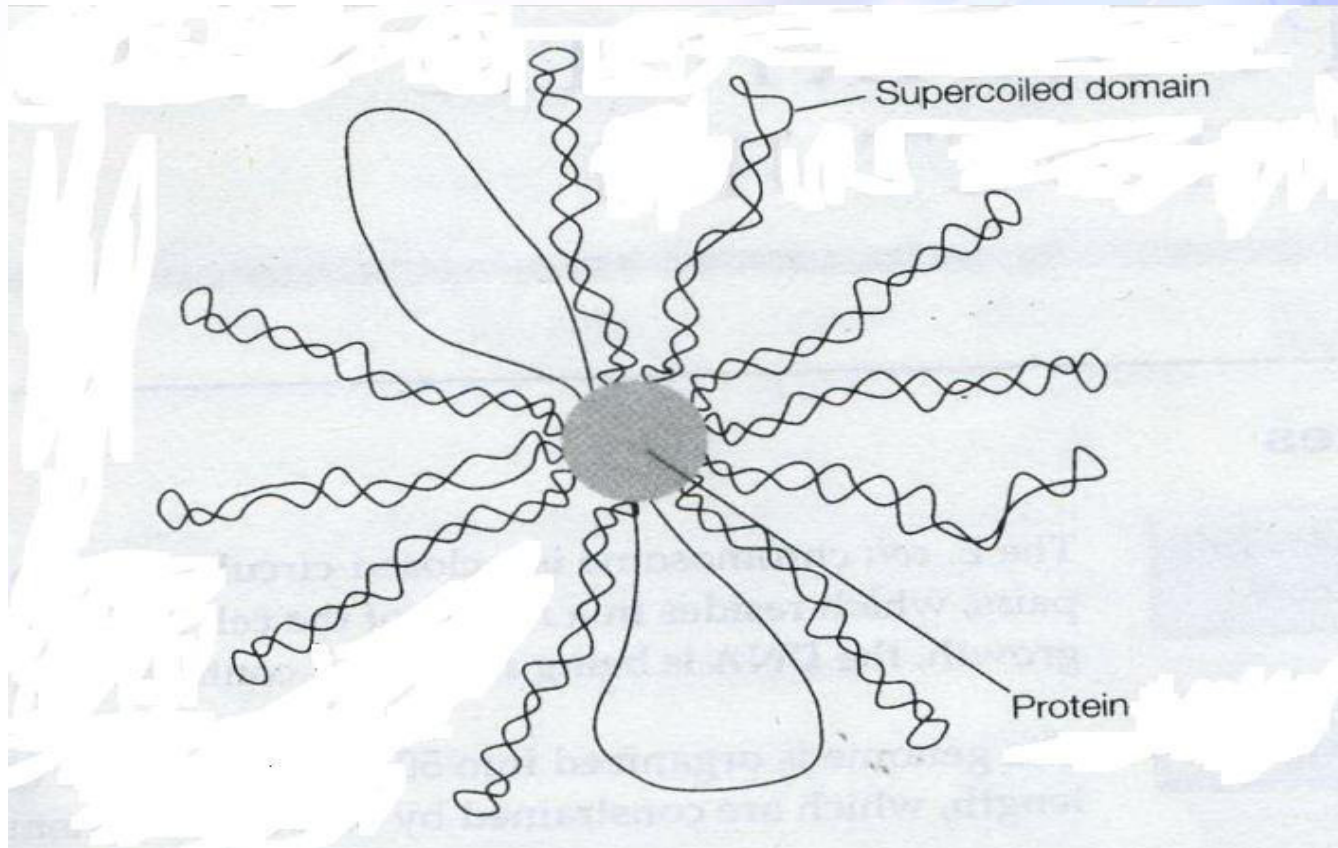
Organization of Genetic Material in Bacteria



Organization of Genetic Material in Bacteria

- If a super-coiled DNA molecule receives a nick, the strain of underwinding is immediately removed, and all the super-coiling is lost.
- Studies confirm that continued nuclease treatment increases number of relaxed loops.

Organization of Genetic Material in Bacteria



Organization of Genetic Material in Bacteria

- The bacterial DNA is arranged in super-coiled loops that are fastened to a central protein matrix, so that each loop is topologically independent from all the others.

Organization of Genetic Material in Bacteria

- So a nick that causes one super-coiled loop to relax would have no effect on other super-coiled loops.
- The super-coiled loops are dynamic structures which change during cell growth & division.

Organization of Genetic Material in Bacteria

- An *E. coli* chromosome is estimated to have about 400 super-coiled loops.
- Each loop has an average length of about 10-20 kbp.

Organization of Genetic Material in Bacteria

- The DNA compaction in a bacterial cell is contributed by super-coiling of loops, macromolecular crowding and DNA-binding proteins.

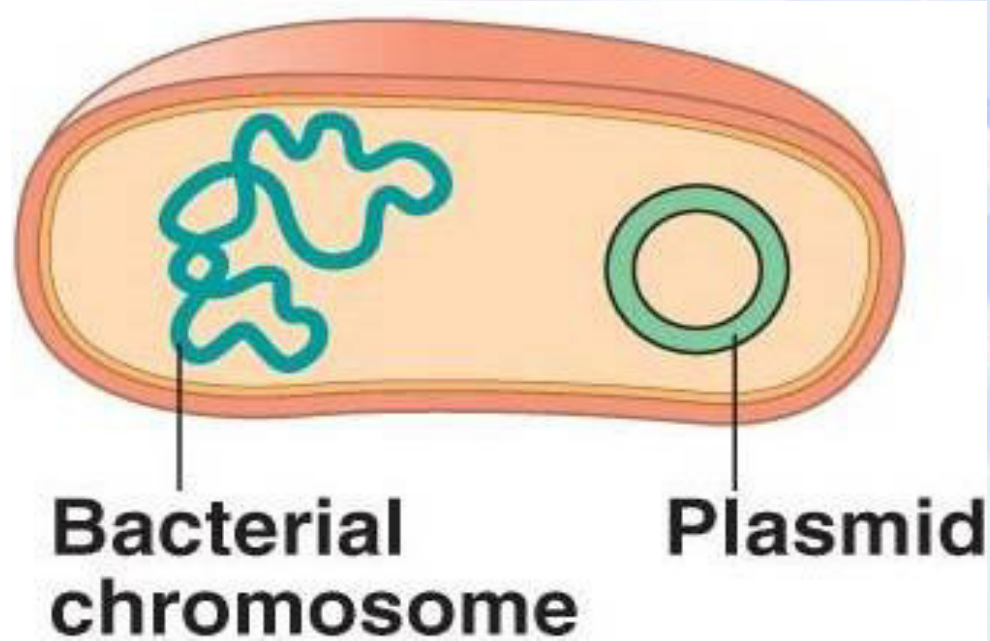
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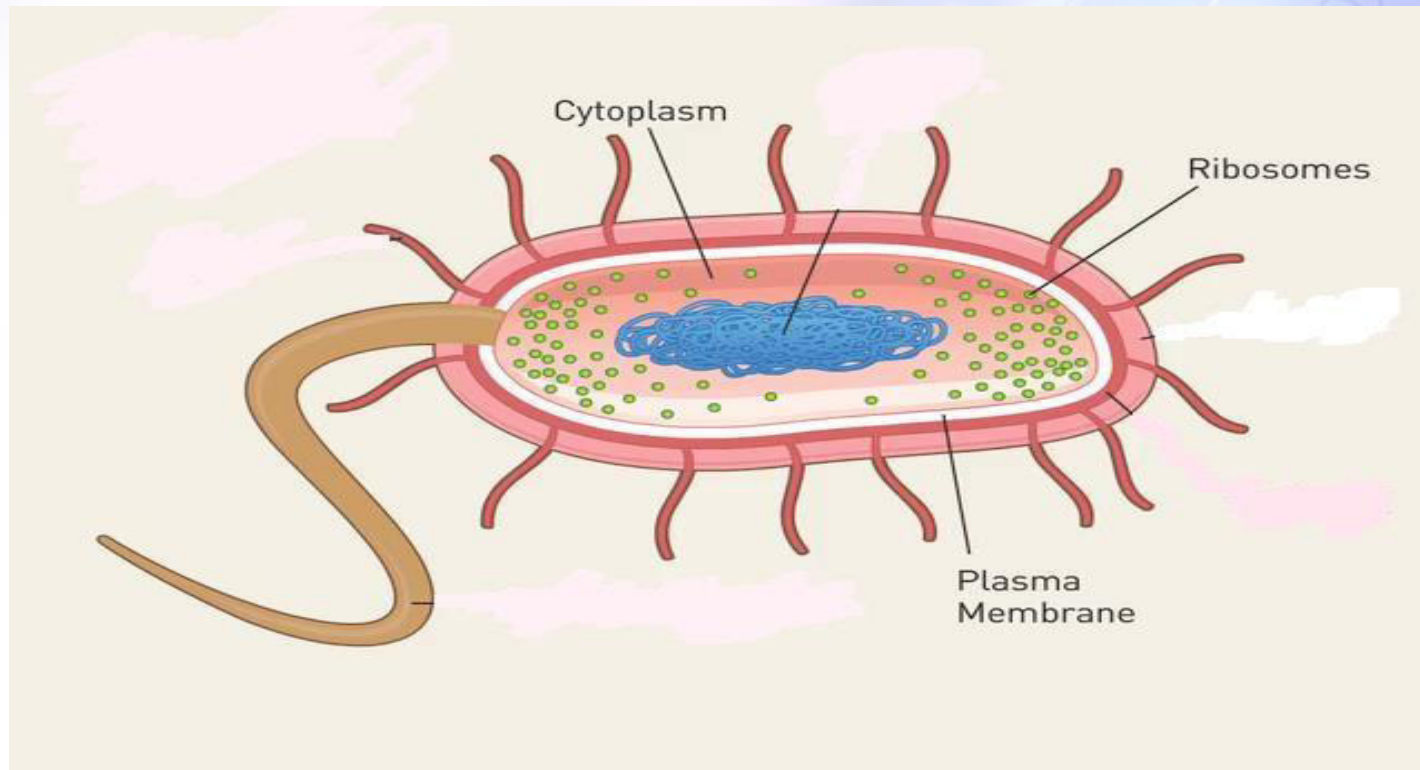
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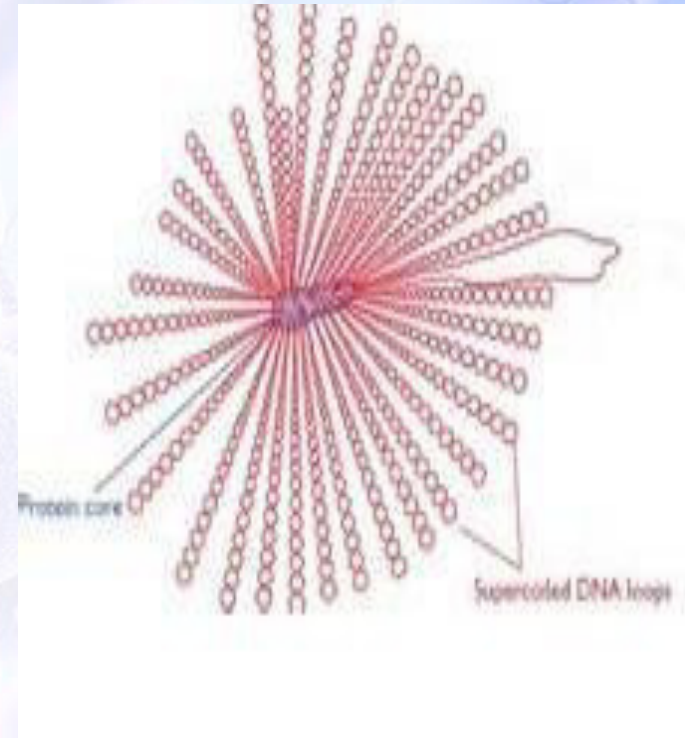
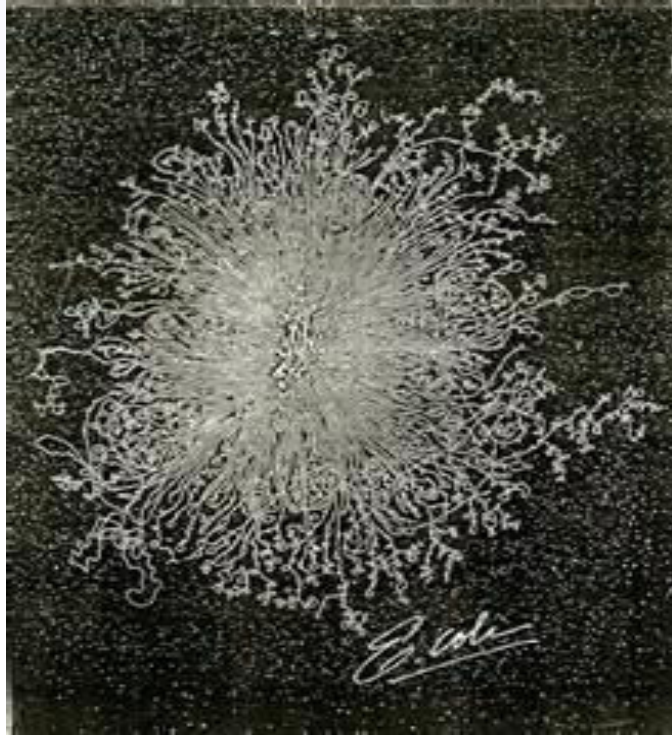
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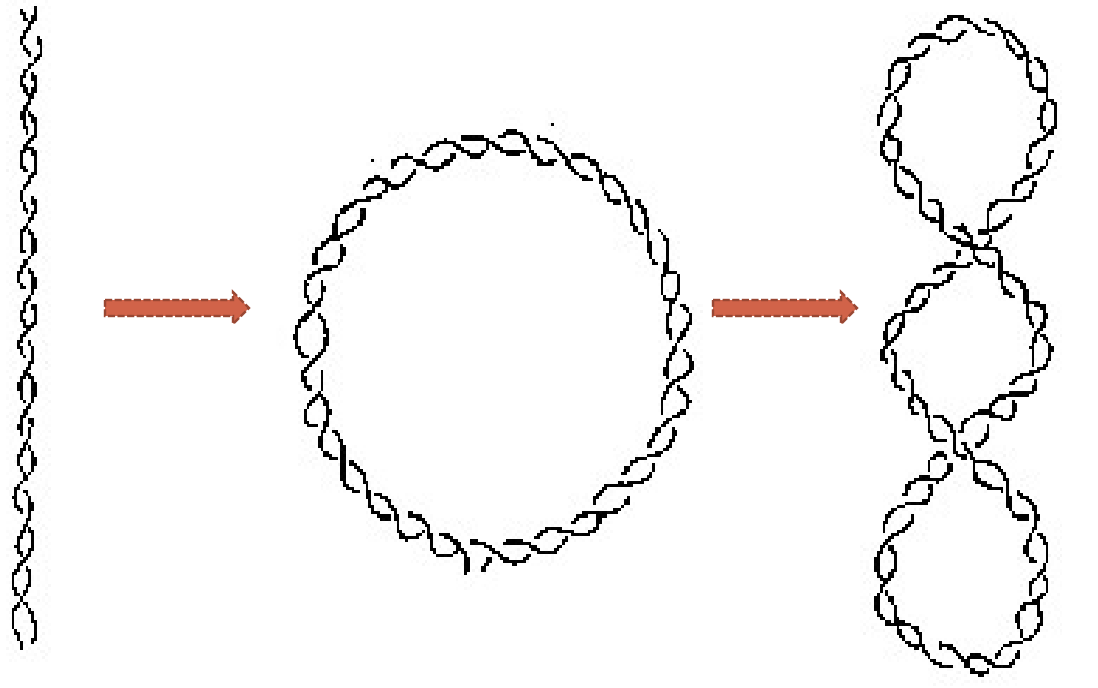
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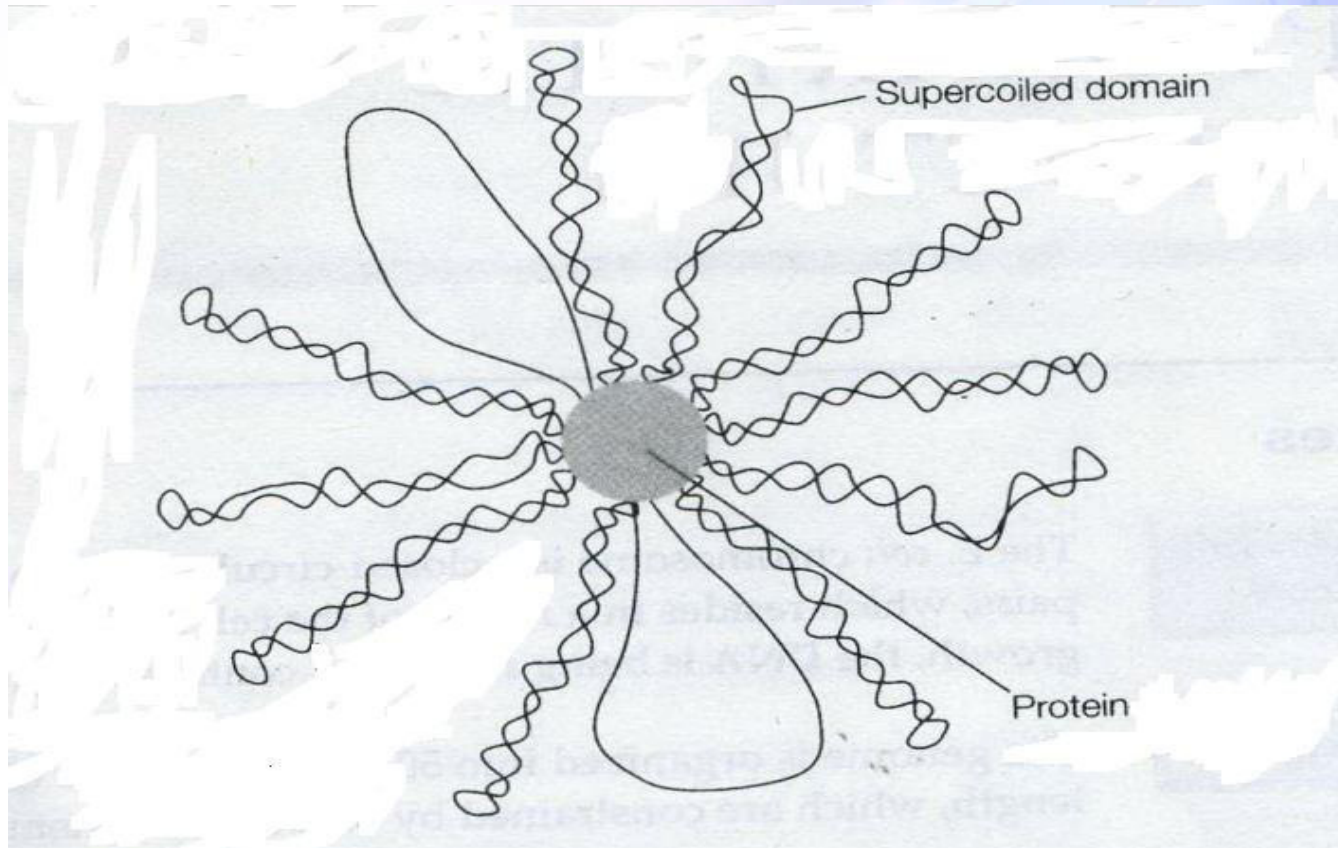
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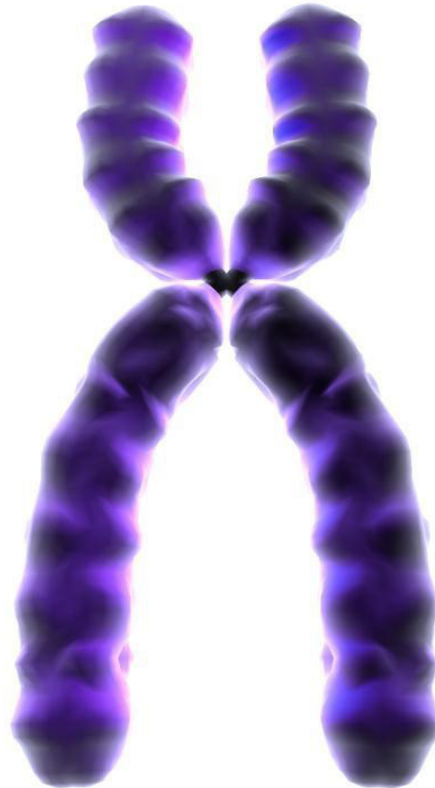
Organization of Genetic Material in Bacteria

