General Biology (Biol-1012)

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MSc. in Ecotoxicology and Env’tal Health

Unit 1. Introduction

1.1 The meaning and scope of biology

Biological Sciences is the study of life and living organisms.

It is also concerned with the physical characteristics and behaviors of organisms.

Therefore, Biology is the science of Living Things. That is why Biology is sometimes known as Life Science. The life sciences can be defined as —a systematic study of living beings or study of nature.

1.2 The origin and nature of life

The question —what is life?

The evolution of life on earth has involved the following sequence of events.

The first living things to appear were the simplest creatures, single-celled organisms. From these came more complex, multi-cellular organisms.

Scientists generally agree that the time from the formation of our solar system until now has been on the order of some 4.5 billion years.

Summary of Theories on Origin of life

1. Theory of Special Creation:

- According to this theory, all the different forms of life that occur today on planet earth have been **created by God, the almighty**.

2. Theory of Spontaneous Generation:

This theory assumed that living organisms could arise suddenly and spontaneously from any kind of non-living matter.

One of the firm believers in spontaneous generation was Aristotle, the Greek philosopher (**384-322 BC**).

3. Theory of Catastrophism:

- A modification of the theory of Special Creation.
- It states that there have been several creations of life by God, each preceded by a catastrophe resulting from some kind of geological disturbance.
- According to this theory, since each catastrophe completely destroyed the existing life, each new creation consisted of life form different from that of previous ones.

4. Cosmozoic Theory (Theory of Panspermia):

- According to this theory, life has reached this planet Earth from other heavenly bodies such as meteorites, in the form of highly resistance spores of some organisms. This idea was proposed by Richter in 1865 and supported by Arrhenius (1908) and other contemporary scientists.
- The theory did not gain any support. This theory lacks evidence, hence it was discarded.

5. Theory of Chemical Evolution:

- This theory is also known as Materialistic Theory or Physico-chemical Theory.
- According to this theory, Origin of life on earth is the result of a slow and gradual process of chemical evolution that probably occurred about 3.8 billion years ago.
- This theory was proposed independently by two scientists - A. I. Oparin, a Russian scientist in 1923 and J.B.S Haldane, an English scientist, in 1928.

Nature and characteristics of life

- Life is defined as a "condition" that distinguishes animals and plants from inorganic materials and dead organisms.

* The most sophisticated form of life is man as a result of this we focuses upon the nature of the life and death of man.

- Man demonstrates three lives or aspects of life:

 Life of the body: which is basic existence demonstrated by the presence of functions. **(Physiology)**

 Life of the mind: contributes effectiveness and scope

 Life of the spirit: spiritual entity contributes maximum

Living tissues and organisms exhibit:

- **Irritability**: the ability to be excited or detect stimuli and to respond to that
- **Growth** and **reproduction**: this consists of the power of multiplication, regeneration and differentiation
- **Adaptability**: permitting both change and maintenance of balances (homeostasis)
- **Metabolism**: the transformation of energy and the use of materials.

- **Excretion**: excretion and osmoregulation are two important homeostatic processes occurring in living cells, helping them to maintain a constant internal environment, or steady state.
- Excretion is the removal from the cell of waste products of metabolism.
- In plant cells the major excretory products are oxygen from photosynthesis and carbon dioxide from cell respiration.

1.3 Scientific methods

- It is a process for experimentation that is used to explore observations and answer questions.
- It is an experimental method of acquiring knowledge.
- It is also the technique used in the construction and testing of a scientific hypothesis.

- The scientific method has five basic steps, plus one feedback step:

 Make an observation.

 Ask a question.

 Form a hypothesis, or testable explanation.

 Make a prediction based on the hypothesis.

 Test the prediction.

 Iterate: use the results to make new hypotheses or predictions.

- **Observation** - Quantitative and qualitative measurements of the world.
- **Inference** - Deriving new knowledge based upon old knowledge.
- **Hypotheses** –A suggested explanation.
- **Rejected Hypothesis** - An explanation that has been ruled out through experimentation.
- **Accepted Hypothesis** - An explanation that has not been ruled out through excessive experimentation and makes verifiable predictions that are true.
- **Experiment** - A test that is used to rule out a hypothesis or validate something already known.
- **Scientific Method** - The process of scientific investigation.
- **Theory** - A widely accepted hypothesis that stands the test of time. Often tested, and usually never rejected.

Summary of the scientific method

- Step 1: Observe behavior or other phenomena
- Step 2: Form a tentative answer or explanation (a hypothesis (guess a reason)
- Step 3: Use your hypothesis to generate a testable prediction
- Step 4: Make systematic, planned observations (data collection)
- Step 5 : Results and Discussion Use the observations to evaluate (support, refute, or refine) the original hypothesis
- Step 6: Conclusion
- Step 7: Recommendation

Chapter review questions

1. List dawn all the steps used in scientific methods
2. Propose a hypothesis in an attempt to find explanations for this curiosity
3. Explain the differences between control and variable group
4. List down the characteristics common to all living things
5. What is a controlled experiment? Why is it essential to have a control group in scientific experiment?
6. Explain the theories on the origin of life.
7. What are the branches of biology?

Unit 2. Biological Molecules

- The molecules of life that are basically found in a living cell and categorized as organic and inorganic molecules in general.
- The organic biomolecules are proteins, carbohydrates, lipids and nucleic acids.
- They are important either structurally or functionally for cells.
- The most commonly known inorganic molecules are water and minerals, which are still important for the normal functioning of the cell.

2.1 Carbohydrates

Made of atoms of carbon, hydrogen and oxygen.

They are an important source of energy and they also provide structural support for cells and help with communication between cells (cell-cell recognition).

They are found in the form of either a sugar or many sugars linked together, called saccharides.

Carbohydrates are polyhydroxy aldehydes or ketones, or substances that yield these compounds on hydrolysis.

Example: Glucose is an aldehyde while fructose is a ketone.

- Based on the number sugar units they contain, they are categorized into three, as follows.
- A single sugar molecule containing carbohydrate is known as a **monosaccharides**, while two and many having are regarded as **disaccharides** and **polysaccharides**, respectively.
- Each of the sugar molecules are bonded together through the **glycosidic linkage/s.**

A. Monosaccharides

- They are simple sugars with multiple OH groups.
- Monosaccharides containing the aldehyde group are classified as aldoses, and those with a ketone group are classified as ketoses.
- All monosaccharides (Aldoses and ketoses) are reducing sugars. This is important in understanding the reaction of sugars with Benedict's reagent.
- However, in water pentoses and hexoses exist mainly in the cyclic form, and it is in this form that they combine to form larger saccharide molecules.

Glucose

- Glucose is the most important carbohydrate fuel in human cells.
- Its concentration in the blood is about 1 gdm^{-3} .
- The small size and solubility in water of glucose molecules allows them to pass through the cell membrane into the cell.
- Two glucose molecules react to form the disaccharide maltose.
- Starch and cellulose are polysaccharides made of glucose units.

Galactose

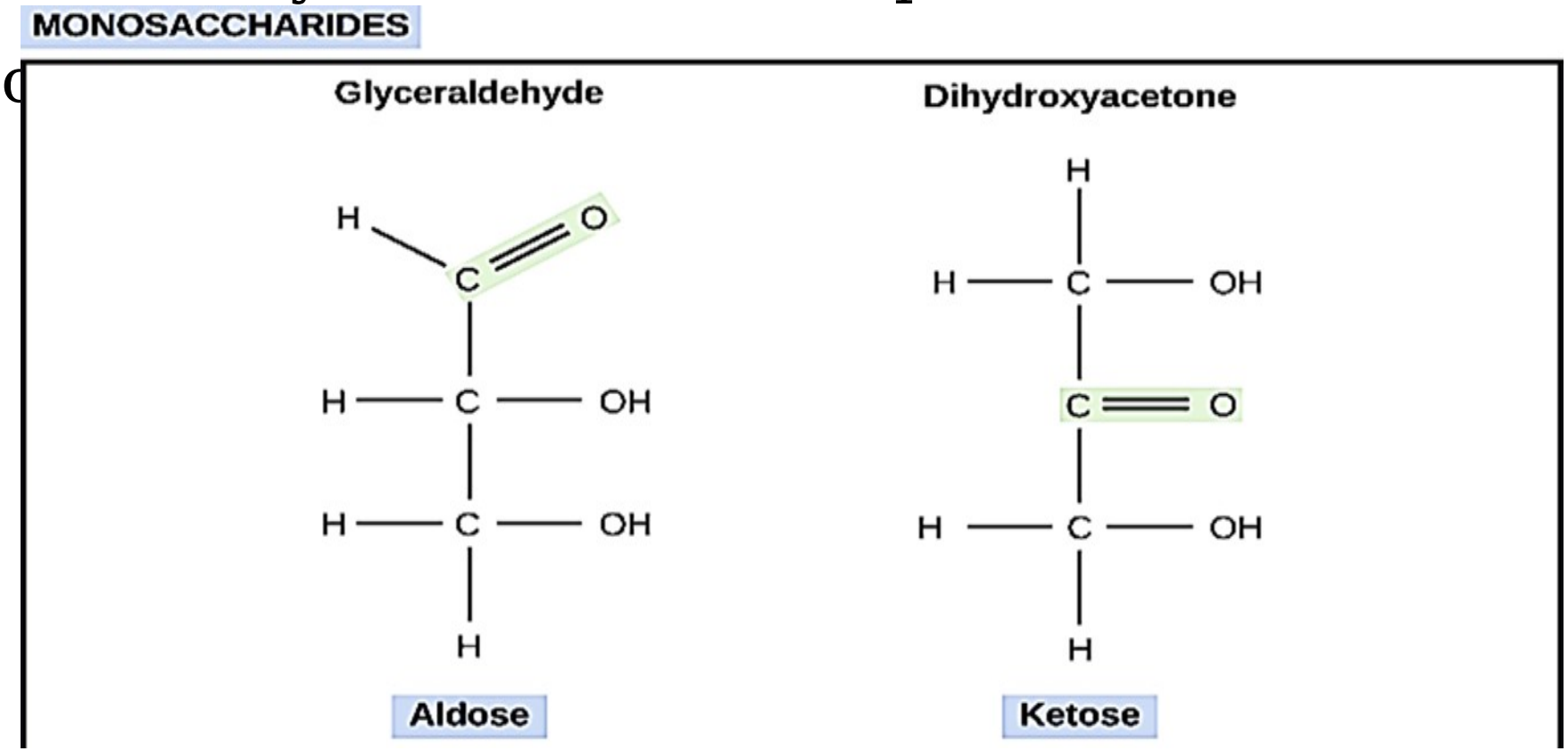
- They can also exist in α and β forms. Galactose reacts with glucose to make the disaccharide **lactose**.

Fructose

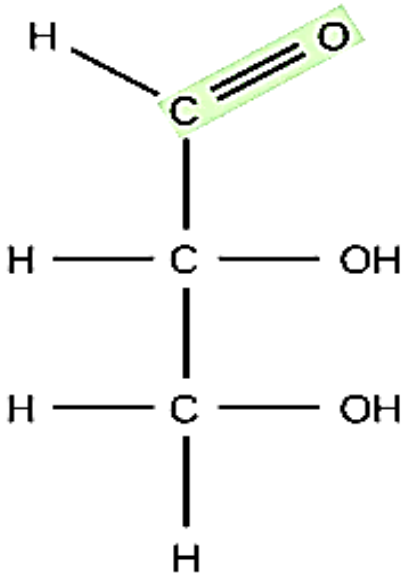
- It also has a five-atom ring rather than a six-atom ring.
- Fructose, glucose and galactose are all hexoses.
- Fructose reacts with glucose to make the disaccharide **sucrose**

Ribose and deoxyribose

- Ribose and deoxyribose are pentoses.
- The ribose unit forms part of a nucleotide of RNA.
- The deoxyribose unit forms part of the nucleotide

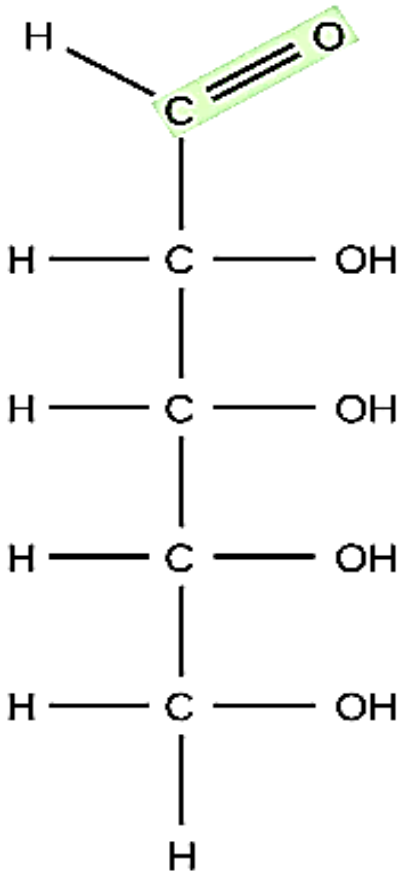


Glyceraldehyde



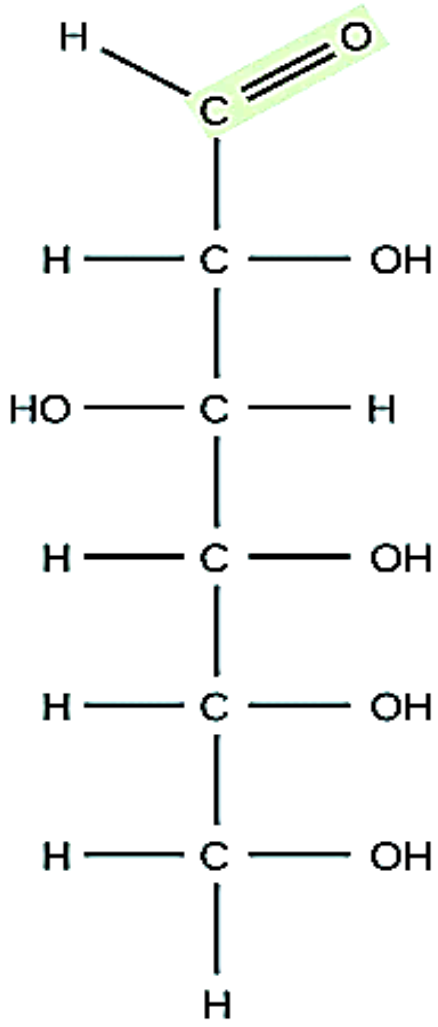
Triose

Ribose



Pentose

Glucose



Hexose

- Figure 1. Monosaccharides are classified based on the position of their carbonyl group and the number of carbons in the backbone.
- **Aldoses** have a carbonyl group at the end of the carbon chain, and **ketoses** have a carbonyl group in the middle of the carbon chain.
- Trioses, pentoses, and hexoses have three, five, and six carbon backbones, respectively.

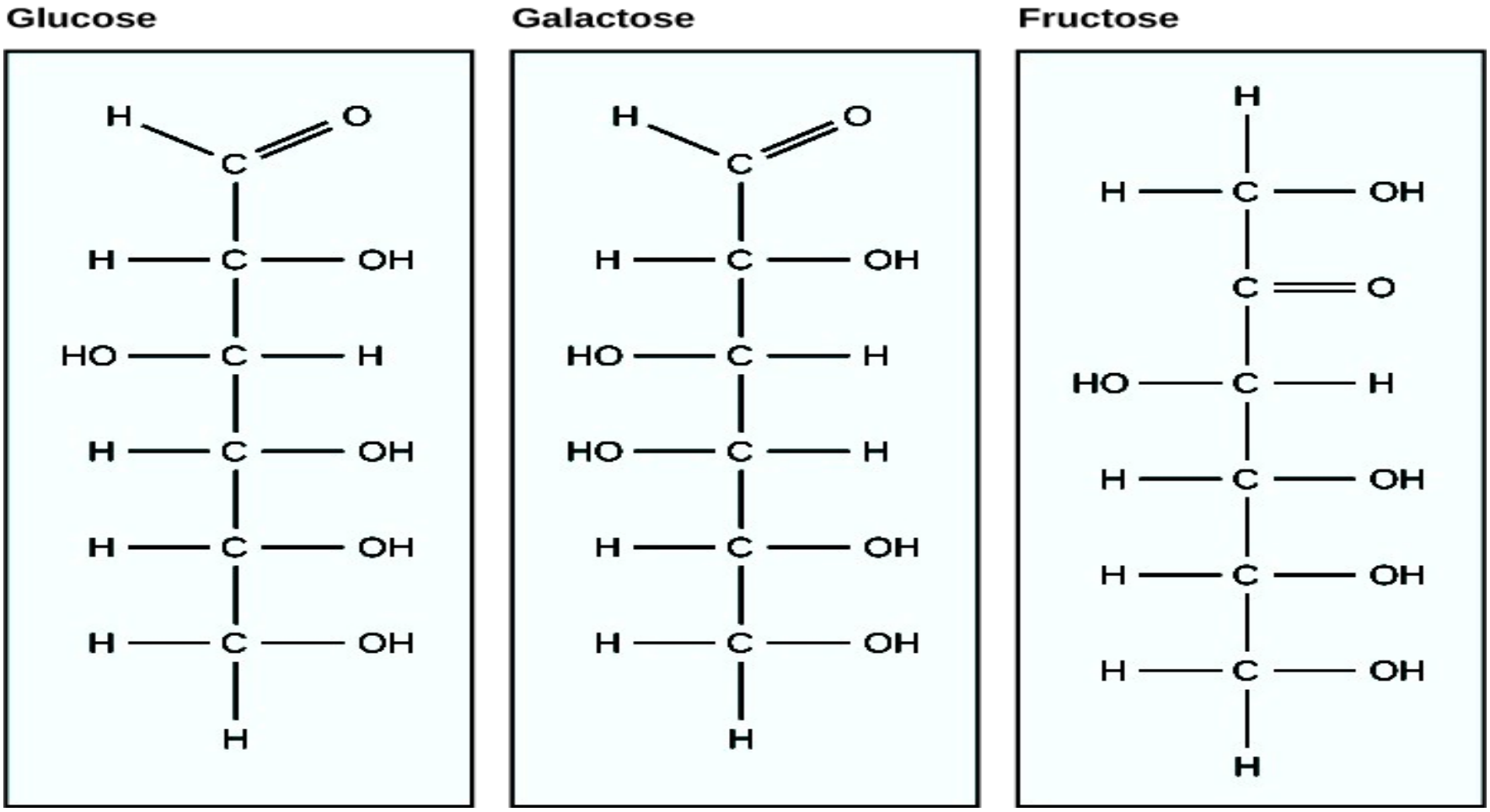
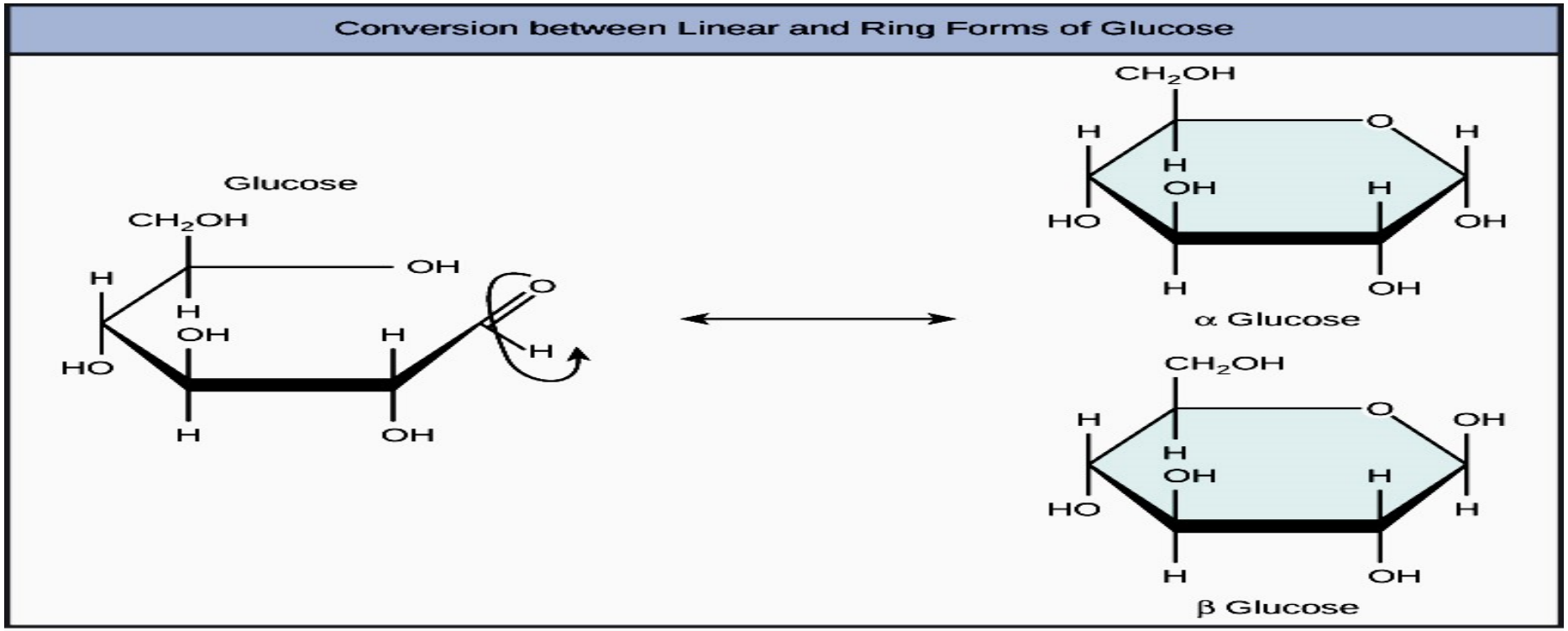


Figure 2. Glucose, galactose, and fructose are all hexoses. They are structural isomers, meaning they have the same chemical formula ($C_6H_{12}O_6$) but a

- Monosaccharides can exist as a linear chain or as ring-shaped molecules; in aqueous solutions they are usually found in ring forms (Figure 3).
- Glucose in a ring form can have two different arrangements of the hydroxyl group (−OH) around the anomeric carbon (carbon 1 that becomes asymmetric in the process of ring formation).
- If the hydroxyl group is below carbon number 1 in the sugar, it is said to be in the alpha (α) position, and if it is above the plane, it is said to be in the beta (β) position.



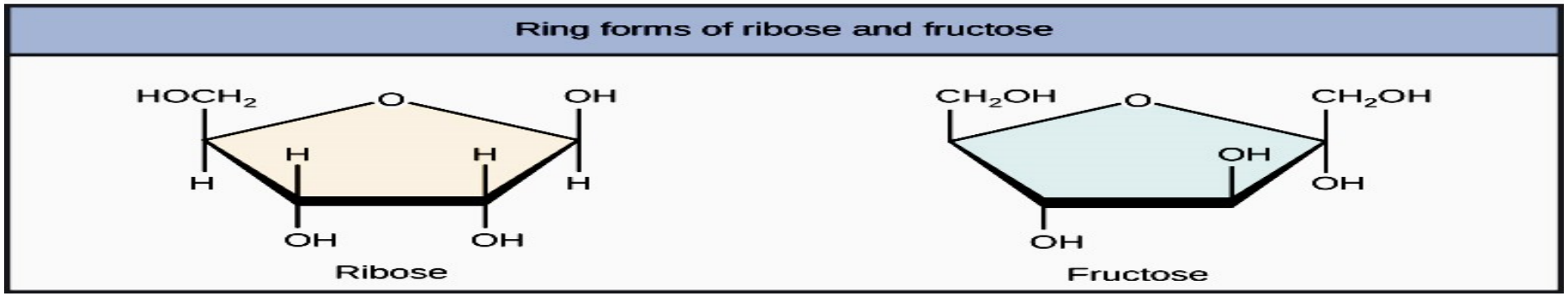
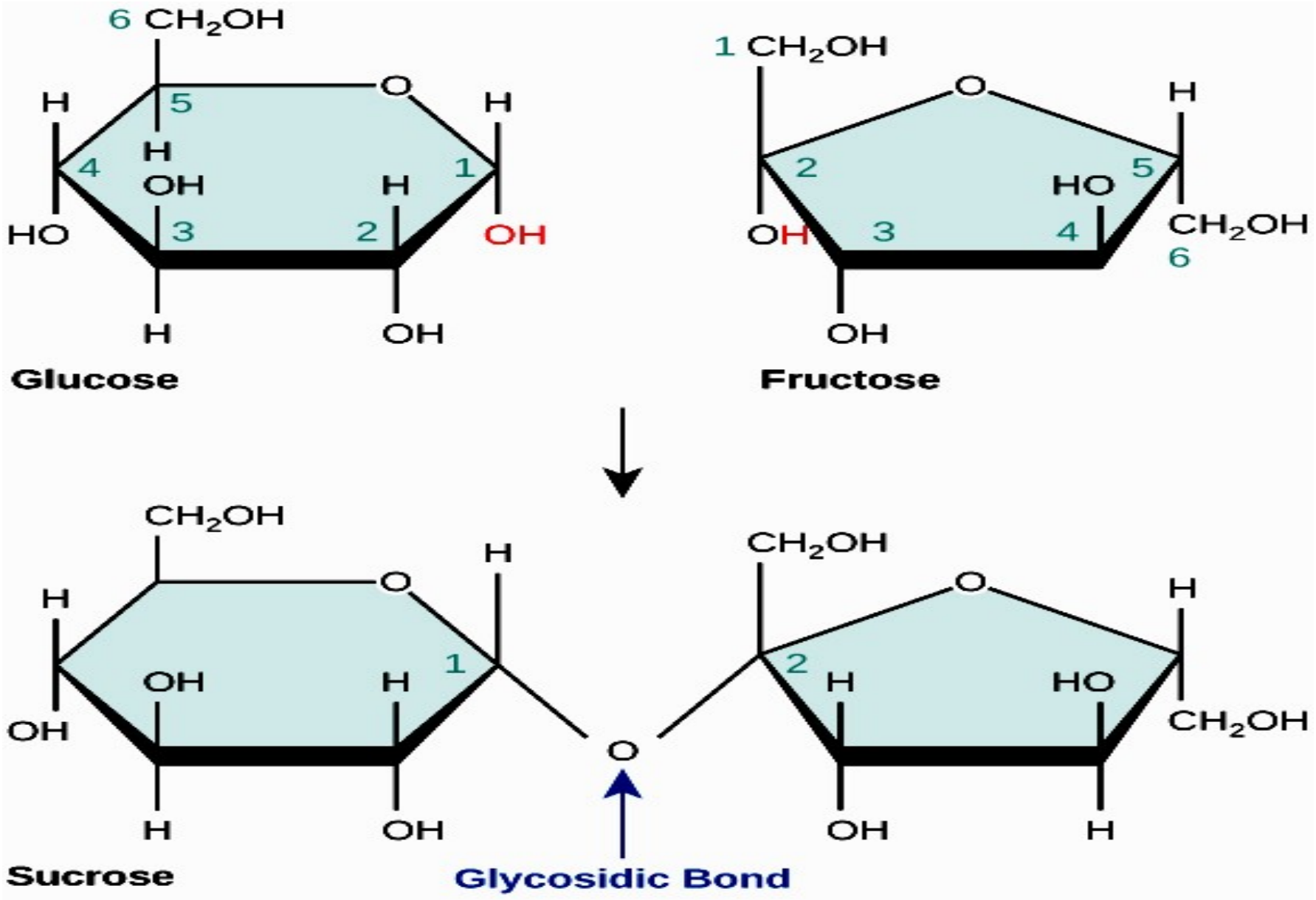


Figure 3. Five and six carbon monosaccharides exist in equilibrium between linear and ring forms. When the ring forms, the side chain it closes on is locked into an α or β position. Fructose and ribose also form rings, although they form five-membered rings as opposed to the six-membered ring of glucose.

B. Disaccharides

- Monosaccharides are rare in nature. Most sugars found in nature are disaccharides.
- Disaccharides are soluble in water.
- **Disaccharides** form when two monosaccharides undergo a dehydration reaction (also known as a **condensation reaction or dehydration synthesis**).
- During this process, the hydroxyl group of one monosaccharide combines with the hydrogen of another monosaccharide, releasing a molecule of water and forming a covalent bond.

- A covalent bond formed between a carbohydrate molecule and another molecule (in this case, between two monosaccharides) is known as a **glycosidic bond** (Figure 4).
- Glycosidic bonds (also called glycosidic linkages) can be of the alpha or the beta type.


6 CH2OH
H
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1
HO
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H
OH
Glucose
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5
HO
OH
3
4
CH2OH
6
OH
Fructose
CH2OH
H
O
H
1
OH
H
OH
H
OH
O
CH2OH
O
H
2
H
HO
CH2OH
OH
H
Sucrose
Glycosidic Bond

- Figure 4 above, Sucrose is formed when a monomer of glucose and a monomer of fructose are joined in a dehydration reaction to form a glycosidic bond.
- By convention, the carbon atoms in a monosaccharide are numbered from the terminal carbon closest to the carbonyl group.
- In sucrose, a glycosidic linkage is formed between carbon 1 in glucose and carbon 2 in fructose.

- The three most important disaccharides are sucrose, lactose and maltose.

- Sucrose is a non-reducing sugar.
- Lactose and maltose are reducing sugars.

* Lactose: glucose and galactose. It is found naturally in milk.
* Maltose, or malt sugar: rxn between two glucose molecules.
* The most common disaccharide is sucrose, or table sugar, which is composed of the monomers glucose and fructose.

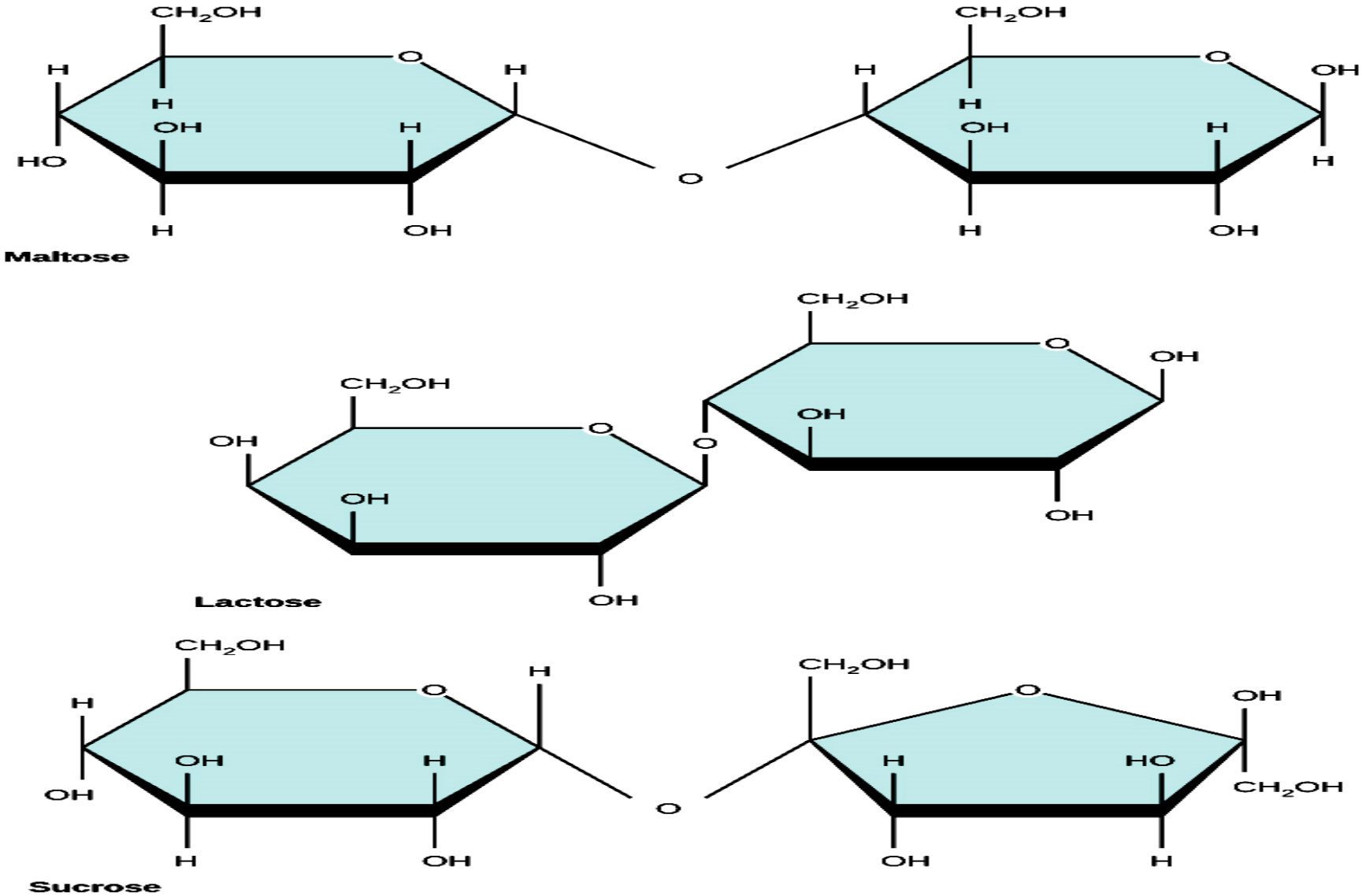


Figure 5. Common disaccharides include maltose (grain sugar), lactose (milk sugar), and sucrose (table sugar).

