Al-Mustaqbal University College

Pharmacy Department / Second Stage

PHYSIOLOGY

L 2: Cell Structure & Function

Dr. Abdulhusein Mizhir Almaamuri

Cytoplasmic Organelles

Cytoplasm

cellular material inside cell

1. Most cellular activities occur here
2. Comprised of:

a. Cytosol: fluid in which other components are suspended

b. Organelles (see below)

c. Inclusions: non-functioning chemicals that may be unique to a given cell type

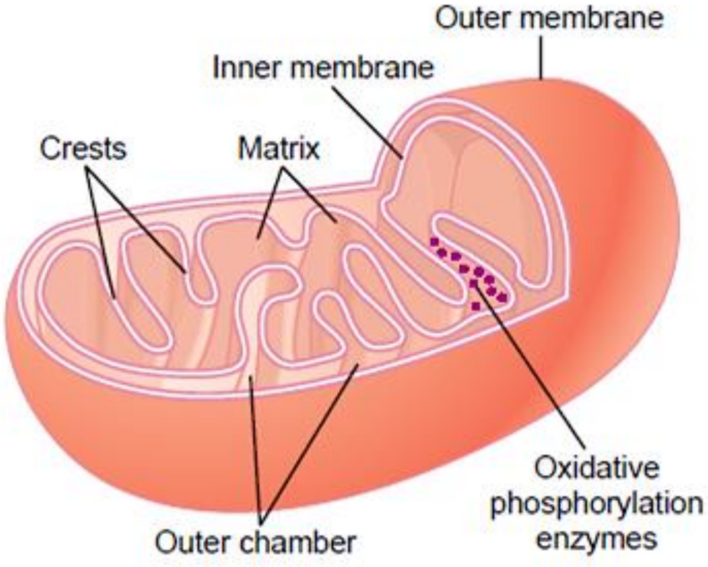
Mitochondria

The mitochondria, are called the "**powerhouses**" of the cell. Without them, cells would be unable to extract enough energy from the nutrients, and essentially all cellular functions would cease. Mitochondria are present in all areas of each cell's cytoplasm, mitochondria are concentrated in the portions of cell that are responsible for the major share of its energy metabolism.

The basic structure of the mitochondrion, is composed mainly of two lipid bilayer–protein membranes: an *outer membrane and* an *inner membrane*

Many foldings of the inner membrane form *shelves onto which oxidative enzymes* are attached. In addition, the inner cavity of the mitochondrion is filled with a ***matrix*** *that contains large* quantities of dissolved enzymes that are necessary for extracting extracting energy from nutrients.

These enzymes operate in association with the oxidative enzymes on the shelves to cause **oxidation** of the nutrients, thereby forming carbon dioxide and water and at the same time releasing energy.



The liberated energy is used to synthesize a “high-energy” substance called ***adenosine triphosphate (ATP).***

.ATP is then transported out of the mitochondrion, and it diffuses throughout the cell to release its own energy wherever it is needed for performing cellular functions.

Mitochondria are **self-replicative**, which means that one mitochondrion can form a second one, a third one, and so on, whenever there is a need in the cell for

increased amounts of ATP. Indeed, the mitochondria contain DNA similar to that found in the cell nucleus.

Ribosomes and the Granular Endoplasmic Reticulum

Attached to the outer surfaces of many parts of the endoplasmic reticulum are large numbers of minute granular particles called *ribosomes. Where these are* present, the reticulum is called the *granular or rough endoplasmic reticulum. The ribosomes are composed of* mixture of RNA and proteins, and they function to synthesize **new protein** molecules in the cell**.**

Agranular Endoplasmic Reticulum

Part of the endoplasmic reticulum has no attached ribosomes. This part is called the *agranular, or smooth, endoplasmic reticulum.*

The agranular reticulum functions for the synthesis of **lipid** substances and for other processes of the cells promoted by intrareticular enzymes.

Golgi Apparatus

The Golgi apparatus, is closely related to the endoplasmic reticulum. It has membranes similar to those of the **agranular** endoplasmic reticulum. This apparatus is prominent in **secretory** cells, where it is located on the side of the cell from which the secretory substances are extruded.

The Golgi apparatus functions in association with the endoplasmic reticulum. In this way, substances entrapped in the **endoplasmic reticulum (ER) vesicles** are transported from the endoplasmic reticulum to the Golgi apparatus.

The transported substances are then processed in the Golgi apparatus to form lysosomes, secretory vesicles, and other cytoplasmic components

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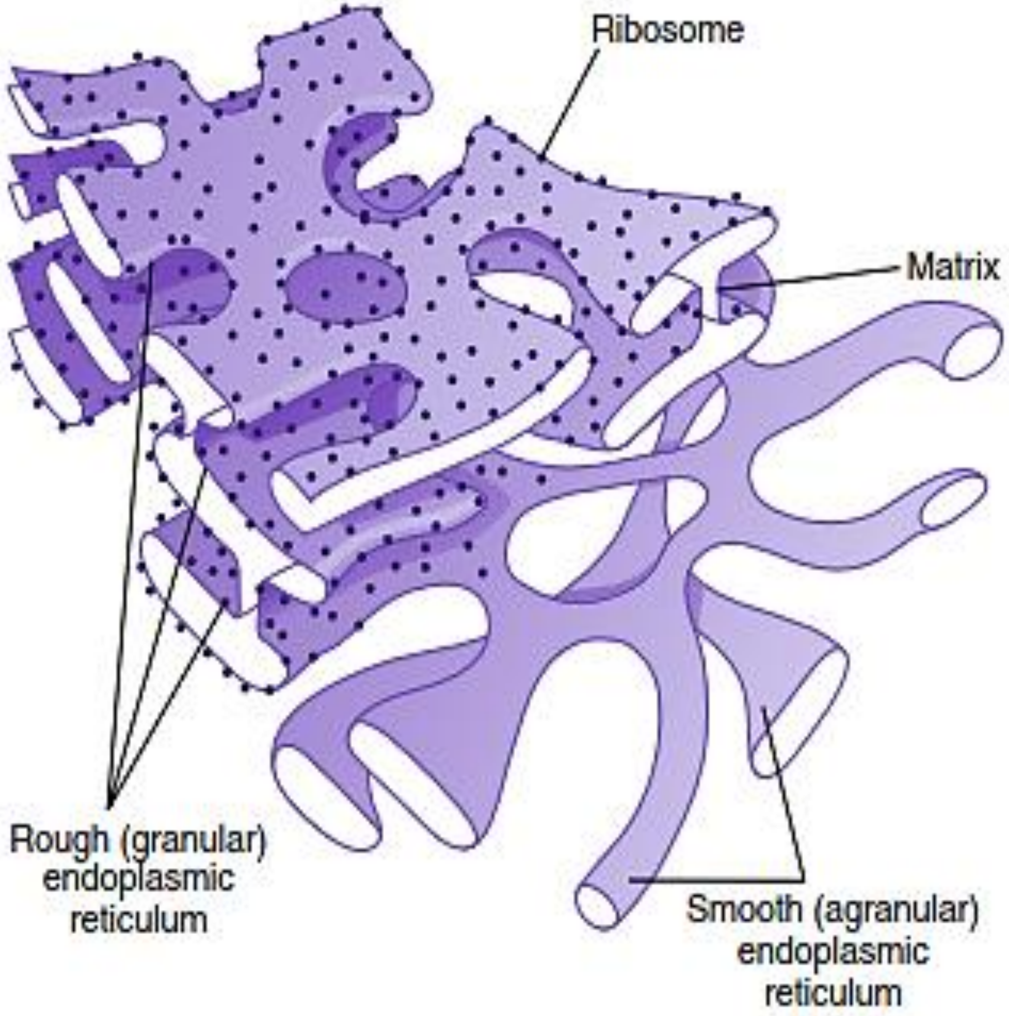


Figure 2-4. Structure of the endoplasmic reticulum.