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Organization of Genetic Material in Eukaryotes

- The genetic material (DNA) of eukaryotic organisms is organized in the form of chromosomes.
- The chromosomes of eukaryotic cells are larger and more complex than those of prokaryotes.

Organization of Genetic Material in Eukaryotes



Organization of Genetic Material in Eukaryotes

- Each un-replicated chromosome consists of a single molecule of DNA.
- If stretched out, some human chromosomes would be several centimetres long.

Organization of Genetic Material in Eukaryotes

- To package such a tremendous length of DNA into this small volume, each DNA molecule is coiled again and again and tightly packed around histone proteins.

Organization of Genetic Material in Eukaryotes

- As eukaryotic chromosomes are not circular, so instead of super-coiling, the mechanism of packaging involves winding the DNA around special proteins, the **histones**.

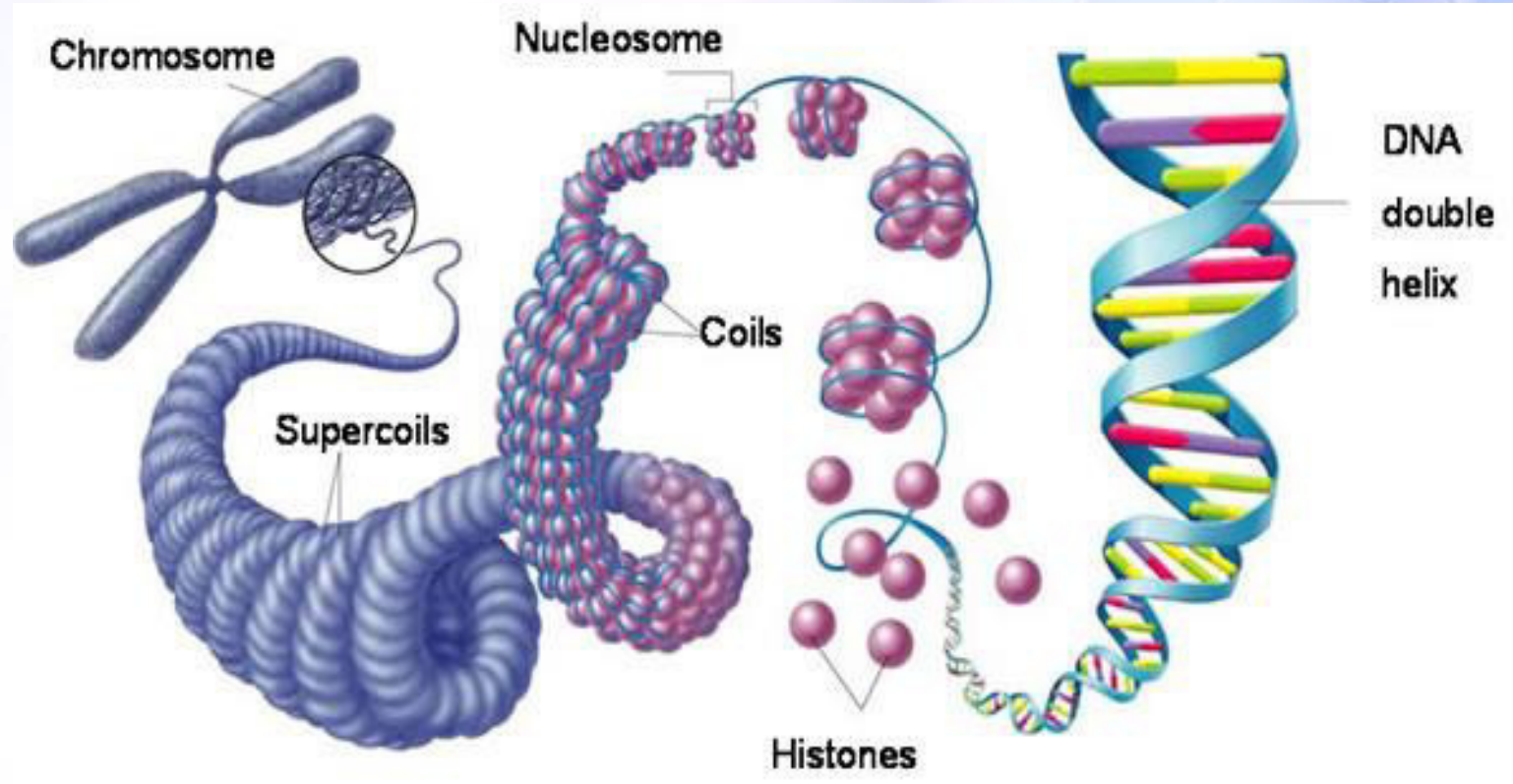
Organization of Genetic Material in Eukaryotes

- DNA with bound histones in the eukaryotes is called as **chromatin**.
- Chromatin consists of roughly spherical subunits, the **nucleosomes**, each containing approx. 200 bp of DNA and nine histones.

Organization of Genetic Material in Eukaryotes

- A condensed mitotic chromosome is about 50,000 times shorter than fully extended DNA.
- Highly condensed chromatin is known as **heterochromatin**.
- The more extended form is known as **euchromatin**.