C. Polysaccharides

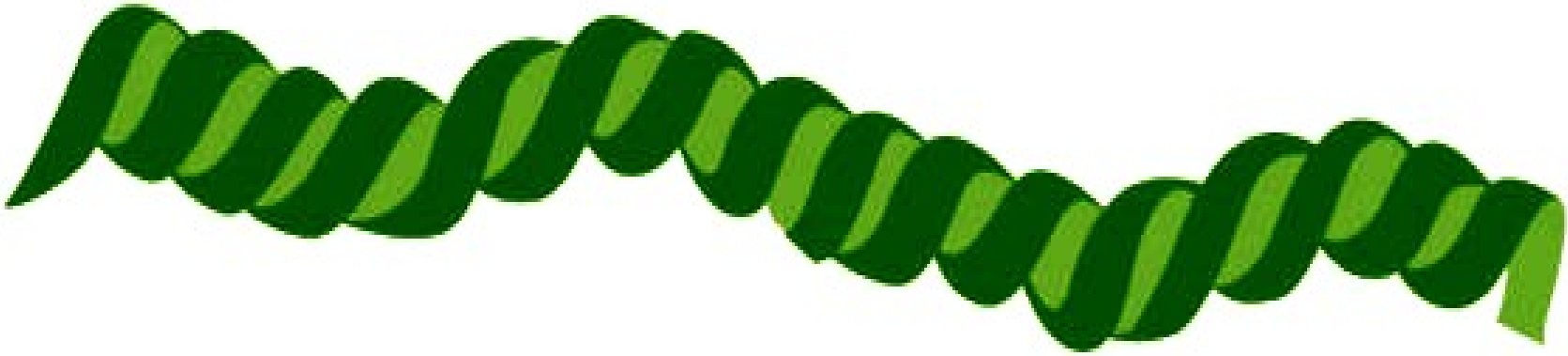
- Monosaccharides can undergo a series of condensation reactions, adding one unit after another to the chain until very large molecules (polysaccharides) are formed. This is called **condensation polymerization**, and the building blocks are called **monomers**.
- **The properties of a polysaccharide molecule depend on**:

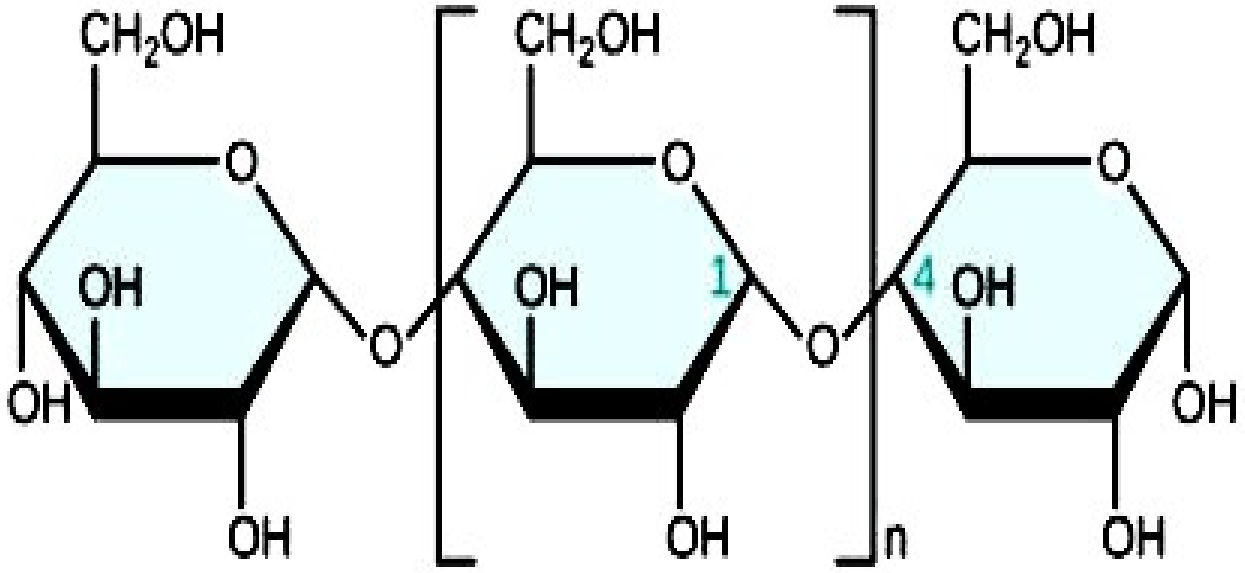
 Its length (though they are usually very long)
 The extent of any branching (addition of units to the side of the chain rather than one of its ends)
 Any folding which results in a more compact molecule

Starch

- Starch is often produced in plants as a way of storing energy.
- It exists in two forms: **amylose** and **amylopectin**. Both are made from α-glucose.
- Starch is made up of glucose monomers that are joined by *α* 1-4 or *α* 1-6 glycosidic bonds.
- **Amylose** is an unbranched polymer of α-glucose (only *α* 1-4 linkages). The molecules coil into a helical structure & forms a colloidal suspension in hot water.
- **Amylopectin** is a branched polymer of α-glucose (connected by α 1-4 and α 1-6 glycosidic linkages) *α* 1-6 linkages at the branch points). It is completely insoluble in

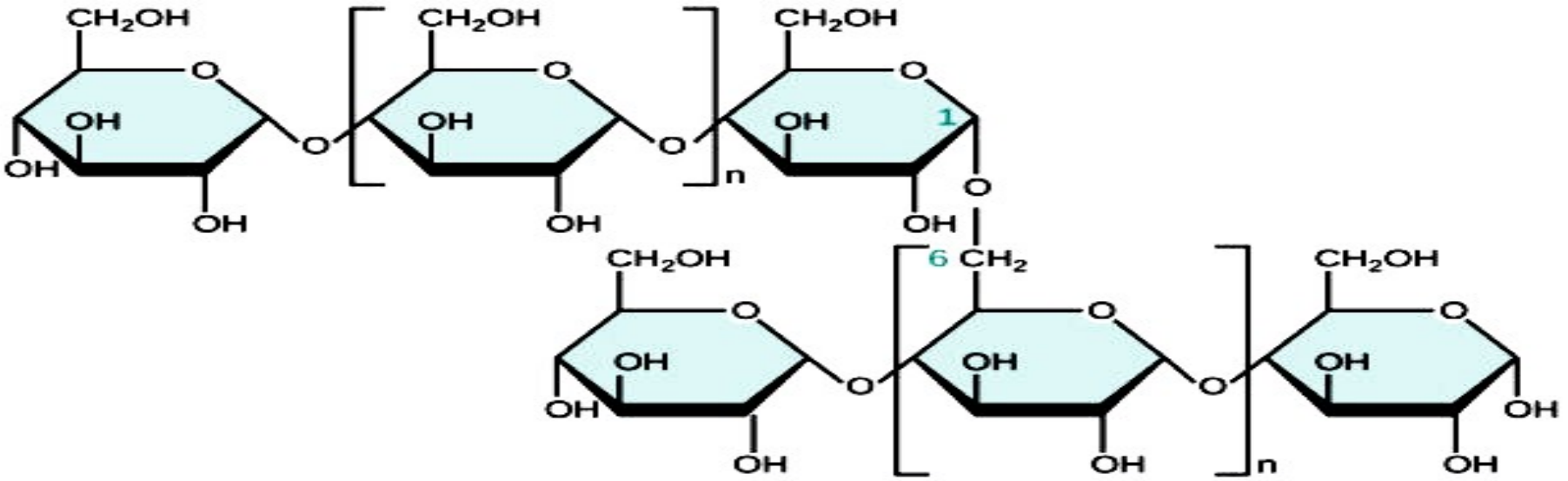
Amylose





Amylopectin





Glycogen

- It is similar in structure to amylopectin but more highly branched.
- It is the storage form of glucose in humans and other vertebrates and is made up of monomers of glucose.
- Glycogen is the animal equivalent of starch and is a highly branched molecule usually stored in liver and muscle cells. Whenever blood glucose levels decrease, glycogen is broken down to release glucose in a process known as **glycogenolysis**.
- Starch from plants is hydrolyzed in the body to produce glucose. Glucose passes into the cell and is used in metabolism. Inside the cell, glucose can be polymerized to make glycogen which acts as a carbohydrate energy store.

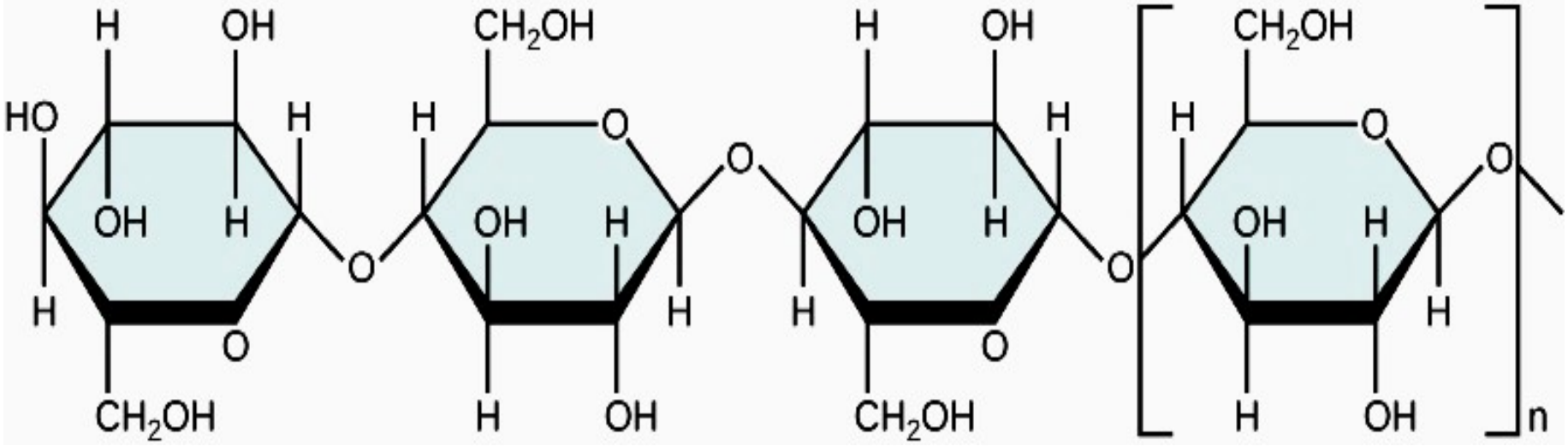
Cellulose

- Cellulose is a third polymer made from glucose. But this time it's made from β-glucose molecules and the polymer molecules are 'straight'.
- Cellulose serves a very different purpose in nature to starch and glycogen. It makes up the cell walls in plant cells. These are much tougher than cell membranes. This toughness is due to the arrangement of glucose units in the polymer chain and the hydrogen-bonding between neighboring chains.
- Cellulose is not hydrolyzed easily and, therefore, cannot be digested so it is not a source of energy for humans. The stomachs of Herbivores contain a specific enzyme called **cellulase** which enables them to digest cellulose.

Cellulose fibers



Cellulose structure



Summary of carbohydrates

- The most abundant organic molecules in nature
- Are polyhydroxy aldehydes or ketones, or substances that yield these compounds on hydrolysis
- Provide a significant part of the energy in the diet of most organisms
- Important source of energy for cells
- Can act as a storage form of energy
- Can be structural components of many organisms
- Can be cell-membrane components mediating intercellular communication
- Can be cell-surface antigens
- Can be part of the body‘s extracellular ground substance
- Can be associated with proteins and lipids
- Part of RNA, DNA, and several coenzymes (NAD+, NADP+, FAD, CoA)

2.2 Lipids

- Lipids are a highly variable group of molecules that include fats, oils, waxes and some steroids.
- They are esters of fatty acids and alcohol (glycerol or chains of alcohols).
- Fatty acids are made mostly from chains of carbon and hydrogen and they bond to a range of other types of atoms to form many different lipids.
- The primary function of lipids is **to store energy**.
- A lipid called a **triglyceride** is a fat if it is solid at room temperature and oil if it is liquid at room temperature.

In addition, triglycerides are stored in the fat cells, also called **adipocytes** or **lipocytes**

- Various types of lipids occur in the human body:

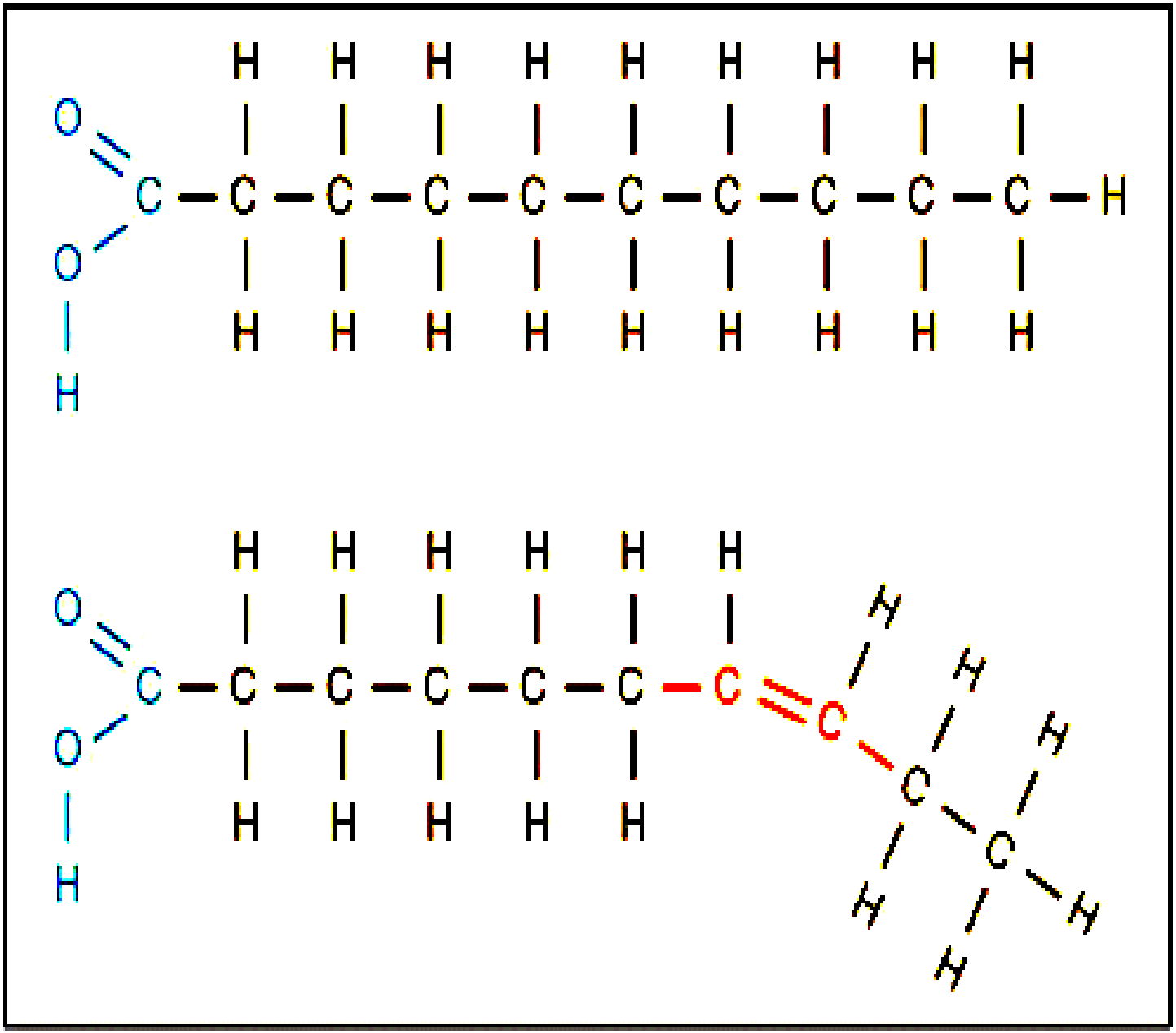
- **triglycerol** * **cholesterol**
- **polar lipids**, which include **phospholipids**, **glycolipids** and **sphingolipids**.

Plant leaves are coated with lipids called **waxes** to prevent water loss, and the honeycomb in a beehive is made of beeswax.

- Lipids that have tail chains with only single bonds between the carbon atoms are called saturated fats because no more hydrogens can bond to the tail.
- Lipids that have at least one double bond between carbon atoms in the tail chain can accommodate at least one more hydrogen and are called unsaturated fats.
- Fats with more than one double bond in the tail are called polyunsaturated fats.

(a) Saturated

(b) Unsaturated



Properties of lipids

- Insoluble in water
- Longer chains More hydrophobic, less soluble
- Double bonds increase solubility
- Melting points: Depend on chain length and saturation

  Unsaturated fatty acids are liquid at room temperature.

Importance of lipids

 As the main component of cell membranes (phospholipids)

 Insulation of heat and water,

2.3 Proteins

A protein is a compound made of small carbon compounds called amino acids.

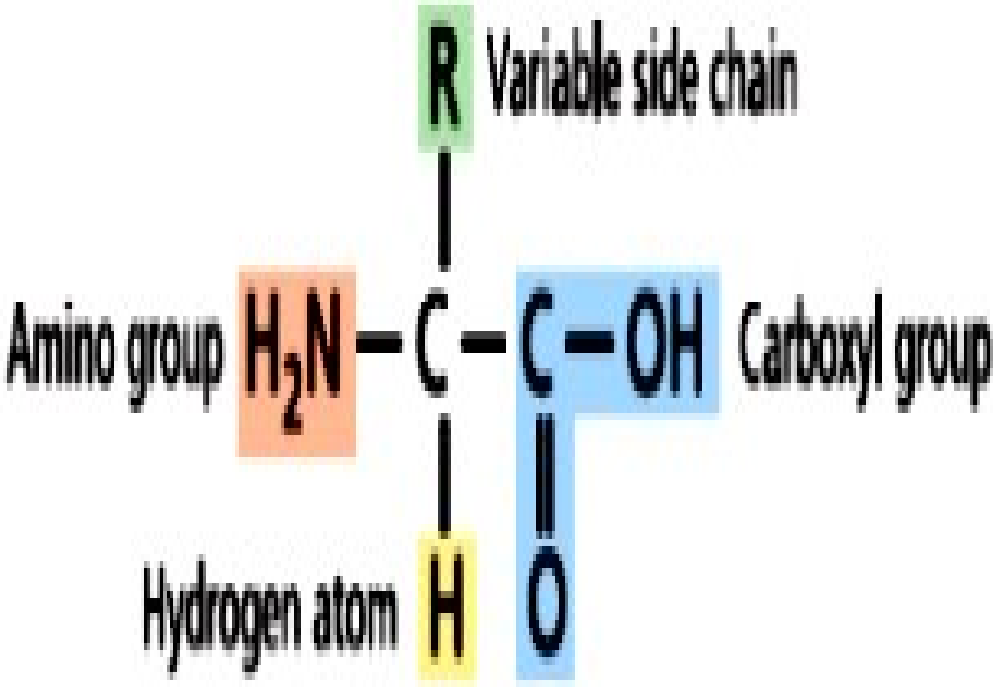
Amino acids are small compounds that are made of carbon, nitrogen, oxygen, hydrogen, and sometimes sulfur.

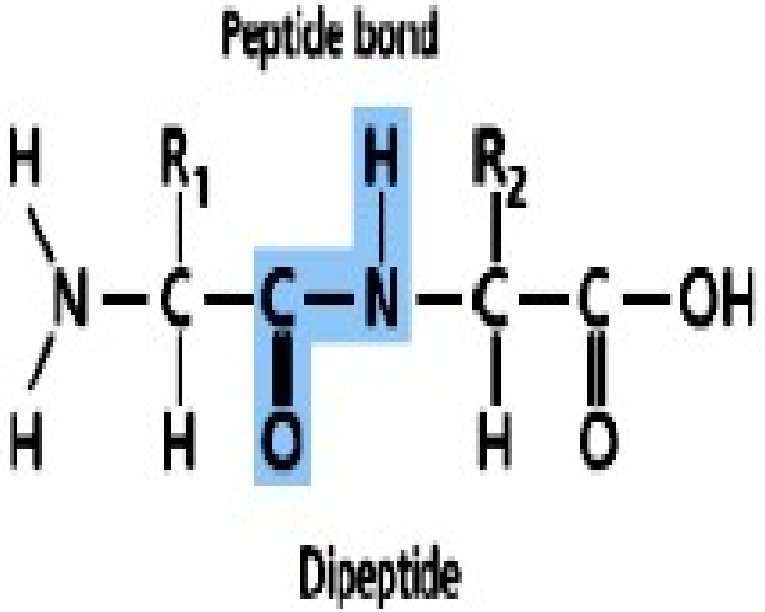
Recall that carbon can form four covalent bonds. One of those bonds is with hydrogen. The other three bonds are with an amino group (–NH2), a carboxyl group (–COOH), and a variable group (–R).

Several covalent bonds called peptide bonds join amino acids together to form proteins, which are also shown in fig. below.

A peptide forms between the amino group of one

ɔup of another.





- Based on the variable groups contained in the different amino acids, proteins can have up to four levels of structure.

The number of amino acids in a chain and the order in which the amino acids are joined define the protein‘s primary structure (the hormone insulin). After an amino acid chain is formed, it folds into a unique three-dimensional shape, which is the protein‘s secondary structure (e.g. glucagon and fibroin in silk)

A protein might contain many helices, pleats, and folds. The tertiary structure of many proteins is globular, such as enzymes (Amylase and pepsin) and antibodies, and

- Proteins make up about 15% of your total body mass and are involved in nearly every function of your body. For example, your muscles, skin, and hair all are made of proteins.
- Your cells contain about 10,000 different proteins that provide structural support, transport substances inside the cell and between cells, communicate signals within the cell and between cells, speed up chemical reactions, and control cell growth.

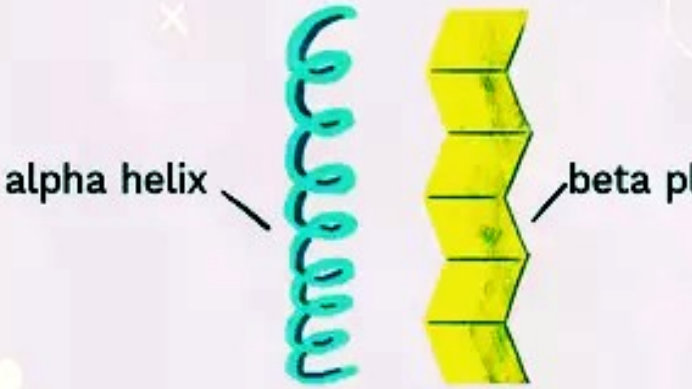
- The structure of a protein may be: globular or fibrous be depending on its particular role.
- Globular proteins are generally compact, soluble, and spherical in shape.
- Fibrous proteins are typically elongated and insoluble.
- There are four structural levels of protein: primary, secondary, tertiary, and quaternary.
- These levels determine the shape and function of a protein and are distinguished from one another by the degree of complexity in a polypeptide chain.

- A single protein molecule may contain one or more of these protein structure levels and the structure and complexity of a protein determine its function.
- Collagen, for example, has a super-coiled helical shape that is long, stringy, strong, and rope-like—collagen is great for providing support.
- Hemoglobin, on the other hand, is a globular protein that is folded and compact. Its spherical shape is useful for maneuvering through blood vessels.

Types of Protein Structures



Primary Structure



Secondary Structure



Tertiary Structure



Quaternary Structure

ThoughtCo.

- **Antibodies** are specialized proteins that defend the body against antigens or foreign invaders. One way antibodies counteract antigens is by immobilizing them so that they can be destroyed by white blood cells.
- **Contractile proteins** are responsible for muscle contraction and movement.

Examples of these proteins include actin, which controls muscle contraction and myosin, which powers the tasks carried out by actin by supplying it with energy.

- **Enzymes** are proteins that facilitate and speed up biochemical reactions. Notable enzymes include lactase and pepsin.
- **Hormonal proteins** are messenger proteins that help coordinate certain bodily functions. Examples include insulin, oxytocin, and somatotropin.
- Insulin regulates glucose metabolism by controlling blood-sugar concentrations in the body, oxytocin stimulates contractions during childbirth, and somatotropin is a growth hormone that stimulates protein production in muscle cells.

- **Structural proteins** are fibrous and tough, this formation making them ideal for supporting various other proteins such as keratin, collagen, and elastin.
- Keratins strengthen protective coverings such as skin, hair, quills, feathers, horns, and beaks.
- Collagen and elastin provide support to connective tissues like tendons and ligaments.

- **Storage proteins** reserve amino acids for the body until ready for use. Examples of storage proteins include ovalbumin, which is found in egg whites, and casein, a milk-based protein. Ferritin is another protein that stores iron in the transport protein, hemoglobin.
- **Transport proteins** are carrier proteins that move molecules from one place to another in the body.

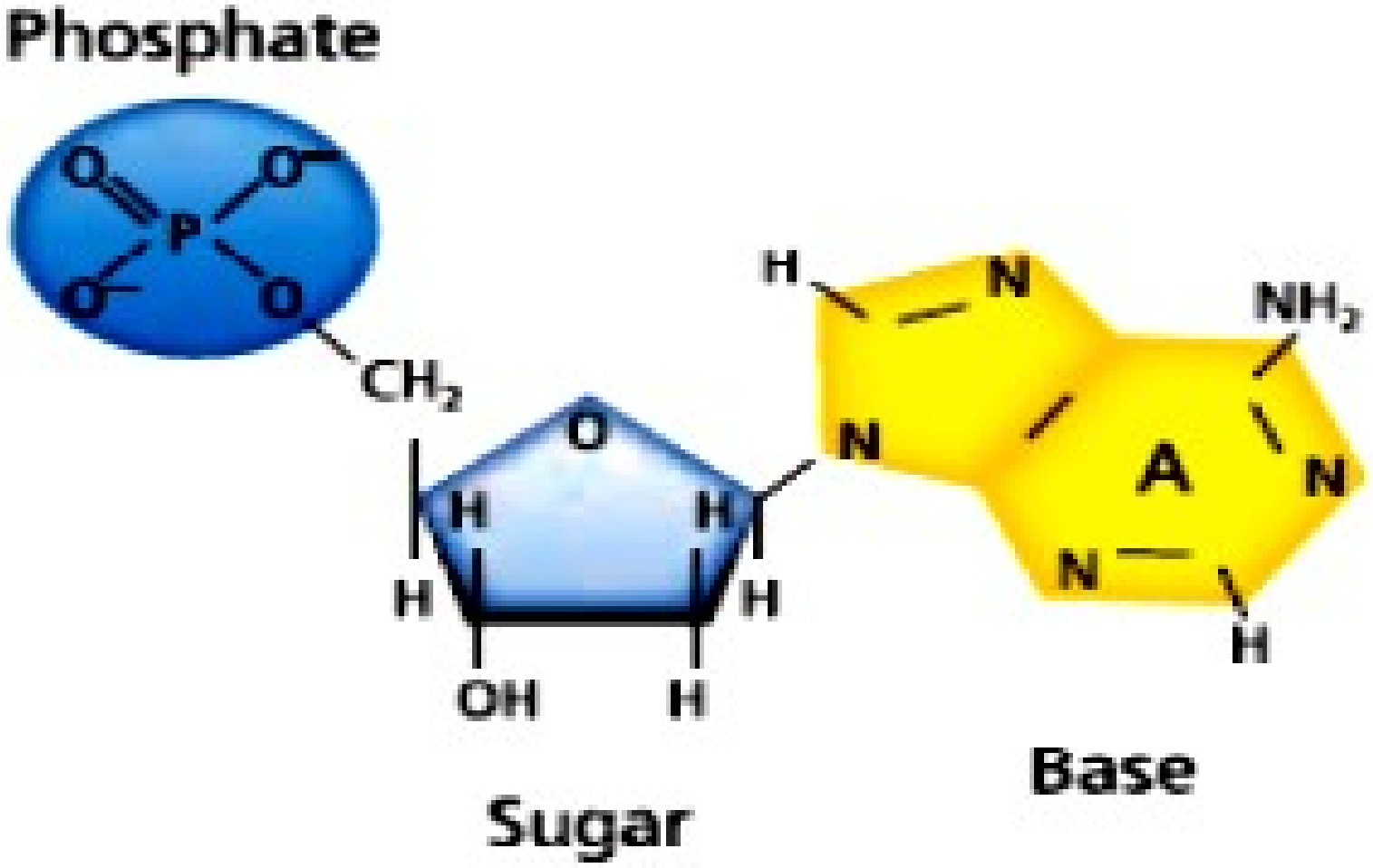
Hemoglobin is one of these and is responsible for transporting oxygen through the blood via red blood cells.

Cytochromes, another type of transport protein, operate in the electron transport chain as electron carrier proteins.

2.4 Nucleic acids

- **Nucleic acids** are complex macromolecules that store and transmit genetic information.
- Nucleic acids are made of smaller repeating subunits called **nucleotides** which are composed of carbon, nitrogen, oxygen, phosphorus, and hydrogen atoms.
- Nucleotides have three units a phosphate, a nitrogenous base, and a ribose sugar.

Nucleotide structure



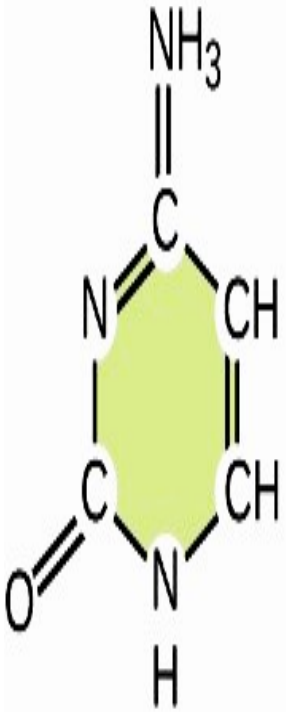
- There are two types of nucleic acids in living organisms: deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).
- In nucleic acids such as DNA and RNA, the sugar of one nucleotide bonds to the phosphate of another nucleotide. There are five different bases found in nucleotide subunits that make up DNA and RNA, Adenine, Cytosine, Guanine, Thymine and Uracil. Each of these nitrogenous base that sticks out from the chain is available for hydrogen bonding with other bases in other nucleic acids.

The difference b/n Purines and Pyrimidines

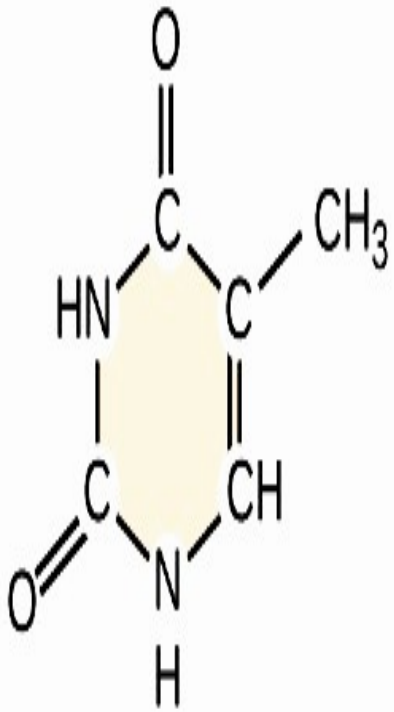
	Purines	Pyrimidines
Structure	Double carbon-nitrogen ring with four nitrogen atoms	Single carbon-nitrogen ring with two nitrogen atoms
Size	Bigger	Smaller
Source	Adenine and Guanine in both DNA and RNA	Cytosine in both DNA and RNA Uracil only in RNA Thymine only in DNA

pyrimidines

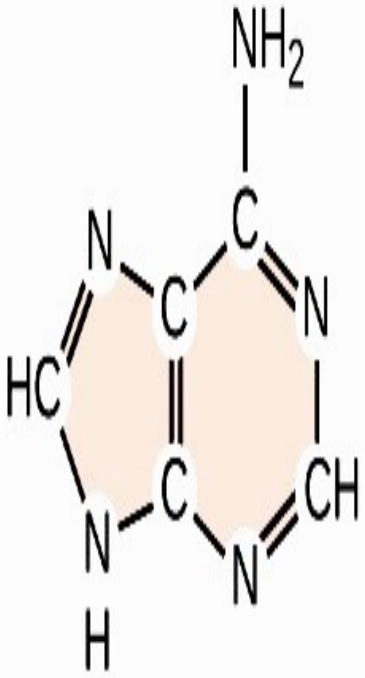
purines



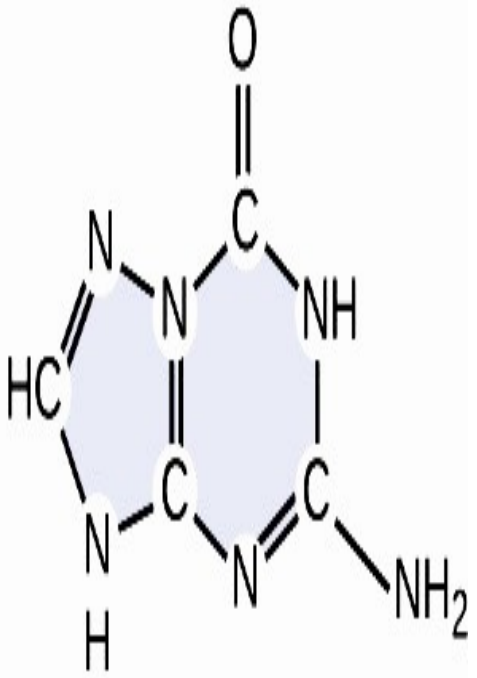
cytosine
C



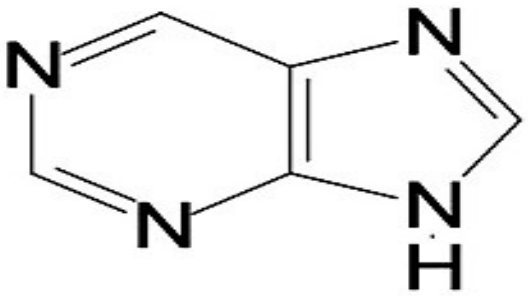
thymine (in DNA)
T



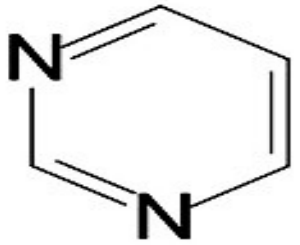
adenine
A



guanine
G



Purine



Pyrimidine

A nucleotide with three phosphate groups is adenosine triphosphate (ATP).

ATP is a storehouse of chemical energy that can be used by cells in a variety of reactions. ATP releases energy when the bond between the second and third phosphate group is broken.

2.5 Vitamins

- Vitamins are organic compounds that are needed in small amounts for metabolic activities.
- Many vitamins help enzymes function well.
- Vitamin D is made by cells in your skin.
- Some B vitamins and vitamin K are produced by bacteria living in the large intestine.
- Some vitamins that are fat-soluble can be stored in small quantities in the liver and fatty tissues of the body. Other vitamins are water-soluble and cannot be stored in the body.

2.6 Water

- Water molecules are formed by covalent bonds that link two hydrogen (H) atoms to one oxygen (O) atom, and each water molecule has the same structure.
- Water molecules have an unequal distribution of charges and are called polar molecules, meaning that they have oppositely charged regions.

➢ **Hydrogen bonds are responsible for four important properties of water.**

* Universal solvent (adhesion)
* Less dense as a solid
* High specific heat
* Surface tension

Biological importance of water

1. It is a place to live:
2. Water is a polar solvent.
3. Water has the ability to ionize molecules, which are necessary for life.
4. Water has high specific heat and a high latent heat of vaporization.
5. Water has ideal viscosity and high surface tension.
6. Water density decreases under 4◦C.
7. The freezing point of water decreases if it has substances dissolved in it.
8. Water can turn into vapor in temp. lower than boiling point (100◦C).
9. Water rise in capillary tubes.
10. Water as a reactant:
11. Water serve as a medium of fertilization:
12. It is an agent of seed germination, stomata closing and opening, growth,…….

