Biochemistry for 3rd year Chemistry B.Sc. students
Semester: II   Aca. Year: 2012E.C

Chapter -1-

Introduction to Biochemistry

What is Biochemistry ?

✓*It is the chemistry of living organisms which deals the composition of a particular organism, the scientific study of the chemical substances (body substance) like enzymes, carbohydrates, amino acids, fats, proteins, hormones, DNA, RNA, etc of processes and reactions that occur in living organisms.*

✓Biochemistry describes their origin, formation, function, deficiency symptoms etc and also it tries to explain life in terms of biochemical reactions.

✓One can understand well all the chemical reactions happening at the molecular level in a living cell or living being through the study of **biochemistry**.

1.2. what is the scope of study of biochemistry?

The major scope of biochemistry is the complete understanding of living cells at the chemical and molecular level through the study of the structure and function of bio-molecules.

To achieve this objective, biochemists have wanted to isolate the numerous molecules found in the cells, determine their structures, and analyze how they are function.

1.3. Chemical vs Biochemical Reactions

Chemical Reactions

-Takes place in test tubes, beakers, flasks…

-Takes place in larger volume

-Generally takes place at high temperatures (to make reaction rates high).

Biochemical Reactions

-In a living cell

-In a restricted area (living Cell, even in organelle)

-Takes place at the constant temperature of the organism.

<u>Chemical Reactions</u>

-The rate of the reaction can be controlled by changing the pH.

-Sometimes require electrical energy to take place.

-Can be catalyzed by agents (Catalysts, metals Etc).

<u>Biochemical Reactions</u>

-pH is constant, generally about ≈ 7.3

-Electrical Energy is not possible.

-Catalyzed by protein agents (Enzymes)- Thus very well controlled- according to the need of the cell)

1.4. The major chemical elements of the human body

There are about 92 element occurring naturally in nature.

From these 92 elements, only about 25 elements are needed to build living organisms.

Not all these element found in all living cell.

- ✓ C, H, O and N are the most frequently found elements in the cells forming about 96%, and with S&P 97% of the human body mass.
- ✓ Also the trace-elements which are found in small quantity in the cells are very important in biological processes.

- Carbon is more abundant in living organisms than it is in the rest of the universe.
- These elements depend on **carbon** for there molecular backbone and can form stable covalent bonds.
- The relative amounts of these six elements vary among organisms.

Chemical compounds in the cell can be divided into two major group:

- Organic
- Inorganic

1. Organic compounds are:

- Chemical compounds **contain C as base &H** (exception are **carbon monoxide, carbon dioxide, carbides and carbonates** which are typically considered as inorganic)
- Are usually found in and originate from living organism.
- Usually consist of macromolecules (large molecules).

There are 4 main group of organic compounds in the cells:

- ✓ Carbohydrates, Lipids, Proteins, Nucleic acids

The carbohydrates are made up of carbon, hydrogen and oxygen. The ratio of hydrogen to oxygen atoms in a molecule usually 2:1.

2. Inorganic compounds are:

- Chemical compounds that **do not contain C as base**
- Usually a smaller and simpler than organic compounds
- Founds in cells; like water, **acids**, alkalis and mineral salts

1.5. The constituents of the cells

The basic unit of all forms of life is cell.