Organization of Genetic Material in Eukaryotes



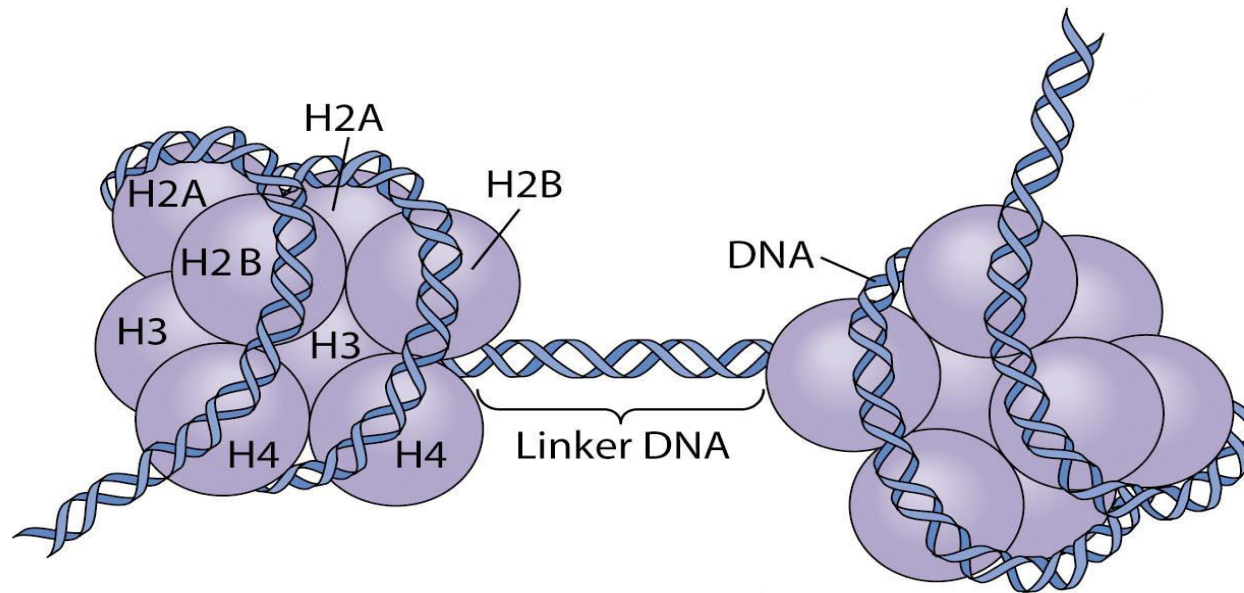
Histone Proteins

- Most abundant proteins in the chromatin are histones.
- There are nine types of histones including two each of H2A, H2B, H3 and H4 and one of H1.

Histone Proteins

- These histones fall in five major classes i.e., H1, H2A, H2B, H3 and H4.
- A typical human cell contains about 60 million copies of each kind of histone.

Histone Proteins



Histone Proteins

- All histones have a high percentage of arginine and lysine but the lysine-to-arginine ratio differs in each type of histone.

Histone Proteins

- The positively charged side chains of lysine and arginine enable histones to bind to the negatively charged phosphate groups of the DNA.

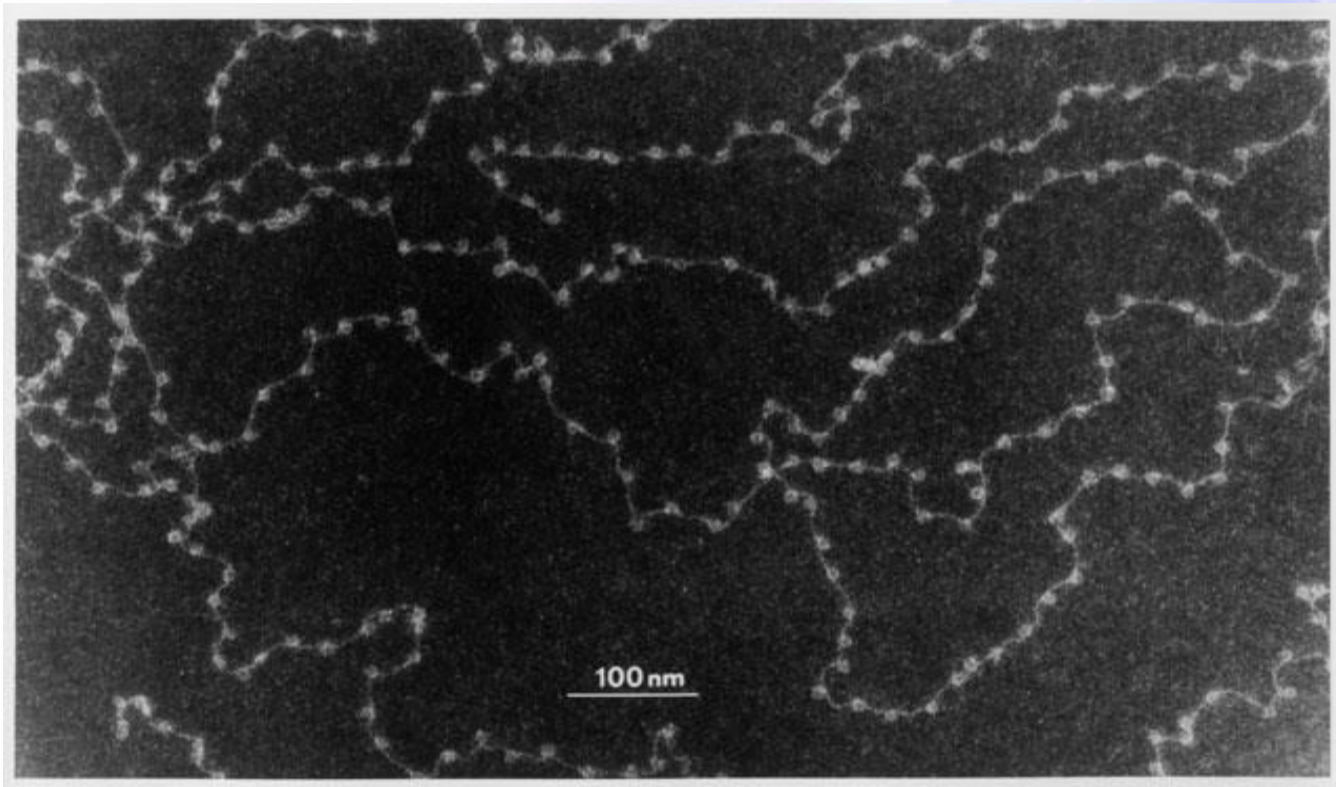
Histone Proteins

- The electrostatic attraction is an important stabilizing force in the chromatin.

The Nucleosome

- The uncondensed chromatin resembles beads on a string when viewed under the electron microscope.
- Each bead is a nucleoprotein complex called **nucleosome**.

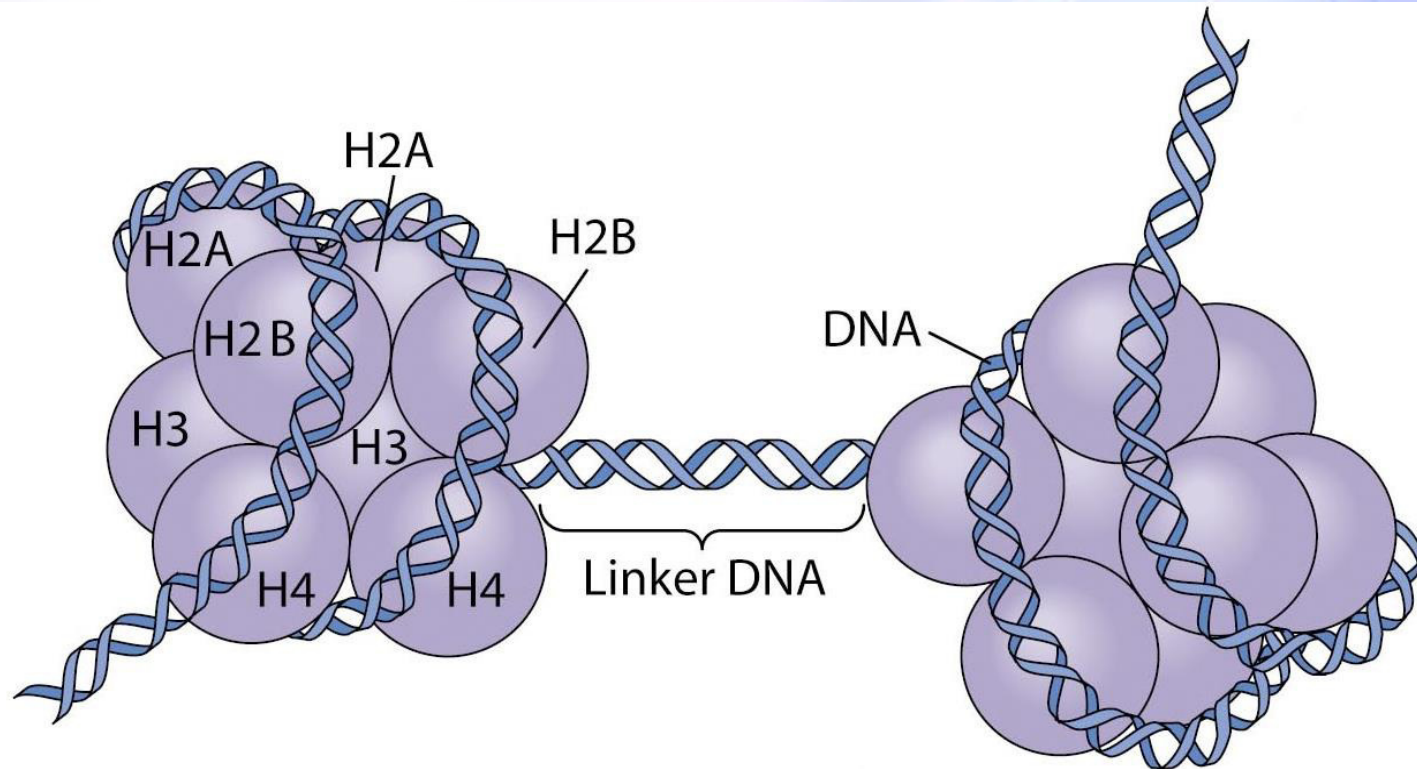
The Nucleosome



The Nucleosome

- Each nucleosome is formed by winding DNA fibre around a protein assembly consisting of eight histone molecules.
- The DNA connecting two nucleosomes is called **linker DNA**.

The Nucleosome



The Nucleosome

- The size of the linker DNA between the nucleosomes varies among different organisms and even different organs of the same organism.

The Nucleosome

- The length of DNA wrapped around nucleosomes also varies from one organism to the other ranging from about 170-240 bp.

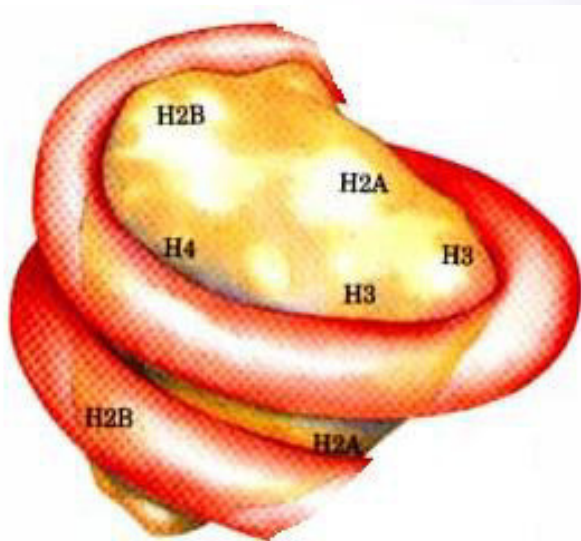
The Nucleosome

- Prolonged nuclease digestion of chromatin cleaves additional nucleotides.
- The structure that remains is the nucleosome core particle.

The Nucleosome

- The nucleosome core particle consists of an octameric protein complex (two copies of each H2A, H2B, H3 & H4) with a 146 bp DNA fragment wound around it.