2.7 Minerals

- Minerals are inorganic compounds used by the body as building material, and they are involved with metabolic functions.
- For example, the mineral iron is needed to make hemoglobin and it binds to hemoglobin in red blood cells and is delivered to body cells as blood circulates in the body.
- Calcium, and other minerals, is an important component of bones and is involved with muscle and nerve functions and they serve as cofactors for enzymes.
- Magnesium is an important component of the green pigment, chlorophyll, involved in photosynthesis.

Unit summary

- Carbon compounds are the basic building blocks of living organisms.
- Biological macromolecules are formed by joining of small carbon compounds into polymers.
- There are four types of biological macromolecules; carbohydrates, proteins, lipids and nucleic acids
- Monosaccharides undergo condensation to form disaccharides and poly saccharides through the glycosidic linkages
- Peptide bonds join amino acids in proteins.
- Lipids are esters of fatty acids and alcohols
- Chains of nucleotides form nucleic acids.

Chapter Review Questions

1. Explain if an unknown substance found on a meteorite is determined to contain no trace of carbon, can scientists conclude that there is life at the meteorite's origin?
2. List and compare the four types of biological macromolecules.
3. Identify the components of carbohydrates and proteins.
4. Discuss the importance of amino acid order to a protein‘s function.
5. Given the large number of proteins in the body, explain why the shape of an enzyme is important to its function.
6. Compare and contrast the functions of carbohydrates

Unit 3. The cellular basis of life

- In the late 1600s, an English scientist named Robert Hook was the first to observe plant cells with a crude microscope. Then, almost a century and a half later, in the 1830‘s two German scientists proposed that all living things are composed of cells (their names were Mathias Schleiden and Theodore Schwann).
- A German pathologist, Rudolph Virchow extended this idea by contending that cells arise only from other cells.

3.1 The cell theory

- The observations of Hooke, Leeuwenhoek, Schleiden, Schwann, Virchow, and others led to the development of the cell theory.
- **The cell theory states that**:

❖ All living things are made of cells and their products.

❖ New cells are created by old cells dividing into two (All cells arise from pre-existing cells (continuity of life from one generation to another has a cellular basis)

❖ Cells are the basic building units of life.

- **A typical eukaryotic cell has 3 major parts**:

- The **plasma membrane**: the outer boundary of the cell.
- The **cytoplasm**: the intracellular fluid packed with organelles, small structures that perform specific cell functions.
- The **nucleus**: an organelle that controls cellular activities. Typically the nucleus resides near the cells center.

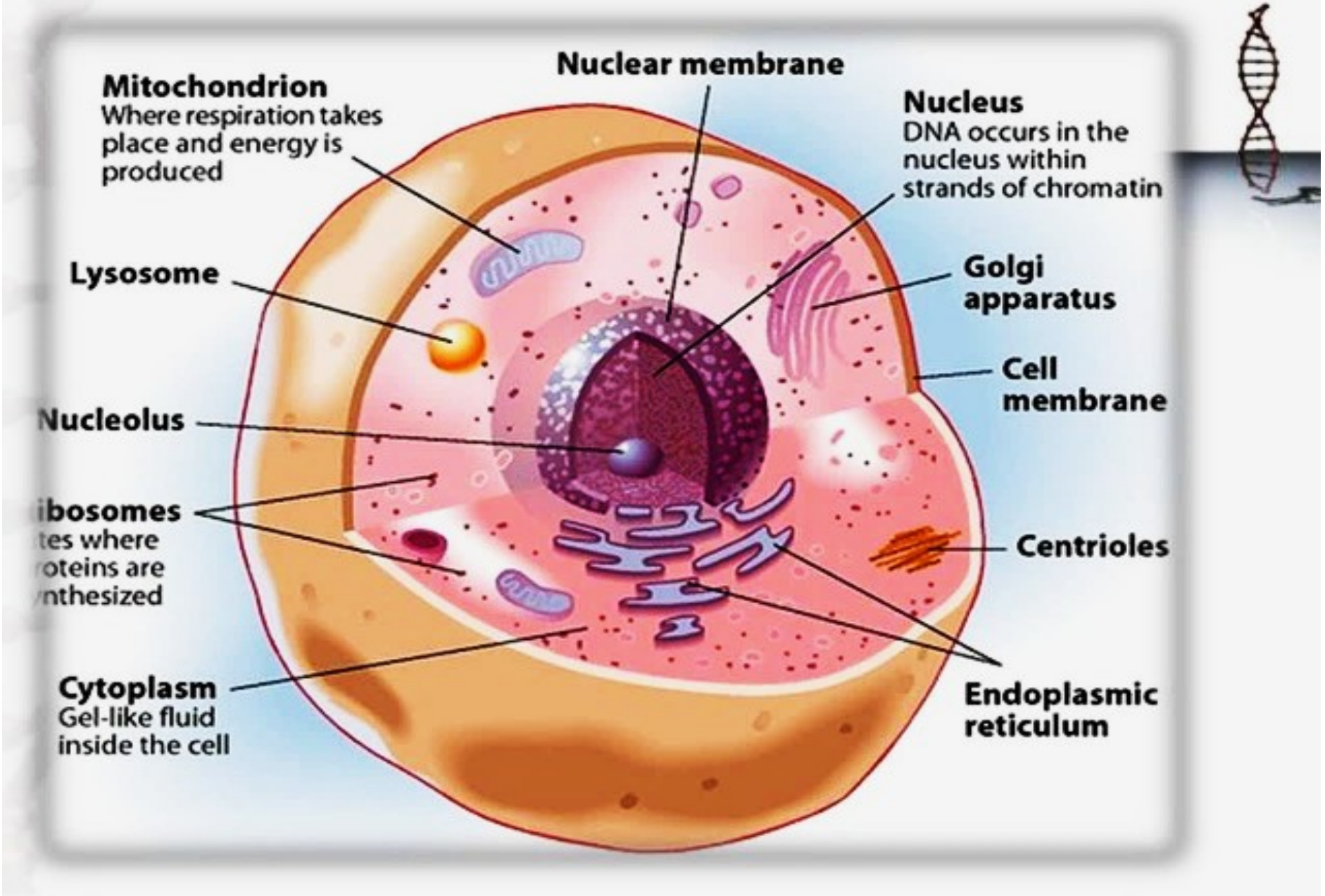


Fig: 3.1. Generalized animal cell

3.1.1 Cell organelles

- An organelle is a specialized subunit within a cell that has a specific function.
- In eukaryotes an organelle is a membrane bound structure found within a cell.
- Prokaryotes are cells that do not have membrane bound organelles.
- These organelles are found in the cytoplasm, a viscous liquid found within the cell membrane that houses the organelles and is the location of most of the action happening in a cell.

- There are two kinds of cell organelles on the basis of membrane covering; membranous and non-membranous organelles.
- Endoplasmic reticulum (Rough and Smooth), Golgi bodies, mitochondria, chloroplasts, nucleus, lysosomes, peroxisomes and vacuoles are membranous whereas,
- Non-membrane bound cell organelles are ribosomes (70s and 80s), centrosomes, cilia and flagella, microtubules, basal bodies and microfilaments.

3.1.2 Structure and function of organelles

* Nucleus:

- It is distinctly oval or spherically shaped largest central structure surrounded by a double-layered membrane.
- In the nucleus, DNA directs protein synthesis and serves as a genetic blueprint during cell replication.
- DNA gives codes, or instruction for directing synthesis of specific structure and enzymes proteins within the cell. By monitoring these protein synthesis activities, the nucleus indirectly governs most cellular activities and serves as the cell‘s master.

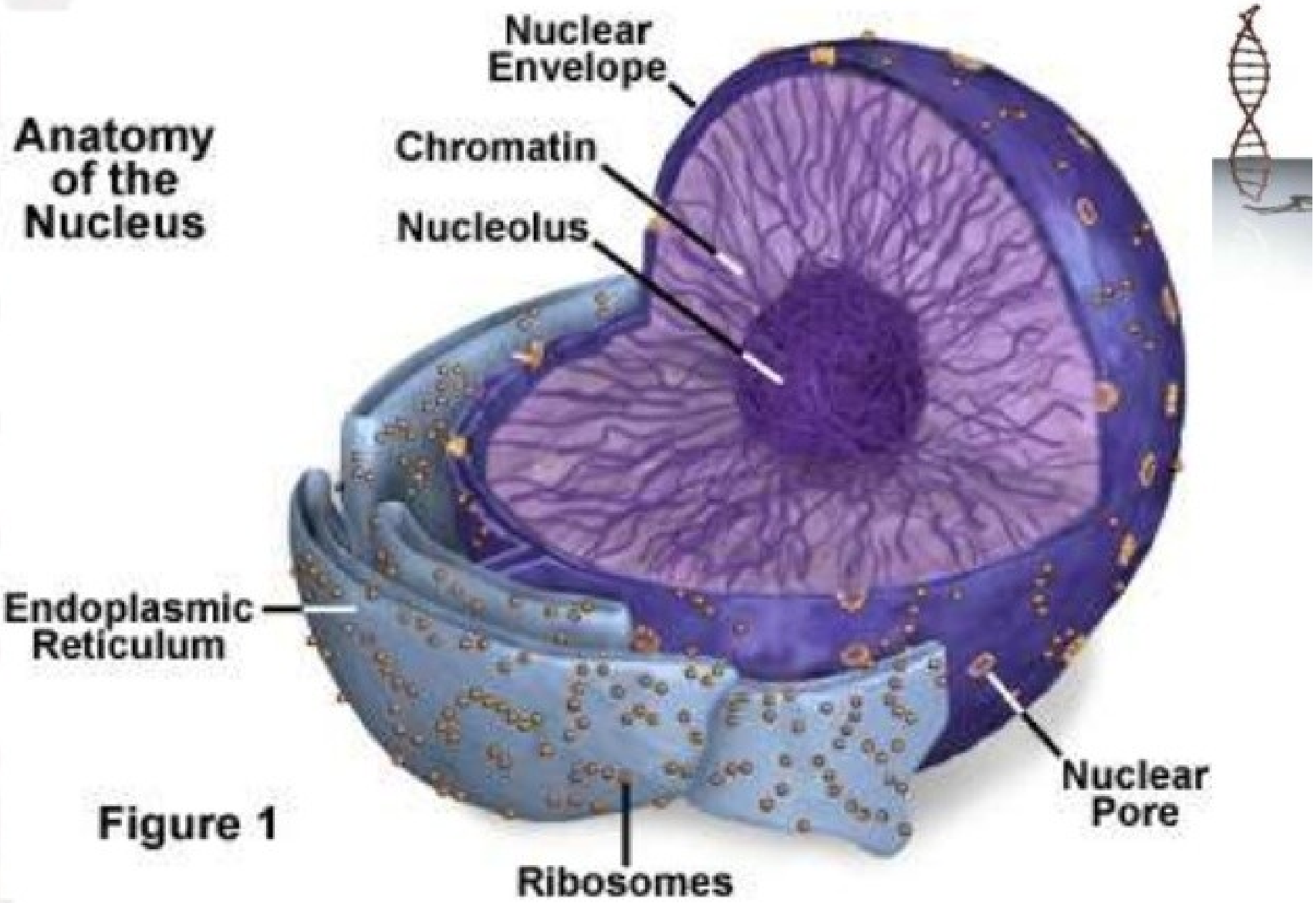
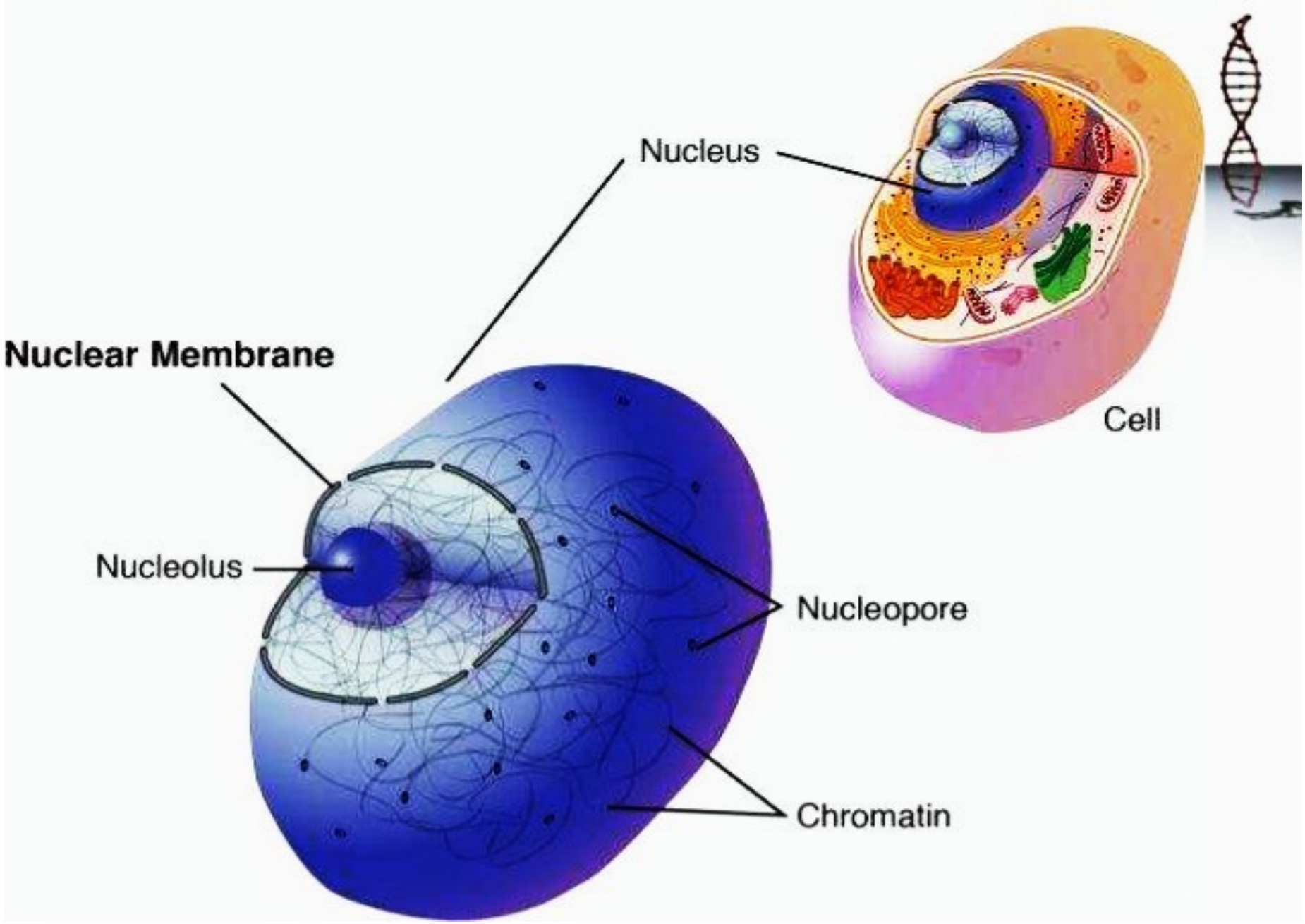

Anatomy of the Nucleus
Nuclear Envelope
Chromatin
Nucleolus
Endoplasmic Reticulum
Nuclear Pore
Ribosomes

Figure 1


Nucleus
Cell
Nuclear Membrane
Nucleolus
Nucleopore
Chromatin

Three types of RNA are involved in protein synthesis.

- At first, DNA‘s genetic code for a particular protein is transcribed into a **mRNA**, which leaves nucleus through the nuclear pores of the nuclear membrane.
- And, within the cytoplasm, mRNA delivers the coded message to the **rRNA**, which "**reads" message/code and translates it into the appropriate amino acids sequence** for the designated protein being synthesized.
- Finally, **tRNA,** which **transfers the appropriate amino acids within the cytoplasm** to their designated site in the protein under production.

- During cell replication, DNA ensures the continuing of the identical types of cell line within the body. Furthermore, in the gametes, the DNA blueprint serves to pass the genetic characteristics to future generation.
- **Generally, the nucleus may be:**

  * rounded; e.g. in hepatocytes

  * indented (segmented); e.g. in neutrophils

  * binucleated; e.g. in parietal cells, cardiac muscle cells.

  * multinucleated; e.g. in osteoclasts, skeletal muscle cells.

  * very large (many DNA); e.g. in megakaryocytes.

  * absent; e.g. in mature erythrocytes, blood platelets

- The nucleus is surrounded by a nuclear envelope and contains chromatin and one or more nucleoli.
- **The Nuclear envelope:**
  * surrounds nuclear material
  * consists of outer and inner membrane
  * perforated at intervals by nuclear pores
  * through this pores most ions and water soluble molecules to transfer b/n nucleus and cytoplasm

* Chromatin:

- The term chromatin means "colored material" and refers to the fact that this material is easily stained for viewing with microscope, and it is composed mainly of coils DNA bound to basic protein called histones.
- The DNA is so long that it has to be packed in an organization manner or it would get entangled like unraveled ball of string.

* Nucleoli:

- The nuclei of most cells contain one or more lightly stained structures called nucleoli that actively engage in synthesizing of ribosomes. The nucleolus, unlike most of the organelles, does not have a limiting membrane. Instead, it is simply a structure that contains large amounts of RNA and protein of the type found in ribosomes.

* **Cytoplasm:** is the material of cell interior not occupied by the nucleus, containing a number of distinct, highly organized membrane-enclosed structures- the organelles- dispersed within a complex jelly like marrow called the **cytosol**.

* **Endoplasmic reticulum (ER)** a fluid-filled membrane system extensively present throughout the cytosol.

- The two different types are the rough ER and the smooth ER.

The rough Endoplasmic Reticulum:

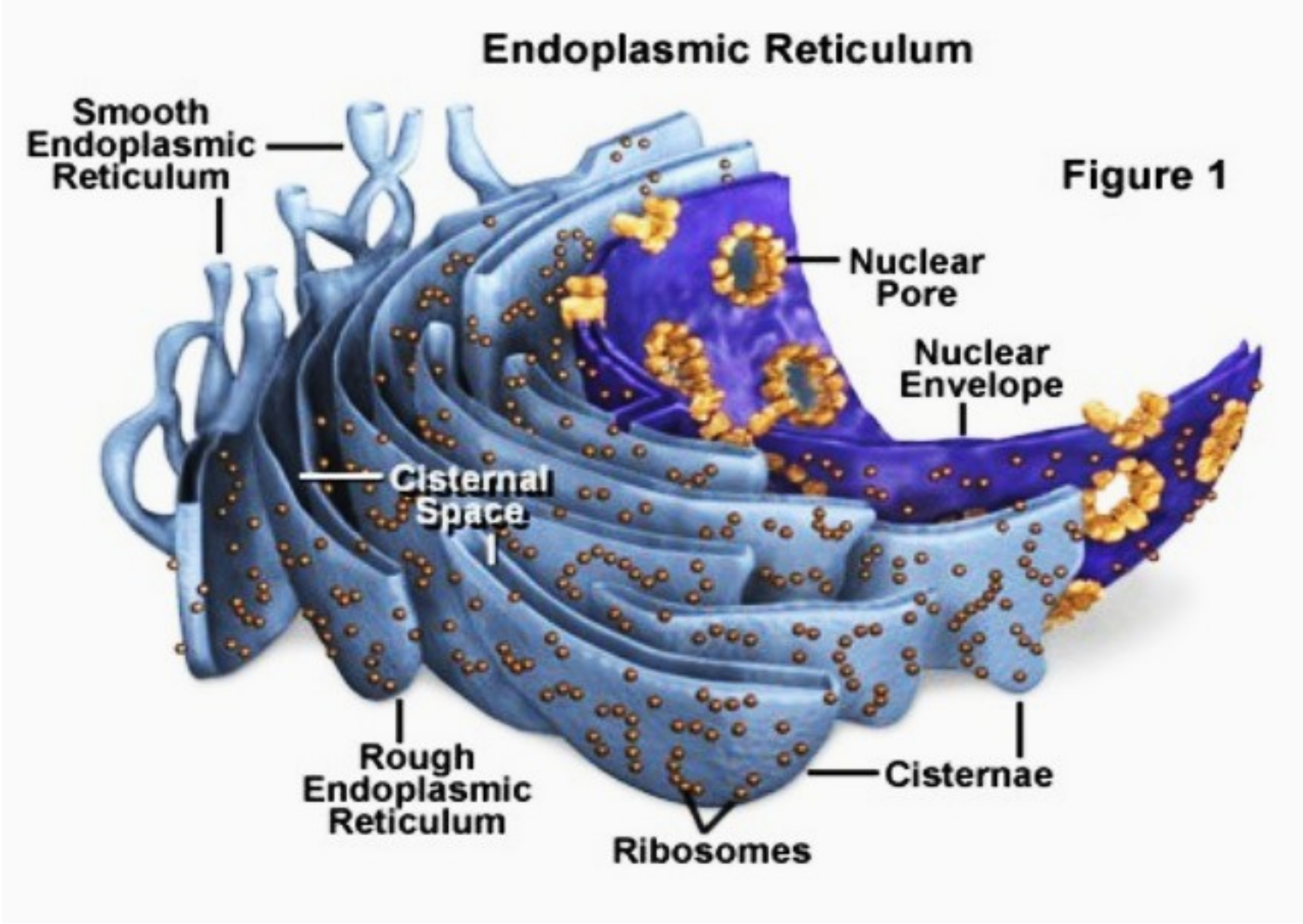
- It contains ribosomes, which are **the workshop where proteins are synthesized**. Some ribosomes are free dispersed throughout the cytosol.
- Some proteins for export as secretory products (hormones or enzymes). Other proteins are transported to sites within the cell for use in the construction of new plasma membrane or new organelle membrane.
- Each ribosome is involved in producing only one type of protein.
- The free ribosomes synthesize enzyme proteins that are used intra cellularly within the cytosol.

*** Smooth Endoplasmic Reticulum:**

- Since it does not have ribosomes, it looks smooth and does not produce proteins.
- It serves a variety of other functions that differ in cell types.
- In most cells, the smooth ER is scarce and serves in packaging and discharging site for protein molecules that are to be transported from the ER.

- Some specialized cells have an extensive smooth ER, which has additional functions as follows:

- lipid metabolism- cells that synthesize steroid hormones.
- contains enzymes for synthesis of lipids.
- a special role in skeletal muscle cells. They have an elaborate network which stores ionic calcium and plays a crucial role in the process of muscle contraction.
- In liver cells, the smooth ER contains enzymes involved in detoxifying harmful endogenous


Endoplasmic Reticulum
Smooth Endoplasmic Reticulum
Figure 1
Nuclear Pore
Nuclear Envelope
Cisternal Space
Rough Endoplasmic Reticulum
Cisternae
Ribosomes

* Golgi complex:

- It performs the following important functions:

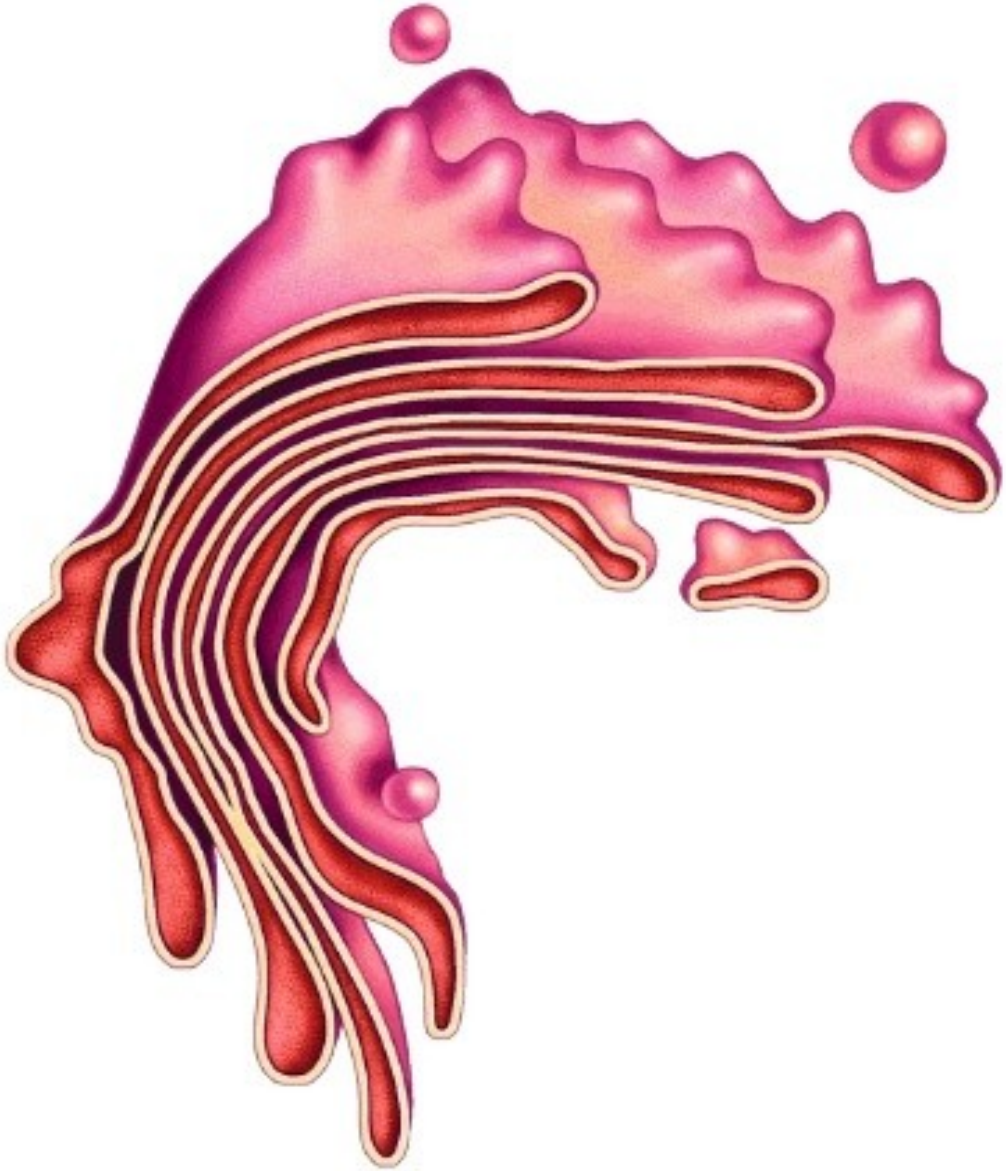
1. Processing the raw material into finished products.

In the Golgi complex, the raw proteins from the ER are modified into their final state mainly by adjustment made in the sugar attached to the protein.

2. Sorting and directing finished product to their final destination.

According to their function and destination, different types of products are segregated by the Golgi

GOLGI COMPLEX



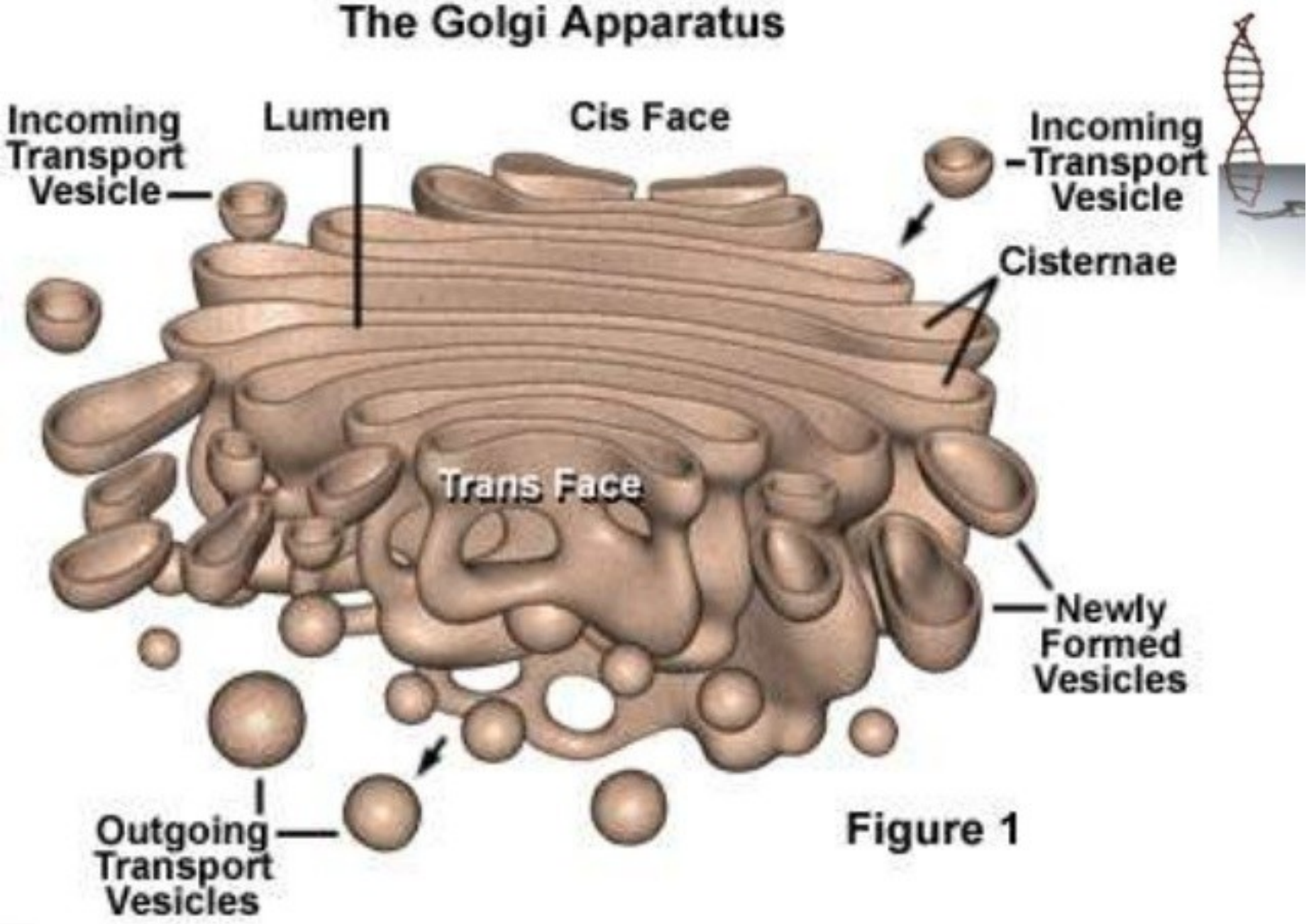

The Golgi Apparatus
Incoming Transport Vesicle
Lumen
Cis Face
Incoming Transport Vesicle
Cisternae
Trans Face
Newly Formed Vesicles
Outgoing Transport Vesicles

Figure 1

* Lysosomes:

They serve as the intracellular —digestive system.

They are membrane-enclosed sacs containing powerful hydrolytic enzymes capable of digesting and removing unwanted cellular debris and foreign materials such as bacteria that have been internalized within the cell.

The process by which worn-out organelles are digested is called **autophagy** a human liver cell recycles about half its content every week.

* Peroxisome:

- Peroxisome is membrane-enclosed sacs containing oxidative enzymes and catalase that detoxify various wastes.
- Oxidative enzymes need oxygen to remove hydrogen from specific substance/molecule; such reactions are important in detoxifying various waste products within the cell or foreign compounds that have entered in, such as ethanol consumed in alcoholic drinks (in liver and kidneys).
- The major product generated is hydrogen peroxide; hydrogen peroxide itself is a powerful oxidant.

- Peroxisome also contains catalase, and **antioxidant** enzyme decomposing hydrogen peroxide into harmless water and oxygen.
- It is shorter and smoother than lysosome and several hundreds may present in one cell.
- Peroximal disorders disrupt the normal processing of lipids and can severely disrupt the normal function of the nervous system by altering the structure of the nerve cell membrane

* Mitochondria

- Mitochondria are the “power houses‘‘ of a cell.
- Their number varies depending on the energy needs of each particular cell types.
- ATP is the universal energy carrier the common energy currency of the body. Cells can —cash in ATP to pay the energy —price for running the cellular machine.
- To get immediate usable energy cells can split terminal phosphate bond of ATP, which yields ADP with phosphate group attached - plus inorganic phosphate (Pi) plus energy.