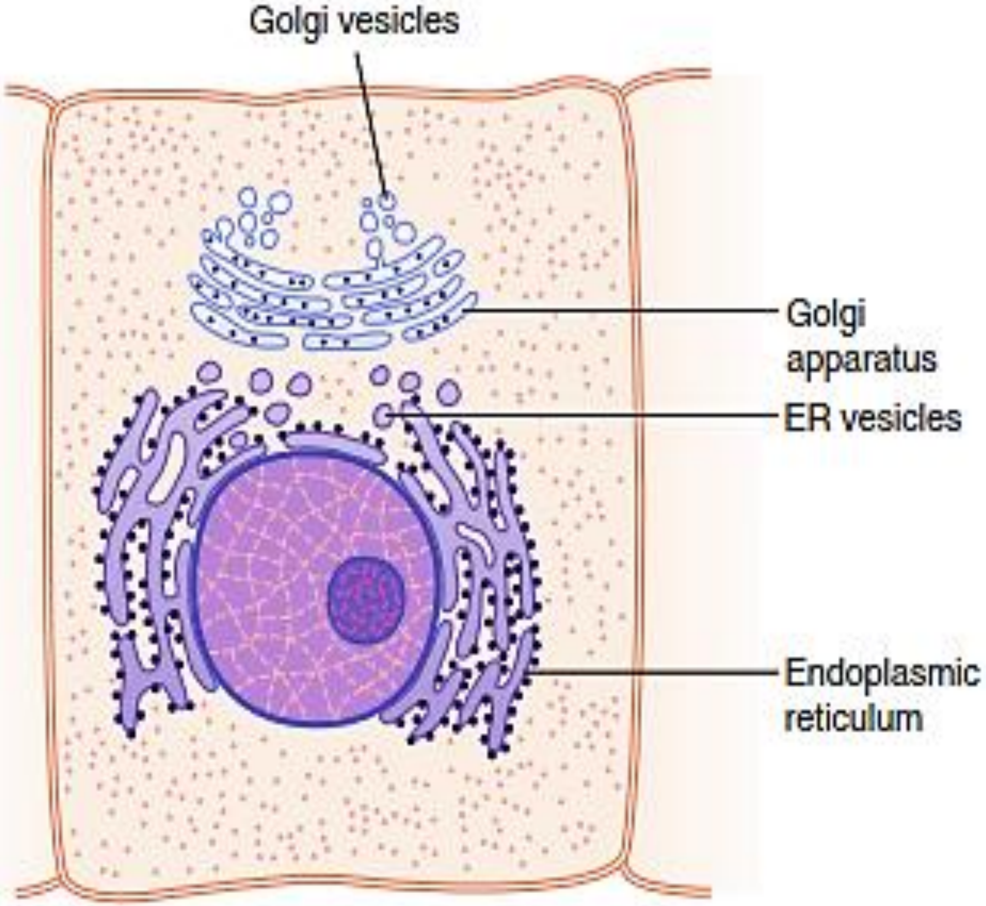


Figure 2-5. A typical Golgi apparatus and its relationship to the endoplasmic reticulum (ER) and the nucleus.

Lysosomes:, are vesicular organelles that form by breaking off from the Golgi apparatus and then dispersing throughout the cytoplasm.

The lysosomes provide an *intracellular digestive system that allows the cell to digest*

(1) damaged cellular structures,

(2) food particles that have been ingested by the cell, and

(3) unwanted matter such as bacteria.

It is surrounded by a typical lipid bilayer membrane and is filled with large numbers of small granules, which are protein aggregates of as many as 40 different *hydrolase (digestive) enzymes. A* ***hydrolytic enzyme*** *is* capable of splitting an organic compound into two or more parts by combining hydrogen from a water molecule with one part of the compound and combining the hydroxyl portion of the water molecule with the other part of the compound.

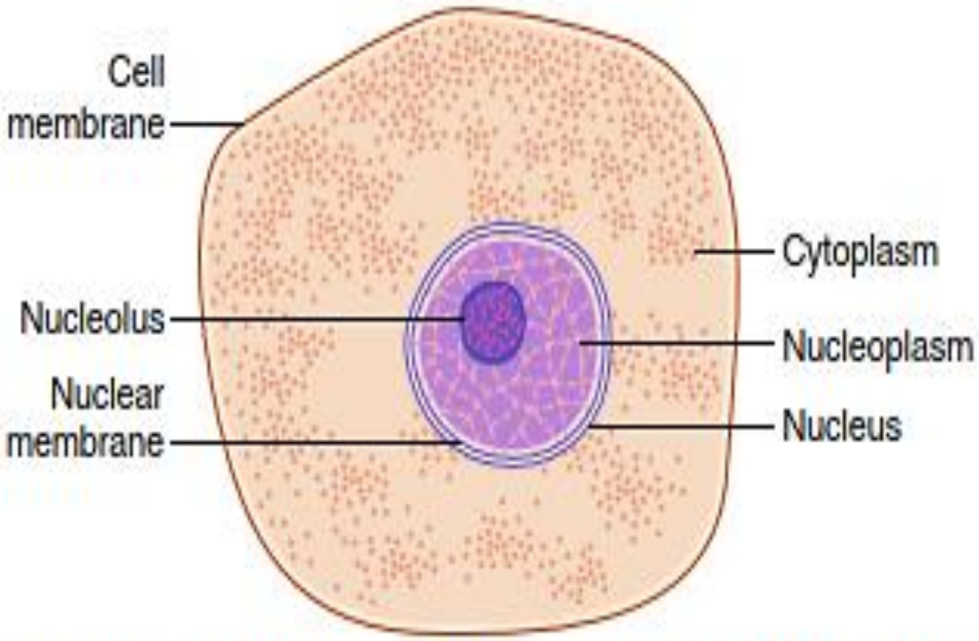


Figure 2-1. Illustration of cell structures visible with a light microscope.