The Nucleosome



**NUCLEASE
DIGESTS
LINKER DNA**



**nucleosome
core particle**



Cell Division

Life Span & Continuity

**All living organisms
have a limited life span.**

**The essence of life is to
propagate.**

**Cells are the basic unit
of life.**

**Cell division is the
basic process that
ensures the continuity
of life.**

The Necessity

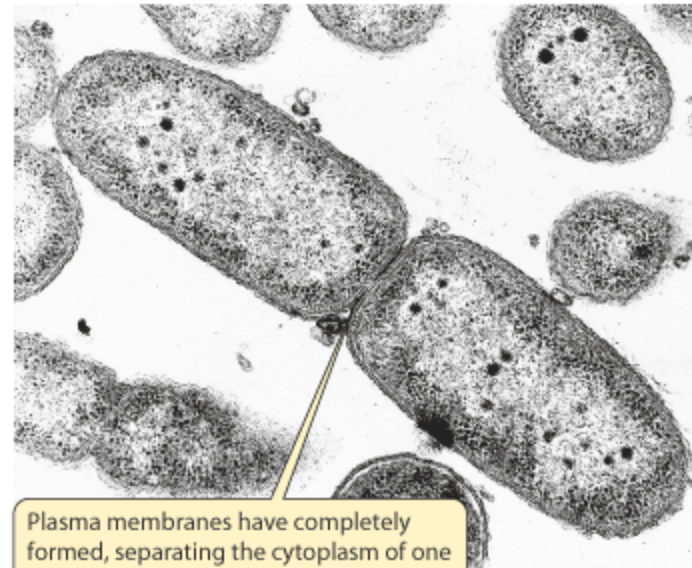
**Unicellular organisms
propagate by splitting
into two cells.**

**Multicellular organisms:
replace damaged or
senescent cells.**

**Billions of cells die each
day in humans, (blood
epithelia)**

**Meiosis: Organisms shuffle
genes.**

Even the Prokaryotes Do It

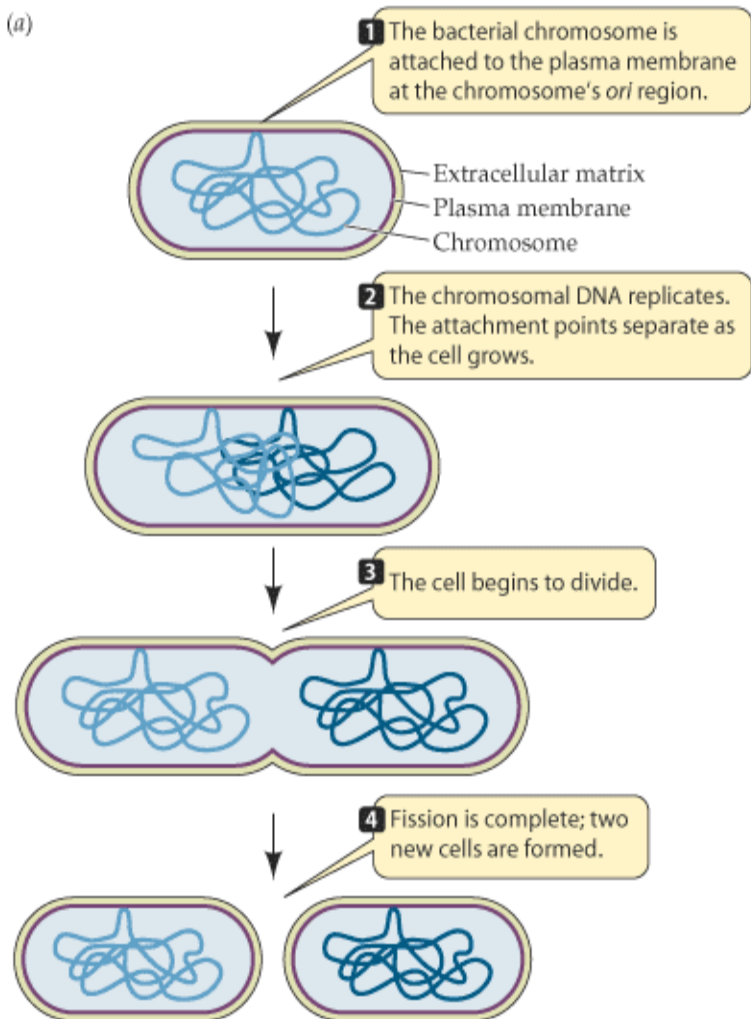


Plasma membranes have completely formed, separating the cytoplasm of one cell from that of the other. Only a small gap of cell wall remains to be completed.

Favorable Conditions

20 - 40 min

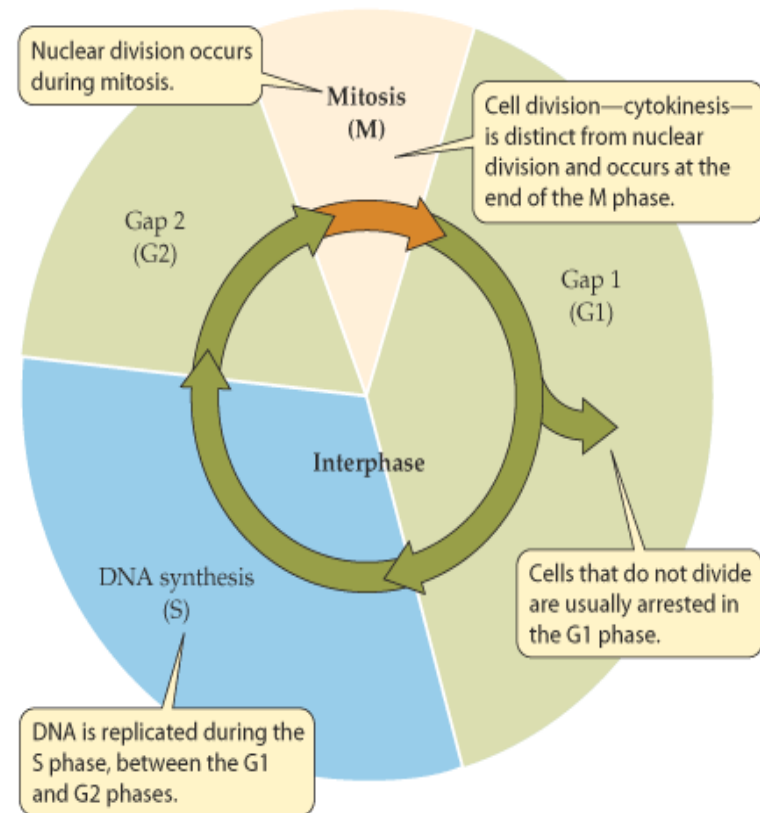
(a)

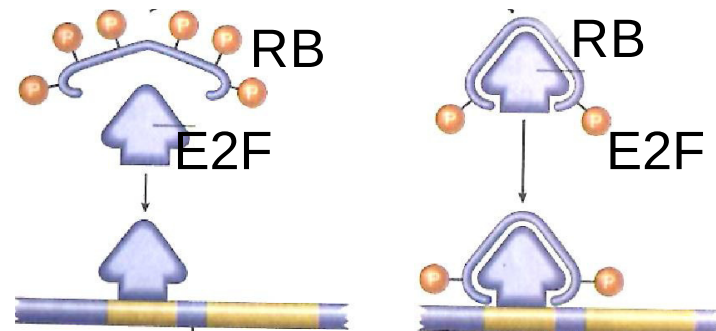
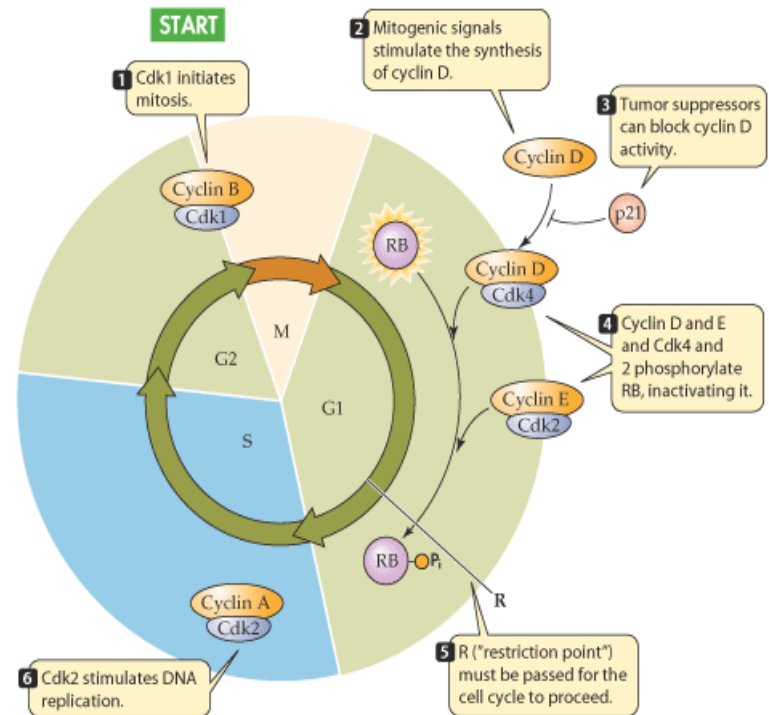


END

Cell Cycle

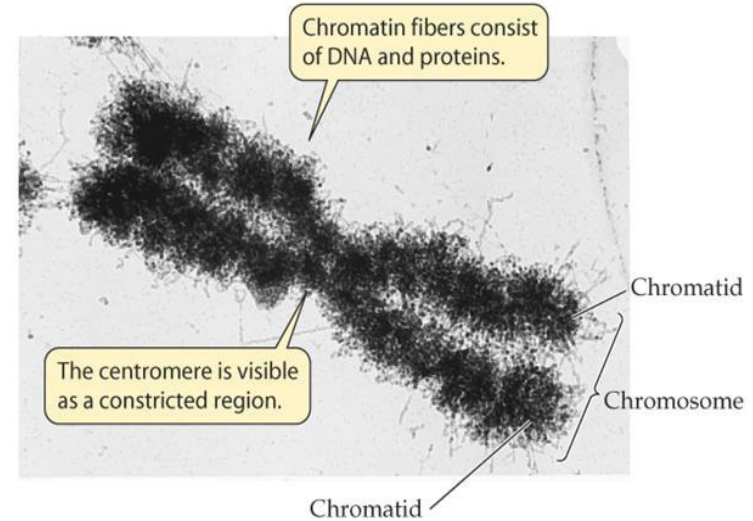
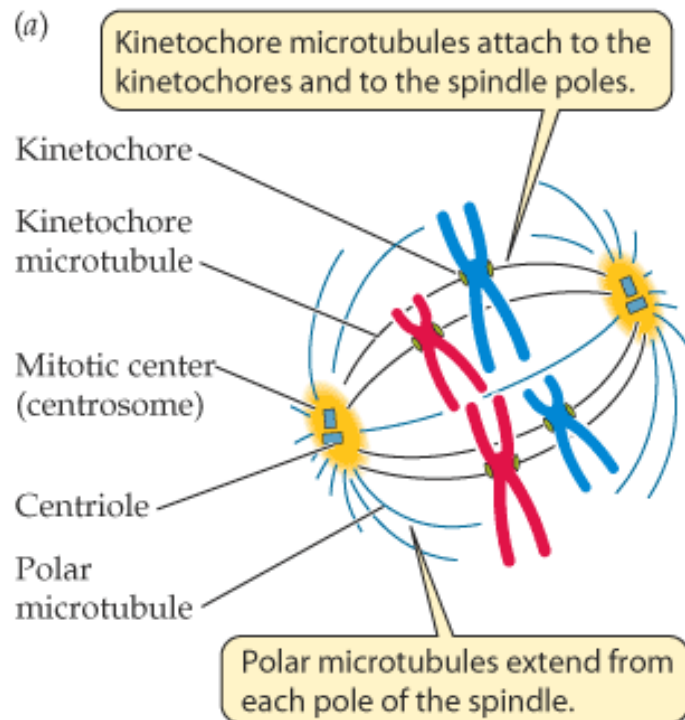
Cell Cycle



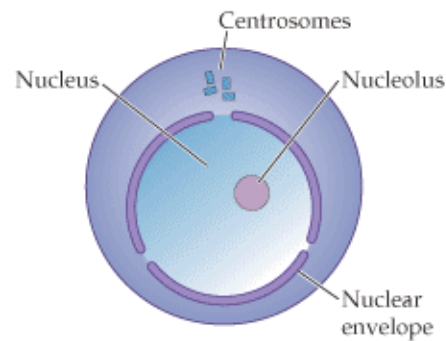
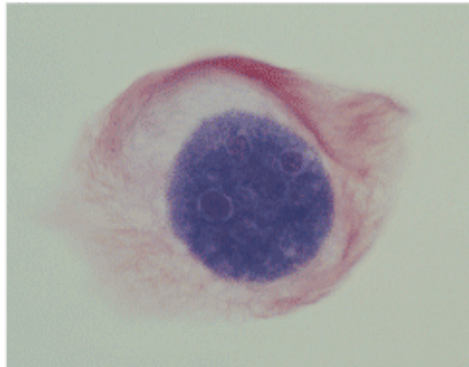


END

Mitosis

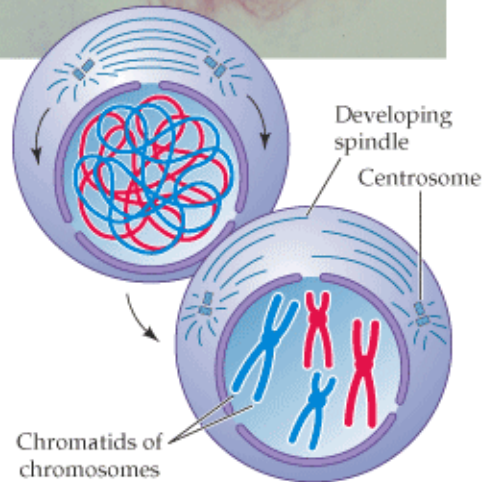
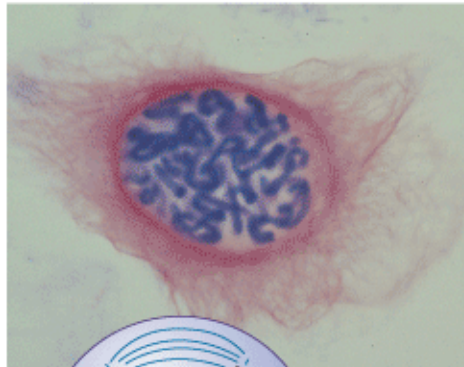


Interphase



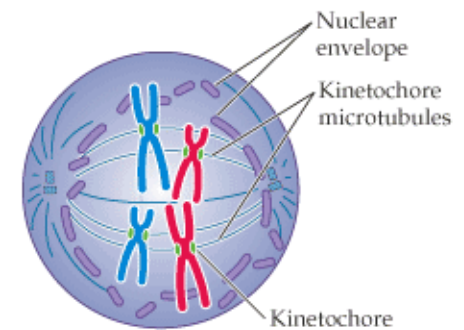
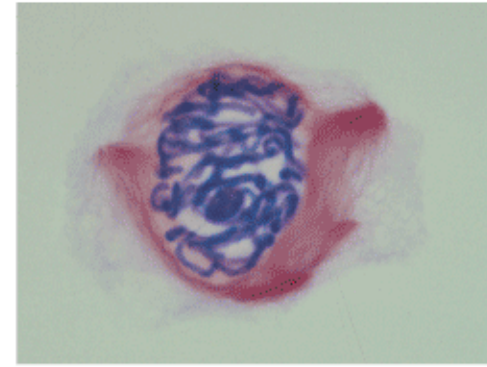
- 1** During the S phase of interphase, the nucleus replicates its DNA and centrosomes.