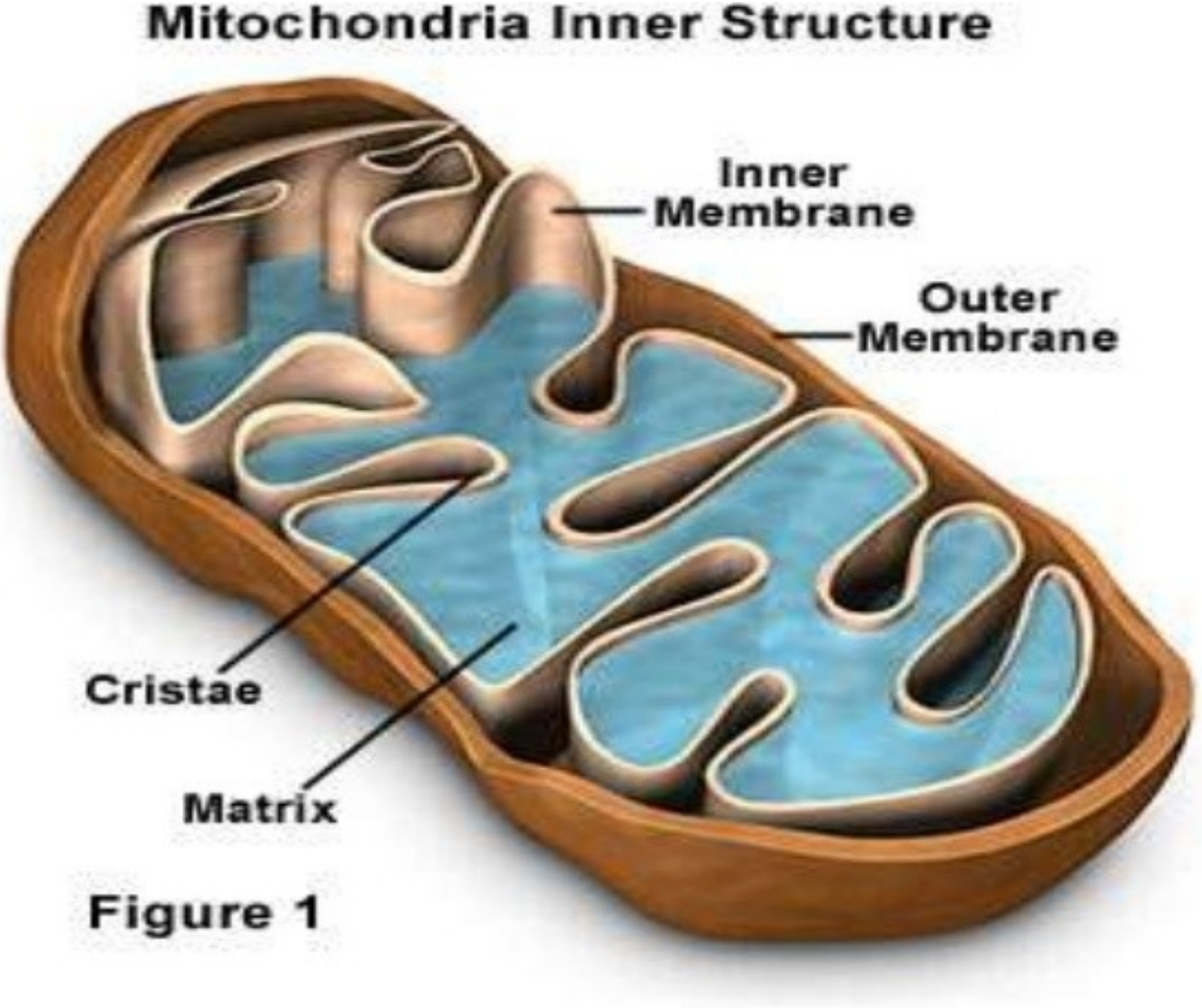

Mitochondria Inner Structure
Inner Membrane
Outer Membrane
Cristae
Matrix

Figure 1

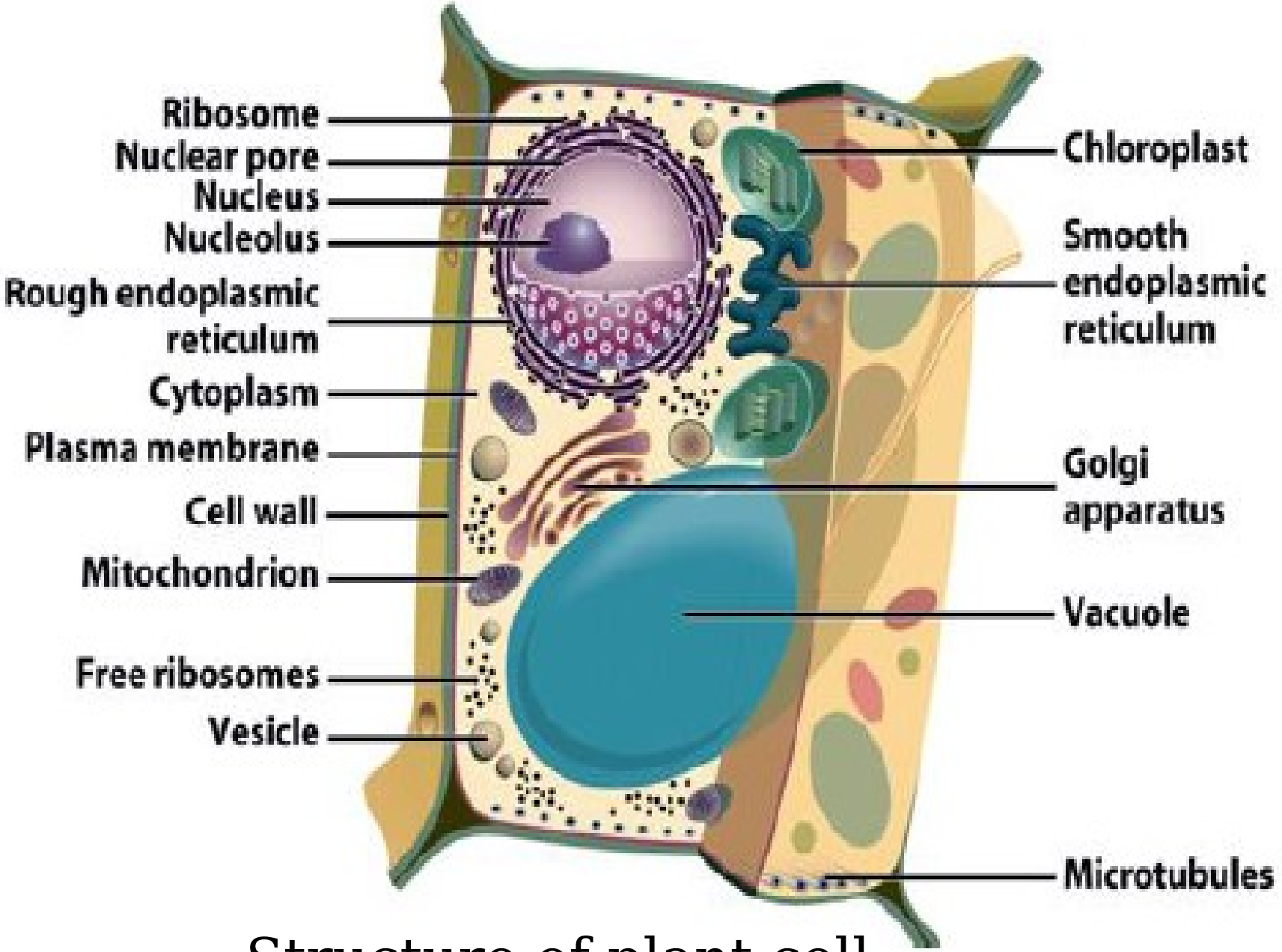
* Mitochondria are unusual organelles in two ways:

 In the matrix they have their own unique DNA called mitochondrial DNA.

 Mitochondria have the ability to replicate themselves even when the cell to which they belong is not undergoing cell division.

*** Chloroplasts**

- Chloroplasts are useful organelles among plastids as they highly participate in the process of photosynthesis
- They are located in outer surface of the cell to receive enough light.



Structure of plant cell

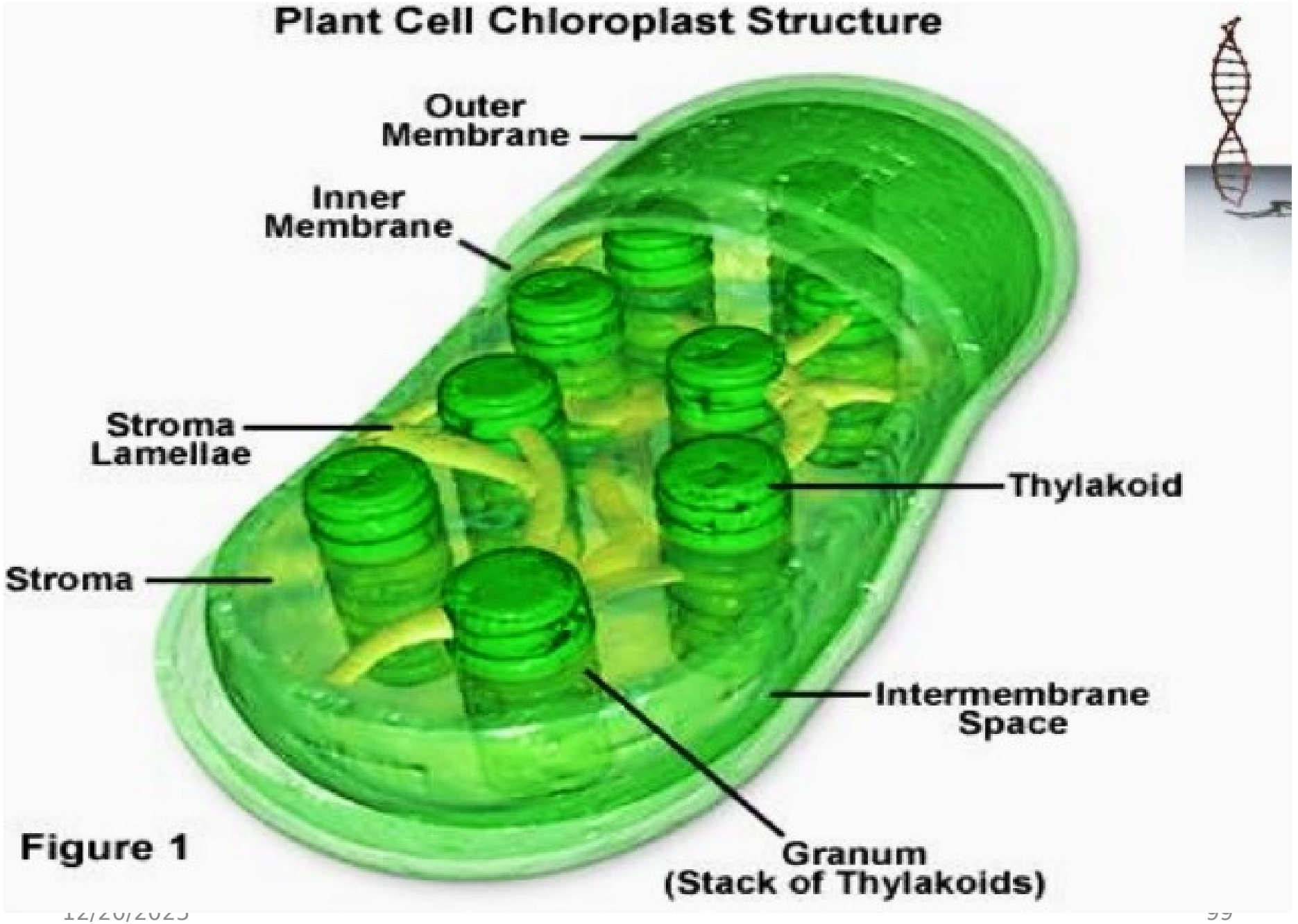

Plant Cell Chloroplast Structure
Outer Membrane
Inner Membrane
Stroma Lamellae
Thylakoid
Stroma
Intermembrane Space
Granum (Stack of Thylakoids)

Figure 1

* Vesicles

- They are membrane bound sacs that are used to store or transport substances around the cell. Lysosomes are actually Vesicles.

❖ Vacuoles

- They are essentially larger Vesicles, and they are formed by the joining together of many Vesicles. They are membrane bound organelles that have no specific shape and contain water with a number of different compounds within it.
- Their function varies greatly depending on the type of cell they are part of. In plant cells they are important in maintaining Turgor Pressure.

* Cytoskeleton

- It is a complex protein network that act as the bone and muscle of the cell.
- Generally, cytoskeletons determine/ provide the:

 shape of a cell

 structural support

 organizing its contents

 substances movement through cell (cilia, flagella and intracytoplasmic vesicles)

 contribute to movements of the cell as a whole.

* Plasma/cell membrane

- The plasma membrane is extremely thin layer of lipids and proteins forming outermost boundary of living cell and enclosing the intracellular fluid.
- It serves as a mechanical barrier that traps needed molecules within the cell;
- It plays an active role in determining the composition of cell by selective permeability of substances to pass between the cell and its environment.

- All plasma membrane are made up of lipids and proteins plus small amount of carbohydrates.

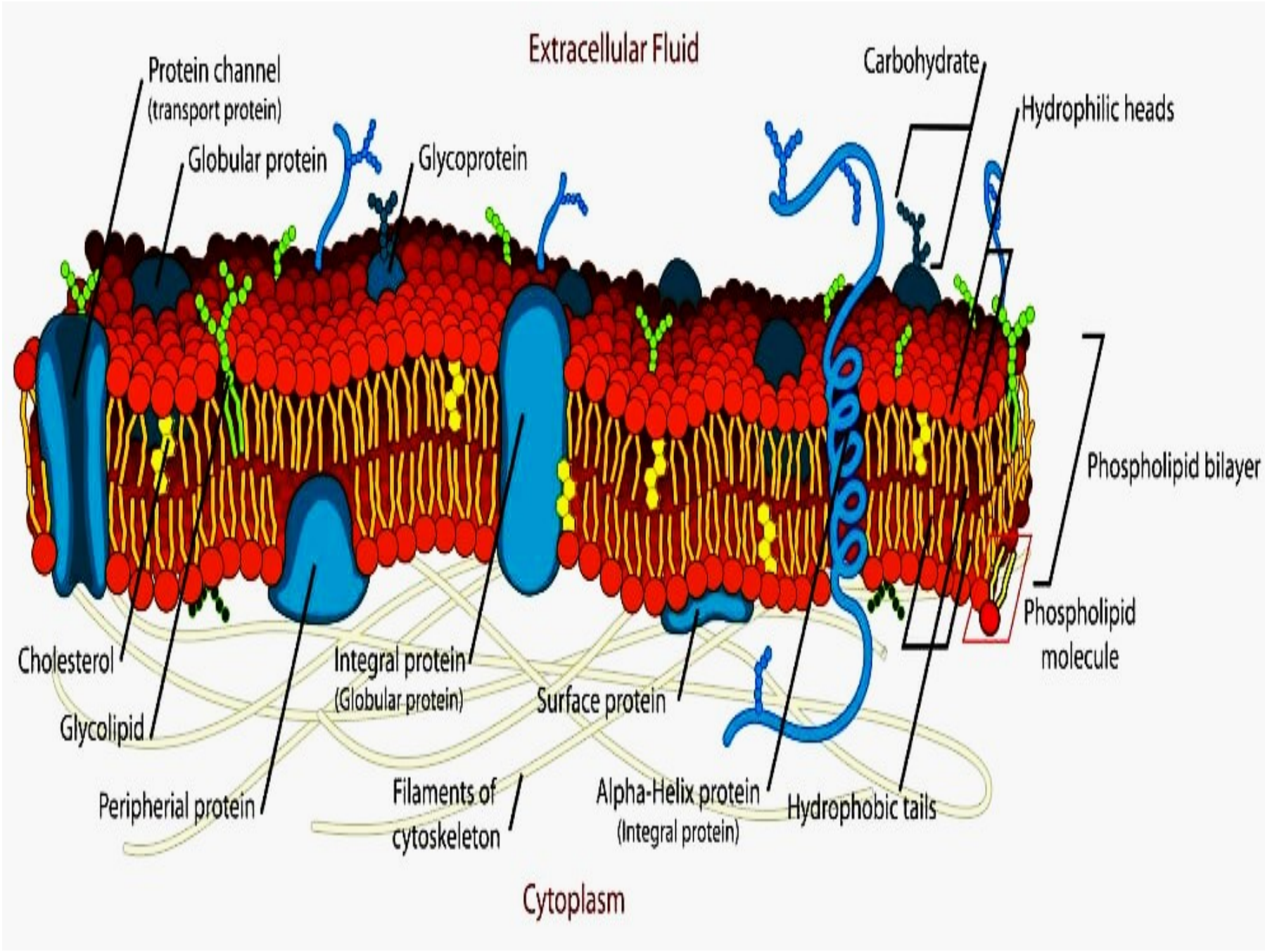
- **Phospholipids** are most abundant with a lesser amount of cholesterol.
- Phospholipids have a polar charged head having a negatively charged phosphate group and two non-polar (electrically neutral) fatty acid tails.
- The polar end is hydrophilic (water loving) because it can interact with water molecule, which is also polar; the non-polar end is hydrophobic (water fearing) and will not mix with water.

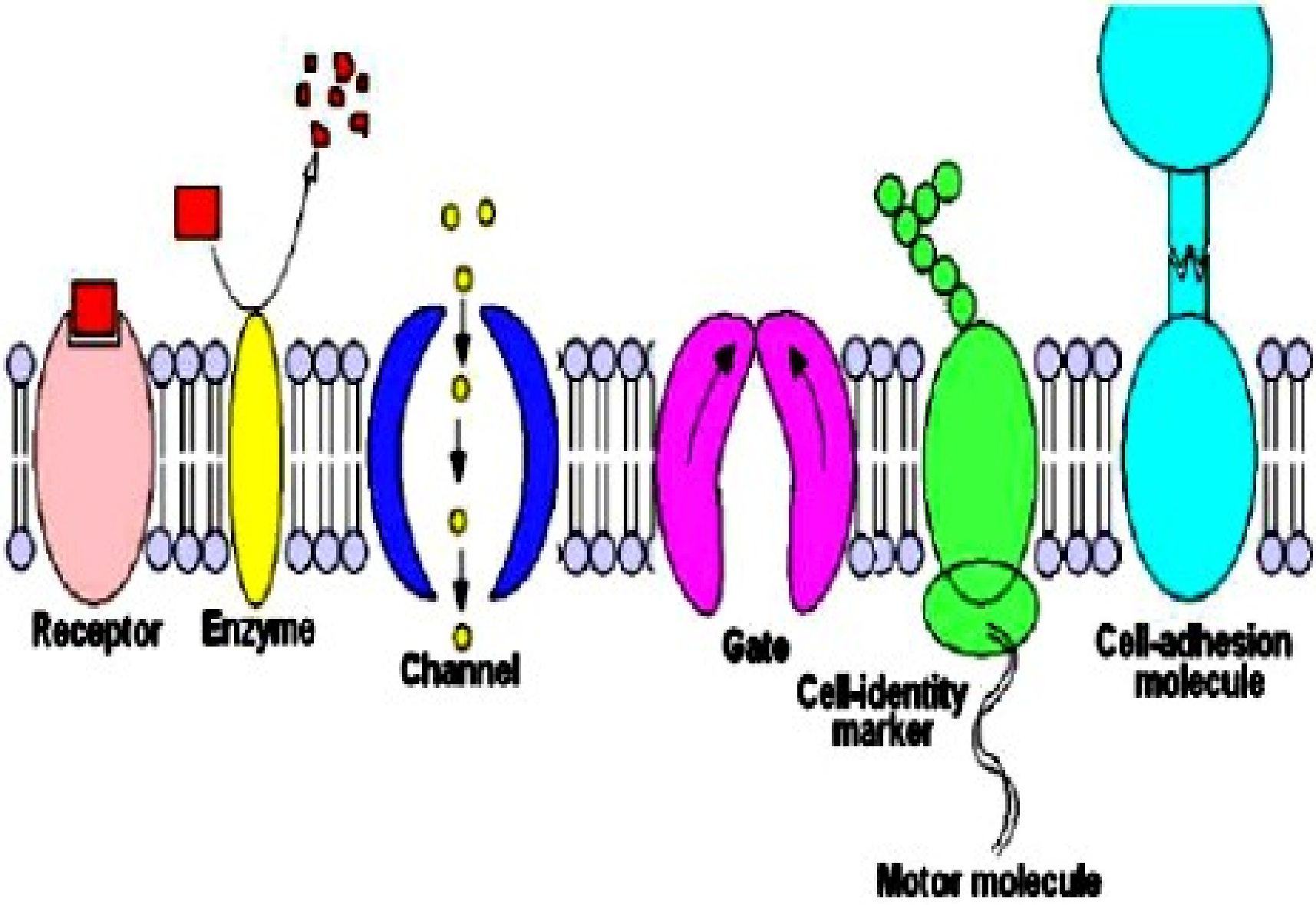
- **Cholesterol** provides to the fluidity as well as the stability; which lies in between the phosphate molecules, preventing the fatty acid chain from packing together and crystallizing that could decrease fluidity of the membrane.
- Cholesterol also exerts a regulatory role on some of the membrane proteins. For fluidity of the membrane, it gives flexibility to the cell to change its shape; transport processes are also dependent on the fluidity of the lipid bilayer.

❖ **Membrane proteins have the following special functions**:

- 1. Such channels allow ions selectively to pass through without coming in direct contact with lipid interior.
- 2. Other proteins serve as carrier molecule that transport specific molecule that cannot cross on their own. They differ in cells, e.g., thyroid epithelial cell possesses carriers for iodine.
- 3. Many proteins on the outer surface serve as ‘receptor sites‘ that recognize and bind with specific molecules in the cell environment.

- 4. Another group of proteins act as membrane-bound enzymes that control specific chemical reactions on either side of the plasma membrane.
- 5. They maintain cell shape arranged as filaments network on the inner side.
- 6. Other proteins function as cell adhesion molecules (CAMs).
- 7. Some proteins, especially in conjunction with carbohydrate are important in the cell‘s ability to recognize ‘self and in cell-to-cell interactions’.


Extracellular Fluid
Protein channel
(transport protein)
Globular protein
Glycoprotein
Carbohydrate
Hydrophilic heads
Phospholipid bilayer
Phospholipid
molecule
Cholesterol
Glycolipid
Peripherial protein
Integral protein
(Globular protein)
Surface protein
Filaments of
cytoskeleton
Alpha-Helix protein
(Integral protein)
Hydrophobic tails
Cytoplasm



Membrane proteins

- **Membrane Carbohydrate:** Short-chain carbohydrate on the outer membrane surface serves as self-identity marker enabling cells to identify and interact with each other in the following ways:
- Recognition of self and cell-to-cell interactions.
- Carbohydrate-containing surface markers are important in growth. Cells do not overgrow their own territory.
- Some cell adhesion molecules have carbohydrate, on the outermost tip where they participate in cell adhesion activity.

Functions of biological membranes

- **The phospholipid bilayers:** provide the basic structure of the membrane and they also restrict entry and exit of polar molecules and ion. The other molecules in the membrane have a variety of function:
- **Channel protein and carrier protein**: these proteins are involved in the selective transport of polar molecule and ion across the membrane
- **Enzymes:** membrane proteins sometimes act as enzymes, For example, the microvilli on epithelial cells lining some part of the gut contain digestive enzymes in their cell surface membrane

- **Receptor molecules:** proteins have very specific shapes and this makes them ideal as receptor molecules for chemical signaling between cells.
- For example, hormones are chemical messengers, which circulate in the blood but, only bind to specific target cells, which have the correct receptors sites.
- Neurotransmitters, the chemicals that enable nerve impulses from one nerve cell to the next, also fit into specific receptor proteins in nerve cells.

- **Antigens:** these act as cell identity markers or "name tag". They are glycoproteins that is proteins with branching carbohydrates side chains like antennae.
- **Glycolipids:** involved in cell-cell recognition. They may act as a receptor sites for chemical signals. With glycoproteins they also involved in sticking the correct cell together in tissues.

  Eg. sperm recognition of ova
- **Energy Transfer:** in photosynthesis and respiration proteins take part in the energy transfer systems.
- **Cholesterol**: acts like a plug or socket, reducing even further the escape or entry of polar molecules through the membrane

3.1.3 Cellular diversity

- Cells are found in different organisms, and are very diverse in their size, shape and their internal structure and this also applies to cells found in the same organism. This diversity is influenced by their roles and function within organism‘s body.

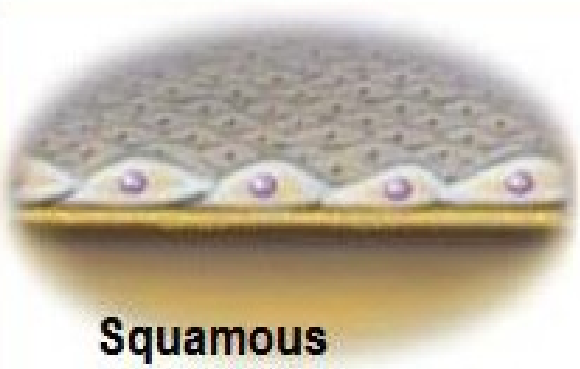
3.1.3.1 Cell Shape

- Cells have different shapes due to appropriate function. It is possible to find other cells which are flat, most of these cells are body cells and their function is protecting and covering body surface. Nerve cells have long extensions.

- Skin cells have a shape which is flat.
- Egg cells have shape which is like sphere, and some bacteria are rod in shape.
- Some plant cells are rectangular.

3.1.3.2 Cell Size

- Some cell can be seen without using magnification instruments as they are enough to be seen by the naked eye.
- Example, egg of birds/reptiles and a neuron cell of giraffe, which is 2 meters in length.



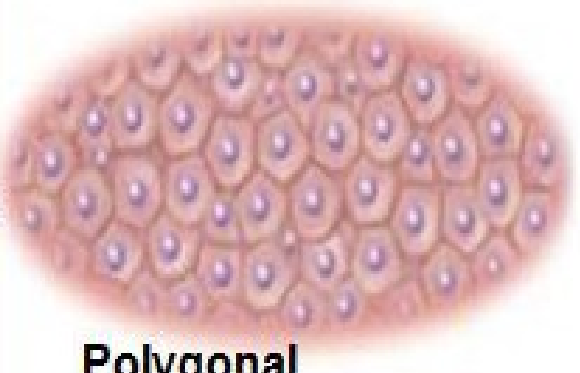
Squamous



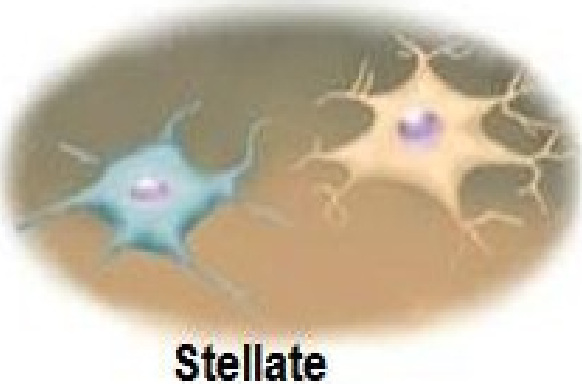
Cuboidal



Columnar



Polygonal



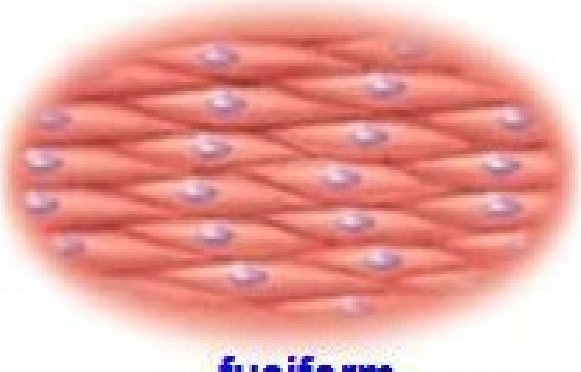
Stellate



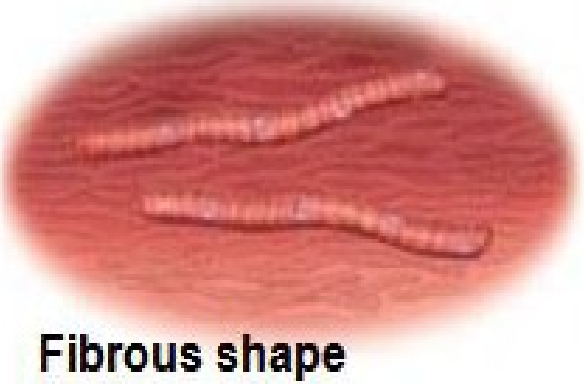
Spheroid/ ovoid



Discoid shape - RBC



fusiform



Fibrous shape

3.1.4 Transport across the cell membranes

- The plasma membrane is selectively permeable. Lipid-soluble substances and small ions can passively diffuse through the plasma membrane down their electro-chemical gradients.
- Highly lipid-soluble particles are able to dissolve in the lipid bilayer and pass through the membrane. Uncharged/non-polar molecules, oxygen, carbon dioxide and fatty acids are highly lipid-soluble and readily permeate the membrane.
- Charged particle sodium/potassium ions and polar molecules such as glucose and proteins have low lipid solubility, but are very soluble in water.

- Particles with low lipid-permeability and too large for channels, cannot permeate the membrane on their own. The phospholipid bilayer is a good barrier around cells, especially to water soluble molecules.
- However, for the cell to survive some materials need to be able to enter and leave the cell.
- There are 4 basic mechanisms:

1. Diffusion and facilitated diffusion
2. Osmosis
3. Active transport
4. Bulk transport

- Two forces are involved in facilitating movement across the plasma membrane**:**

- 1. Forces that do not require the cell to expend energy for movement – **Passive force**
- 2. Forces requiring energy (as ATP) to be expended to transport across the membrane - **Active force**

*** Diffusion**

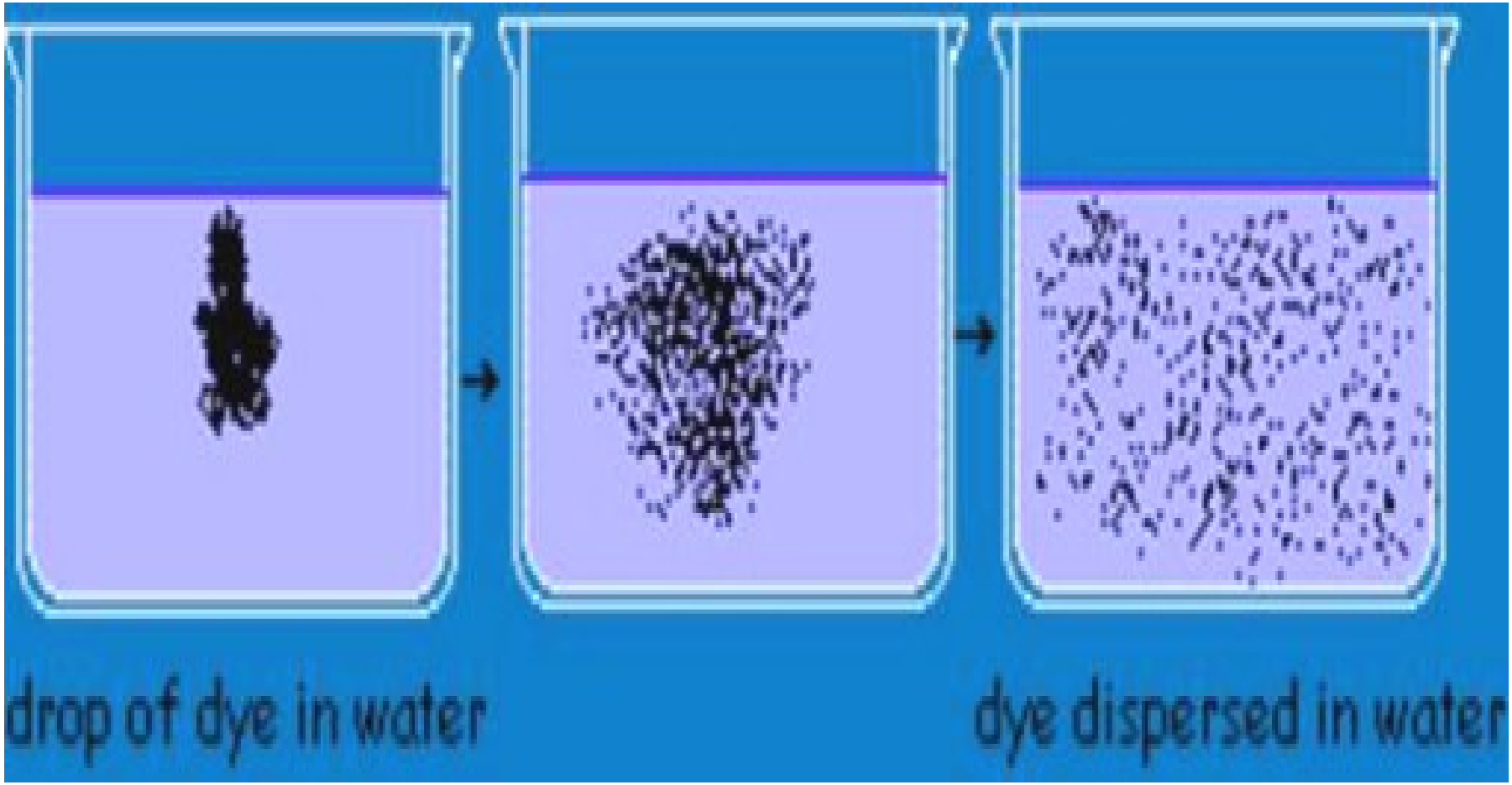
- It is the net movement of molecules (or ions) from a region of their high concentration to a region of their lower concentration.
- The molecules move down a concentration gradient.
- Molecules have kinetic energy, which makes them move about randomly.

- All molecules in liquid and gases are in continuous random motion in any direction as they have more room to move before colliding with another.
- The greater the concentration, the greater the possibility of collision. Such a difference in concentration in molecules between two adjacent areas is chemical/concentration gradient.
- The net movement of the molecule by diffusion will be from the higher area of concentration to the area of lower concentration.