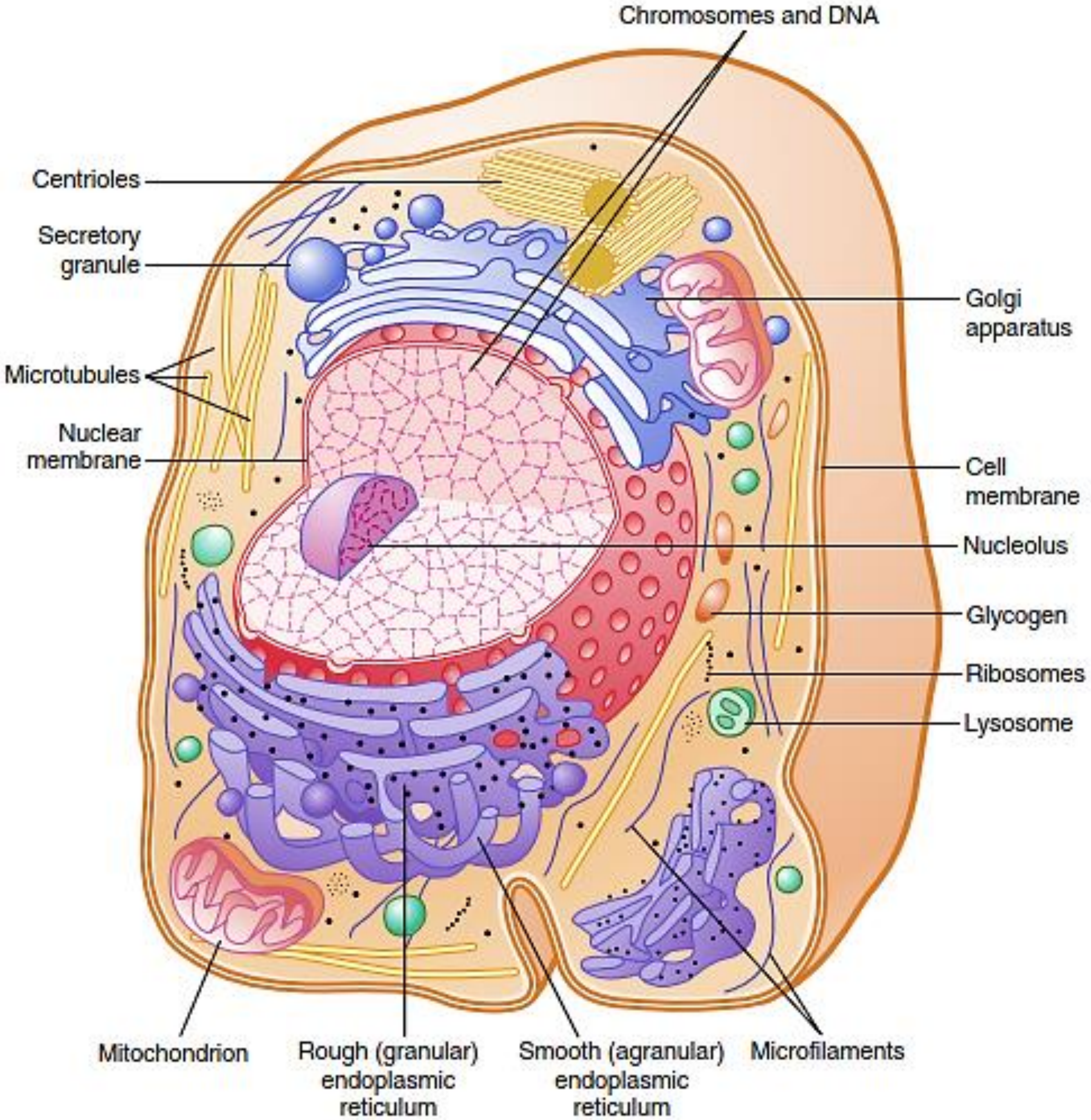


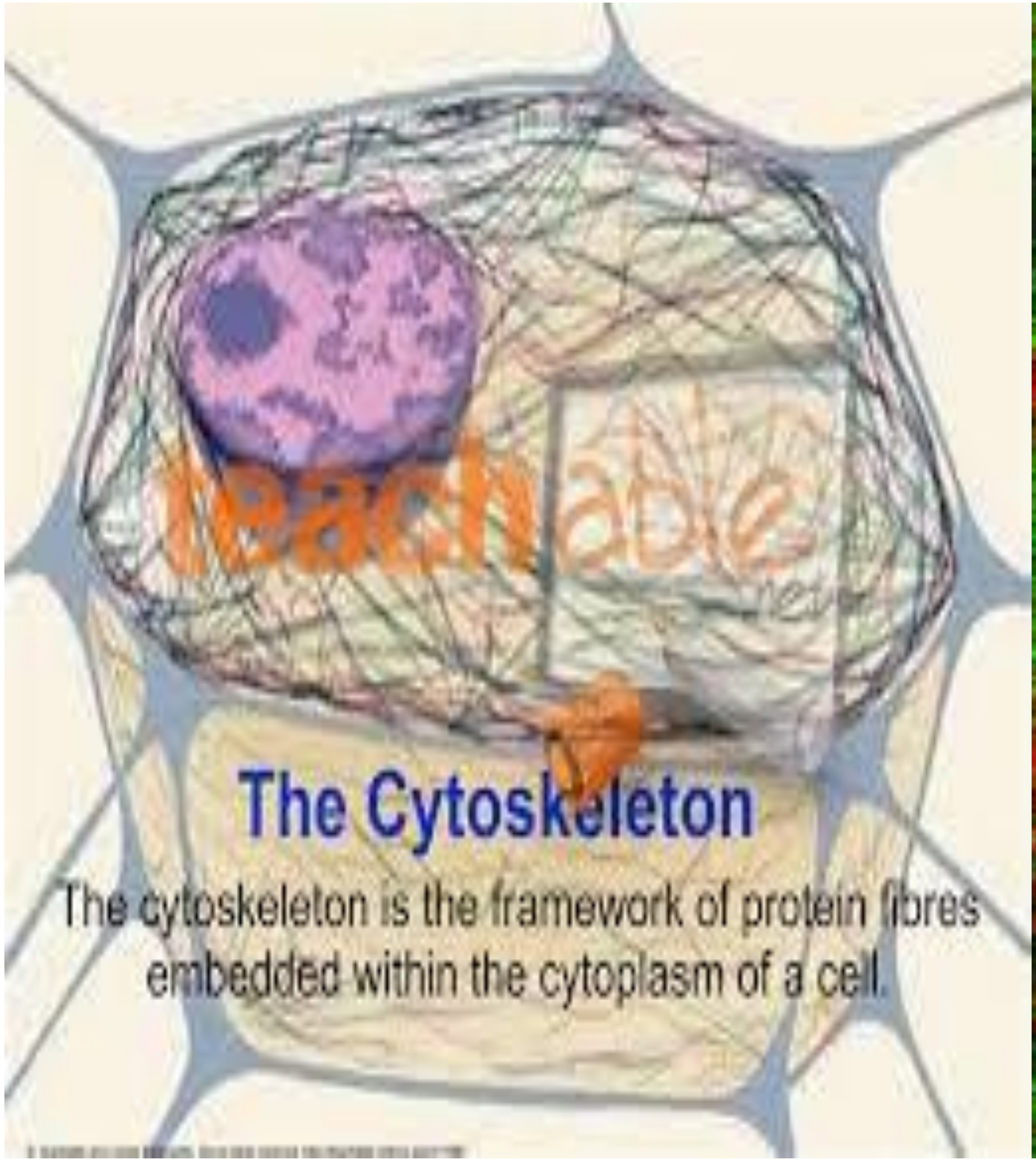
Figure 2-2. Reconstruction of a typical cell, showing the internal organelles in the cytoplasm and nucleus.

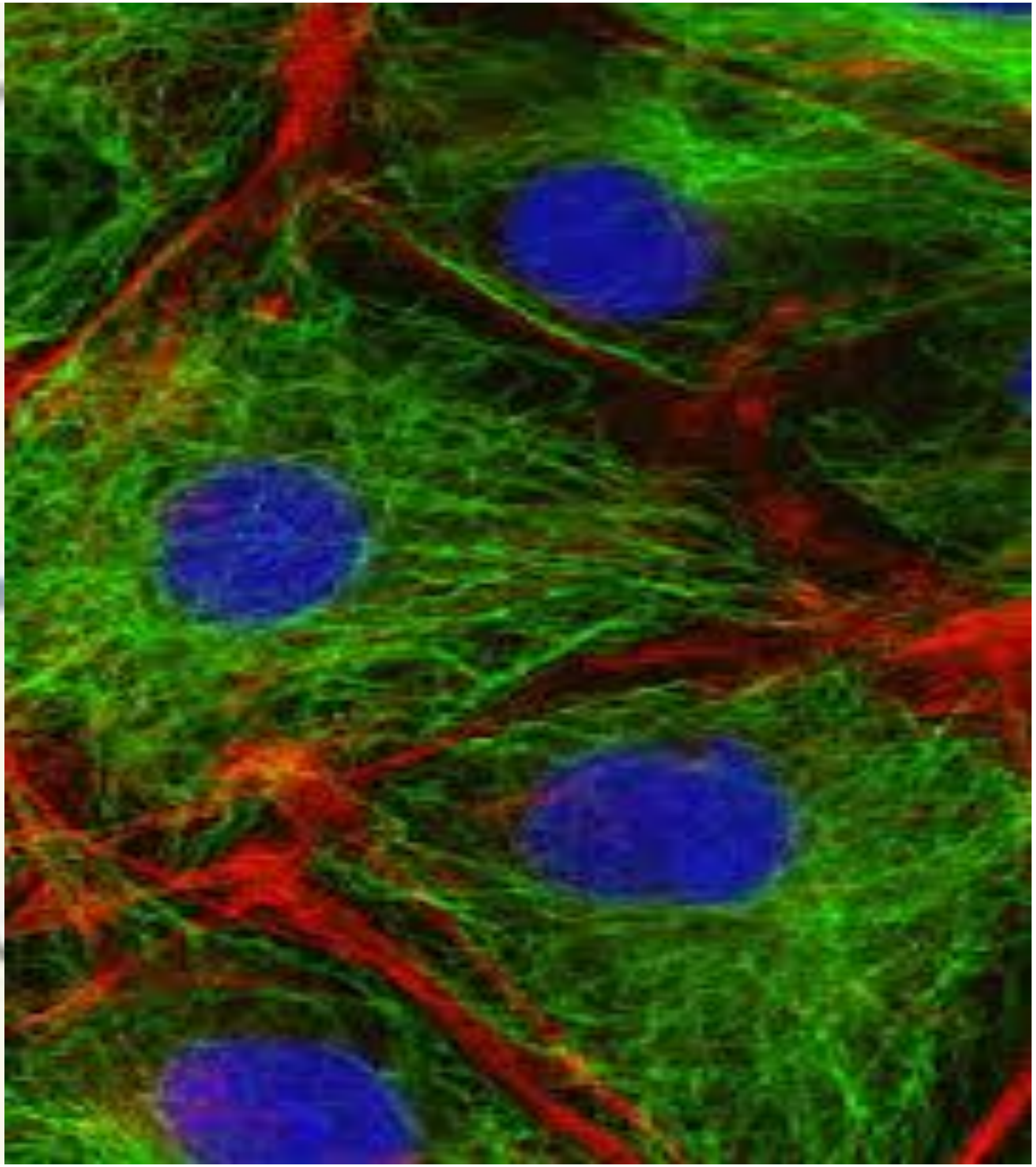
Peroxisomes

Peroxisomes are similar physically to lysosomes, but they are different in two important ways. **First**, they are believed to be formed by self-replication (or perhaps by budding off from the smooth endoplasmic reticulum) rather than from the Golgi apparatus. **Second**, they contain oxidases rather than hydrolases.