Prophase



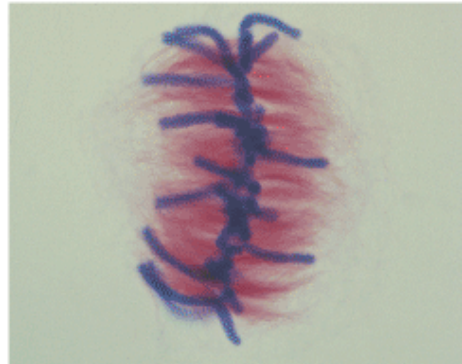
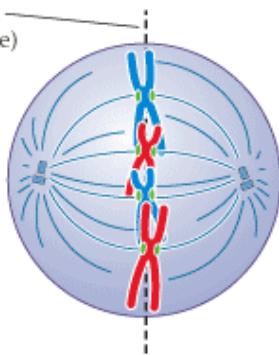
- 2** The chromatin coils and supercoils, becoming more and more compact and eventually condensing into visible chromosomes. The chromosomes consist of identical, paired sister chromatids.

Prometaphase



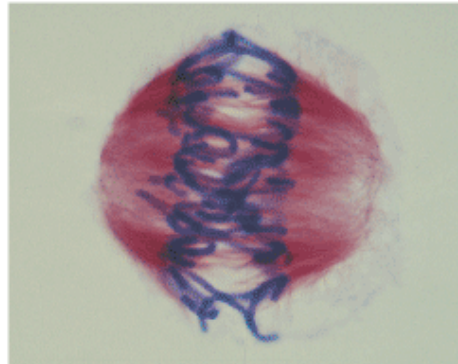
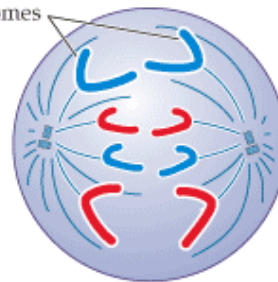
- 3** The nuclear envelope breaks down. Kinetochore microtubules appear and connect the kinetochores to the microtubule organizing centers.

Metaphase

Equatorial
(metaphase)
plate

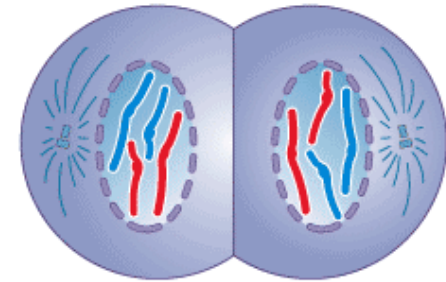
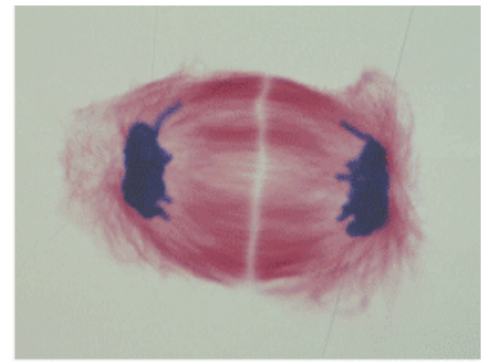
- 4** The centromeres (regions connecting paired chromatids) become aligned in a plane at the cell's equator.

Anaphase

Daughter
chromosomes

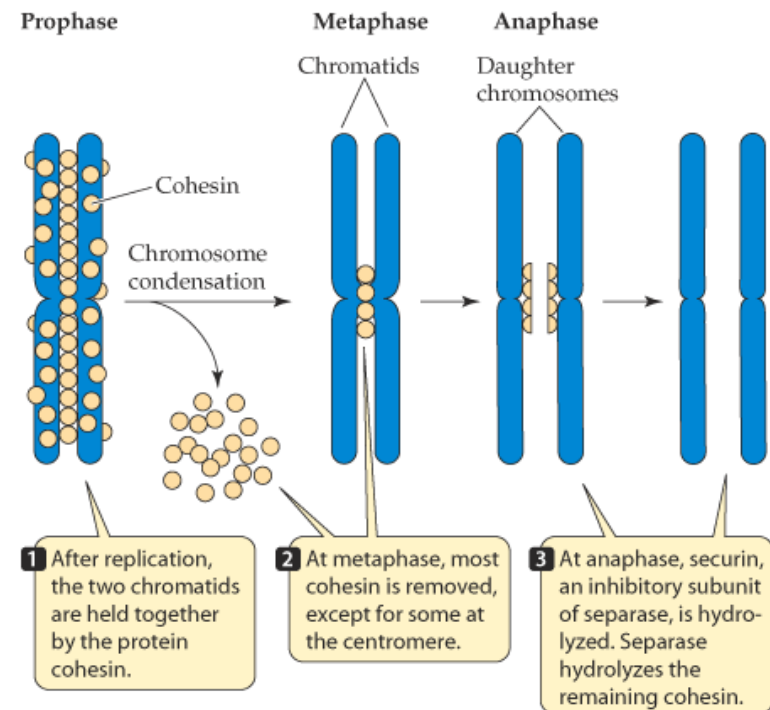
- 5** The paired sister chromatids separate, and the new daughter chromosomes begin to move toward the poles.

Telophase



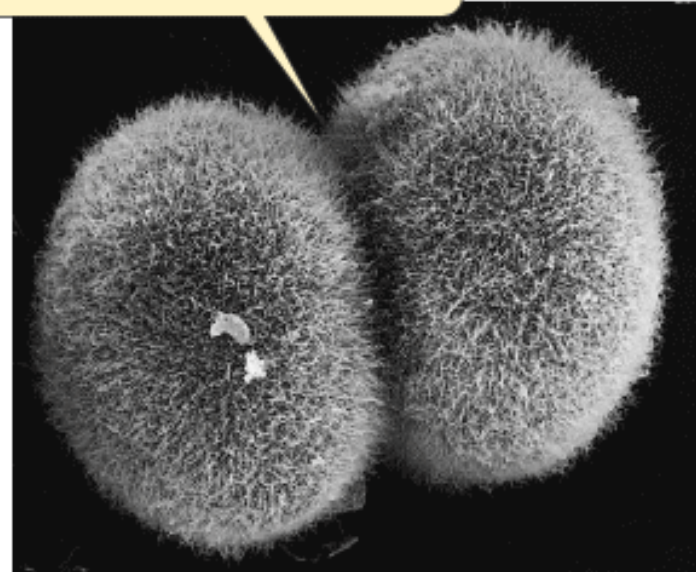
- 6** The daughter chromosomes reach the poles. Telophase passes into the next interphase as the nuclear envelopes and nucleoli re-form and the chromatin becomes diffuse.

The Glue

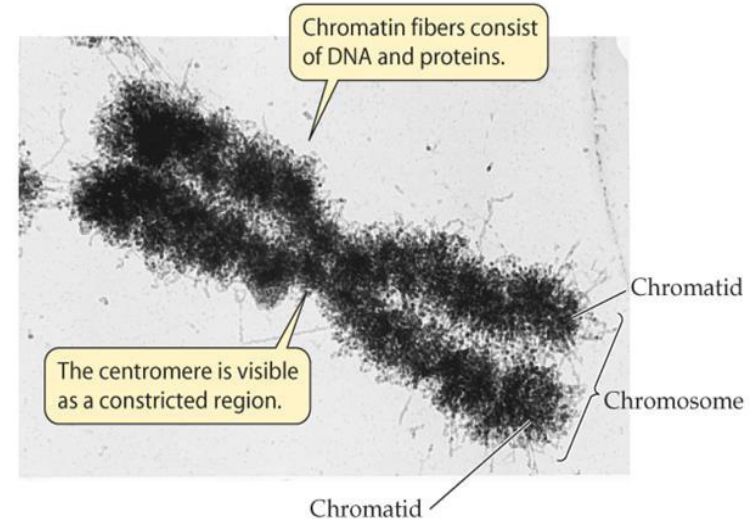
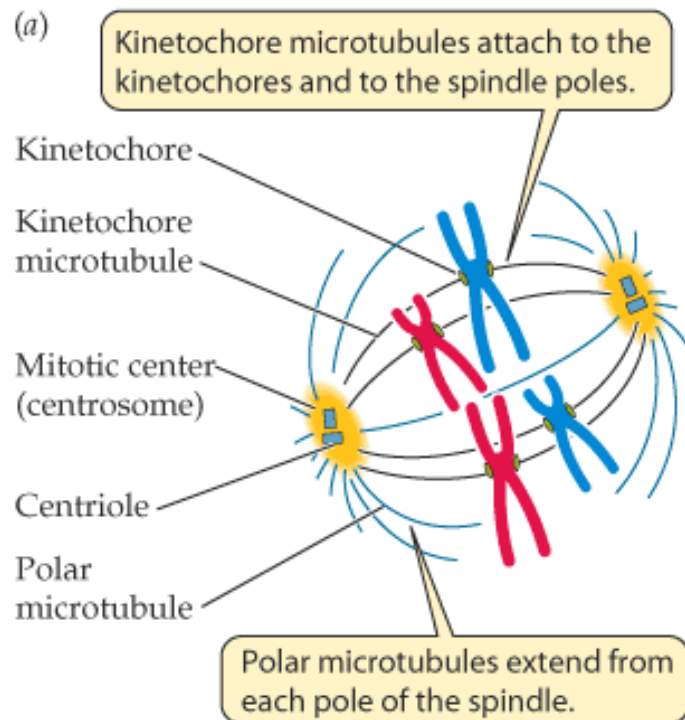


Cytokinesis

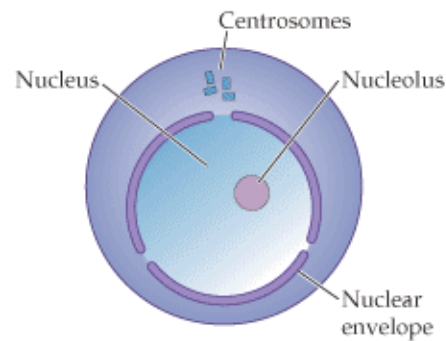
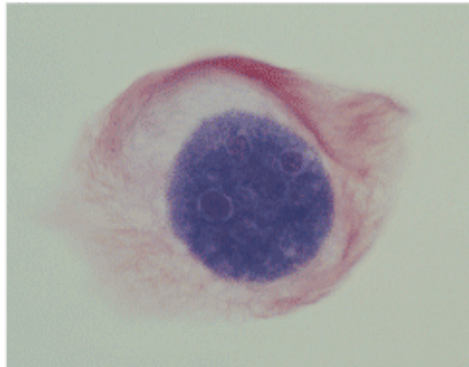
The division furrow has completely separated the cytoplasms of these two daughter cells, although their surfaces remain in contact.