- Certain additional factors that influence the rate of net diffusion across a membrane are:

1. permeability of the membrane
2. surface area of the membrane
3. molecular weight of the substance (lighter one diffuses rapidly)
4. distance through which diffusion must take place

- **N.B:-** Increasing all the factors increases rate of net diffusion, except distance - thickness, that if increased, decreases the rate of diffusion; and

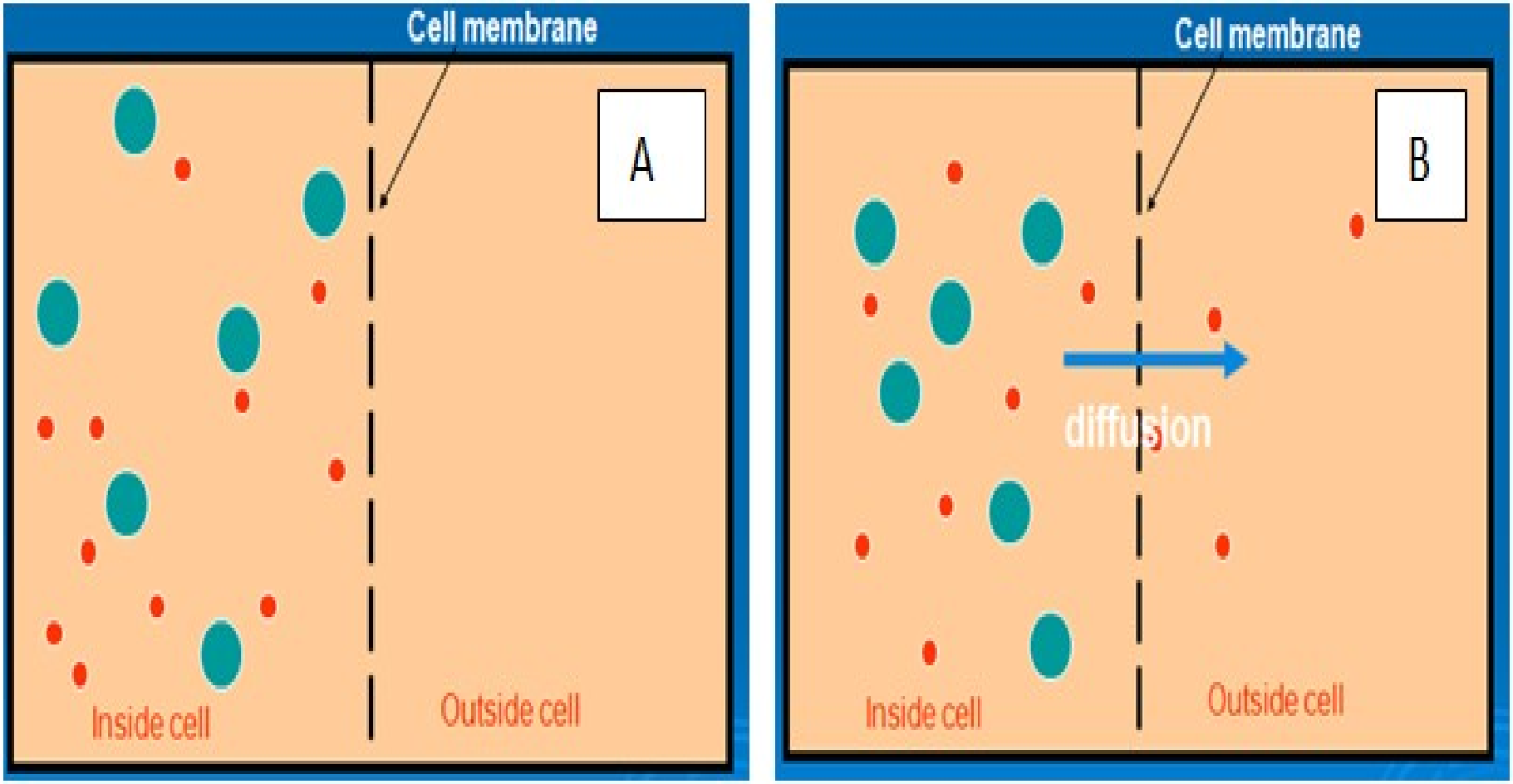


Diffusion of molecules

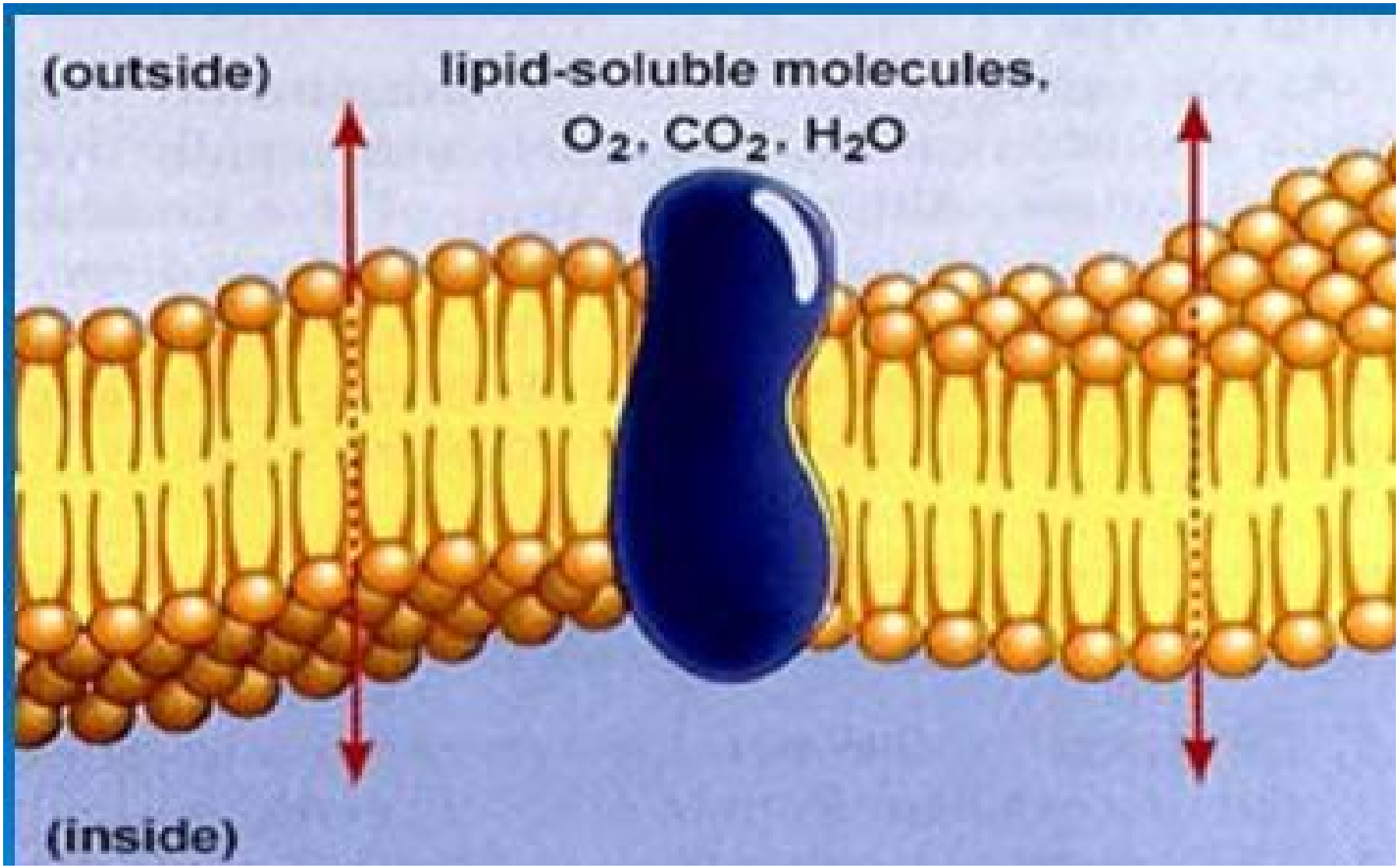
As a result of diffusion, molecules reach an equilibrium where they are evenly spread out. This is when there is no net movement of molecules from either side.

Movement along electrical gradient

- Movement of charged particles is also affected by their electrical gradient.
- If a relative difference in charges exists between two adjacent areas, the cations tend to move towards more negatively charged area, whereas the anions tend to move toward the more positively charged areas.
- The simultaneous existence of an electrical and concentration (chemical) gradient for a particular ion is referred to as an electro-chemical gradient.



Concentration gradient (A) and diffusion (B)



Diffusion of lipid molecules

Carrier- Mediated Transport

All carrier proteins distance the thickness of the plasma membrane and are able to undergo reversible changes in shape so that specific binding site can alternately be exposed at either side of the membrane.

Carrier- Mediated transport displays three characteristics:

- **1. Specificity:** each cell possesses protein specified to transport a specific substance or few closely-related chemical compounds.
- Amino acid cannot bind to glucose carrier, but similar amino acids may use the same carrier.

- **2. Saturation**: limited number of carrier site are available within a particular plasma membrane for a specific molecule. This limit is known as **transport maximum** (Tm).
- The substance's rates of transport across the membrane are directly related to its concentration. When the Tm is reached, the carrier is saturated, and the rate of transport is maximum.
- Further increase in the substance concentration is not accompanied by corresponding increase in the rate of transport.

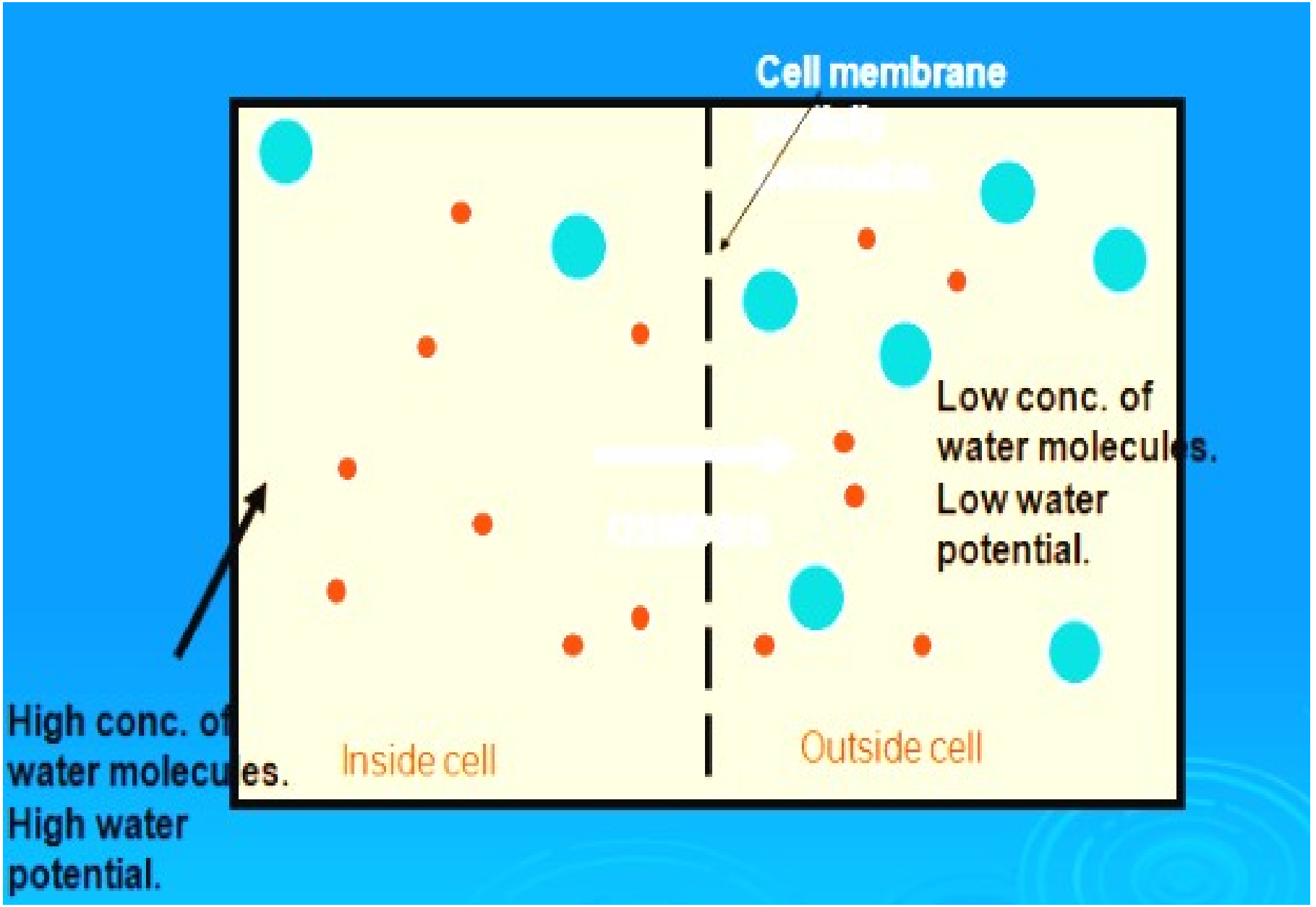
- **3. Competition:** Several closely related compounds may compete for ride across the plasma membrane on the same carrier.

* Facilitated Diffusion

- Facilitated diffusion uses a carrier protein to facilitate the transfer of a particular substance across the membrane ''downhill'' from higher to lower concentration.
- This process is passive and does not require energy because movement occurs naturally down a concentration gradient.

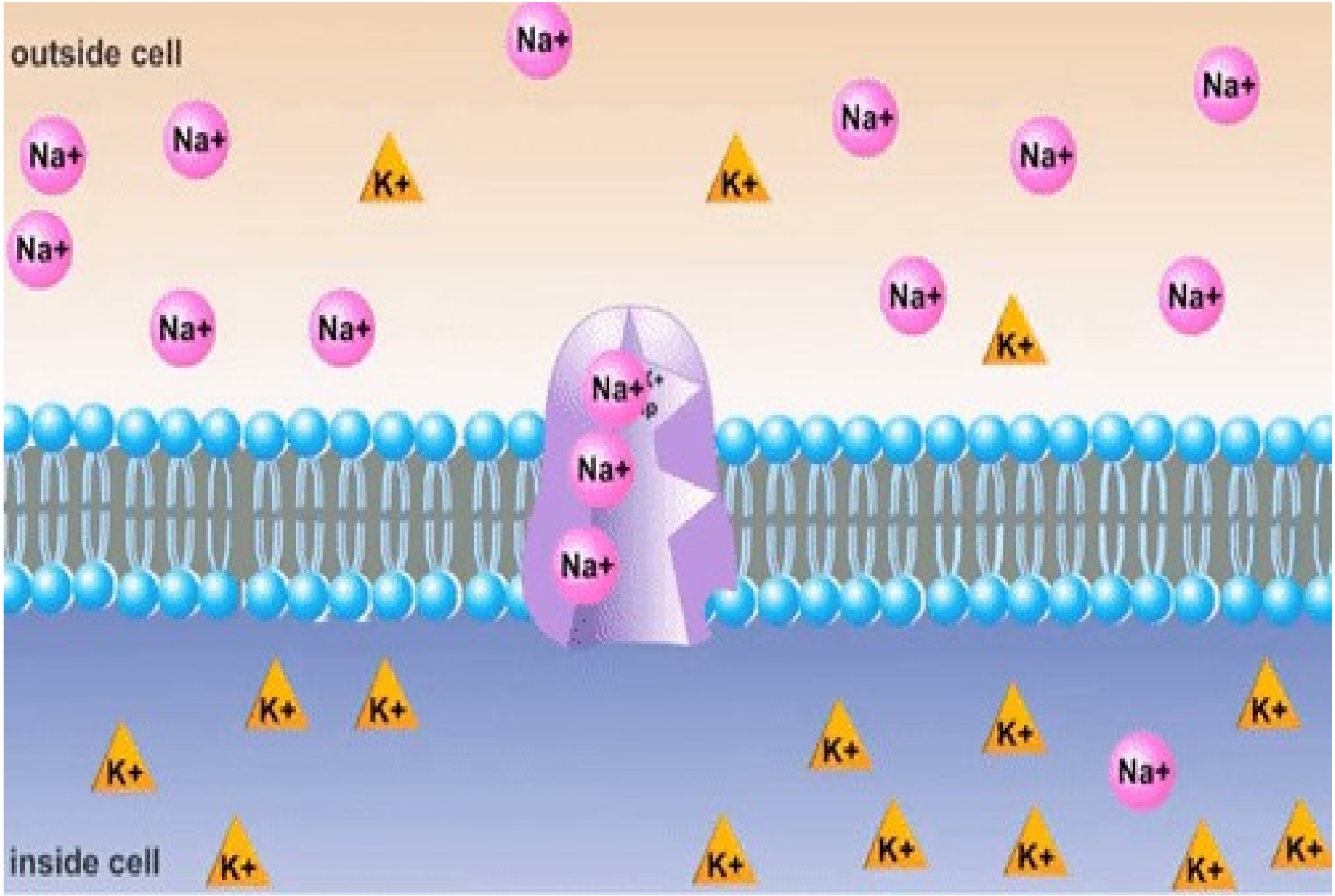
* Osmosis

- Osmosis is the net diffusion of water down its own concentration gradient.
- Water can readily permeate the plasma membrane. The driving force for diffusion of water is its concentration gradient from area of higher water concentration (low solute) to the area of lower water (high solute) concentration. This net diffusion of water is known as osmosis.
- Special mechanisms are used to transport selected molecules unable to cross the plasma membrane on their own.


Cell membrane
Low conc. of water molecules. Low water potential.
High conc. of water molecules. High water potential.
Inside cell
Outside cell

* Active transport

- It is an energy consuming transport of molecules or ions across a membrane against its natural tendency to diffuse in the opposite direction.
- The movement of molecules in active transport is in one direction only; unlike diffusion that is reversible the energy is supplied by the broke down of ATP, which energy carrier is made in respiration.
- It requires the carrier to expend energy to transfer its passenger ''uphill'' against a concentration gradient from an area of lower concentration to an area of higher concentration.



Sodium-Potassium pump

- **Na^+-K^+-pump plays three important roles:**

- 1. It establishes sodium and potassium concentration gradients across the plasma membrane of all cells; these gradients are important in the nerve and muscle to generate electrical signals.
- 2. It helps to regulate cell volume by controlling the concentration of solutes inside the cell and thus minimizing osmotic effects that would induce swelling or shrinking of the cell.
- 3. The energy used to run the pump also indirectly serves as the energy source for the co-transport of glucose and amino acids across the membrane (intestine and kidney cell).

How molecules cross cell membrane

	Active/ Passive	Molecules that Move	Direction	Energy Needed?	Protein Needed?
Diffusion	Passive	small, hydrophobic	down gradient (toward low conc.)	no	no
Osmosis	Passive	water	toward high conc. of solutes	no	no
Facilitated Diffusion	Passive	any (specific transporter)	down gradient (toward low cons.)	no	yes
Active Transport	Active	any (specific transporter)	specific: in or out, dep. on transporter	yes	yes

Bulk Transport

Exocytosis and Endocytosis

- **Vesicular Transport:** The special cell membrane transport system selectively transports ions and small polar molecules. But large polar molecules and even multimolecular material may leave or enter the cell, such as hormone secretion or ingestion of invading microbe by leukocytes.
- Transport into the cell is termed **endocytosis**, whereas transport out of the cell is called **exocytosis**.

- **Endocytosis** occurs by an in folding or extension of cell surface membrane to form a vesicle or vacuole. It is of two types.

- **Phagocytosis (cell eating)** material taken up is in solid form. Cells specializing in the processes are called phagocytes and are said to be phagocytic. The sac formed during the uptake is called a phagocytic vacuole.
- **Pinocytosis (cell drink)** material taken up is in liquid form. Vesicles formed are extremely small, in which case the process is known as micropinocytosis and the vesicles as micro-pinocytic vesicles. Pinocytosis is used by the human egg cell to take up nutrients from the surrounding follicle cells.

- **Exocytosis** is the reverse process of endocytosis.

- Waste materials such as solid and undigested remains from phagocytic vacuoles may be removed from cells or useful materials may be secreted.
- Secretion of enzymes from the pancreas is achieved in this way.
- Plant cells use exocytosis to export the materials needed to form cell wall.

Comparison b/n Exocytosis & Endocytosis

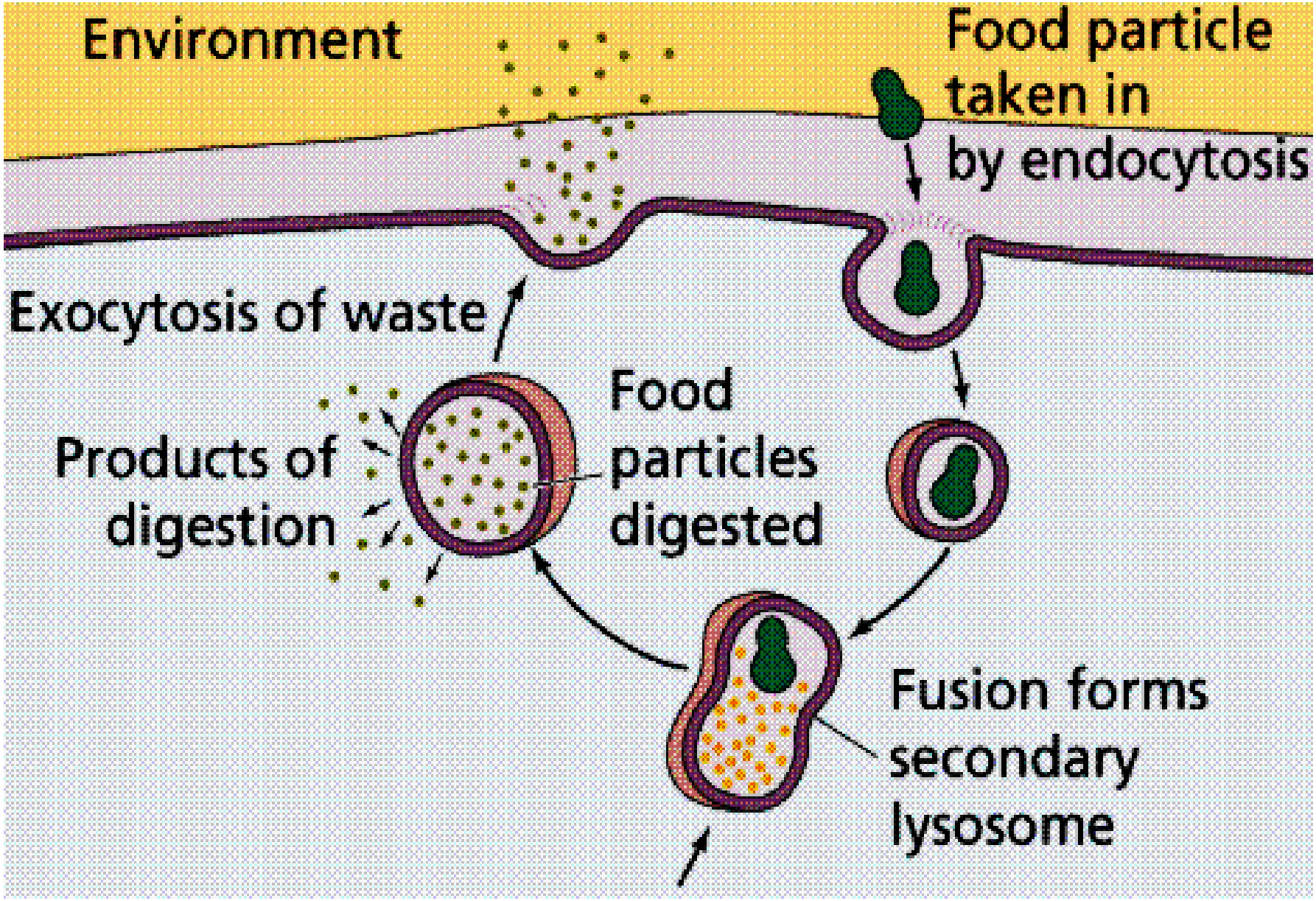
* Exocytosis

- It results is expelling molecules outside the cell.
- This process leads to the destruction of vesicles.
- There is a discharge of enzymes, hormones, proteins, and glucose. All these constituents are used for the functioning of other body parts.
- Example 1: Neurotransmitters released from the neuron cells.
- Example 2: In case of an infection, the cells communicate among themselves, and strengthen the immune system of the body by the process of exocytosis.
- This process helps in expelling wastes from the body.

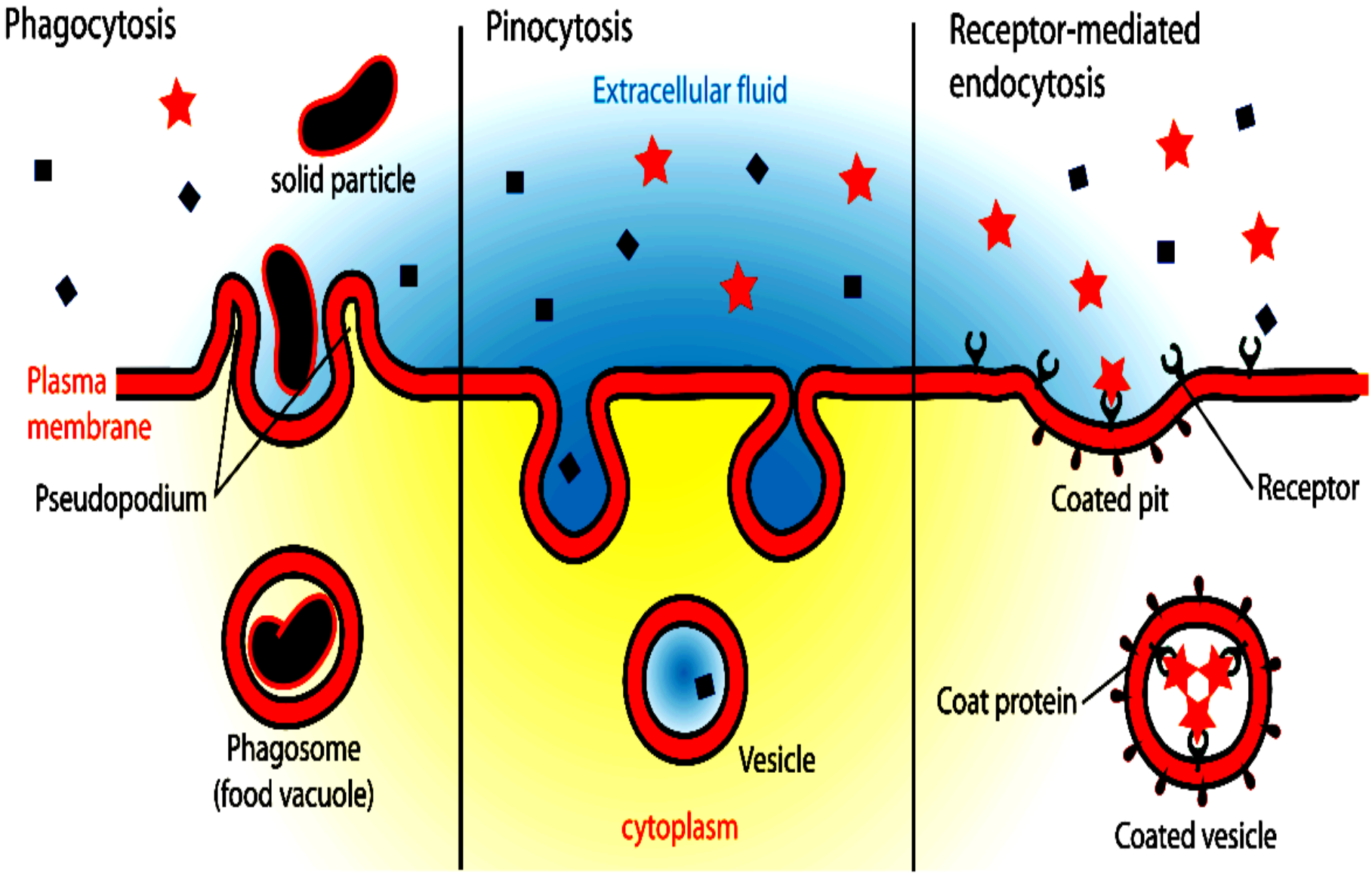
* Endocytosis

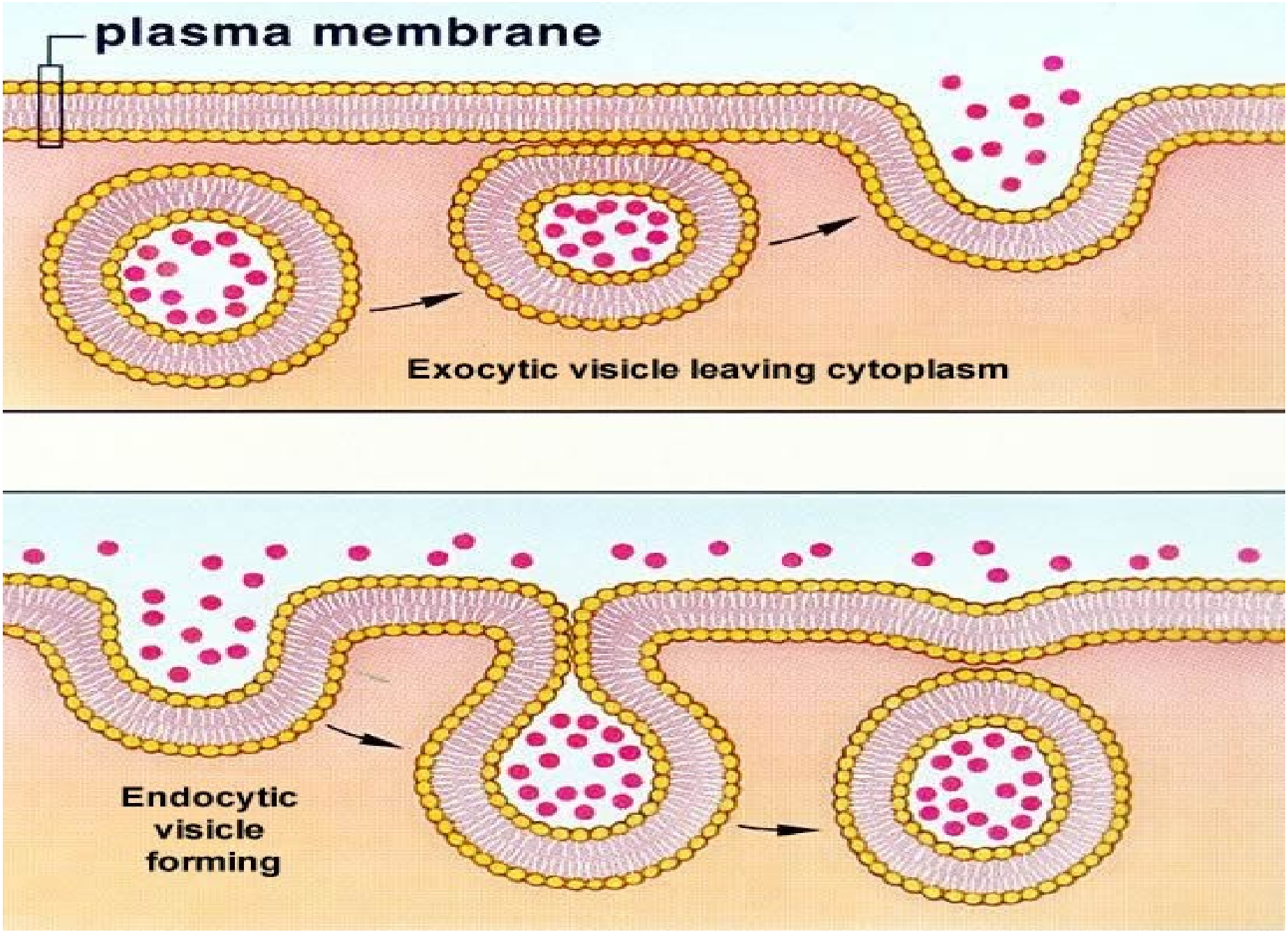
- It helps to ingest molecules towards the cell interior.
- This process leads to creation of vesicles.
- By this process, nutrients, food particles, and proteins are received by the body cells. Apart from this, some bacteria and pathogens can also gain entry into the body through this process.
- Example 1: The body cells engulf pathogens and destroy them.
- Example 2: Endocytosis is used in case of cell migration and adhesion related functions.
- This process serves as a signal receptor.

➢ Thus, the processes of exocytosis and endocytosis are opposite, as well as complementary to each other. These mechanisms are very important for the existence and


Environment
Food particle taken in by endocytosis
Exocytosis of waste
Products of digestion
Food particles digested
Fusion forms secondary lysosome

Endocytosis




plasma membrane
Exocytic visicle leaving cytoplasm
Endocytic visicle forming

Unit 4
Cellular Metabolism and Metabolic Disorders

4.1 Cellular metabolism

- Living organisms are unique in that they can extract energy from their environments and use it to carry out activities such as movement, growth and development, and reproduction.
- Their cells extract energy in the enzyme-mediated chemical reactions that take place in living matter (metabolism).

- **Metabolism** is the sum of chemical reactions that takes place within a living organism that provides energy for vital processes (**catabolic reactions**) and synthesizing of new organic materials (**anabolic reactions**).
- In metabolism, a series of chemical reactions in which the product of one reaction is the substrate for the next reaction is called a **metabolic pathway.**
- Catabolic pathways release energy by breaking down larger molecules into smaller molecules.

- Anabolic pathways use the energy released by catabolic pathways to build larger molecules from smaller molecules, insuring the continual flow of energy within an organism.
- The reactants and products of these chemical reactions are **metabolites**.
- The major classes of metabolites include proteins, carbohydrates, nucleotides, lipids, coenzymes, and cofactors.

- Polar metabolites are soluble in aqueous solutions and include most sugars, purines and pyrimidines, nucleotides and nucleosides, etc.
- These metabolites include most of the reactants and products involved in cellular respiration (e.g., glycolysis, the Krebs's cycle, or in other pathways) and in the production of building blocks for synthesis of large biopolymers such as DNA, RNA, proteins, and oligosaccharides.
- The nonpolar metabolites are commonly lipids. These metabolites function in energy storage, membrane structure, and signal transduction.

4.1.1 Enzymes and their role in metabolism

- In many cases, heat may be a catalyst, but this is inefficient because heat cannot be applied to molecules in a controlled fashion. Thus, most chemical reactions require biological catalyst called enzymes.

What are enzymes and why they are needed?

- Enzymes are protein catalysts that speed biochemical reactions by facilitating the molecular rearrangements that support cell function.
- Enzymes speed up (**catalyze**) chemical reactions; in some cases, enzymes can make a chemical reaction millions of times faster than it would have been without it.

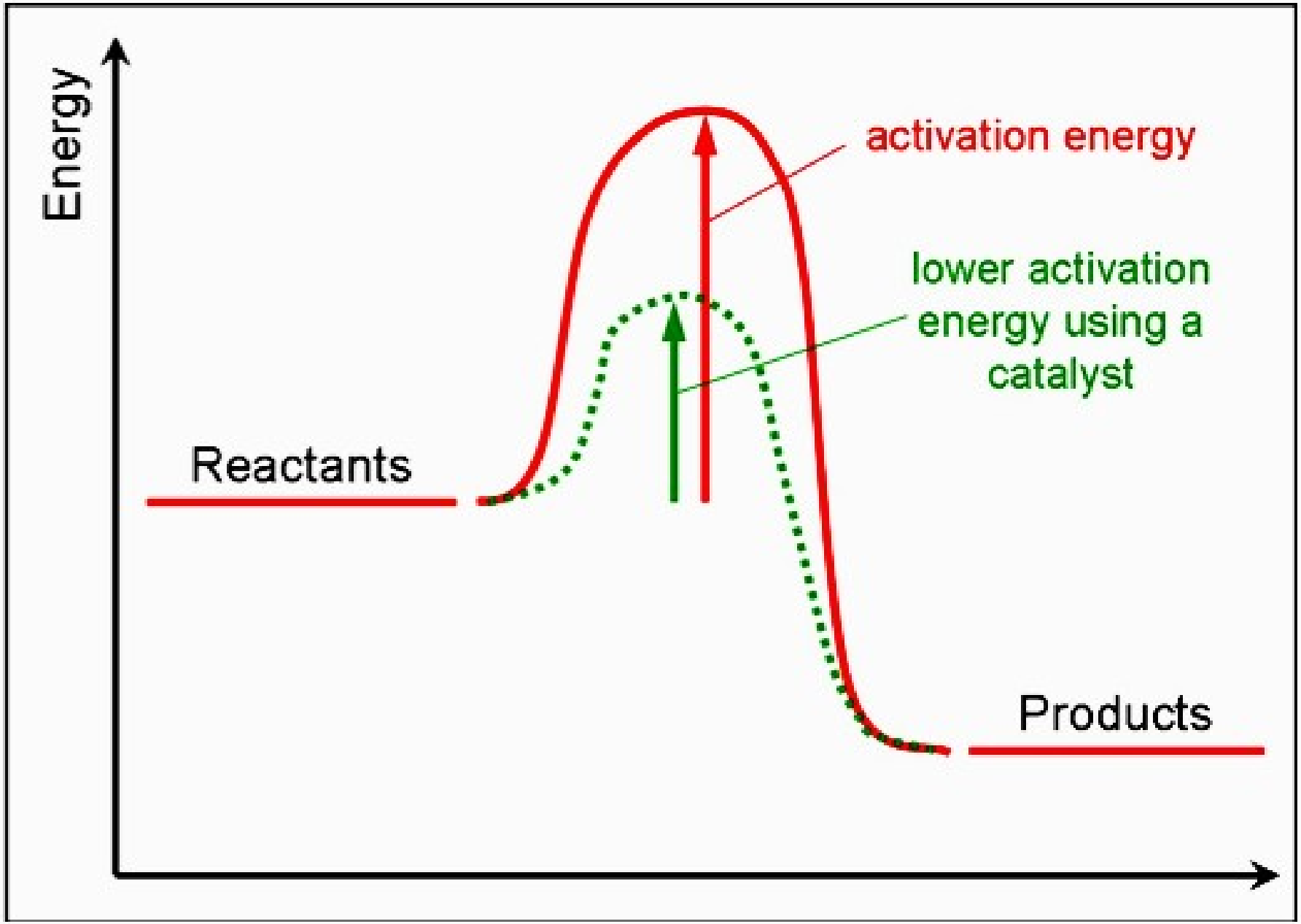
- Enzymes bind with particular reactants until the chemical reaction occurs, then free themselves.