Cytoskeleton

All cells have a **cytoskeleton,** a system of fibers that not only maintains the structure of the cell but also permits it to change shape and move. The cytoskeleton is made up primarily of microtubules, intermediate filaments, and microfilaments, along with proteins that anchor them and tie them together. In addition, proteins and organelles move along microtubules and microfilaments from one part of the cell to another propelled by molecular motors.


teachable.net
The Cytoskeleton
The cytoskeleton is the framework of protein fibres embedded within the cytoplasm of a cell.



Cilia, Microvilli & Flagella

Microvilli: increase surface area; absorption

Cilia & flagella: made of micro- tubules set in a special way, for movement.

Nucleus

’’control center’’ for cellular function; contains genetic material

Number of nuclei:

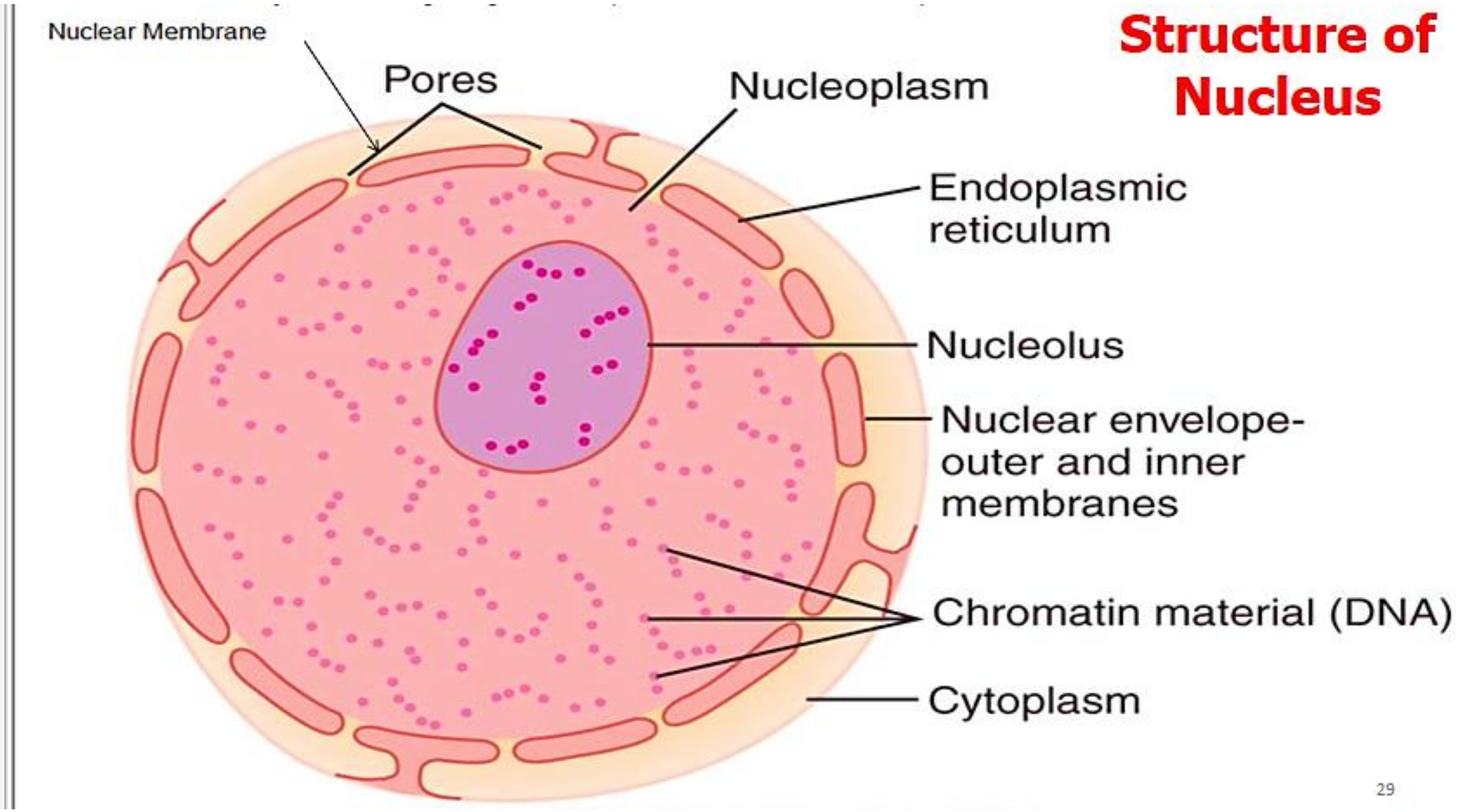
1. Most cells have a single nucleus
2. Large cells (those with a large amount of cytoplasm) have to be *multinucleate*
3. Red blood cells: only cell lacking a nucleus

Structures of Nucleus

1. Nuclear envelope

Double membrane: inner and outer

- Outer membrane is continuous with ER, Nuclear pores, Selectively permeable
    - "Envelope" as its a double-membrane of phospholipid bilayer (vis cell membrane) sets what comes in and out



2. Nucleoli

- No membrane
- Ribosomes subunits are assembled here
- Its large in a growing cells,
- Chromatin: (DNA region) nuclear regions coding for RNA.

3. Chromatin

Chromatin: DNA + globular histone

DNA (blueprint of life) carries the genetic information, consists of two strands arranged into a ladder-like structure called a ''Double Helix'' that made up of millions of tiny subunits ''Nucleotides'' joined by a hydrogen bond.

Each nucleotide consists of phosphate group, pentose sugar & nitrogenous base.

- Nucleosome: major unit of chromatin, units of eight histone wrapped by DNA molecule