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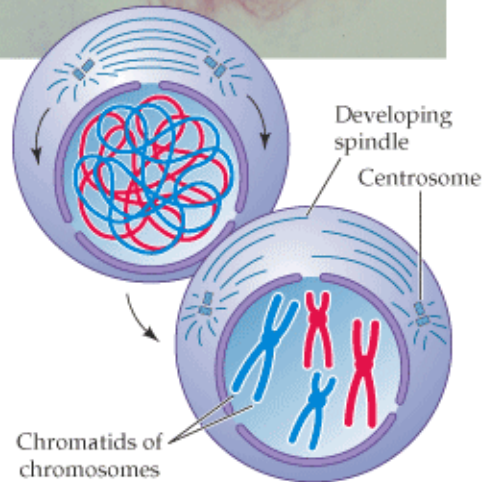
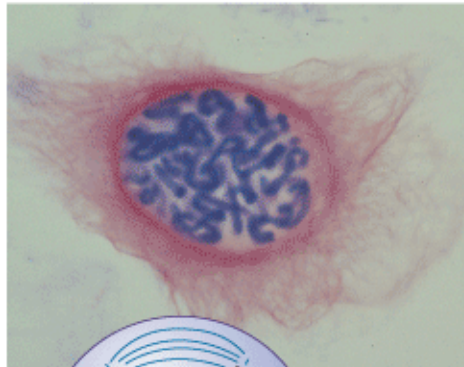


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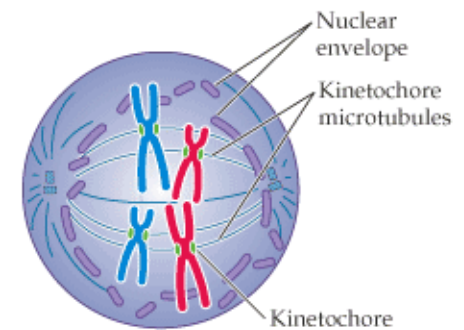
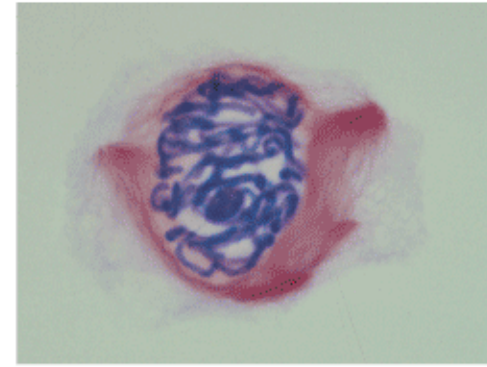
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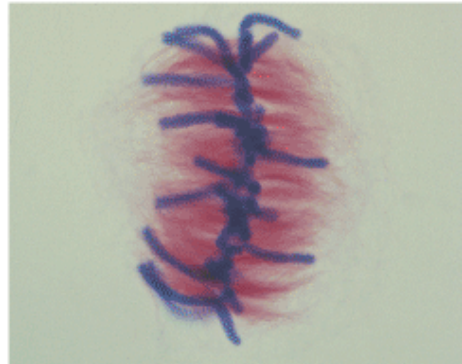
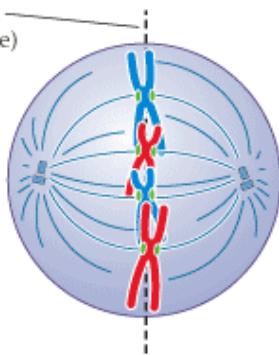
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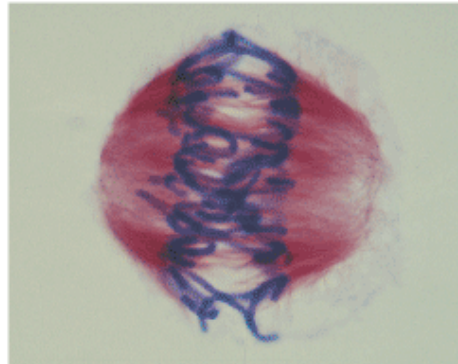
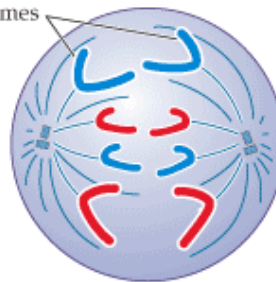
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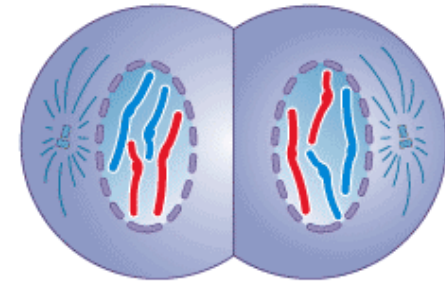
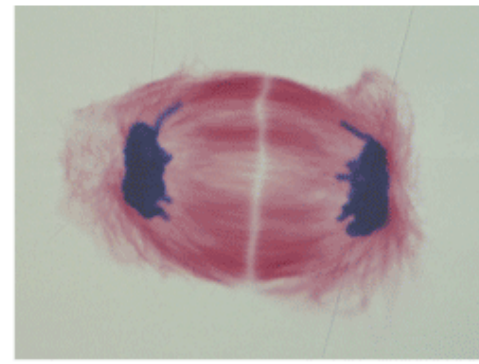
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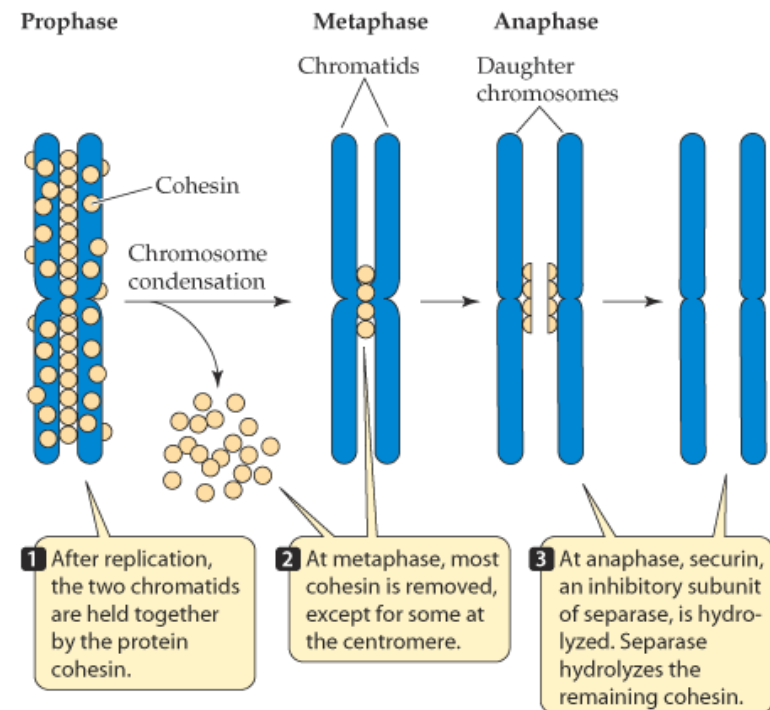
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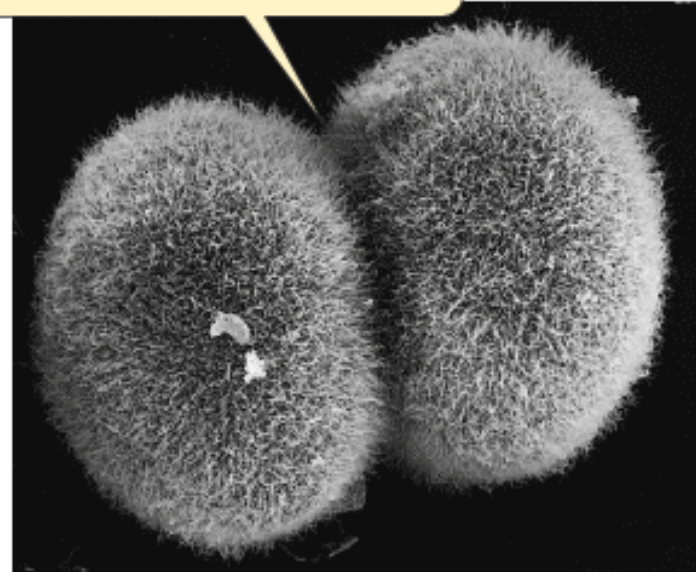
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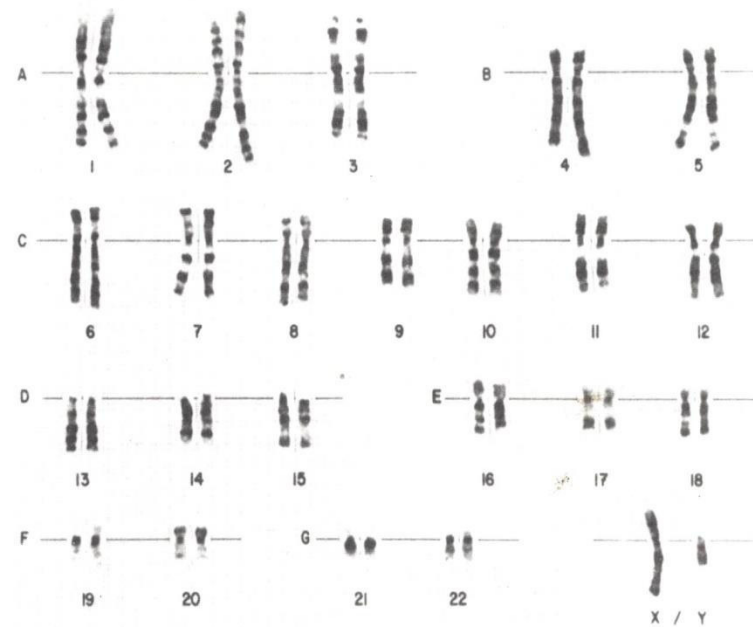
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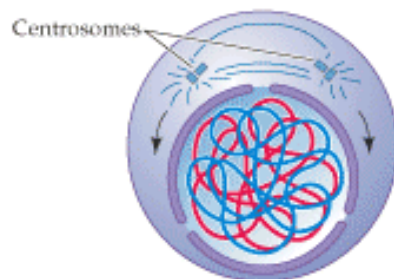
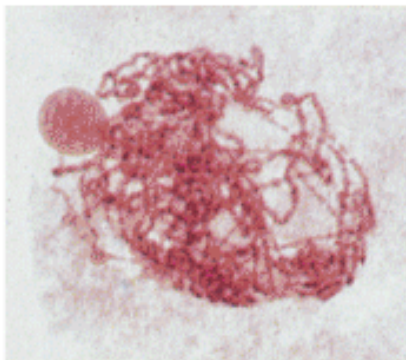
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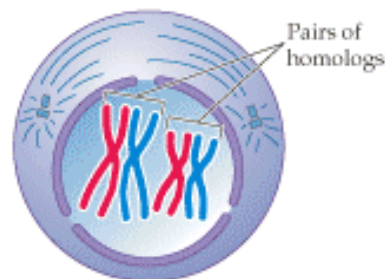
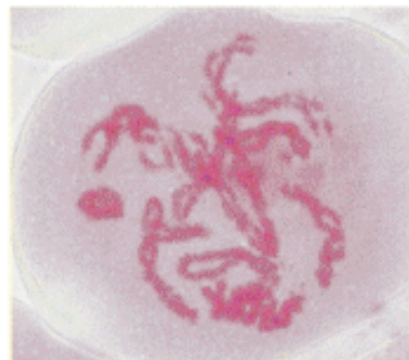
Meiosis I

Karyotype

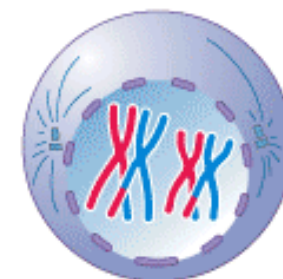
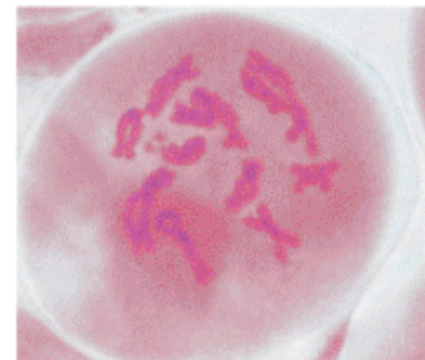


MEIOSIS I**Early Prophase I**

1 The chromatin begins to condense following interphase.

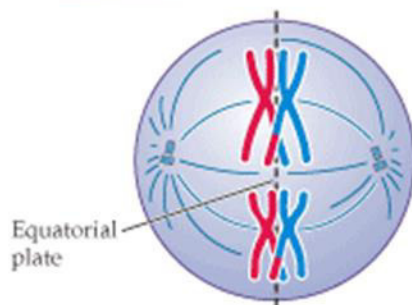
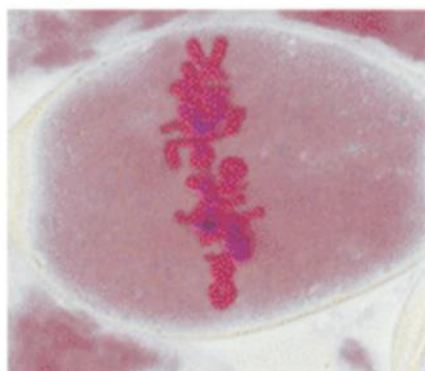
Mid-Prophase I

2 Synapsis aligns homologs, and chromosomes condense. Homologs are shown in different colors indicating those coming from each parent. In reality, their differences are very small, usually comprising different alleles of some genes.

Late Prophase I–Prometaphase

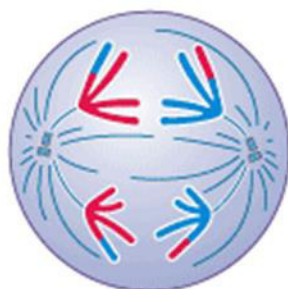
3 The chromosomes continue to coil and shorten. Crossing over results in an exchange of genetic material. In prometaphase the nuclear envelope breaks down.