How do enzymes speed up chemical reactions?

- Enzymes speed up reactions by lowering activation energy. Many enzymes change shape when substrates bind. This is termed "induced fit", meaning that the precise orientation of the enzyme required for catalytic activity can be induced by the binding of the substrate.

What is activation energy?

Activation energy is the minimum energy required to cause a process (such as a chemical reaction) to occur.


Energy
activation energy
lower activation energy using a catalyst
Reactants
Products

4.1.2 Chemical nature and classification of enzymes

- All known enzymes are proteins with the exception of recently discovered RNA enzymes. Some enzymes may additionally contain a non-protein group. Enzymes are high molecular weight compounds made up principally of chains of amino acids linked together by peptide bonds.
- Many enzymes require the presence of other compounds (cofactors) before their catalytic activity can be exerted. This entire active complex is referred to as the **holoenzyme**; i.e., apoenzyme (protein portion) plus the cofactor (coenzyme, prosthetic group or metal-ion-activator).

- On the basis of differences in chemical nature, the enzymes may be described as follows:

  - **Conjugate enzyme**: an enzyme which is formed of two parts – a protein part called **apoenzyme** (e.g., flavoprotein) and a non-protein part named cofactor.

The complete conjugate enzyme, consisting of an **apoenzyme** and a **cofactor**, is called **holoenzyme**.

There can be an enzymatic activity only when both components (apoenzyme and cofactor) are present together.

- The cofactor is sometimes a simple divalent metallic ion (e.g. Ca, Mg, Zn, Co, etc), and sometimes a nonprotein organic compound. However, some enzymes require both kinds of cofactors.
- If the cofactor is firmly bound to the apoenzyme, it is called **prosthetic group**. For example, **cytochromes** are the enzymes that possess **porphyrins** (important in biochemistry in a form with a metal atom in the central cavity) as their prosthetic groups.

- If instead of being more or less permanently bound to the apoenzyme; the cofactor attaches itself to the apoenzyme only at the time of reaction, it is called a **coenzyme**.

➢ **Simple enzymes:** are made up of only protein (polypeptide). They contain no chemical groups other than amino acid residues. Digestive enzymes such as pepsin and trypsin are of this nature.

➢ **Metallo-enzymes:** The metal cofactors involved in enzymic reactions are monovalent (K^{+}) and divalent cations (Mg^{++}, Mn^{++} and Cu^{++}).

These may be loosely held by the enzyme, or as in some cases, go into the composition of the molecule itself.

If the metal forms part of the molecule, as iron of hemoglobin or cytochrome is, the enzymes are called metallo-enzymes.

- **Isoenzymes (Isozymes):** At one time it was believed that an organism has only a single enzyme for a given step of a metabolic reaction.
- It was later discovered that a substrate may be acted upon by a number of variants of an enzyme producing the same product.

Classes of enzymes based on the substrate they act up on

S.No.	Type of reaction	Description of reaction	Enzyme class
1.	Oxidation – reduction	Transfer of electrons.	Oxidoreductases
2.	Group transfer	Transfer of a functional group from one molecule to another.	Transferases
3.	Hydrolysis	Cleavage of bonds by the addition of water.	Hydrolases
4.	Nonhydrolytic cleavage	Cleaving/splitting a molecule by nonhydrolytic processes.	Lyases
5.	Isomerization & rearrangements	Rearrangement of atoms to form isomers.	Isomerases
6.	Ligation using energy from ATP	Formation of Carbon and other bonds with energy from ATP.	Ligases

(Source: Concepts in Biochemistry; Rodney Boyer)

4.1.3 Mechanisms of enzyme action

- Mechanisms of enzyme catalysis vary, but are all similar in principle to other types of chemical catalysis in that the crucial factor is a reduction of energy barrier(s) separating the reactants from the products.
- The reduction of activation energy increases the fraction of reactant molecules that can overcome this barrier and form the product.
- An important principle is that since they only reduce energy barriers between products and reactants, enzymes always catalyze reactions in both directions, and cannot affect the equilibrium position.

- An enzyme attracts substrates to its active site, catalyzes the chemical reaction by which products are formed, and then allows the products to dissociate (separate from the enzyme surface).
- The combination formed by an enzyme and its substrates is called the **enzyme–substrate complex**.
- The substrates are attracted to the active site by **electrostatic and hydrophobic forces**, which are called **noncovalent bonds** because they are physical attractions and not chemical bonds.

4.1.4 Factors affecting enzymatic activities

- The activity of an enzyme is affected by its environmental conditions such as temperature and pH. Changing these alter the rate of reaction caused by the enzyme.
- In nature, organisms adjust the conditions of their enzymes to produce an optimum rate of reaction, where necessary, or they may have enzymes which are adapted to function well in extreme conditions where they live.

❖ Temperature

- Increasing temperature increases the **kinetic energy** that molecules possess. In a fluid, this means that there are more random collisions between molecules per unit time.
- Since enzymes catalyze reactions by randomly colliding with substrate molecules, increasing temperature increases the rate of reaction, forming more product.
- However, increasing temperature also increases the vibrational energy that molecules have, specifically (in this case enzyme molecules), which puts strain (damage) on the bonds that hold them together.

- As temperature increases, more bonds, especially the weaker hydrogen and ionic bonds, will break as a result of this strain.
- Breaking bonds within the enzyme will cause the **active site** to change shape. Eventually, the enzyme will become denatured and will no longer function.
- The temperature at which the maximum rate of reaction occurs is called the enzyme's Optimum Temperature. This is different for different enzymes.

❖ pH - Acidity and Basicity

- pH is a measure of the hydrogen ion (H^+) concentration, and therefore a good indicator of the hydroxide ion (OH^-) concentration.
- Lower pH values mean higher H^+ concentrations and lower OH^- concentrations. H^+ and OH^- ions are charged and therefore interfere with hydrogen and ionic bonds that hold together an enzyme, since they will be attracted or repelled by the charges created by the bonds.

- Different enzymes have different optimum pH values. This is the pH value at which the bonds within them are influenced by H^+ and OH^- ions in such a way that the shape of their active site is the most complementary to the shape of their substrate.
- At the optimum pH, the rate of reaction is at an optimum. Any change in pH above or below the optimum will quickly cause a decrease in the rate of reaction, since more of the enzyme molecules will have active sites whose shapes are not (or at least are less) complementary to the shape of their substrate.

- Changing the enzyme and substrate concentrations affect the rate of reaction of an enzyme-catalyzed reaction.
- Changing the concentration of a substance only affects the rate of reaction if it is the limiting factor.
- If it is the limiting factor, increasing concentration will increase the rate of reaction up to a point, after which any increase will not affect the rate of reaction

Substrate concentration

- Increasing substrate concentration increases the rate of reaction. This is because more substrate molecules will be colliding with enzyme molecules, so more product will be formed.
- However, after a certain concentration, any increase will have no effect on the rate of reaction, since substrate concentration will no longer be the limiting factor. The enzymes will effectively become saturated, and will be working at their maximum possible rate.

Enzyme concentration

- Increasing enzyme concentration will increase the rate of reaction, as more enzymes will be colliding with substrate molecules.
- However, this too will only have an effect up to a certain concentration, where the enzyme concentration is no longer the limiting factor.

4.1.5 Enzyme inhibitors

- Enzyme activity can be inhibited in various ways. Inhibition could be reversible or irreversible.

❖ **Reversible inhibition**

❑ **Competitive inhibition**: occurs when molecules very similar to the substrate molecules bind to the active site and prevent binding of the actual substrate.

- Penicillin, for example, is a competitive inhibitor that blocks the active site of an enzyme that many bacteria use to construct their cell walls.

- **Noncompetitive inhibition**: occurs when an inhibitor binds to the enzyme at a location other than the active site.

- In some cases of noncompetitive inhibition, the inhibitor is thought to bind to the enzyme in such a way as to physically block the normal active site. In other instances, the binding of the inhibitor is believed to change the shape of the enzyme molecule, thereby deforming its active site and preventing it from reacting with its substrate.

- This latter type of noncompetitive inhibition is called **allosteric inhibition**; the place where the inhibitor binds to the enzyme is called the allosteric site. Frequently, an end-product of a metabolic pathway serves as an allosteric inhibitor on an earlier enzyme of the pathway.
- This inhibition of an enzyme by a product of its pathway is a form of **negative feedback**.

- **Activators:** Allosteric control can involve stimulation of enzyme action as well as inhibition.

- An activator molecule can be bound to an allosteric site and induce a reaction at the active site by changing its shape to fit a substrate that could not induce the change by itself.
- Common activators include hormones and the products of earlier enzymatic reactions.
- Allosteric stimulation and inhibition allow production of energy and materials by the cell when they are needed and inhibit production

❖ Irreversible inhibition

- Irreversible inhibitors usually covalently modify an enzyme, and inhibition can therefore not be reversed.
- Irreversible inhibitors often contain reactive functional groups.
- Irreversible inhibition is different from reversible enzyme inactivation.
- Irreversible inhibitors are generally specific for one class of enzyme and do not inactivate all proteins; they do not function by destroying protein structure but by specifically altering the active site of their target

4.2 Bioenergetics and biosynthesis

4.2.1 Cellular respiration

The function of cellular respiration is to harvest electrons from carbon compounds, such as glucose, and use that energy to make Adenosine Tri Phosphate (ATP). ATP is used to provide immediate energy for cells to do work. This catabolic process can be divided into 3 phases.

- **Phase I** - Breakdown of large complex biomolecules like polysaccharides, proteins and lipids into their respective building blocks (**hydrolysis**). The chemical

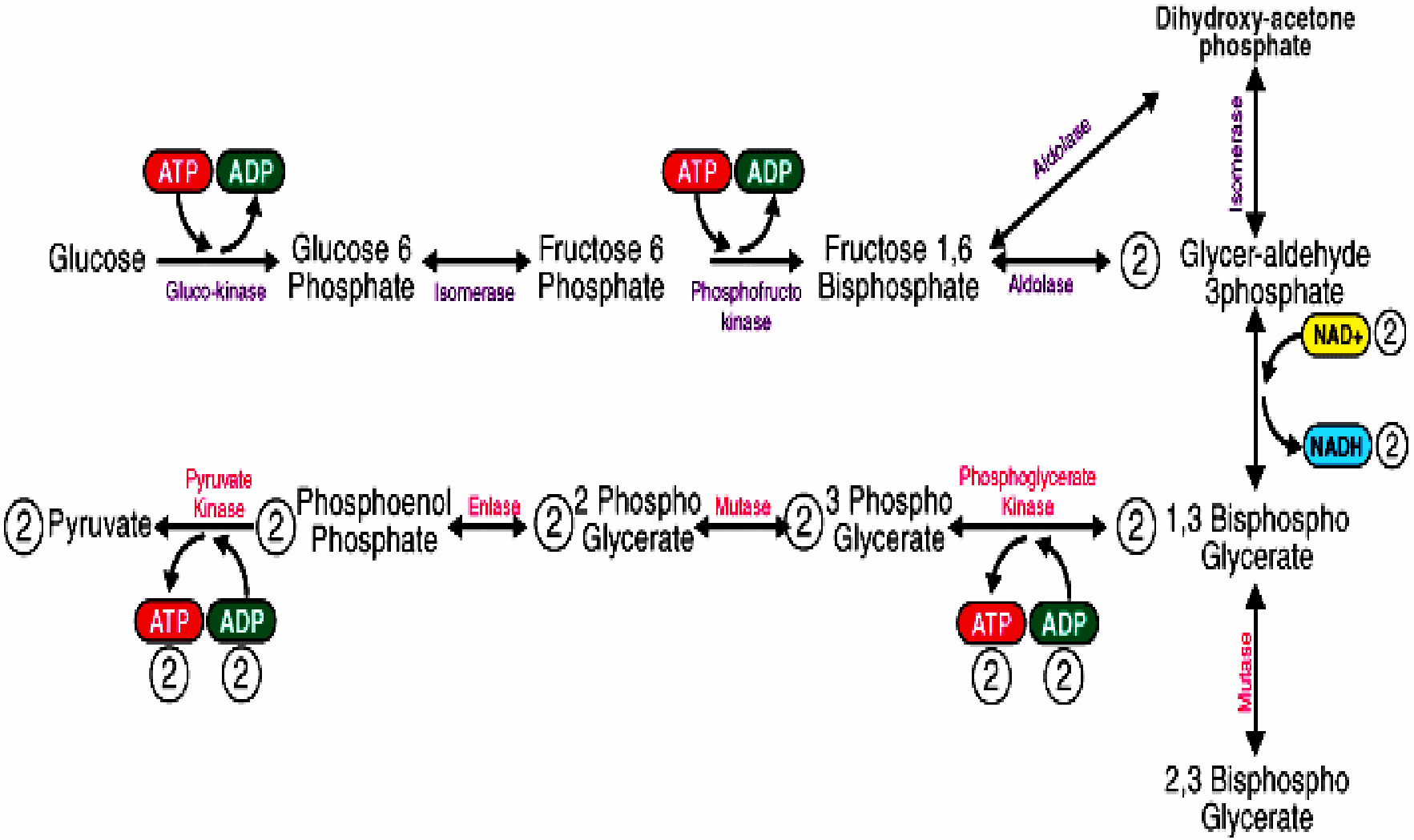
- **Phase II** - These building blocks are usually oxidized to a common intermediate, acetyl - CoA. Additionally, pyruvate or other citric acid cycle intermediates may also be formed (in glycolysis and other pathways).
- **Phase III** – This consists of the citric acid cycle (i.e. oxidation of acetyl - CoA to CO_2, formation of NADH and $FADH_2$) followed by electron transport and oxidative phosphorylation. Energy released by electron transport to O_2 is coupled to ATP synthesis. This cycle is responsible for the release of much energy (TCA cycle and ETC).

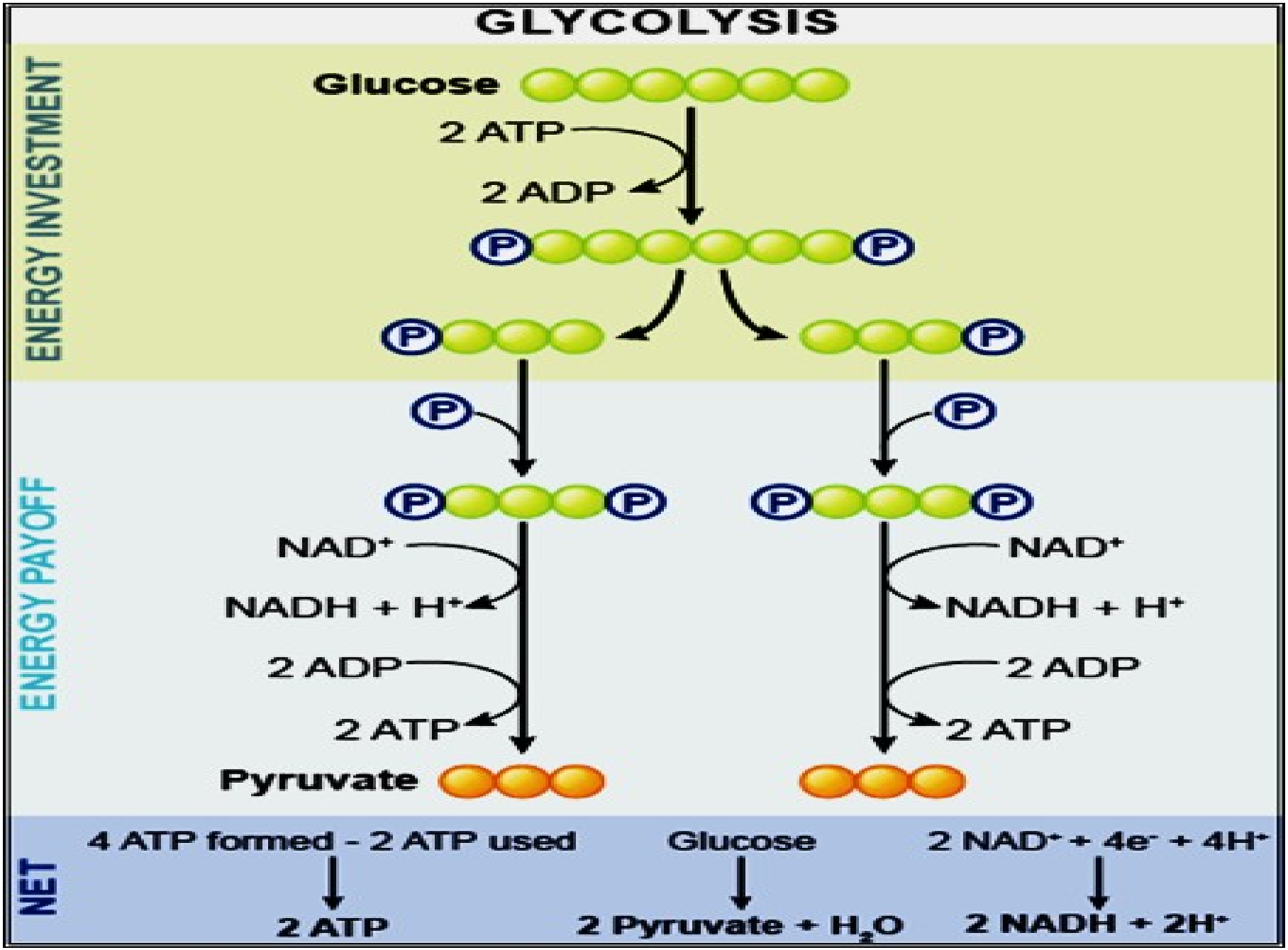
- Cellular respiration occurs in two main parts: glycolysis and aerobic respiration.
- The first stage, glycolysis, is an anaerobic process.
- Aerobic respiration includes the Krebs cycle and electron transport chain.
- Aerobic metabolic processes require oxygen.

4.2.1.1 Glycolysis: anaerobic respiration

- Glucose is a key metabolite in metabolism. Various pathways that are concerned with the utilization, storage, and regeneration of glucose exist.
- Glycogen is synthesized when glucose supply is high, and its degradation helps to maintain the blood glucose level when we are fasting.
- When glycogen is depleted, more glucose is synthesized from starch in gluconeogenesis.
- Gluconeogenesis occurs in the liver and in the kidneys.

PATHWAY OF GLYCOLYSIS




GLYCOLYSIS
ENERGY INVESTMENT
Glucose
2 ATP
2 ADP
ENERGY PAYOFF
NAD+
NADH + H+
2 ADP
2 ATP
Pyruvate
NET
4 ATP formed – 2 ATP used
2 ATP
Glucose
2 Pyruvate + H2O
2 NAD+ + 4e- + 4H+
2 NADH + 2H+

- Glycolysis, which translates to "splitting sugars", is the process of releasing energy within sugars.
- In glycolysis, a six-carbon sugar known as glucose is split into two molecules of a three-carbon sugar called pyruvate.
- This multistep process yields two ATP molecules containing free energy, two pyruvate molecules, two high energy, electron-carrying molecules of NADH, and two molecules of water.

Glycolysis

- It is the process of breaking down glucose.
- It can takes place with or without oxygen.
- It produces two molecules of **pyruvate**, two molecules of **ATP**, two molecules of **NADH**, and two molecules of **water**.
- It takes place in the **cytoplasm**.
- There are 10 enzymes involved in breaking down sugar. The 10 steps of glycolysis are organized by the order in which specific enzymes act upon the system.
- In the presence of oxygen, glycolysis is the first stage of cellular respiration.
- In the absence of oxygen, glycolysis allows cells to make small amounts of ATP through a process of fermentation.

The 10 steps of glycolysis

Step 1: The enzyme **hexokinase** phosphorylates or adds a phosphate group to glucose in a cell's cytoplasm. In the process, a phosphate group from ATP is transferred to glucose producing glucose 6-phosphate or G6P. One molecule of ATP is consumed during this phase.

Step 2: The enzyme **phosphoglucomutase** isomerizes G6P into its isomer fructose 6-phosphate or F6P. Isomers have the same molecular formula as each other but different atomic arrangements.

- Step 3: The kinase **phosphofructokinase** uses another ATP molecule to transfer a phosphate group to F6P in order to form fructose 1,6-bisphosphate or FBP. One ATP molecule has been used so far.
- Step 4: The enzyme **aldolase** splits fructose 1,6-bisphosphate into a ketone and an aldehyde molecule. These sugars, dihydroxyacetone phosphate (DHAP) and glyceraldehyde 3-phosphate (GAP), are isomers of each other.
- Step 5: The enzyme **triose-phosphate isomerase** rapidly converts DHAP into GAP (these isomers can inter-convert).
- GAP is the substrate needed for the next step of glycolysis.

- Step 6: The enzyme **glyceraldehyde 3-phosphate dehydrogenase** (GAPDH) serves two functions in this reaction.
- First, it dehydrogenates GAP by transferring one of its hydrogen (H^+) molecules to the oxidizing agent nicotinamide adenine dinucleotide (NAD^+) to form NADH + H^+.
- Next, GAPDH adds a phosphate from the cytosol to the oxidized GAP to form 1,3-bisphosphoglycerate (BPG). Both molecules of GAP produced in the previous step undergo this process of dehydrogenation and phosphorylation.

- Step 7: The enzyme **phosphoglycerokinase** transfers a phosphate from BPG to a molecule of ADP to form ATP. This happens to each molecule of BPG. This reaction yields two 3-phosphoglycerate (3 PGA) molecules and two ATP molecules.
- Step 8: The enzyme **phosphoglyceromutase** relocates the P of the two 3 PGA molecules from the third to the second carbon to form two 2-phosphoglycerate (2 PGA) molecules.

- Step 9: The enzyme **enolase** removes a molecule of water from 2-phosphoglycerate to form phosphoenolpyruvate (PEP). This happens for each molecule of 2 PGA from Step 8.
- Step 10: The enzyme **pyruvate kinase** transfers a P from PEP to ADP to form pyruvate and ATP. This happens for each molecule of PEP. This reaction yields two molecules of pyruvate and two ATP molecules.
- The overall reaction of glycolysis which occurs in the cytoplasm is represented simply as:

$C_6H_{12}O_6$ + 2 NAD^+ + 2 ADP + 2 P —–> 2 pyruvic acid,

($CH_3(C=O)COOH$ + 2 ATP + 2 NADH + 2 H^+

Summary on Glycolysis

- Glycolysis is derived from the Greek words (glykys = *sweet and* lysis = *splitting*). It is a universal catabolic pathway in the living cells.
- **Glycolysis can be defined as** the sequence of reactions for the breakdown of Glucose (6-carbon molecule) to two molecules of pyruvic acid (3-carbon molecule) under aerobic conditions; or lactate under anaerobic conditions along with the production of small amount of energy.
- This pathway was described by Embden, Meyerhof and Parnas. Hence, it is also called as **Embden-Meyerhof pathway** (EM pathway).

Summary on Glycolysis …

- **Site of Glycolysis**

- Glycolysis occurs in the cytoplasm of virtually all the cells of the body.

- **Types of Glycolysis**

- **Aerobic Glycolysis**: It occurs when oxygen is plentiful. Final product is **pyruvate** along with the production of Eight ATP molecules.
- **Anaerobic Glycolysis**: It occurs when oxygen is scarce. Final product is **lactate** along with the production of two ATP molecules.

➢ Steps of Glycolysis

- Glycolysis is an extramitochondrial pathway and is carried by a group of eleven enzymes. Glucose is converted to pyruvate in 10 steps by glycolysis.
- **The glycolytic pathway can be divided into two phases:**

➢ Preparatory Phase :

- This phase is also called **glucose activation phase**. In the preparatory phase of glycolysis, two molecules of ATP are invested and the hexose chain is cleaved into two triose phosphates.
- During this, phosphorylation of glucose and it's conversion to glyceraldehyde-3-phosphate take place.
- The steps 1, 2, 3, 4 and 5 together are called as the preparatory phase.

➢ Payoff Phase :

- This phase is also called **energy extraction phase**. During this phase, conversion of glyceraldehyde-3-phophate to pyruvate and the coupled formation of ATP take place.
- Because glucose is split to yield two molecules of D-Glyceraldehyde-3-phosphate, each step in the payoff phase occurs twice per molecule of glucose.
- The steps after 5 constitute preparatory phase.

Net energy (ATP) yield per molecule of Glucose in Glycolysis

Energy Yield in Aerobic Glycolysis

Step	Enzyme	Source	No. of ATP
1	Hexokinase	–	-1
3	Phosphofructokinase	–	-1
6	Glyceraldehyde-3-phosphate dehydrogenase	NADH	(+3) x 2 = +6
7	Phosphoglycerate kinase	ATP	(+1) x 2 = +2
10	Pyruvate kinase	ATP	(+1) x 2 = +2

Energy Yield in Anaerobic Glycolysis

Step	Enzyme	Source	No. of ATP Formed or consumed
1	Hexokinase	–	-1
3	Phosphofructokinase	–	-1
7	Phosphoglycerate kinase	ATP	(+1) x 2 = +2
10	Pyruvate kinase	ATP	(+1) x 2 = +2
Net Yield			2 ATPs

Significance of the Glycolysis Pathway

- It is the only pathway that is taking place in all the cells of the body.
- It is the only source of energy in erythrocytes.
- In strenuous exercise, when muscle tissue lacks enough oxygen, anaerobic glycolysis forms the major source of energy for muscles.
- The glycolytic pathway may be considered as the preliminary step before complete oxidation.
- The glycolytic pathway provides carbon skeletons for synthesis of non-essential amino acids as well as glycerol part of fat.
- Most of the reactions of the glycolytic pathway are reversible, which are also used for gluconeogenesis.

4.2.1.2 TCA cycle : Aerobic respiration

- One fate of **pyruvate** is that it enters to TCA cycle for complete oxidation. But there are intermediate processes that convert pyruvate to a acetyl-CoA.
- The enzyme complex converts pyruvate into Acetyl-CoA by the following chemical changes:

- Decarboxylation of pyruvate (loss of CO_2)
- Formation of acetyl group
- Linkage of acetyl group to coenzyme A forming acetyl - CoA.

The Tricarboxylic Acid (TCA) Cycle (Phase III)

- The TCA cycle also called Krebs or Citric acid cycle, is considered as central pathway of aerobic metabolism, as it serves two purposes-bioenergetics and biosynthesis:

➢ **1. Bioenergetic** - The cycle carries out complex degradation of acetyl group in acetyl - CoA to CO2, resulting in release of energy (ATP or GTP) and reducing power (NADH and FADH2).

- TCA oxidizes two-carbon units, producing two molecules of CO2, one molecule of GP, and high-energy electrons in the form of NADH and FADH2.

Steps of the TCA or Krebs cycle or CA Cycle

- **Step 1:** First the acetyl CoA (a two carbon molecule) joins with oxaloacetate (4 carbon molecule) to form citrate (6 carbon molecule).
- **Step 2:** The citrate is then converted to isocitrate (isomer of citrate)
- **Step 3:** Isocitrate is then oxidized to alpha-ketoglutarate (a five carbon molecule) which results in the release of carbon dioxide. One NADH molecule is also formed in this step.

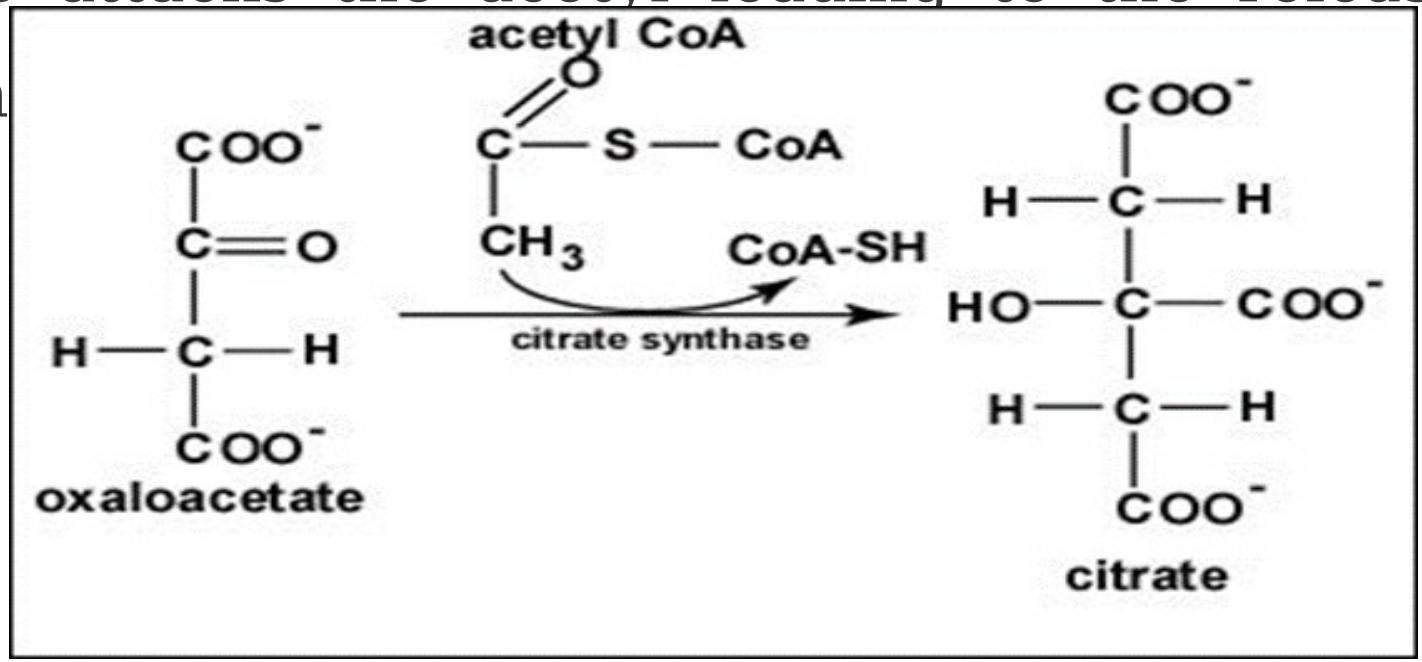
- The enzyme responsible for catalyzing this step is isocitrate dehydrogenase. This is a rate limiting step as isocitrate dehydrogenase is an allosterically controlled enzyme.
- **Step 4:** Here alpha-ketoglutarate is oxidized to form a 4 carbon molecule which picks up coenzyme A forming succinyl CoA. This conversion also forms a NADH molecule.
- **Step 5:** Succinyl CoA is then converted to succinate (4 carbon molecule) and one GTP molecule is produced.

- **Step 6:** Succinate is converted into fumarate (4 carbon molecule) and a molecule of $FADH_2$ is produced.
- **Step 7:** Fumarate is converted to malate (another 4 carbon molecule).
- **Step 8:** Malate is then converted into Oxaloacetate and NADH is also produced here.

Reactions of Krebs Cycle

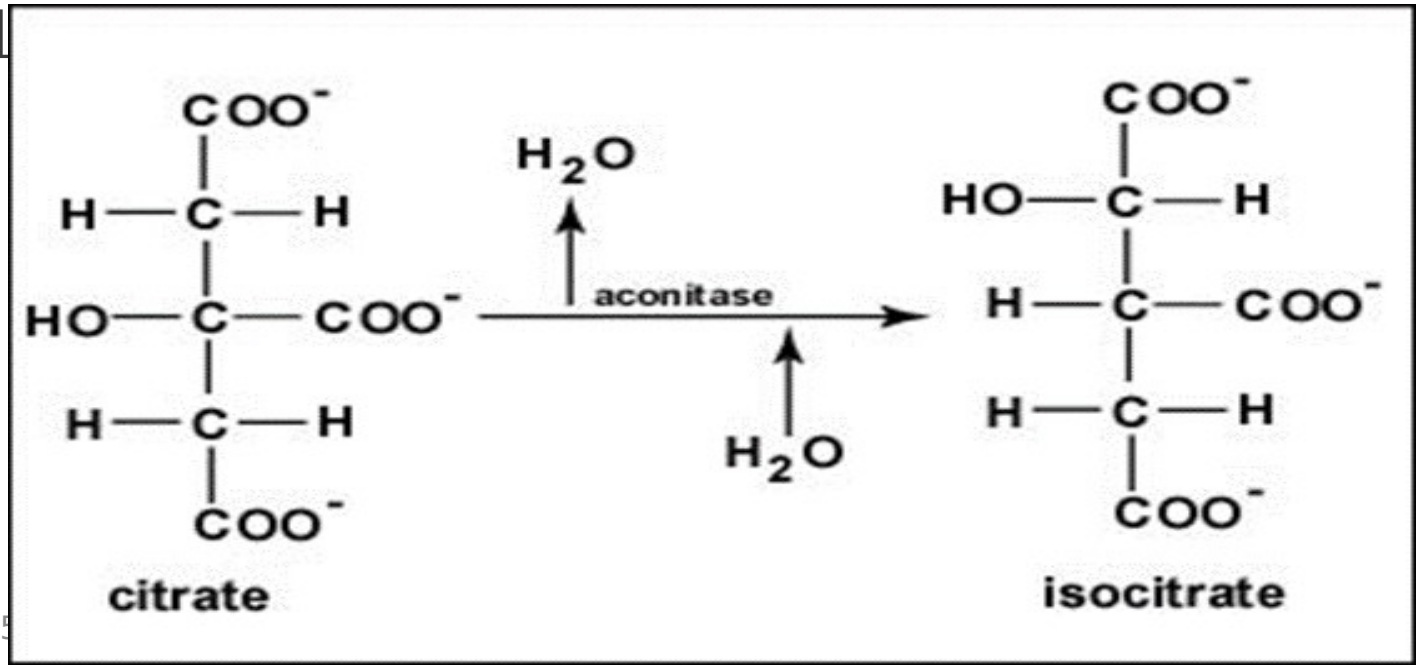
Reaction 1: Formation of Citrate: The condensation of **acetyl-CoA** with **oxaloacetate** to form **citrate**, catalyzed by **citrate synthase**.