Chromosomes: prior to cell division, chromatin condenses to form chromosomes -

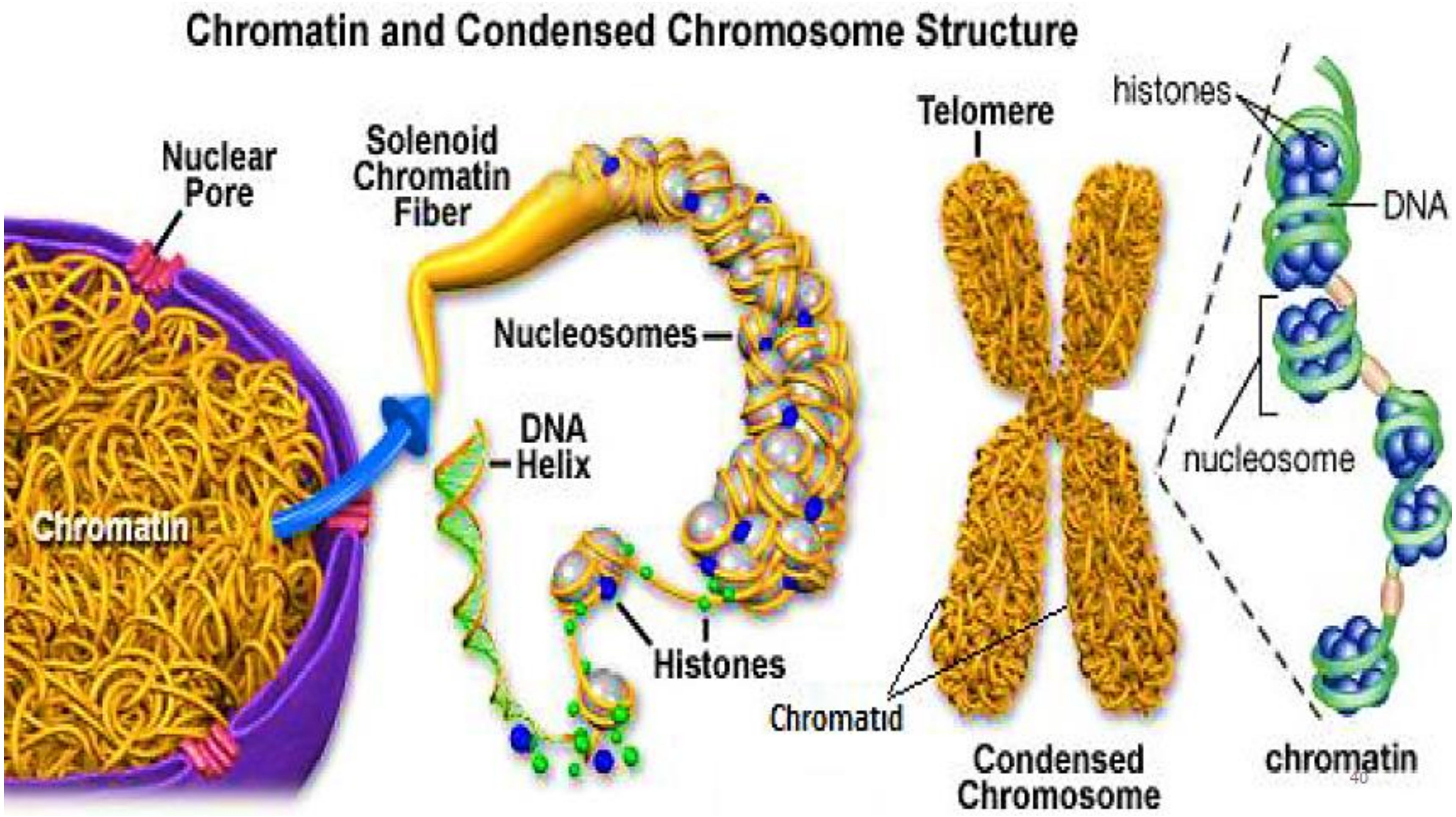
Genes: DNA unit has a unique sequence of bases that code for a special protein & regulate how other genes are expressed.

All cells of an organism contain the same genetic information but they do not all express the same genes.

Cells differentiate by genes that are activated.

Chromosomes: before cell division, chromatin condenses to form chromosomes.

Genome: is the total genetic information encoded in DNA, includes both the genes & the non-coding sequences of the DNA.



Functional Systems of the Cell

ENDOCYTOSIS—INGESTION BY THE CELL

If a cell is to live and grow and reproduce, it must obtain nutrients and other substances from the surrounding fluids. Most substances pass through the cell membrane by the processes of **diffusion** and ***active transport***

Diffusion involves simple movement through the membrane caused by the random motion of the molecules of the substance. Substances move through cell membrane pores or, in the case of lipid-soluble substances, through the lipid matrix of the membrane.

Active transport involves actually carrying a substance through the membrane by a physical protein structure that penetrates all the way through the membrane. These active transport mechanisms are so important to cell function.

Large particles enter the cell by a specialized function of the cell membrane called ***endocytosis***. The principal forms of endocytosis are ***pinocytosis*** and ***phagocytosis.*** Pinocytosis means the ingestion of minute particles that form vesicles of extracellular fluid and par- ticulate constituents inside the cell cytoplasm. Phagocytosis means the ingestion of large particles, such as bacteria, whole cells, or portions of degenerating tissue.

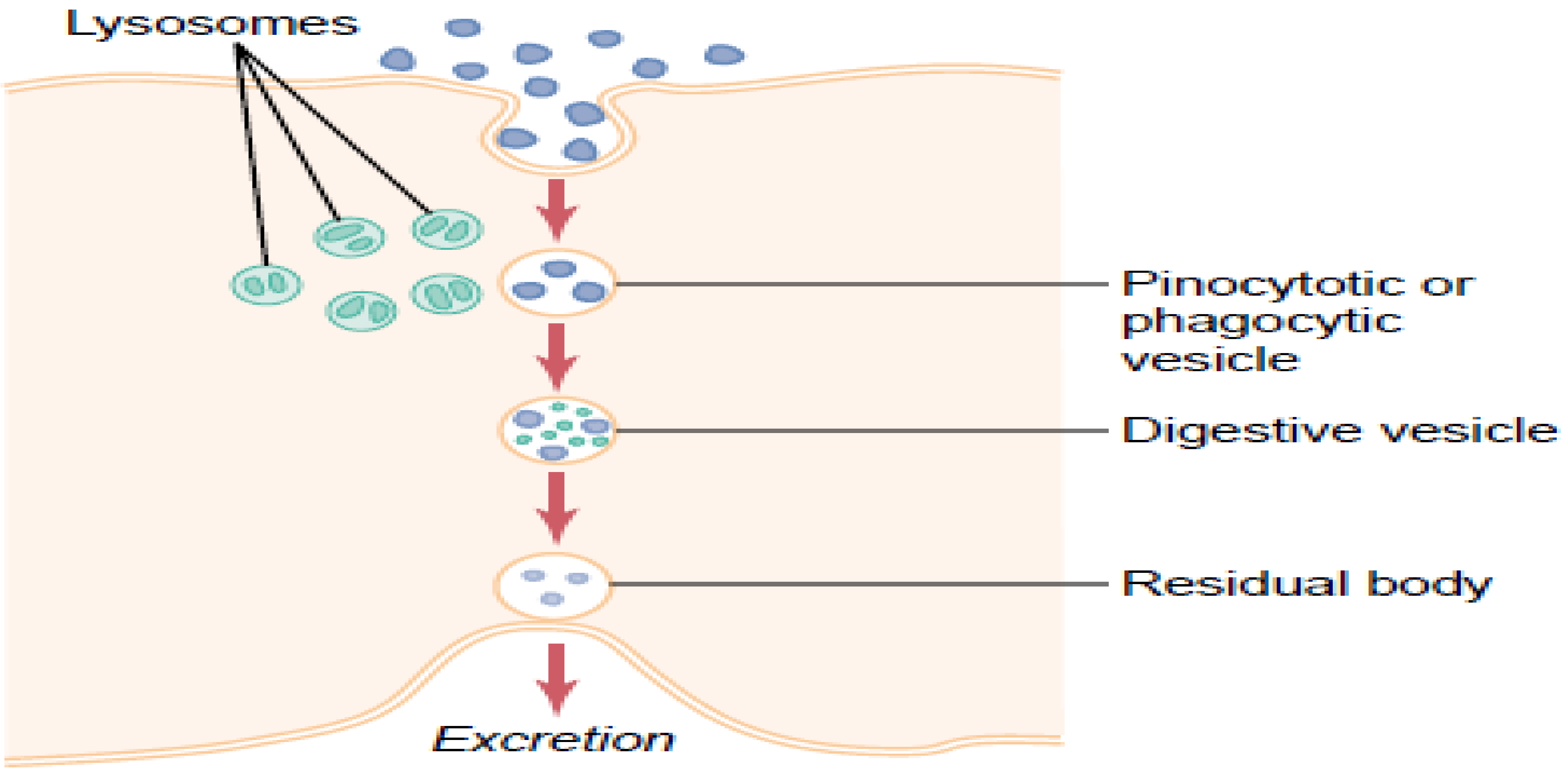


Figure 2–12

Digestion of substances in pinocytotic or phagocytic vesicles by enzymes derived from lysosomes.