Metaphase I



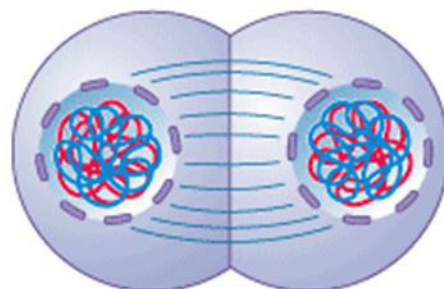
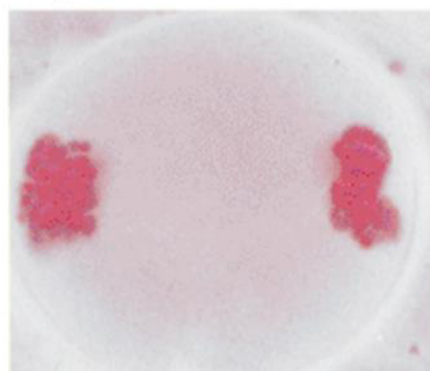
4 The homologous chromosomes line up on the equatorial (metaphase) plate.

Anaphase I



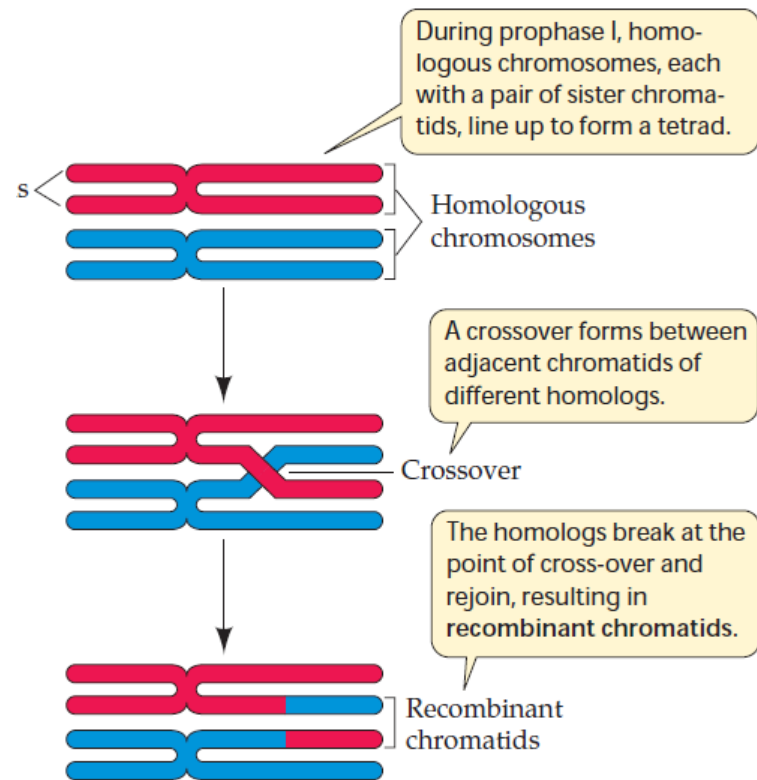
5 The homologous chromosomes (each with two chromatids) move to opposite poles of the cell.

Telophase I



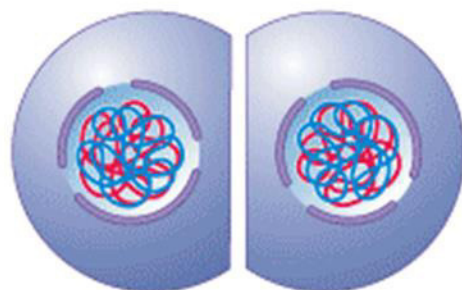
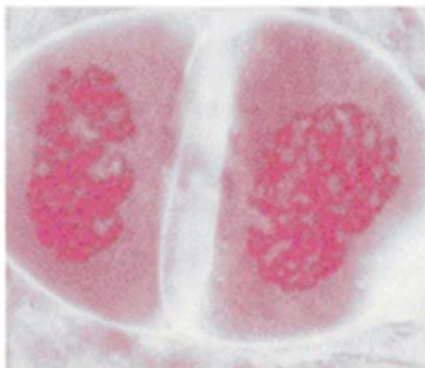
6 The chromosomes gather into nuclei, and the original cell divides.

Genetically Diverse Chromosomes

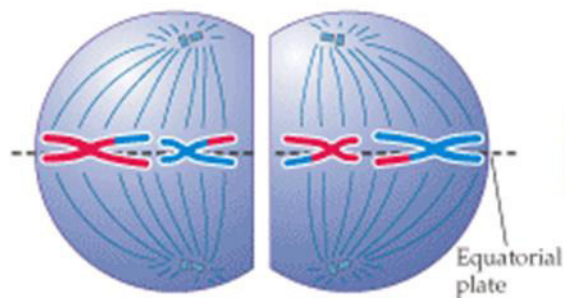
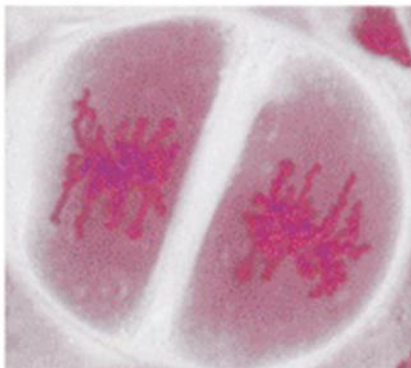


END

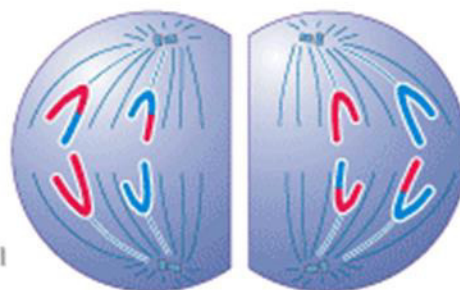
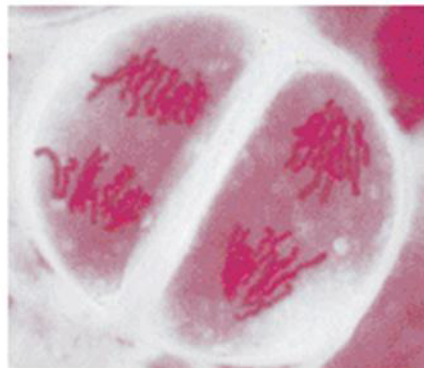
Meiosis II

MEIOSIS II**Prophase II**

7 The chromosomes condense again, following a brief interphase (interkinesis) in which DNA does not replicate.

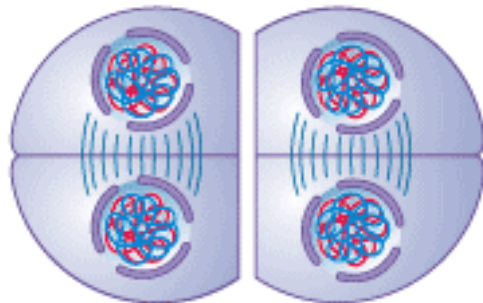
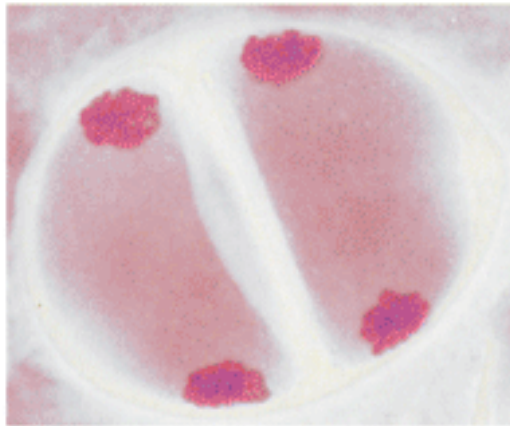
Metaphase II

8 Kinetochore of the paired chromatids line up across the equatorial plates of each cell.

Anaphase II

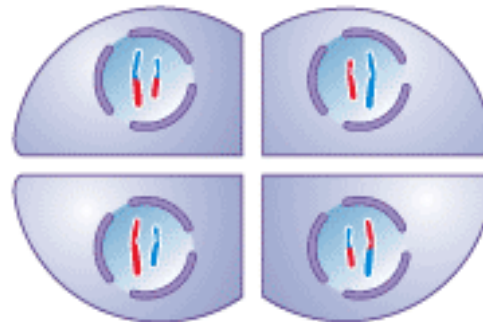
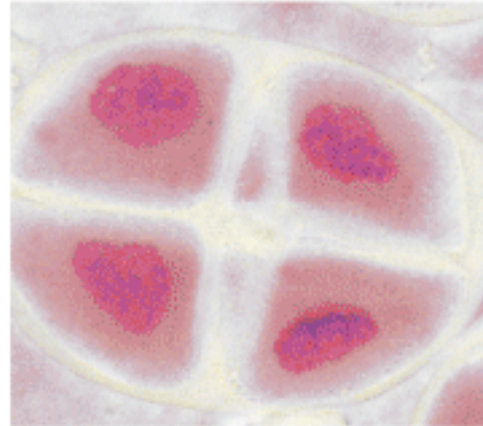
9 The chromatids finally separate, becoming chromosomes in their own right, and are pulled to opposite poles. Because of crossing over in prophase I, each new cell will have a different genetic makeup.

Telophase II



- 10** The chromosomes gather into nuclei, and the cells divide.

Products



- 11** Each of the four cells has a nucleus with a haploid number of chromosomes.

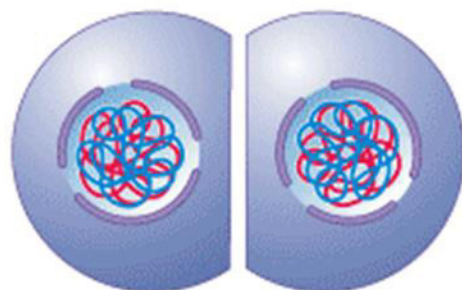
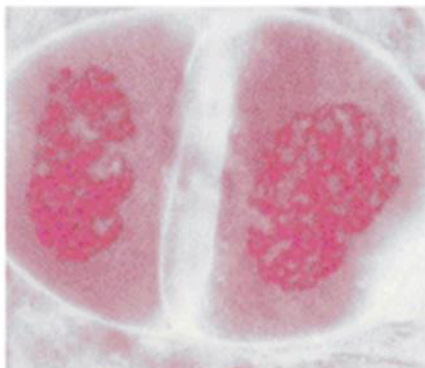
Features

Reduces chromosome number from diploid to haploid

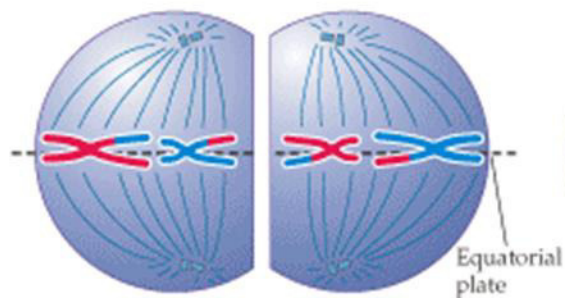
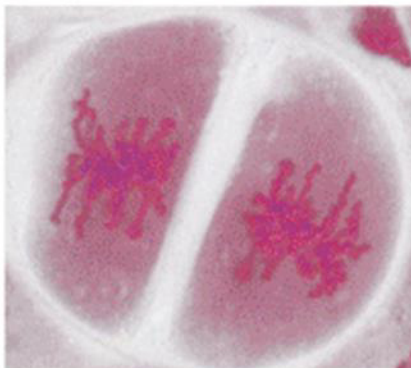
Ensures each of the haploid products has a complete set of chromosomes

Promotes genetic diversity among the products.