Once oxaloacetate is joined with acetyl-CoA, a water molecule attacks the acetyl leading to the release of coenzym



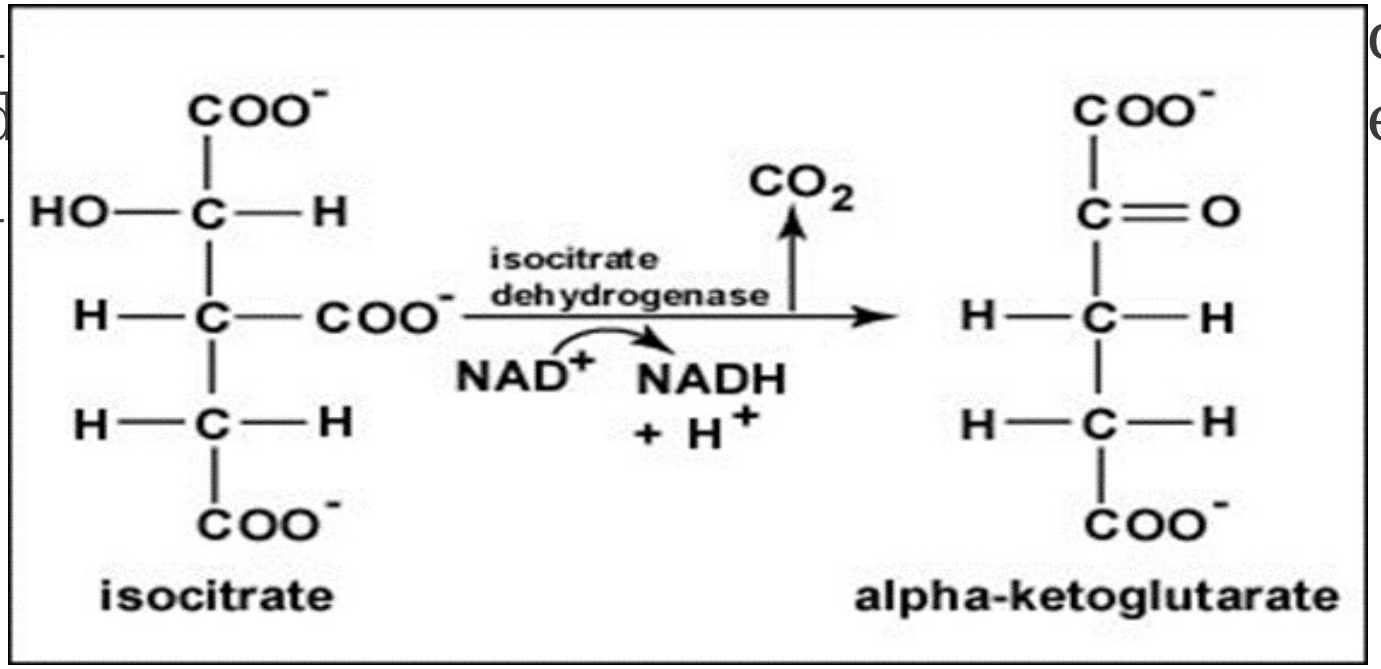
Reaction 2: Formation of Isocitrate: The **citrate** is rearranged to form an isomeric form, **isocitrate** by an enzyme **aconitase.**

•In this reaction, **a water molecule is removed** from the citric acid and then put back on in another location. The overall effect of this conversion is that the –OH group is moved from the 3′ to the 4′ position on the molecule. This transformation yields the molecul



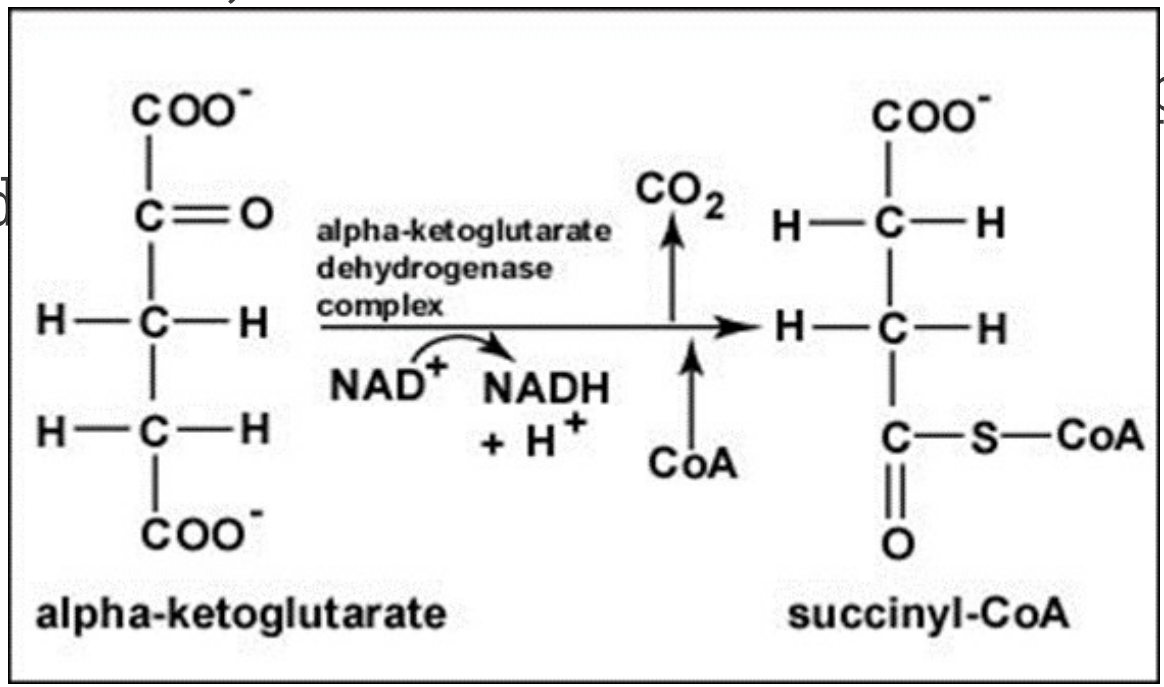
Reaction 3: Oxidation of Isocitrate to α-Ketoglutarate:

- In this step, isocitrate dehydrogenase catalyzes oxidative decarboxylation of **isocitrate** to form **α-ketoglutarate.**
- In the reaction, generation of NADH from NAD is seen. The enzyme **isocitrate dehydrogenase** catalyzes the oxidation of the –OH group a d an intermed ecule removed

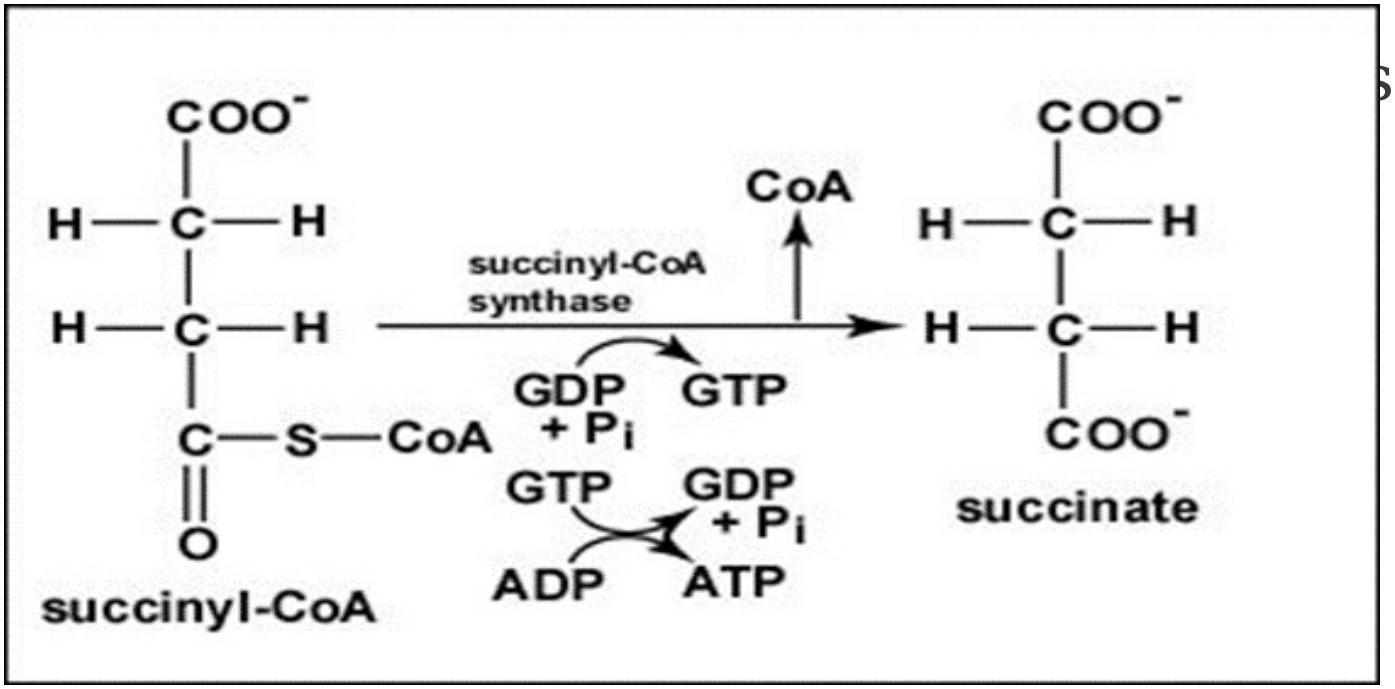


Reaction 4: Oxidation of α-Ketoglutarate to Succinyl-CoA:

- **Alpha-ketoglutarate** is oxidized, carbon dioxide is removed, and coenzyme A is added to form the 4-carbon compound **succinyl-CoA**.
- During this oxidation, NAD^+ is reduced to NADH + H^+. The enzyme **pha-ketoglutarate d**

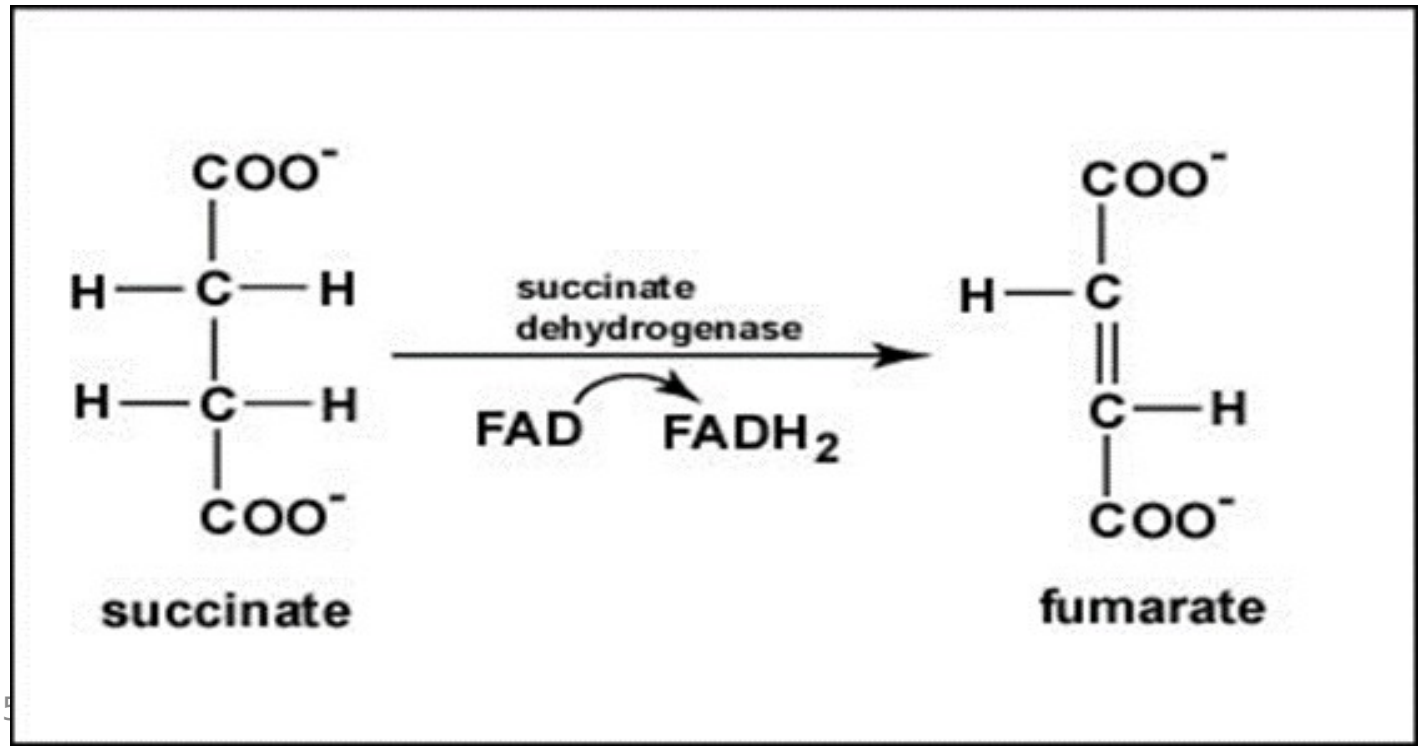


Reaction 5: Conversion of Succinyl-CoA to Succinate: The CoA is removed from **succinyl-CoA** to produce **succinate.** The energy released is used to make guanosine triphosphate (GTP) from guanosine diphosphate (GDP) and Pi by substrate-level phosphorylation. GTP can then be used to make ATP. The s this reaction.



Reaction 6: Oxidation of Succinate to Fumarate:

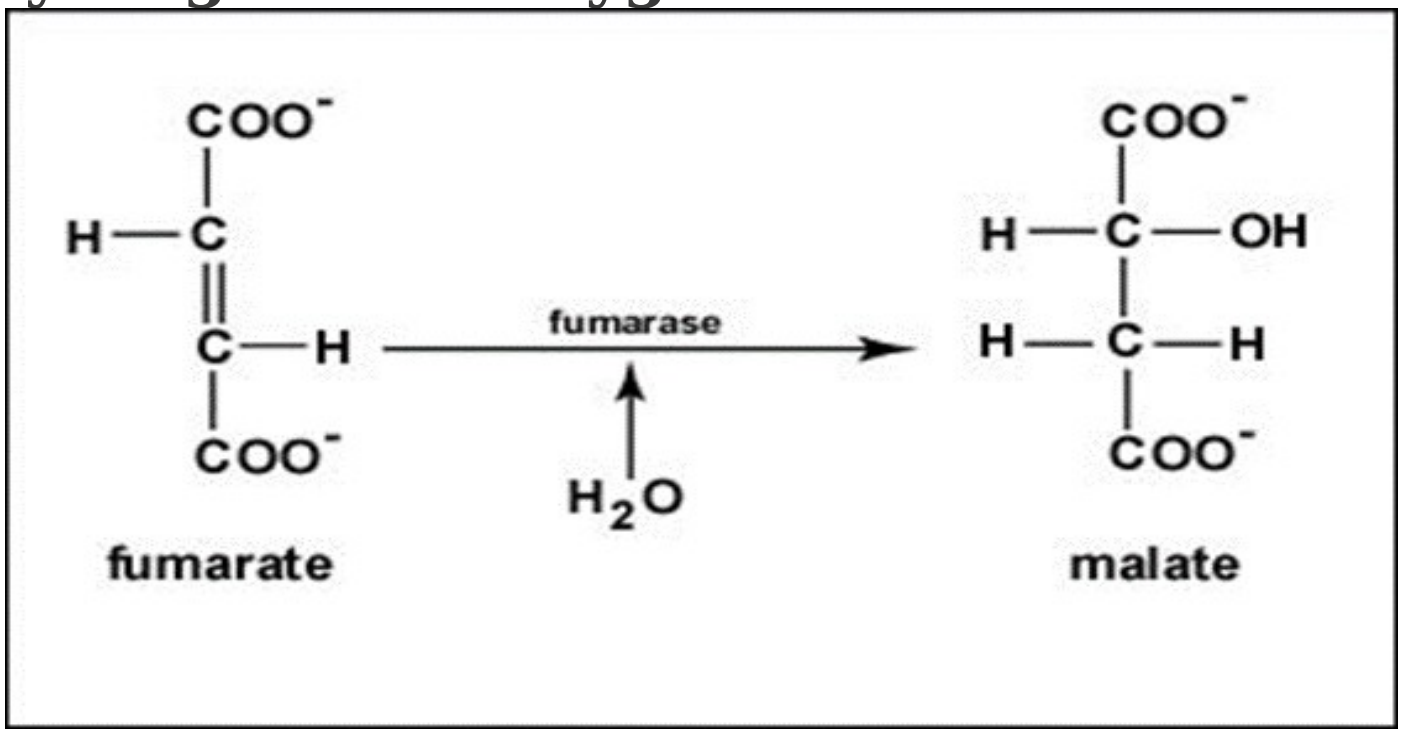
- **Succinate** is oxidized to **fumarate**.
- During this oxidation, FAD is reduced to FADH2. The enzyme **succinate dehydrogenase** catalyzes the removal of two hydrogens from succinate.



Reaction 7: Hydration of Fumarate to Malate:

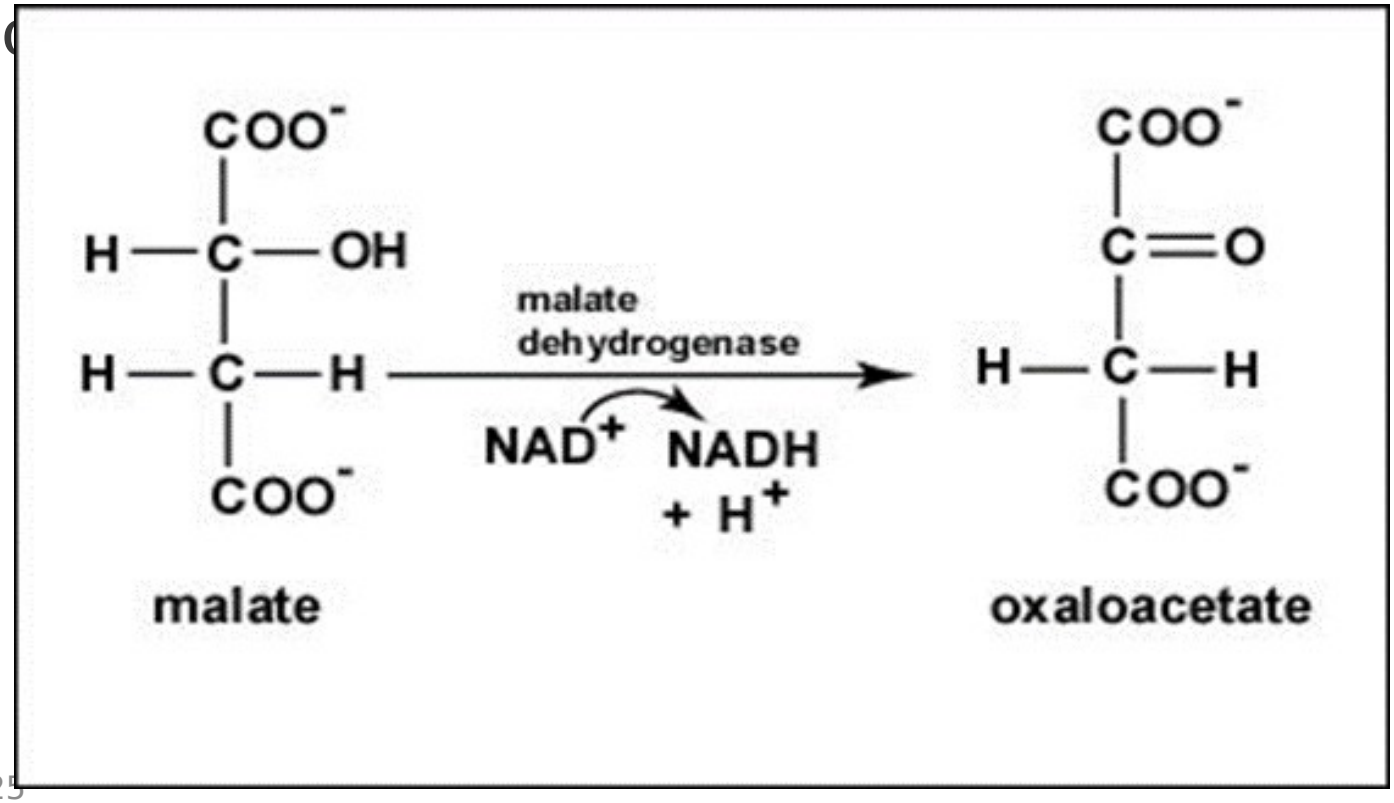
The reversible hydration of **fumarate** to **L-malate** is catalyzed by **fumarase (fumarate hydratase).**

Fumarase continues the rearrangement process by adding **Hydrogen and Oxygen** back into the substrate that had



Reaction 8: Oxidation of Malate to Oxaloacetate:

- **Malate** is oxidized to produce **oxaloacetate**, the starting compound of the citric acid cycle by **malate dehydrogenase**. During this oxidation, NAD^+ is reduce



The Net Equation:

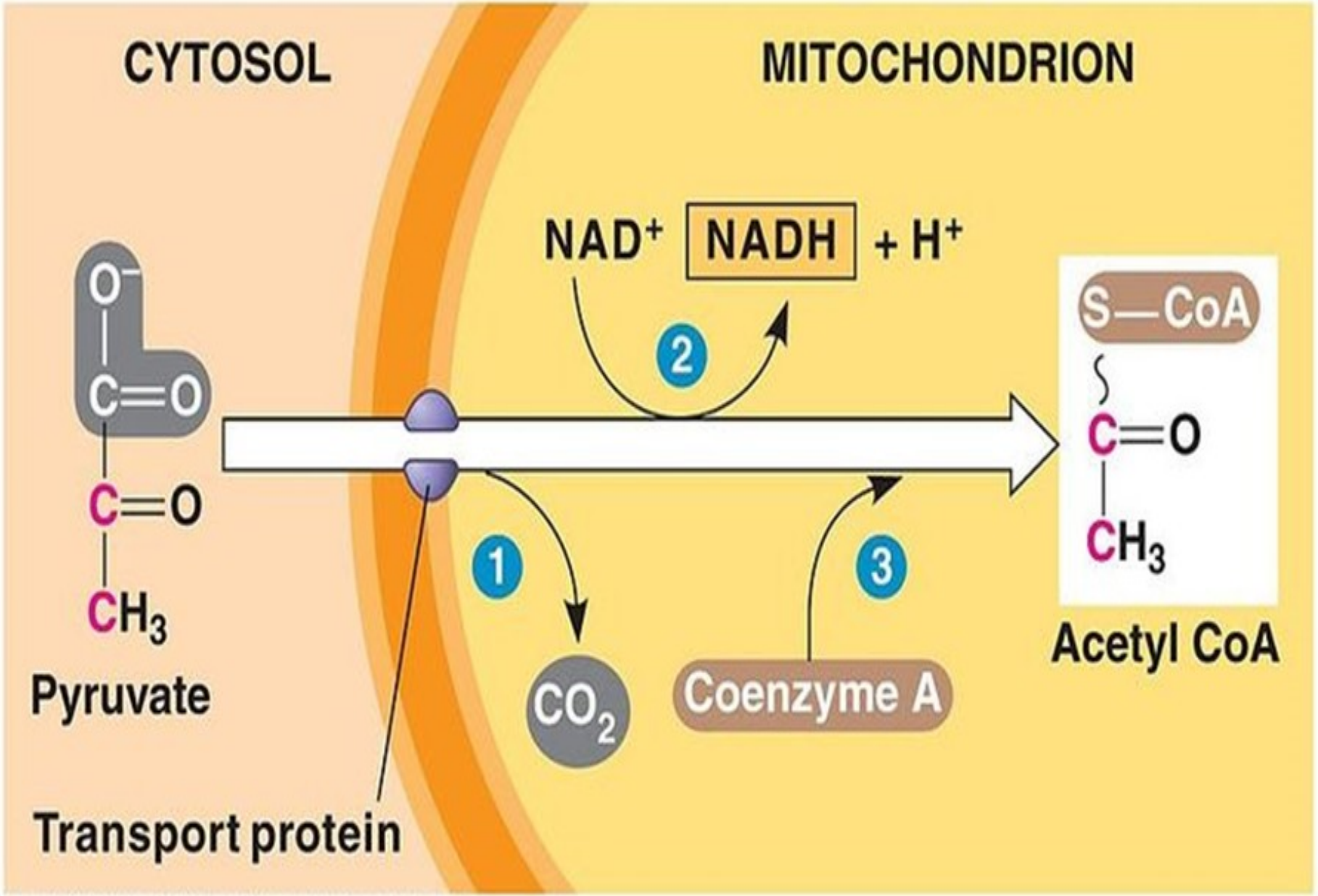
Acetyl CoA + 3 NAD + FAD + ADP + HPO_4^{-2} ———> $2\ CO_2$ + CoA + 3 $NADH^+$ + $FADH^+$ + ATP

ATP Generation:

- **Total ATP = 12 ATP**
- 3 NAD = 9 ATP
- 1 FAD = 2 ATP
- 1 ATP = 1 ATP

Significance of Krebs Cycle

- Intermediate compounds formed during Krebs cycle are used for the synthesis of biomolecules like amino acids, nucleotides, chlorophyll, cytochromes and fats etc.
- Intermediate like succinyl CoA takes part in the formation of chlorophyll.
- Amino Acids are formed from α- Ketoglutaric acid, pyruvic acids and oxaloacetic acid.
- Krebs cycle (citric Acid cycle) releases plenty of energy (ATP) required for various metabolic activities of cell.
- By this cycle, carbon skeletons are got, which are used in process of growth and for maintaining the cells.



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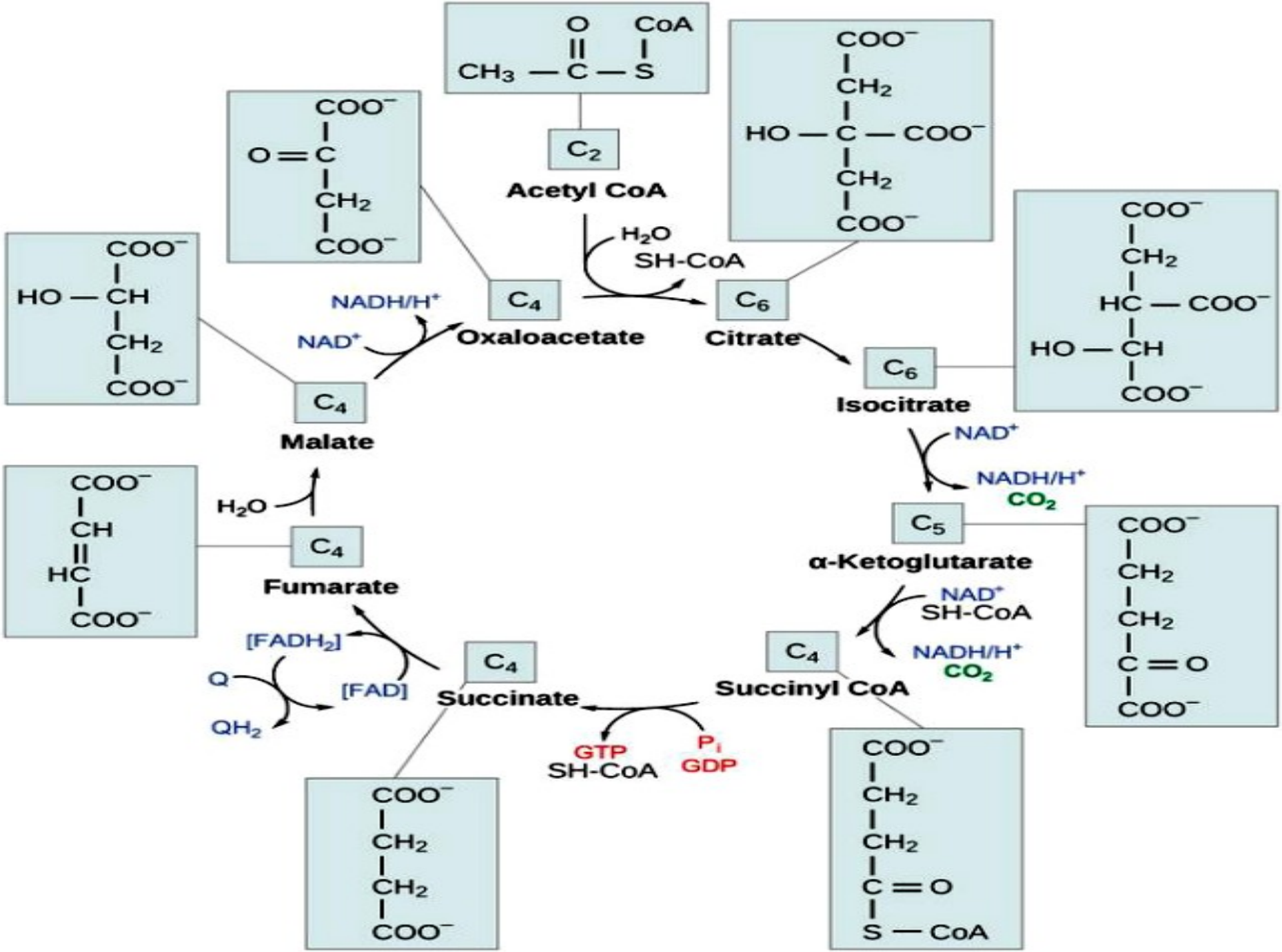
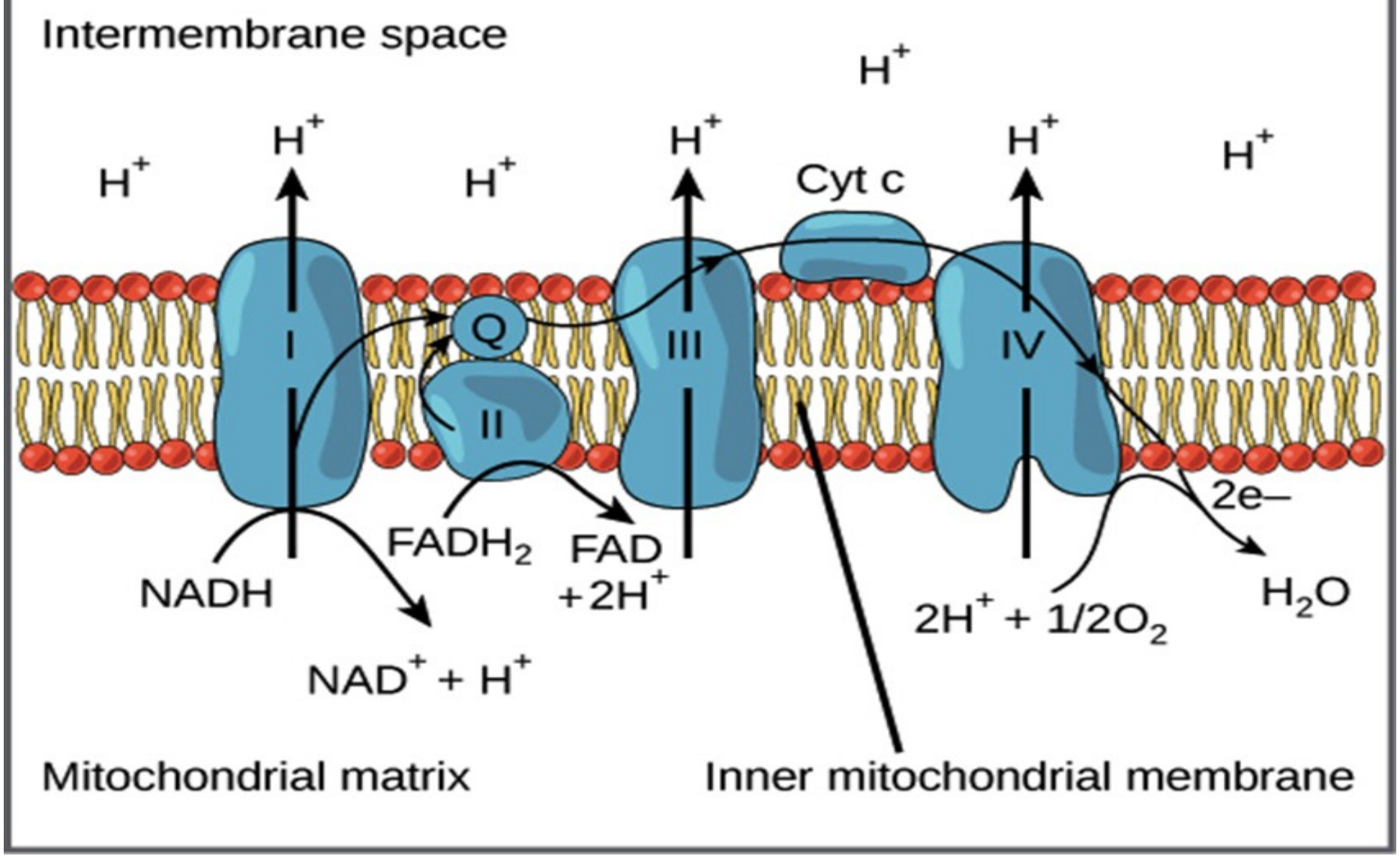
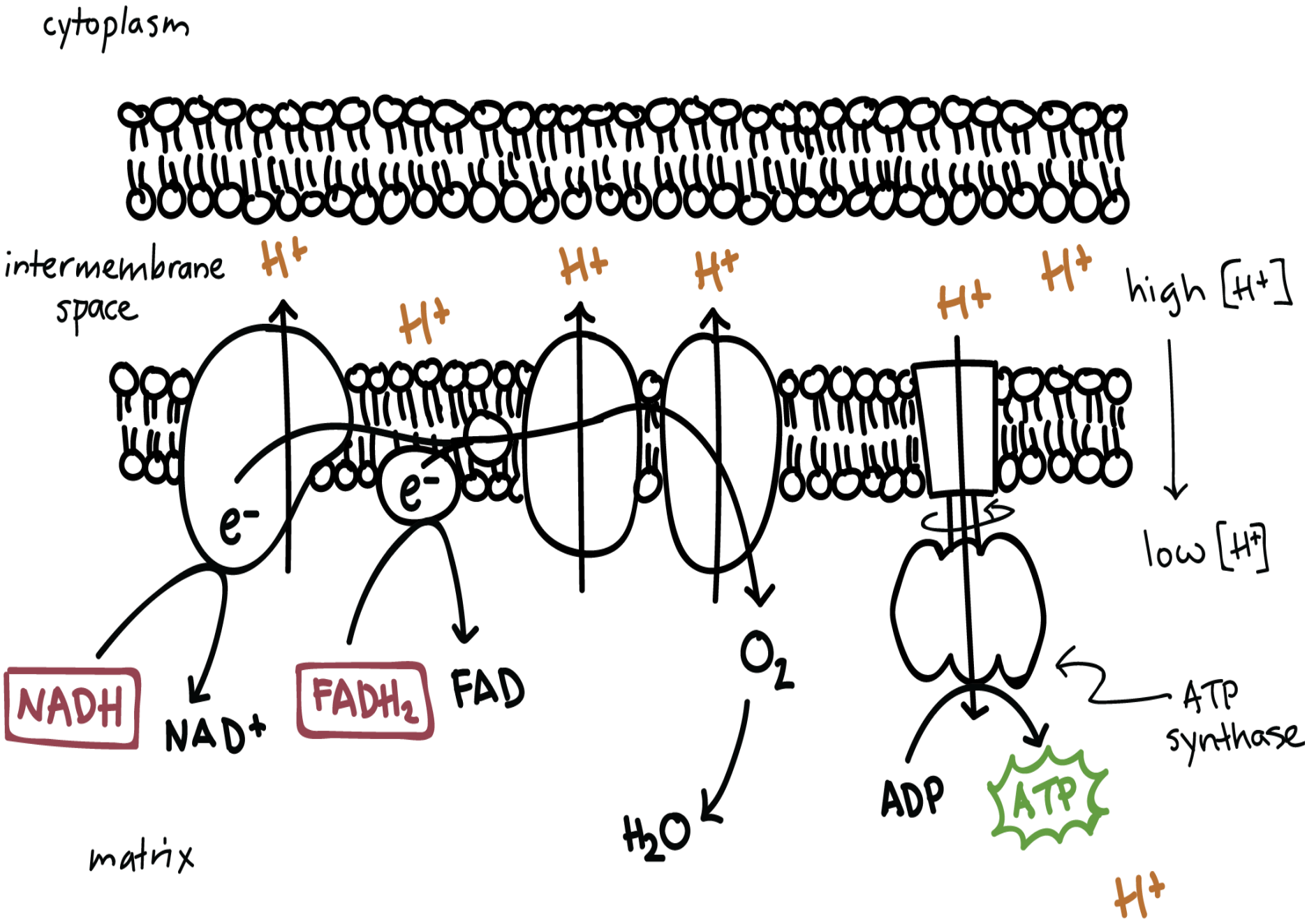

CoA
CH_3 — C — S
O
C_2
Acetyl CoA
H_2O
SH-CoA
C_6
Citrate
HO — C — COO⁻
CH_2
COO⁻
C_4
Oxaloacetate
O = C
CH_2
COO⁻
NADH/H⁺
NAD^+
C_4
Malate
HO — CH
CH_2
COO⁻
H_2O
C_4
Fumarate
HC
CH
$[FADH_2]$
[FAD]
Q
QH_2
C_4
Succinate
GTP
SH-CoA
P_i
GDP
C_4
Succinyl CoA
S — CoA
C = O
CH_2
C_6
Isocitrate
HC — COO⁻
HO — CH
NAD^+
NADH/H⁺
CO_2
C_5
α-Ketoglutarate
C = O
NAD^+
SH-CoA
NADH/H⁺
CO_2

- In aerobic respiration, electron transport is the final step in the breakdown of glucose.
- It is the point at which most of the ATP is produced. High-energy electrons and hydrogen ions from NADH and $FADH_2$ produced in the Krebs cycle are used to convert ADP to ATP.
- It is a series of proteins and organic molecules found in the inner membrane of the mitochondria. Electrons are passed from one member of the transport chain to another in a series of redox reactions. Energy released in these reactions is captured as a proton

Electron Transport Chain




cytoplasm
intermembrane space
H+
H+
H+
H+
H+
H+
high [H+]
low [H+]
e-
e-
NADH
NAD+
FADH2
FAD
O2
H2O
ATP synthase
ADP
ATP
H+
matrix

- Together, the electron transport chain and chemiosmosis (the movement of ions across a selectively permeable membrane, down their electrochemical gradient) make up **oxidative phosphorylation**. The key steps of this process, shown in simplified form in the diagram above, include:

- **Delivery of electrons by NADH and $FADH_2$.** Reduced electron carriers (NADH and $FADH_2$ from other steps of cellular respiration transfer their electrons to molecules near the beginning of the transport chain. In the process, they turn back into NAD^+ and FAD, which can be reused in other steps of cellular respiration.