Transport of Substances through Cell Membranes

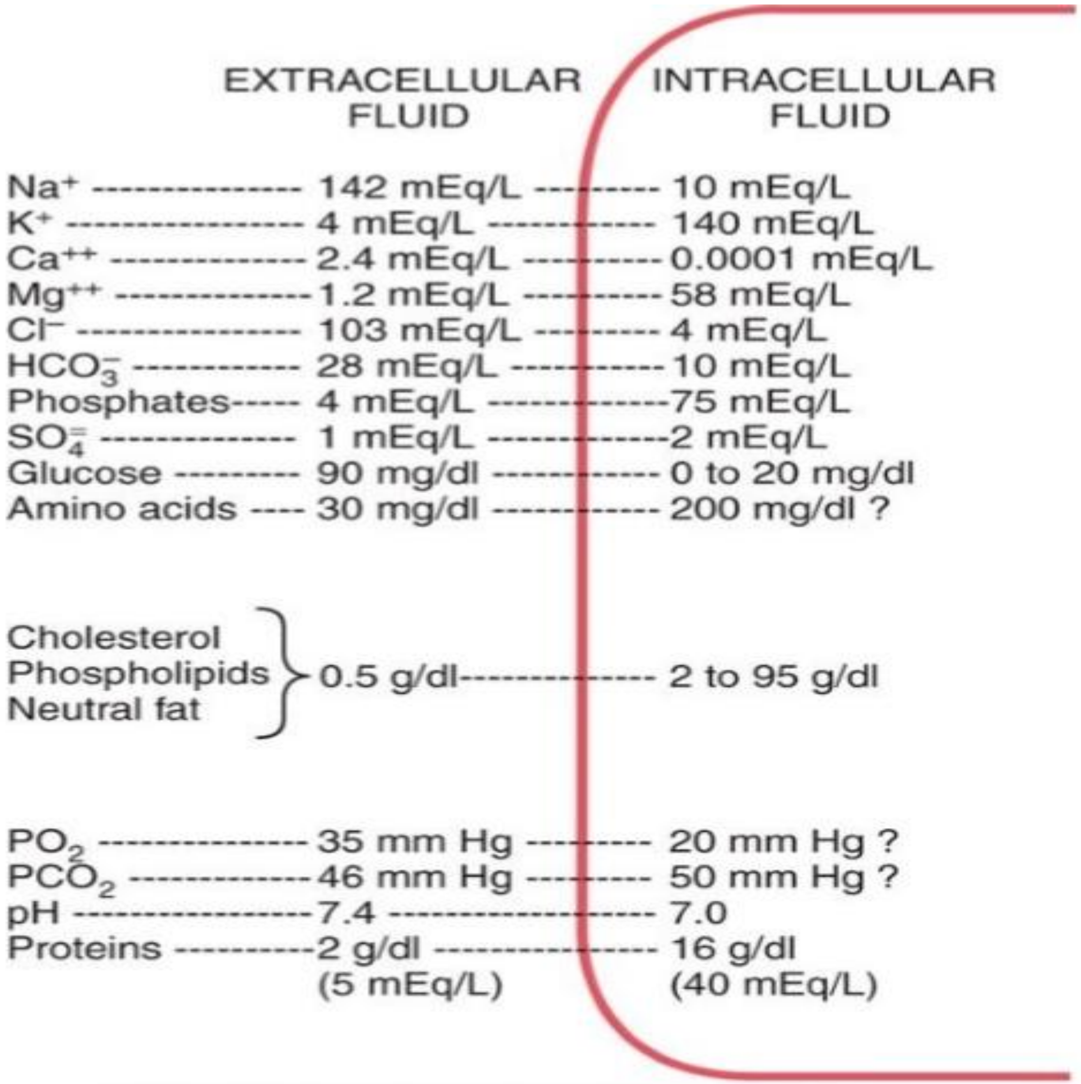


Figure 1: *Chemical compositions of extracellular and intracellular fluids.*

Transport of Substances through Cell Membranes

The ECF contains a large amount of Na^+ & Cl^- but only a small amount of K^+.
The opposite is true of the ICF for these ions.
But the conc. of phosphates and proteins in the ICF > in the ECF.

These differences are extremely important to the life of the cell.
The lipid bilayer of cell membrane is not miscible with either the ECF or the ICF.
Therefore, it constitutes ***a barrier against*** movement of water molecules and water-soluble substances between the ECF and ICF compartments.

However, few substances can penetrate this lipid bilayer, diffusing directly through the lipid substance itself; this is true mainly of ***lipid-soluble substances***.

Transport of Substances through Cell Membranes

The protein molecules in the membrane have entirely different properties for transporting substances.

Their molecular structures interrupt the continuity of the lipid bilayer, constituting an alternative pathway through the cell membrane.

Most of these penetrating proteins, therefore, can function as transport proteins.

Different proteins function differently:-

Channel proteins: Have watery spaces all the way through the molecule and allow free movement of water, as well as selected ions or molecules.

Carrier proteins: Bind with molecules or ions that are to be transported; conformational changes in the protein molecules then move the substances through the interstices of the protein to the other side of the membrane.

Both the channel proteins and the carrier proteins are usually highly selective for the types of molecules or ions that are allowed to cross the membrane.

"Diffusion" Versus "Active Transport."

Diffusion:

Random molecular movement of substances molecule either through intermolecular spaces in the membrane or in combination with a carrier protein.
The energy that causes diffusion is the energy of the normal kinetic motion of matter.

Active transport:

Movement of ions or other substances across the membrane in combination with a carrier protein in such a way that the carrier protein causes the substance to move ***against*** an energy gradient, such as from a low concentration state to a high-concentration state.

This movement requires an additional source of energy besides kinetic energy.

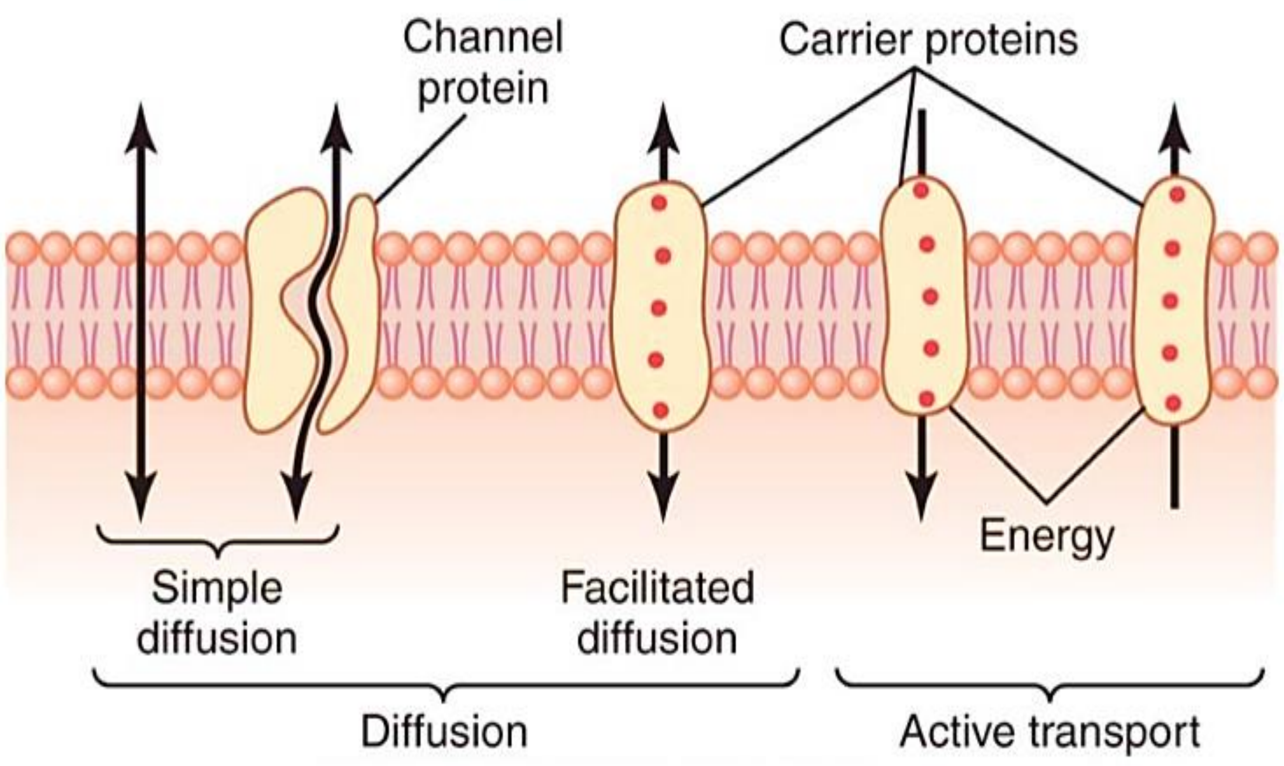


Figure 2: *Transport pathways through the cell membrane, and the basic mechanisms of transport.*

Diffusion Through the Cell Membrane

This is divided into two subtypes: (1) simple diffusion and (2) facilitated diffusion.
Simple diffusion:
Kinetic movement (of molecules or ions) through a membrane opening or through intermolecular spaces **without** any interaction with carrier proteins in the membrane.
Simple diffusion can occur through the cell membrane by two pathways:
(1) Through the interstices of the lipid bilayer if the diffusing substance is lipid soluble and
(2) Through watery channels that penetrate all the way through some of the large transport proteins
The rate of diffusion is determined by the:
Amount of substance available,
Velocity of kinetic motion, and
Number and sizes of openings in the membrane through which the molecules or ions can move. -

Facilitated diffusion:
Requires interaction of a carrier protein.
The carrier protein aids passage of the molecules or ions through the membrane by binding chemically - *with them and shuttling them through the membrane in this form.*

Diffusion of Lipid-Soluble Substances Through the Lipid Bilayer

Lipid solubility of a substance is one of the most important factors that determine the rapidly of diffuses through the lipid bilayer.