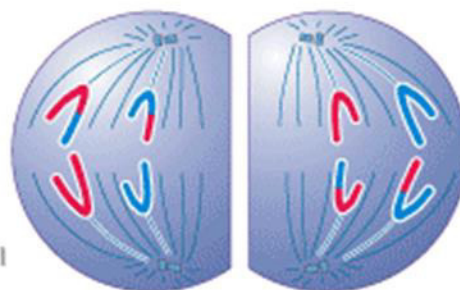
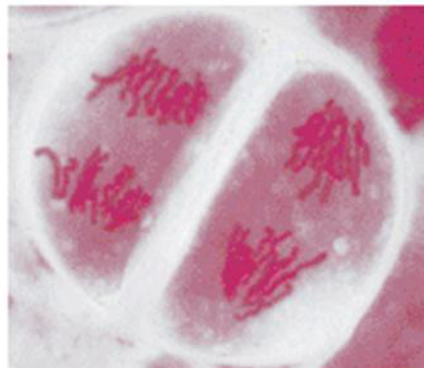
Meiosis II

MEIOSIS II**Prophase II**

7 The chromosomes condense again, following a brief interphase (interkinesis) in which DNA does not replicate.

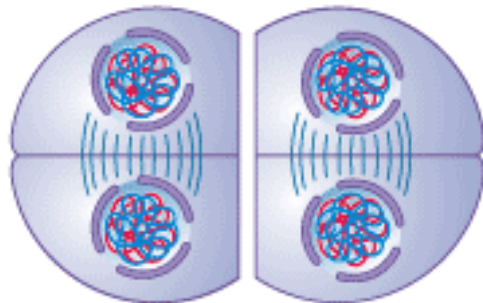
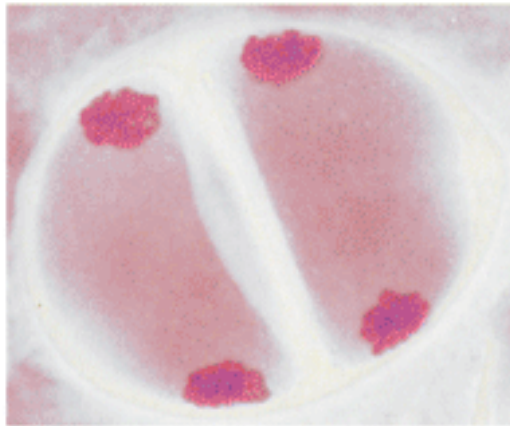
Metaphase II

8 Kinetochore of the paired chromatids line up across the equatorial plates of each cell.

Anaphase II

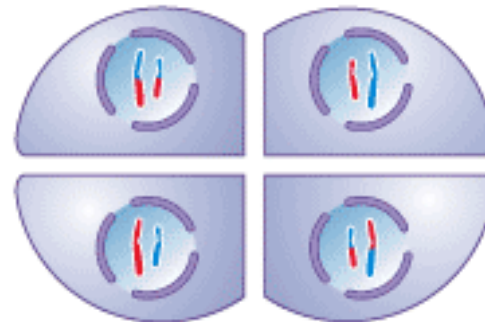
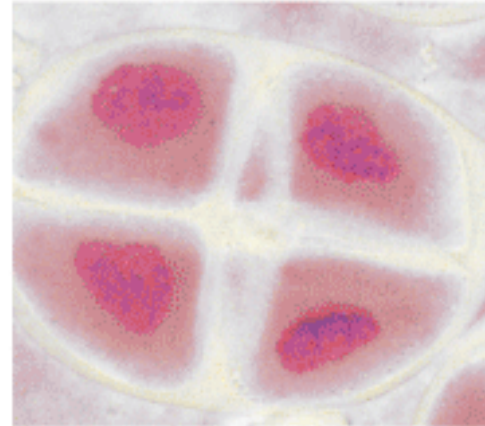
9 The chromatids finally separate, becoming chromosomes in their own right, and are pulled to opposite poles. Because of crossing over in prophase I, each new cell will have a different genetic makeup.

Telophase II



10 The chromosomes gather into nuclei, and the cells divide.

Products



11 Each of the four cells has a nucleus with a haploid number of chromosomes.

Features

Reduces chromosome number from diploid to haploid

Ensures each of the haploid products has a complete set of chromosomes

Promotes genetic diversity among the products.

Cell Biology

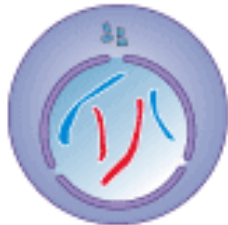
The Comparison

The background of the slide features an abstract geometric design. It consists of several overlapping triangular and quadrilateral shapes in shades of teal and light blue. Two prominent orange lines intersect near the center of the slide, one running diagonally from the top right and the other horizontally from the left. The overall effect is a modern, clean aesthetic.

The Comparison

MITOSIS

Parent cell ($2n$)

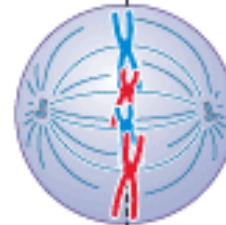


Prophase



No synapsis of homologous chromosomes

Metaphase



Individual chromosomes align at the equatorial plate.

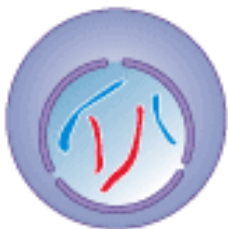
Anaphase



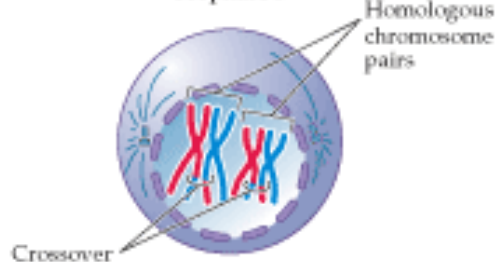
Centromeres separate. Sister chromatids separate during anaphase, becoming daughter chromosomes.

MEIOSIS

Parent cell ($2n$)

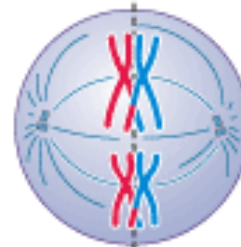


Prophase I



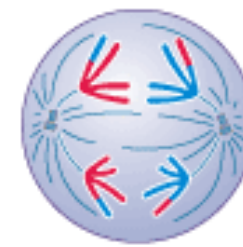
Synapsis and crossing over of homologs

Metaphase I



Homologous pairs align at the equatorial plate.

Anaphase I



Centromeres do not separate; sister chromatids remain together during anaphase; homologs separate; DNA does not replicate before subsequent prophase.

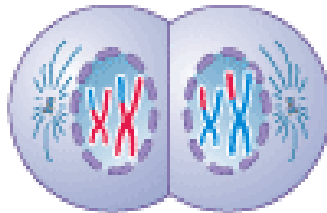
The Comparison

Two daughter
cells (each $2n$)

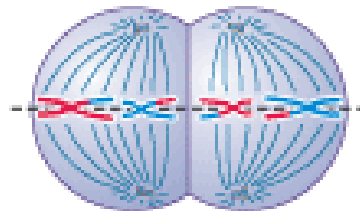


Mitosis is a mechanism for constancy:
The parent nucleus produces two
identical daughter nuclei.

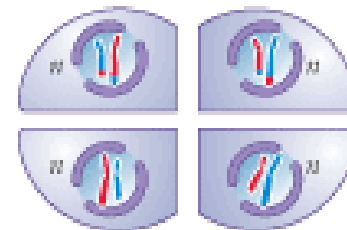
Telophase I



Metaphase II



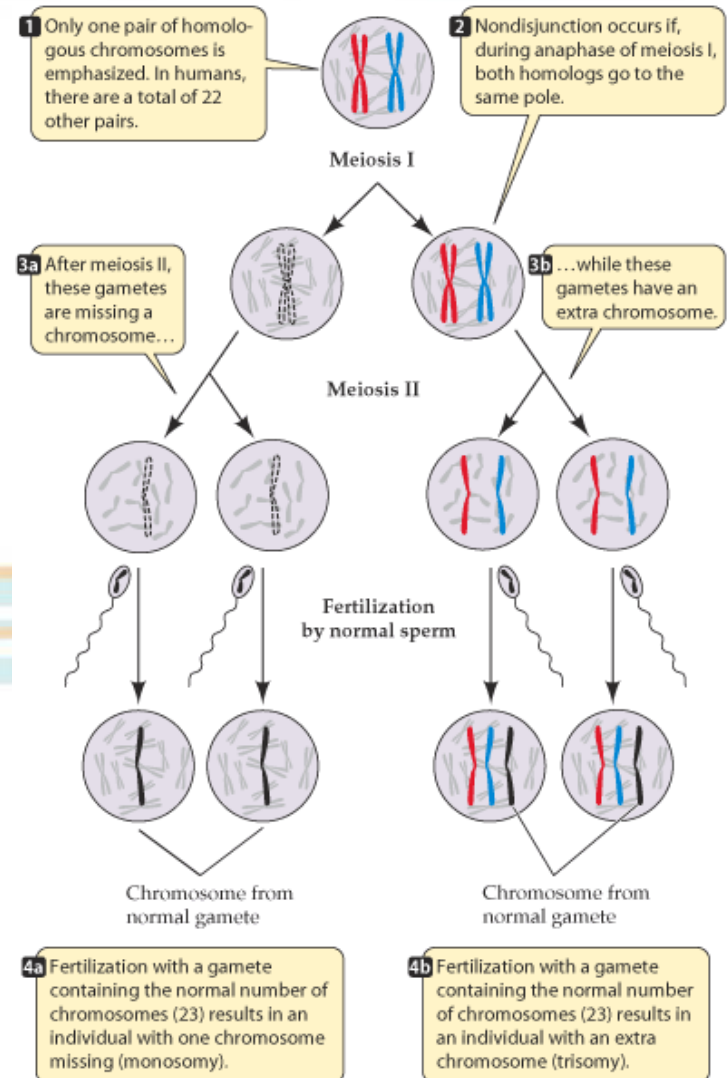
Four daughter
cells (each n)



Chromatids separate.

Meiosis is a mechanism for diversity:
The parent nucleus produces four
different haploid daughter nuclei.

The Common Mistake

**END**

Replication of DNA

- The double-helical model for DNA includes the concept that the two strands are complementary.
- Thus, each strand can in principle serve as the template for making its own partner.

Replication of DNA

- A number of models were proposed to explain the mode of replication of DNA.
- But the **semiconservative model** for DNA replication is the correct one.

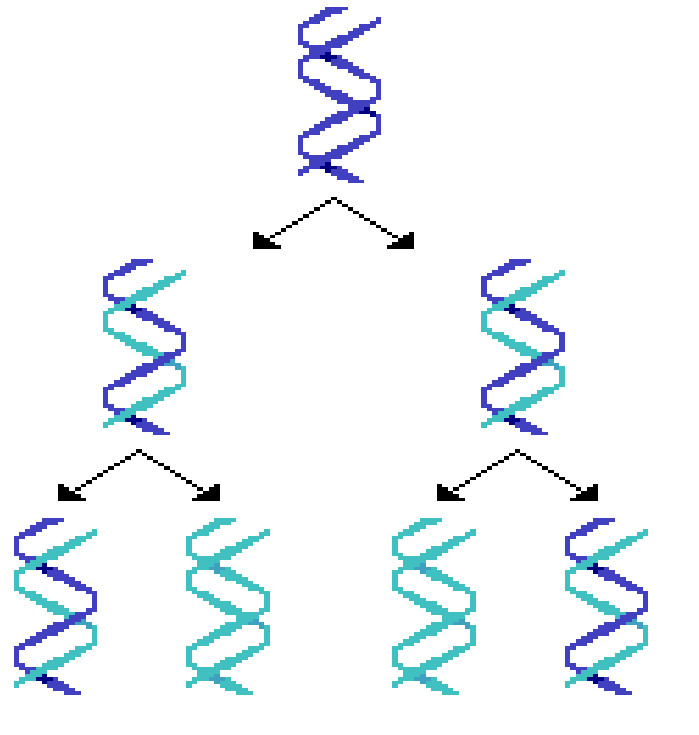
Replication of DNA

- The Watson–Crick model for DNA replication proposed that the two parental strands separate and that each then serves as a template for a new progeny strand.

Replication of DNA

- This is called semiconservative replication because each daughter duplex has one parental strand and one new strand which means that one of the parental strands is “conserved” in each daughter duplex.

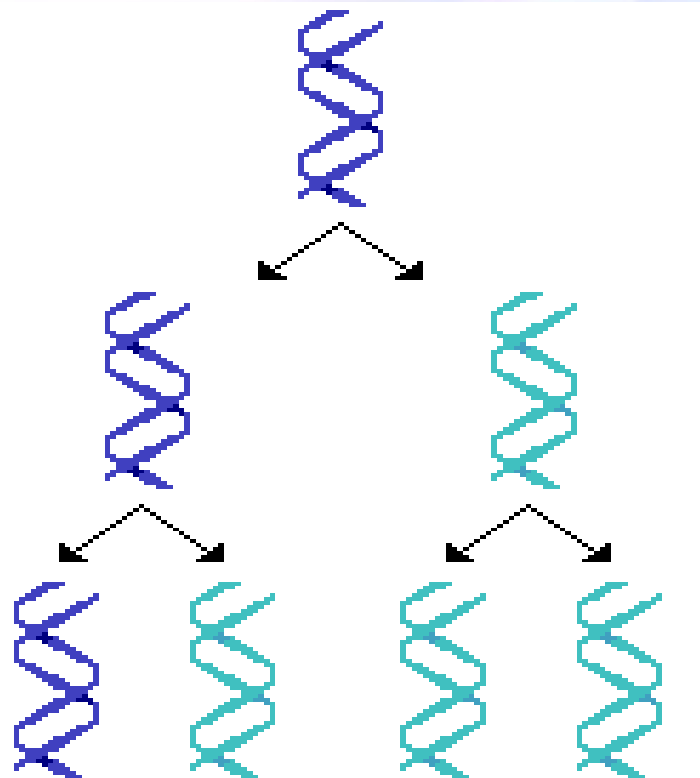
Replication of DNA



Replication of DNA

- Another potential mechanism is **conservative replication**, in which the two parental strands stay together and somehow produce another daughter helix with two completely new strands.

Replication of DNA



Replication of DNA

- Yet another possibility is **dispersive replication**, in which the DNA becomes fragmented so that new and old DNAs coexist in the same strand after replication.

Replication of DNA