- **Electron transfer and proton pumping**. As electrons are passed down the chain, they move from a higher to a lower energy level, releasing energy. Some of the energy is used to pump H^+, moving them out of the matrix and into the intermembrane space. This pumping establishes an electrochemical gradient.
- **Splitting of oxygen to form water**. At the end of the electron transport chain, electrons are transferred to molecular oxygen, which splits in half and takes up H^+ to form water.
- **Gradient-driven synthesis of ATP**. As H^+ ions flow down their gradient and back into the matrix, they pass through an enzyme called ATP synthase, which harnesses the flow of protons to synthesize ATP.

- We'll look more closely at both the electron transport chain and chemiosmosis in the sections below.

The electron transport chain

- The electron transport chain is a collection of membrane-embedded proteins and organic molecules, most of them organized into four large complexes labeled I to IV.
- In eukaryotes, many copies of these molecules are found in the inner mitochondrial membrane. In prokaryotes, the electron transport chain components are found in the plasma membrane.

- As the electrons travel through the chain, they go from a higher to a lower energy level, moving from less electron-hungry to more electron-hungry molecules. Energy is released in these “downhill” electron transfers, and several of the protein complexes use the released energy to pump protons from the mitochondrial matrix to the intermembrane space, forming a proton gradient.
- All of the electrons that enter the transport chain come from NADH and $FADH_2$ molecules produced during earlier stages of cellular respiration: glycolysis, pyruvate oxidation, and the citric acid cycle.

- NADH is very good at donating electrons in redox reactions (that is, its electrons are at a high energy level), so it can transfer its electrons directly to complex I (**Flavin mononucleotide & NADH – dehydrogenase**), turning back into NAD^+. As electrons move through complex I in a series of redox reactions, energy is released, and the complex uses this energy to pump protons from the matrix into the intermembrane space.

- $FADH_2$ is not as good at donating electrons as NADH (that is, its electrons are at a lower energy level), so it cannot transfer its electrons to complex I. Instead, it feeds them into the transport chain through complex II (**Succinate dehydrogenase**), which does not pump protons across the membrane.

- Because of this "bypass," each $FADH_2$ molecule causes fewer protons to be pumped (and contributes less to the proton gradient) than an NADH.
- Since these electrons bypass, and thus do not energize, the proton pump in the first complex, fewer ATP molecules are made from the $FADH_2$ electrons. The number of ATP molecules ultimately obtained is directly proportional to the number of protons pumped across the inner mitochondrial membrane.
- Beyond the first two complexes, electrons from NADH and $FADH_2$ travel exactly the same route. Both complex I and complex II pass their electrons to a small, mobile electron carrier called **ubiquinone** (Q), which is reduced to form **QH_2** and travels through the membrane, delivering the electrons to complex III.

- As electrons move through complex III (**Cytochrome oxidoreductase**), more H^+ ions are pumped across the membrane, and the electrons are ultimately delivered to another mobile carrier called **cytochrome C** (Cyt C) which carries the electrons to complex IV, where a final batch of H^+ ions is pumped across the membrane.
- Complex IV (**cytochrome proteins c, a, and a_3 or cytochrome c oxidase**) passes the electrons to O_2, which splits into two oxygen atoms and accepts protons from the matrix to form water. Four electrons are required to reduce each molecule of O_2 and two water molecules are formed in the process.
- Oxygen is the final electron acceptor in the electron transport system in cellular respiration. Protons and electrons are transferred to oxygen to form water.

❖ Overall, ETC has two important functions:

- Regenerates electron carriers. NADH and $FADH_2$ pass their electrons to the electron transport chain, turning back into NAD^+ and FAD. This is important because the oxidized forms of these electron carriers are used in glycolysis and the citric acid cycle and must be available to keep these processes running.
- Makes a proton gradient. The transport chain builds a proton gradient across the inner mitochondrial membrane, with a higher concentration of H^+ in the intermembrane space and a lower concentration in the matrix. This gradient represents a stored form of energy, and, as we'll see, it can be used to make ATP.

❑ Chemiosmosis

- Complexes I, III, and IV of the electron transport chain are proton pumps. As electrons move energetically downhill, the complexes capture the released energy and use it to pump H^+ ions from the matrix to the intermembrane space. This pumping forms an electrochemical gradient across the inner mitochondrial membrane.
- In the inner mitochondrial membrane, H^+ ions have just one channel available: a membrane-spanning protein known as ATP synthase.
- As ATP synthase turns, it catalyzes the addition of a phosphate to ADP, capturing energy from the proton gradient as ATP. This process, in which energy from a proton gradient is used to make ATP, is called **chemiosmosis**.

ATP yield

Stage	Direct products (net)	Ultimate ATP yield (net)
Glycolysis	2 ATP	2 ATP
	2 NADH	3-5 ATP
Pyruvate oxidation	2 NADH	5 ATP
Citric acid cycle	2 ATP/GTP	2 ATP
	6 NADH	15 ATP
	2 $FADH_2$	3 ATP
Total		30-32 ATP

4.2.2 Biosynthesis

2. Biosynthesis - It supplies precursors for several biosynthetic pathways of amino acids, pyrimidines, purines etc.

 As already mentioned, the TCA cycle is also an important source of biosynthetic precursors. E.g. α-ketoglutarate and oxaloacetate are used for synthesis of a number of amino acids like glutamic acid, aspartic acid etc.

 Succinyl - CoA is used to form porphyrin ring of cytochromes, chlorophyll etc.

 Oxaloacetate can also be converted to phosphoenolpyruvate, which is a precursor of glucose.

 Acetyl - CoA is the starting material for fatty acid biosynthesis.

Requirements of Biosynthesis

- Sometimes all that is required for biosynthesis is for two substances to physically join together to make a new physical substance, which is called a **macromolecule**.

I. **Photosynthesis:** autotrophs convert light energy into chemical energy through photosynthesis.

The importance of photosynthesis

Photosynthesis is essential to all life on earth. It is the only biological process that captures energy from outer space (sunlight) and converts it into chemical energy in the form of Glyceraldehyde 3-phosphate (G3P), which in turn can be made into sugars and other organic compounds such as proteins, lipids, and nucleic acids.

Other variant of photosynthesis

- Commonly known photosynthetic processes is the one known as oxygenic photosynthesis. The other type is termed as anoxygenic photosynthesis.
- The oxygenic photosynthesis is the most common and is seen in plants, algae and cyanobacteria.
- During oxygenic photosynthesis, light energy transfers electrons from water (H_2O) to carbon dioxide (CO_2), to produce carbohydrates. In this transfer, the CO_2 is "reduced," or receives electrons, and the water becomes "oxidized," or loses electrons. Ultimately, oxygen is produced along with carbohydrates.

$$6CO_2 + 12H_2O + \text{Light Energy} \rightarrow C_6H_{12}O_6 + 6O_2 + 6H_2O$$

- ❖ Anoxygenic photosynthesis uses electron donors other than water. The process typically occurs in bacteria such as purple bacteria and green sulfur bacteria, which are primarily found in various aquatic habitats.
- Anoxygenic photosynthesis does not produce oxygen. What is produced depends on the electron donor. For example, many bacteria use the bad-eggs-smelling gas hydrogen sulfide, producing solid sulfur as a byproduct.

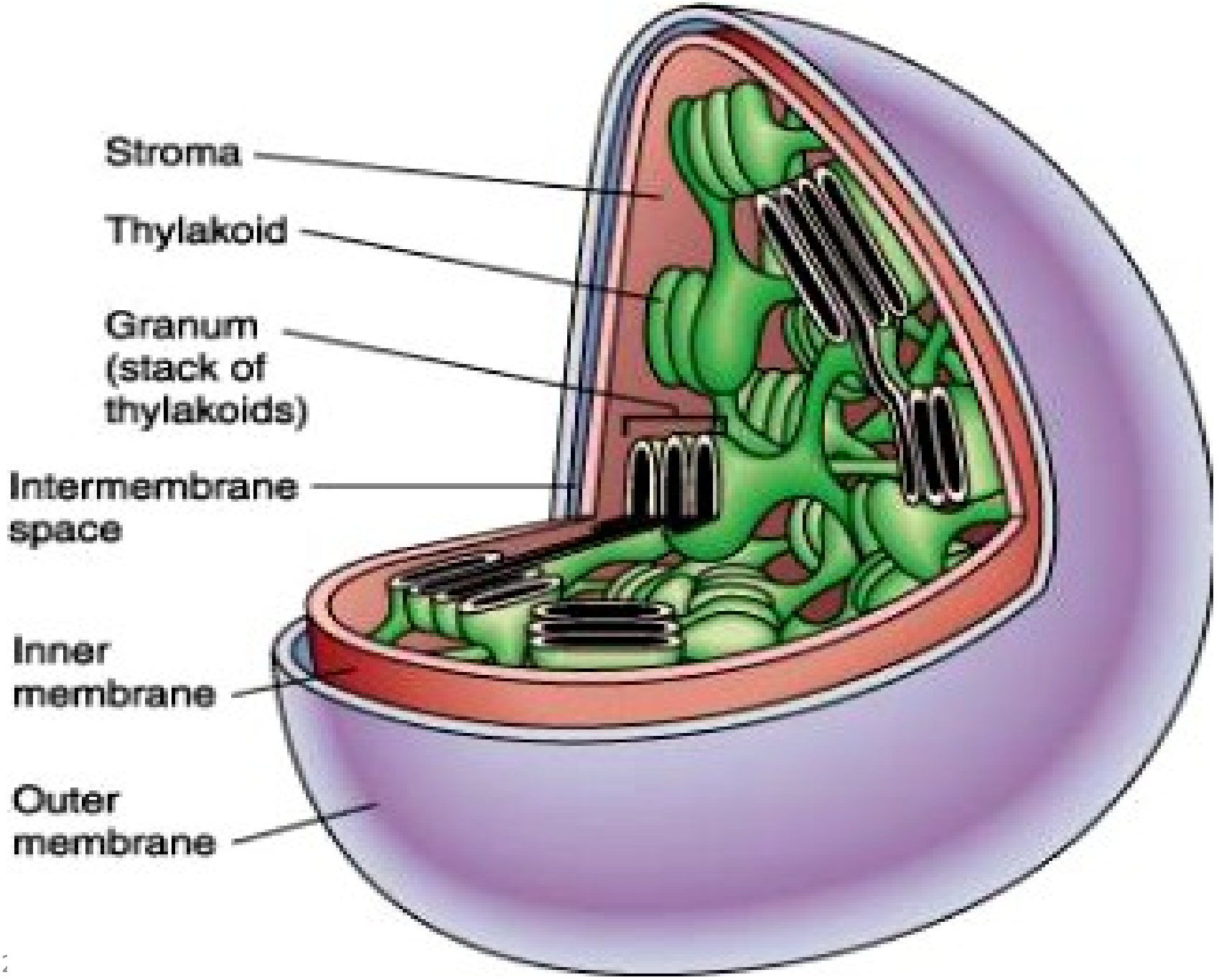
$$CO_2 + 2H_2A + \text{Light Energy} \rightarrow [CH_2O] + 2A + H_2O$$

- The letter A in the equation is a variable and H2A represents the potential electron donor. For example,

4.2.2.1 The photosynthetic apparatus

❖ Plastids

- Photosynthetic eukaryotic organisms contain organelles called plastids in their cytoplasm.
- Plastids generally contain pigments or can store nutrients. Colorless and nonpigmented leucoplasts store fats and starch, while chromoplasts contain carotenoids (any class of yellow to red plant pigments including the carotenes and xanthophylls) and chloroplasts contain chlorophyll.

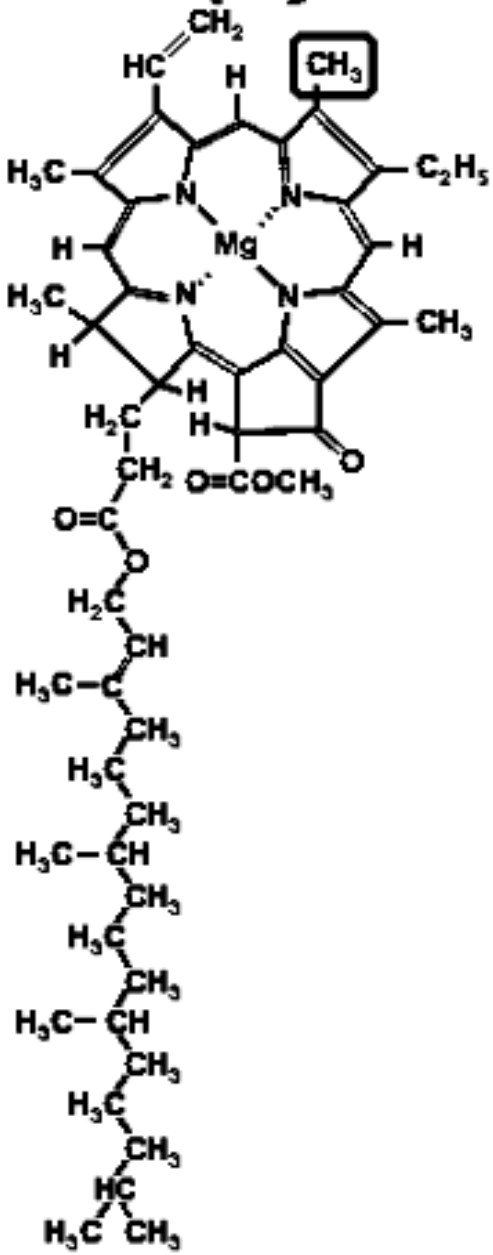

Stroma
Thylakoid
Granum
(stack of
thylakoids)
Intermembrane
space
Inner
membrane
Outer
membrane

Pigments

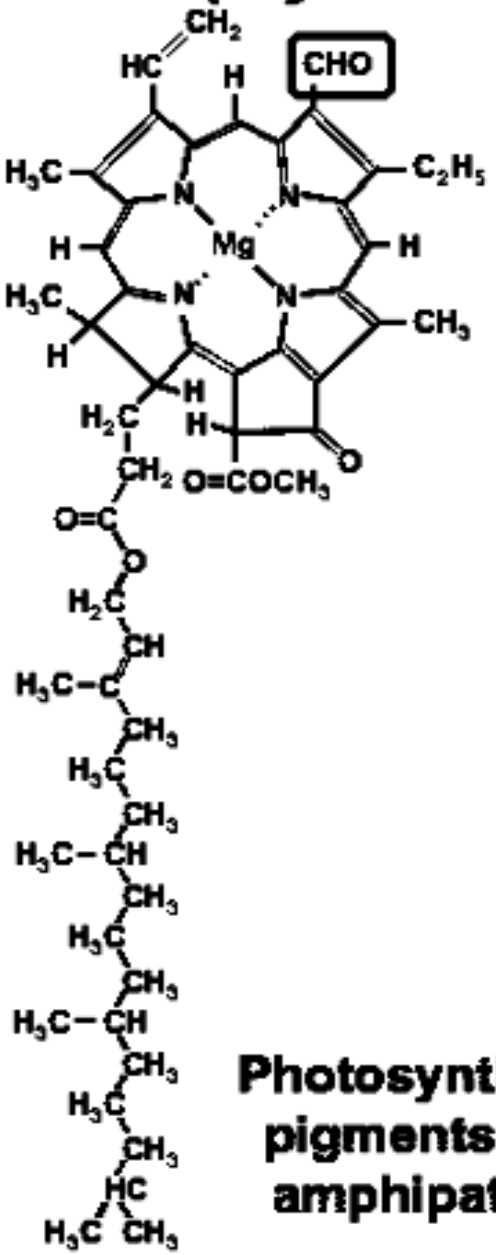
- Pigments are molecules that donate color on plants, algae and bacteria, but they are also responsible for effectively trapping sunlight. Pigments of different colors absorb different wavelengths of light. Below are the three main groups.

 Chlorophylls: These green-colored pigments are capable of trapping blue and red light. Chlorophylls have three subtypes, dubbed chlorophyll a, chlorophyll b and chlorophyll c. There is also a bacterial variant properly named bacteriochlorophyll, which absorbs infrared light. This pigment is mainly seen in purple and green bacteria, which perform anoxygenic photosynthesis.

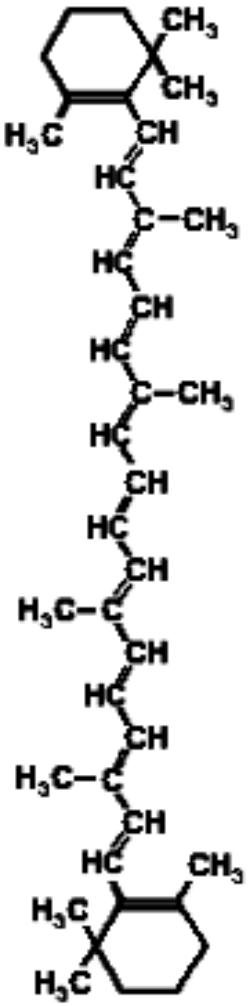
Chlorophyll a



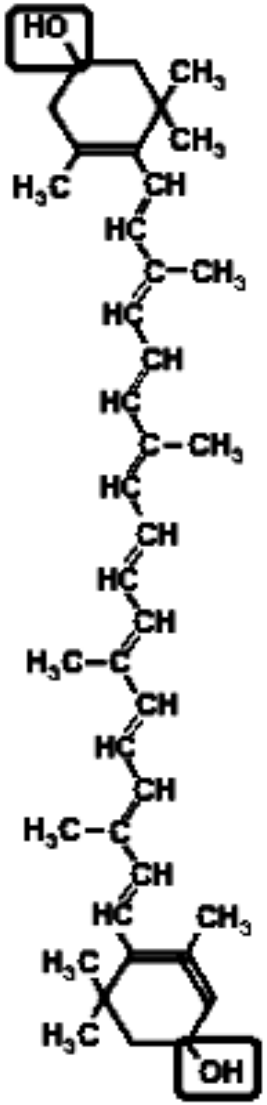
Chlorophyll b



ß-Carotene



Zeaxanthin



Lutein

Photosynthetic pigments are amphipathic

 Carotenoids: These red, orange or yellow-colored pigments absorb bluish-green light. Examples of carotenoids are xanthophyll (yellow) and carotene (orange) from which carrots get their color.

 Phycobilins: These red or blue pigments absorb wavelengths of light that are not as well absorbed by chlorophylls and carotenoids. They are seen in cyanobacteria and red algae.

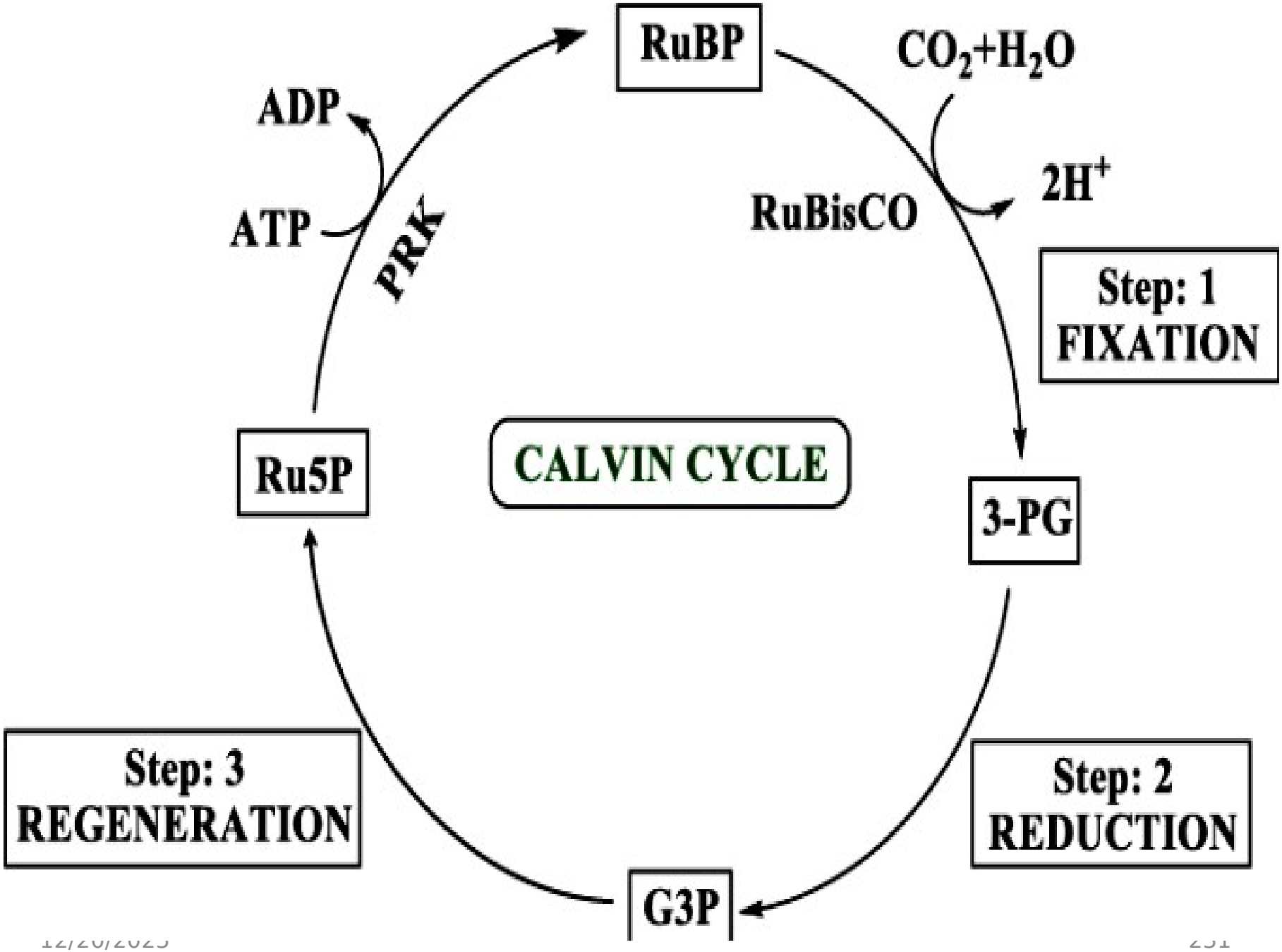
- **Antennae:** Pigment molecules are associated with proteins, which allow them the flexibility to move toward light. These structures effectively capture light energy from the sun, in the form of photons.

- **Reaction centers:** The pigments and proteins, which convert light energy to chemical energy and begin the process of electron transfer, are known as **reaction centers (where water molecules split)**.

4.2.2.2 The photosynthetic process

- The reactions of plant photosynthesis are divided into those that require the presence of sunlight and those that do not.
- Both types of reactions take place in chloroplasts: light-dependent reactions in the thylakoid and light-independent reactions in the stroma.
- **Light-dependent reactions** (also called light reactions): When a photon of light hits the reaction center, a pigment molecule such as chlorophyll releases an electron.

- Light reactions produce ATP and NADPH, which are the rich energy sources that drive dark reactions.
- Although NADPH and ATP provide cells with large amounts of energy, these molecules are not stable enough to store chemical energy for long periods of time. Thus, there is a second phase of photosynthesis called the Calvin cycle in which energy is stored in organic molecules such as glucose.
- **Light-independent reactions** (also called dark reactions and known as the Calvin cycle):
- Three chemical reaction steps make up the Calvin cycle: carbon fixation, reduction and regeneration. These reactions use water and catalysts.


RuBP
CO_2+H_2O
$2H^+$
RuBisCO
Step: 1
FIXATION
3-PG
Step: 2
REDUCTION
G3P
Step: 3
REGENERATION
Ru5P
PRK
ATP
ADP
CALVIN CYCLE

- In the carbon fixation, six carbon dioxide ($6CO_2$) molecules combine with six 5-carbon compounds to form twelve 3-carbon molecules called 3-phosphoglycerat (3-PGA).
- In the second step, the chemical energy stored in ATP and NADPH is transferred to the 3-PGA molecules to form high-energy molecules called **glyceraldehyde 3-phosphates** (G3P). ATP supplies the phosphate groups for forming G3P molecules, while NADPH supplies hydrogen ions and electrons.
- In the third step, two G3P molecules leave the cycle to be used for the production of glucose and other organic compounds.
- In the final step of the Calvin cycle, an enzyme called rubisco converts the remaining ten G3P molecules into 5-carbon molecules called ribulose 1, 5-bisphosphates (**RuBP**). These molecules combine with new carbon dioxide molecules to continue the cycle.

Alternative Pathways

The environment in which an organism lives can impact the organism‘s ability to carry out photosynthesis.

- ❖ C4 plants one adaptive pathway that helps plants maintain photosynthesis while minimizing water loss is called the C4 pathway.
- The C4 pathway occurs in plants such as sugar cane and corn. These plants are called C4 plants because they fix carbon dioxide into four-carbon compounds instead of three-carbon molecules during the Calvin cycle.
- C4 plants also have significant structural modifications in the arrangement of cells in the leaves.

- In general, C_4 plants keep their stomata closed during hot days, while the four carbon compounds are transferred to special cells where CO_2 enters the Calvin cycle. This allows for sufficient carbon dioxide uptake, while simultaneously minimizing water loss.

❖ CAM plants another adaptive pathway used by some plants to maximize photosynthetic activity is called **crassulacean acid metabolism** (CAM photosynthesis).

❖ The CAM pathway occurs in water conserving plants that live in deserts, salt marshes, and other environments where access to water is limited.

- CAM plants, such as cacti, orchids, and the pineapple allow carbon dioxide to enter the leaves only at night, when the atmosphere is cooler and more humid. At night, these plants fix carbon dioxide into organic compounds.
- During the day, carbon dioxide is released from these compounds and enters the Calvin cycle. This pathway also allows for sufficient carbon dioxide uptake, while minimizing water loss.

4.3 Metabolic disorders, diagnosis and treatments

Disorders in metabolism can be inherited, in which case they are also known as inborn errors of metabolism, or they may be acquired during your lifetime.

Inherited metabolic disorders

- Inherited metabolic disorders are one cause of metabolic disorders, and occur when a defective gene causes an enzyme deficiency.
- Metabolic diseases can also occur when the liver or pancreas do not function properly.

- The inherited metabolic disorders, which can be classified based on the type of food-related, building block that they affect,
- **Carbohydrate disorders**; examples include Diabetes insipidus, hereditary fructose intolerance, galactosemia, pyruvate metabolism disorders, etc.
- **Fatty acid oxidation defects**; examples include Gaucher‘s disease, Niemann-Pick disease, Fabry‘s disease, and medium-chain acyl-coenzyme A dehydrogenase (MCAD) deficiency

- **Amino acid disorders**; examples include Tay-Sachs disease, phenylketonuria, tyrosinemia, maple syrup urine disease, and homocystinuria
- Acid-base imbalance, disorders of calcium metabolism, DNA repair-deficiency disorders, Iron metabolism disorders, Mitochondrial diseases, Phosphorus metabolism disorders, Malabsorption syndromes, Water-electrolyte imbalance are some of the disorders associated with metabolism.

Other causes of metabolic disorders

- Metabolic disorders can be due to other factors, such as a combination of inherited and environmental factors. Some of the conditions that can cause metabolic disorders include:
- Alcohol abuse, Diabetes (chronic disease that affects your body‘s ability to use sugar for energy)
- Diuretic abuse, Gout (type of arthritis caused by a buildup of uric acid in the joints)
- Ingestion of poison or toxins, including excessive aspirin, bicarbonate, alkali, ethylene glycol, or methanol
- Kidney failure, Pneumonia, respiratory failure, or collapsed lung
- Sepsis (life-threatening bacterial blood infection)

4.3.1. Risk factors of metabolic disorders

- Certain chronic medical conditions
- Family history of genetic metabolic disorder
- Race and ethnicity
- HIV/AIDS and other diseases
- Age- the risk of metabolic syndrome increases with age.
- Obesity and lack of exercise
- Hormone imbalance
- Insulin resistance: a situation in which a body cannot use insulin properly.

4.3.2 Diagnosis of metabolic disorders

Specifically, metabolic syndrome is diagnosed if **any three of the following five markers** are present:

- Elevated waist circumference:
- Elevated triglycerides: 150 mg/dL or higher
- Reduced high-density lipoprotein (HDL) levels (''good cholesterol): <40 mg/dL in men; <50 mg/dL in women
- Elevated blood pressure: 130/85 mmHg or higher or are already taking blood pressure medications
- Elevated fasting glucose: 100 mg/dL or higher or are already taking glucose-lowering medications

4.3.3 Treatments of metabolic disorders

- Depends on the specific disorder. Inborn errors of metabolism are often treated with nutritional counseling and support, periodic assessment, physical therapy, and other supportive care options.
- Multiple treatment options are available for inherited metabolic disorders and examples include: bone marrow transplantation, enzyme replacement therapy in selected patients, gene therapy in selected patients, medications to reduce symptoms, such as pain or low blood sugar, mineral supplementation, nutritional counseling, surgery to relieve pain or symptoms, vitamin supplementation and etc.

- Acquired metabolic disorder treatment will include normalizing the metabolic balance by both reversing the cause and administering medications.

Summary

- **Phenylketonuria** is an example of an inherited metabolic disorder characterized by an inability to break down one of the building blocks of protein, the amino acid phenylalanine.
- **Type I diabetes**, a disease in which the pancreas does not create enough insulin to maintain balanced blood sugar levels, is a metabolic disorder of sugar metabolism.
- An example of a metabolic disorder affecting fat metabolism is **Gaucher's disease,** which is characterized by a lack of the enzyme glucocerebrosidase.