Example: *O_2, N_2, CO_2, alcohols, and steroid hormones can dissolve directly in the lipid bilayer and diffuse through the cell membrane (in the same manner that diffusion of water solutes occurs in a watery solution). This is because of their high lipid solubility.*

Diffusion of Water and Other Lipid-Insoluble Molecules Through Protein Channels

The Water:

Water is highly insoluble in the membrane lipids
But, it readily passes through channels (**aquaporin**) in protein molecules that penetrate through the membrane.
The rapidity with which water molecules can move through most cell membranes is astounding.

Other lipid-insoluble molecules

Small size and water soluble (*lipid-insoluble*) molecules can pass through the protein pore channels in the same way as water. Large size molecules **cannot** penetration the membrane.

Diffusion Through Protein Pores and Channels-Selective Permeability and "Gating" of Channels

Proteins that form **pores** or **channels** have tubular pathways all the way from the ECF to the ICF.
Integral cell membrane proteins → **Pores** (open tubes through the membrane) - always open.
The pore has diameter and electrical charges → these provide selectivity that permits only certain molecules to pass through.

For example*: the pores aquaporins or water channels, permit rapid passage of water through cell membranes but exclude other molecules.*
At least 13 different types of aquaporins have been found in various cells of the human body.
Aquaporins have a narrow pore that permits water molecules to diffuse through the membrane in single file.
The pore is too narrow to permit passage of any hydrated ions.

Integral cell membrane proteins → **Channels** that:

1. Often selectively permeable to certain substances.

This is related to the characteristics of the channel, such as its diameter, its shape, and the nature of the electrical charges and chemical bonds along its inside surfaces.

***Example**: K^+ channels permit passage of potassium ions across the cell membrane about 1000 times more readily than they permit passage of Na^+ ions.*

2. Their opening or closure is regulated by:

Electrical signals (voltage-gated channels)

The molecular conformation of the gate or of its chemical bonds responds to the electrical potential across the cell membrane.

Chemicals that bind to the channel proteins (ligand-gated channels).

The chemical causes a conformational or chemical bonding change in the protein molecule that opens or closes the gate.

***Example**: The effect of acetylcholine on the so-called acetylcholine channel.*

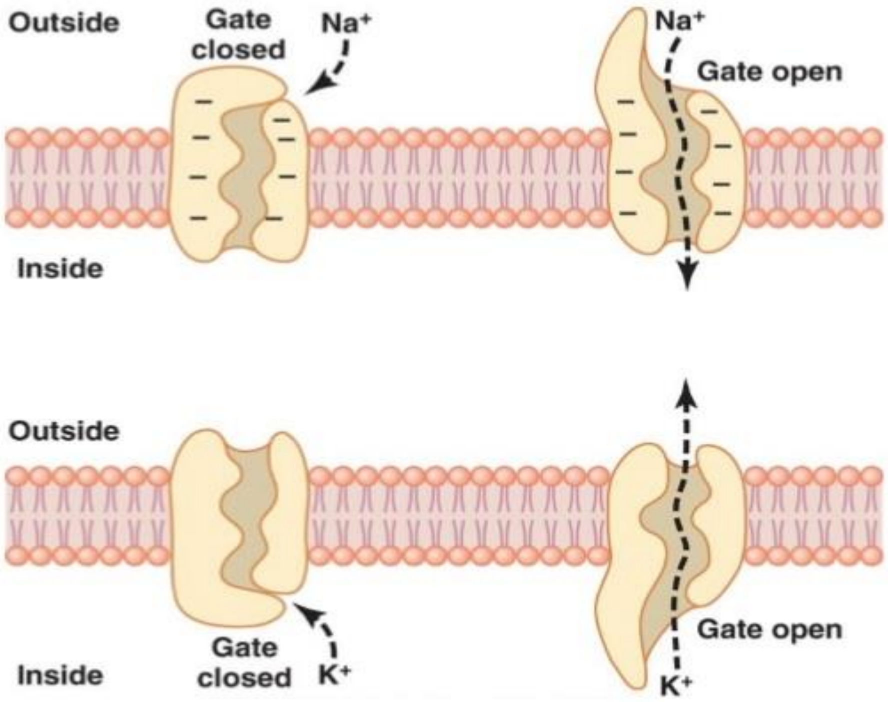


Figure 4: *Transport of sodium and potassium ions through protein channels (**ion channels**). Also shown are conformational changes in the protein molecules to open or close "gates" guarding the channels.*

Facilitated Diffusion

In this way a substance diffuses (transported) through the membrane using a specific carrier protein to help. *Also called carrier-mediated diffusion. The carrier facilitates diffusion of the substance to the other side.*

Difference between the rate of facilitated diffusion & the rate of simple diffusion: ***(see Figure 5)***

In simple diffusion the rate increases proportionately with the concentration of the diffusing substance.

In facilitated diffusion the rate approaches a maximum, called Vmax, as the concentration of the diffusing substance increases.

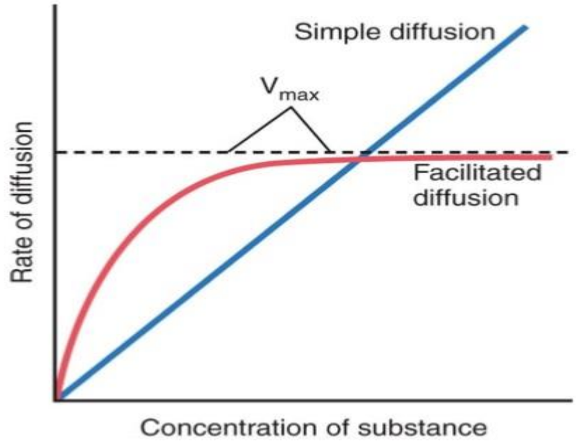


Figure 5: *Effect of concentration of a substance on rate of diffusion through a membrane by simple diffusion and facilitated diffusion. This shows that facilitated diffusion approaches a maximum rate called the V_{max}.*

Steps in the transported by facilitated diffusion:

1. The molecule enters the pore.
2. Bound weakly to the inside of the pore
3. Conformational (chemical change) occurs in the carrier protein [**in a fraction of a second**].
4. The pore now opens to the opposite side of the membrane.
5. Released of the molecule on the opposite side of the membrane.

This is because the binding force of the receptor

is weak thus the thermal motion of the attached mo

***Example**: Among the most important substances*

that cross cell membranes by facilitated diffusion

are glucose and most of the amino acids.

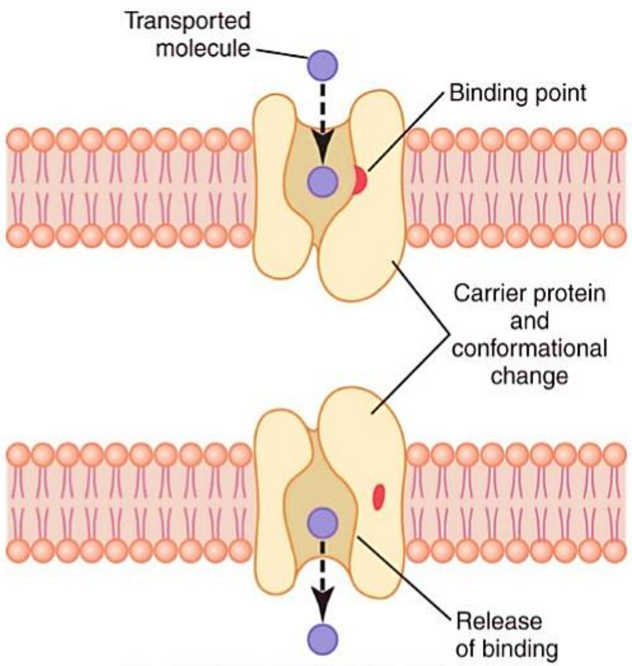


Figure 6: *Postulated mechanism for facilitated diffusion.*

Active Transport" of Substances Through Membranes

Sometimes, a large conc. of a substance is required in the ICF even though the ECF contains only a small conc. ***This is true, for instance, for potassium ions.***
Conversely, it is important to keep the conc. of other ions very low inside the cell even though their conc. in the ECF are great. ***This is especially true for sodium ions.***
Neither of these two effects could occur by simple diffusion. Why?
Because simple diffusion eventually equilibrates conc. on the two sides of the membrane.

Thus instead of simple diffusion, some energy source must cause excess movement of potassium ions to the inside of cells and excess movement of sodium ions to the outside of cells against their conc. or electrical gradients, the process is called ***active transport****.*

Active transport is divided into two types according to the source of the energy used to cause the transport:

In both instances, transport depends on carrier proteins that penetrate through the cell membrane.

Primary Active Transport

The energy is derived directly from breakdown of ATP or of some other high- energy phosphate compound.

Sodium-Potassium Pump

- Among the substances that are transported by primary active transport are Na^+, K^+, Ca^{2+}, H^+, Cl^-, and a few other ions.
- Na^+-K^+ pumps Na^+ ions out of the cell through the cell membrane and at the same time pumps K^+ ions from the outside to the inside. This pump is responsible for maintaining the Na^+ and K^+ conc. differences across the cell membrane, as well as for establishing a negative electrical voltage inside the cells (electrogenic pump). (***See Figure 7***)
  - ✓ *When two potassium ions bind on the outside of the carrier protein and three sodium ions bind on the inside, the ATPase function of the protein becomes activated.*
  - ✓ *This then cleaves one molecule of ATP, splitting it to adenosine diphosphate (ADP) and liberating a high-energy phosphate bond of energy.*
  - ✓ *This liberated energy is then believed to cause a chemical and conformational change in the protein carrier molecule, extruding the three sodium ions to the outside and the two potassium ions to the inside.*

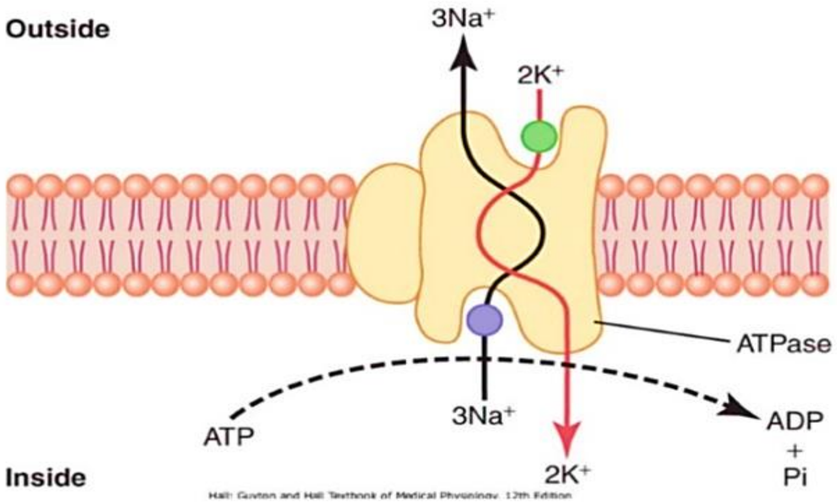


Figure 7: *Postulated mechanism of the sodium-potassium pump. ADP, adenosine diphosphate; ATP, adenosine triphosphate; Pi, phosphate ion.*

Calcium pump

Ca^{2+} ions are maintained normally at extremely low conc. in the cytosol of virtually all cells in the body.

At a conc. about 10,000 times less than that in the ECF fluid.

This is achieved mainly by **two** primary active transport calcium pumps.

One is in the cell membrane and pumps calcium to the ***outside*** *of the cell.*

The other pumps calcium ions into one or more of the intracellular vesicular organelles of the cell, such as the ***sarcoplasmic reticulum*** *of muscle cells and the* ***mitochondria*** *in all cells.*

Primary Active Transport of Hydrogen Ions

At two places in the body, primary active transport of hydrogen ions is important: ➢

In the gastric glands of the stomach. -

In the late distal tubules and cortical collecting ducts of the kidneys. -

Secondary Active Transport

The energy is derived secondarily from energy that has been stored in the form of ionic conc. differences of secondary molecular or ionic substances between the two sides of a cell membrane, created originally by primary active transport

"Co-Transport" and "Counter-Transport"

When Na^+ ions transported → out of cell by primary active transport → develop conc. gradient across the membrane (high out and low in) → this gradient represents a storehouse of energy.

(because the excess sodium outside the cell membrane is always attempting to diffuse to the interior)

In **"Co-Transport":** Under appropriate conditions, this diffusion energy of Na^+ can pull other substances along with the Na^+ through the cell membrane. This phenomenon is called co-transport; it is one form of secondary active transport. ***Example**: Glucose and many amino acids are transported into most cells against large conc. gradients (**See Figure 8**).*

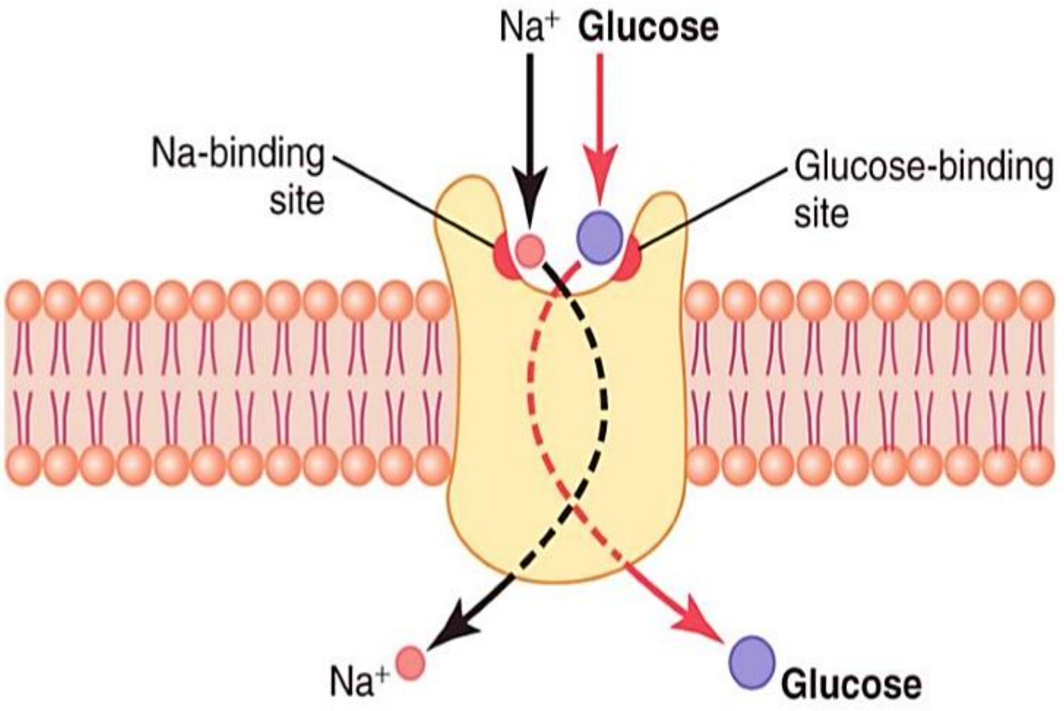


Figure 8: *Postulated mechanism for sodium co-transport of glucose.*

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