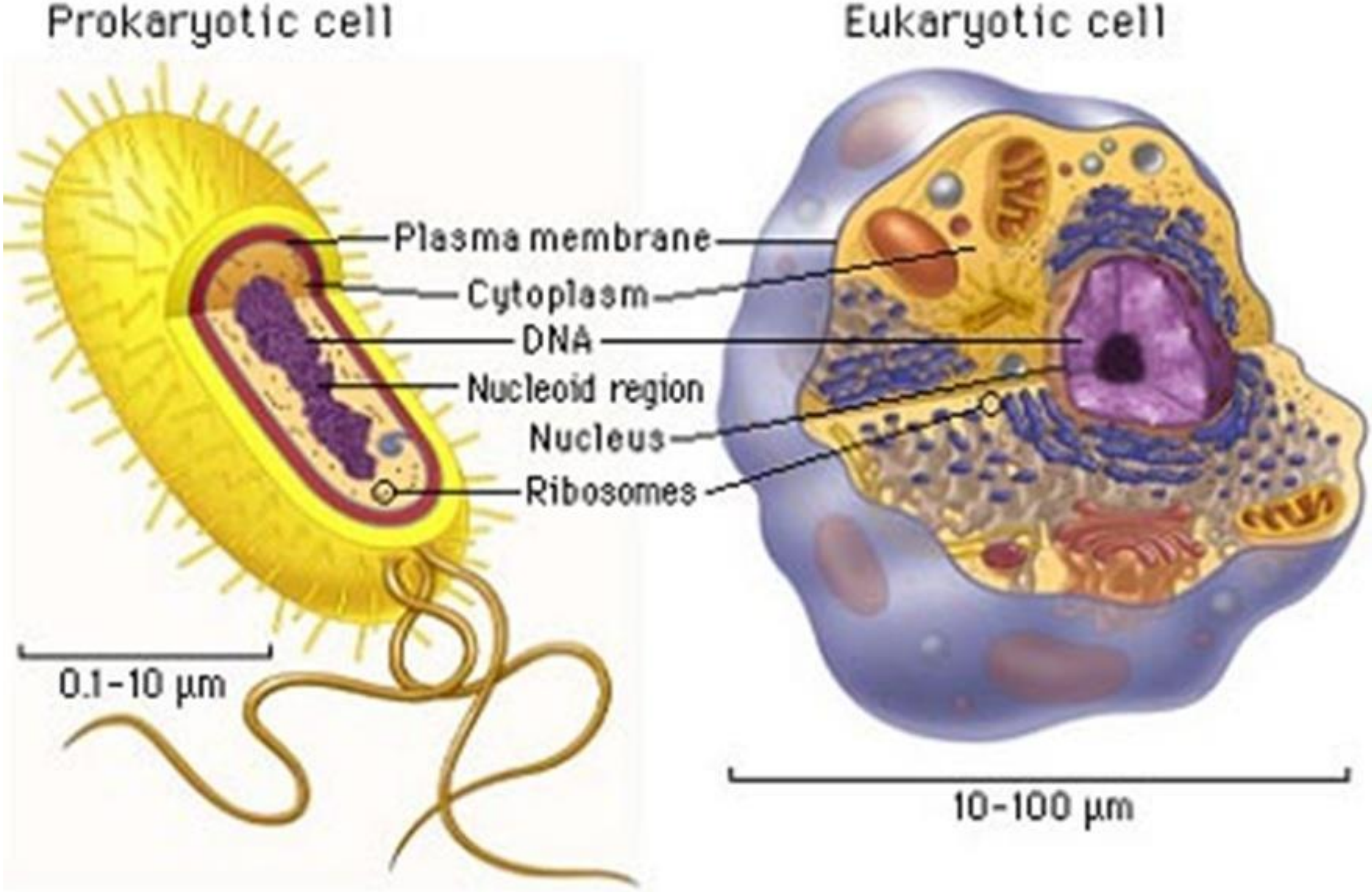
A cell is a collection of living matter enclosed by a barrier that separates the cell from its surroundings.

The Cell Theory states that:

1. All living organisms are composed of one or more cells.
2. The cell is the basic unit of structure, function in all organisms.
3. All new cells arise from other preexisting living cells by the process of cell division.

There are two main categories of cells:

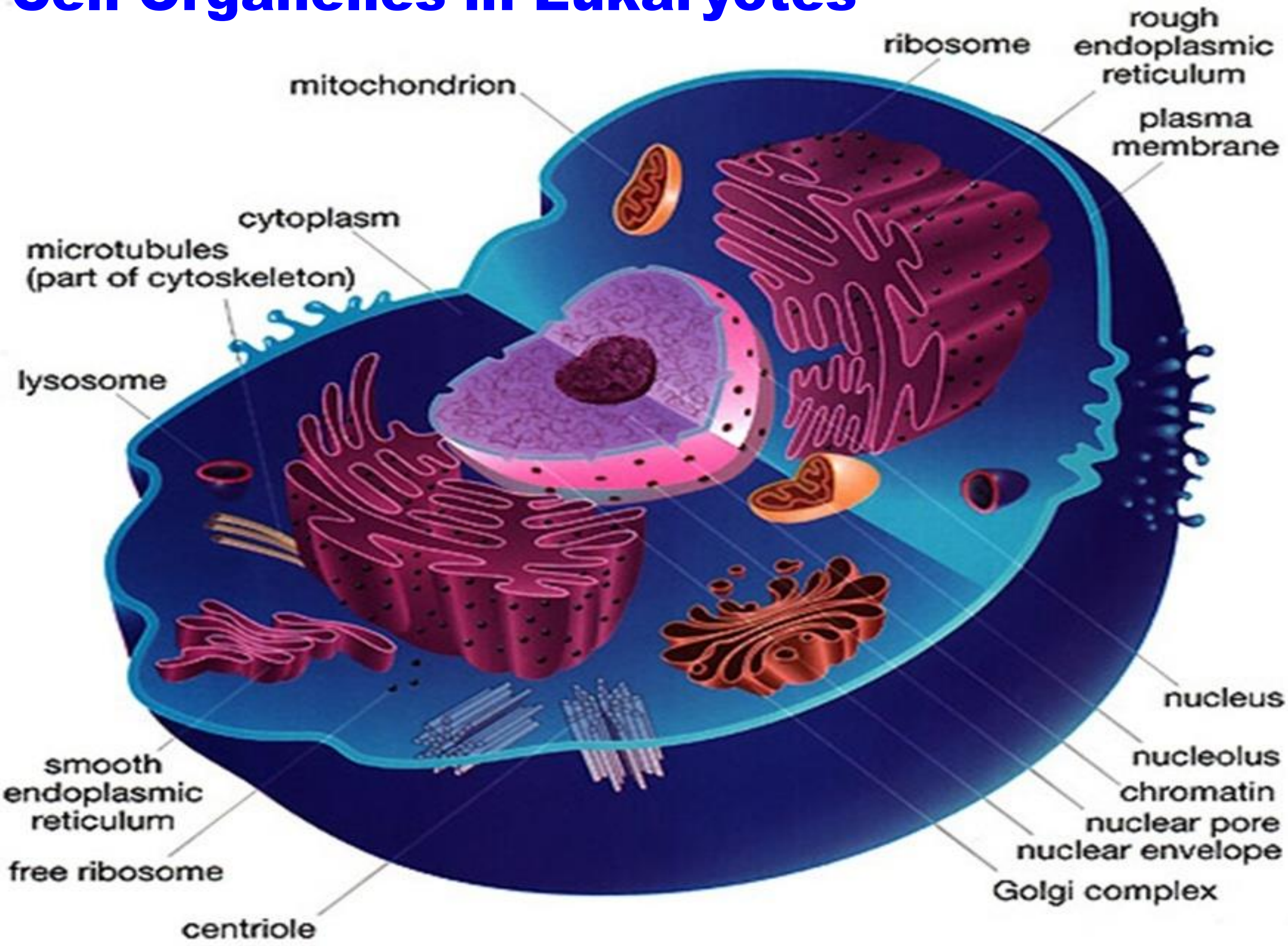
- **Prokaryote (prokaryotic cells)**
  - Bacteria
  - Have **no membrane-bound** nucleus
  - Nucleic acid is usually found in “loops” in the cytoplasm
  - Usually smaller than eukaryotes
  - Have fewer non membrane bound organelles than eukaryotes
- **Eukaryotes (eukaryotic cells)**
  - All organisms except bacteria are eukaryotes
  - Have a **membrane-bound** nucleus where DNA is located
  - Larger
  - More organelles
  - Two types of **eukaryotic cells; plant &animals cells.**


Prokaryotic cell
Eukaryotic cell
Plasma membrane
Cytoplasm
DNA
Nucleoid region
Nucleus
Ribosomes
0.1–10 μm
10–100 μm

Chemistry of Organelles

- **Organelle** = “little organs”
  - Specialized structures that perform specific jobs in the cell
- Found only in eukaryotic cells
- Many are “membrane-bound” (a membrane surrounds the organelle)
- **Cytosol** (the intracellular fluid) is the liquid found inside cells (watery matrix that organelles float in).
- **Cytoplasm**: Everything in a cell except the nucleus

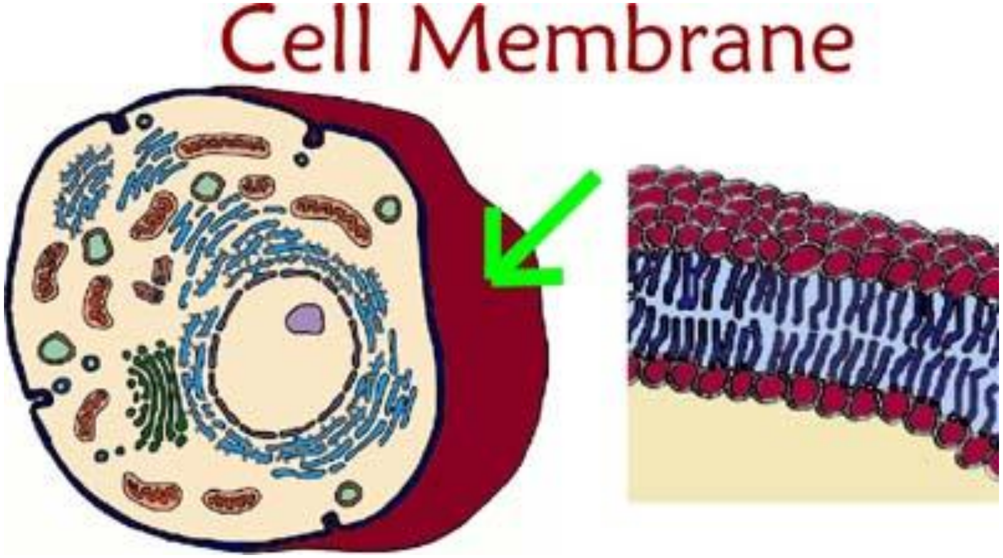
Cell Organelles in Eukaryotes



✓Cell Membrane

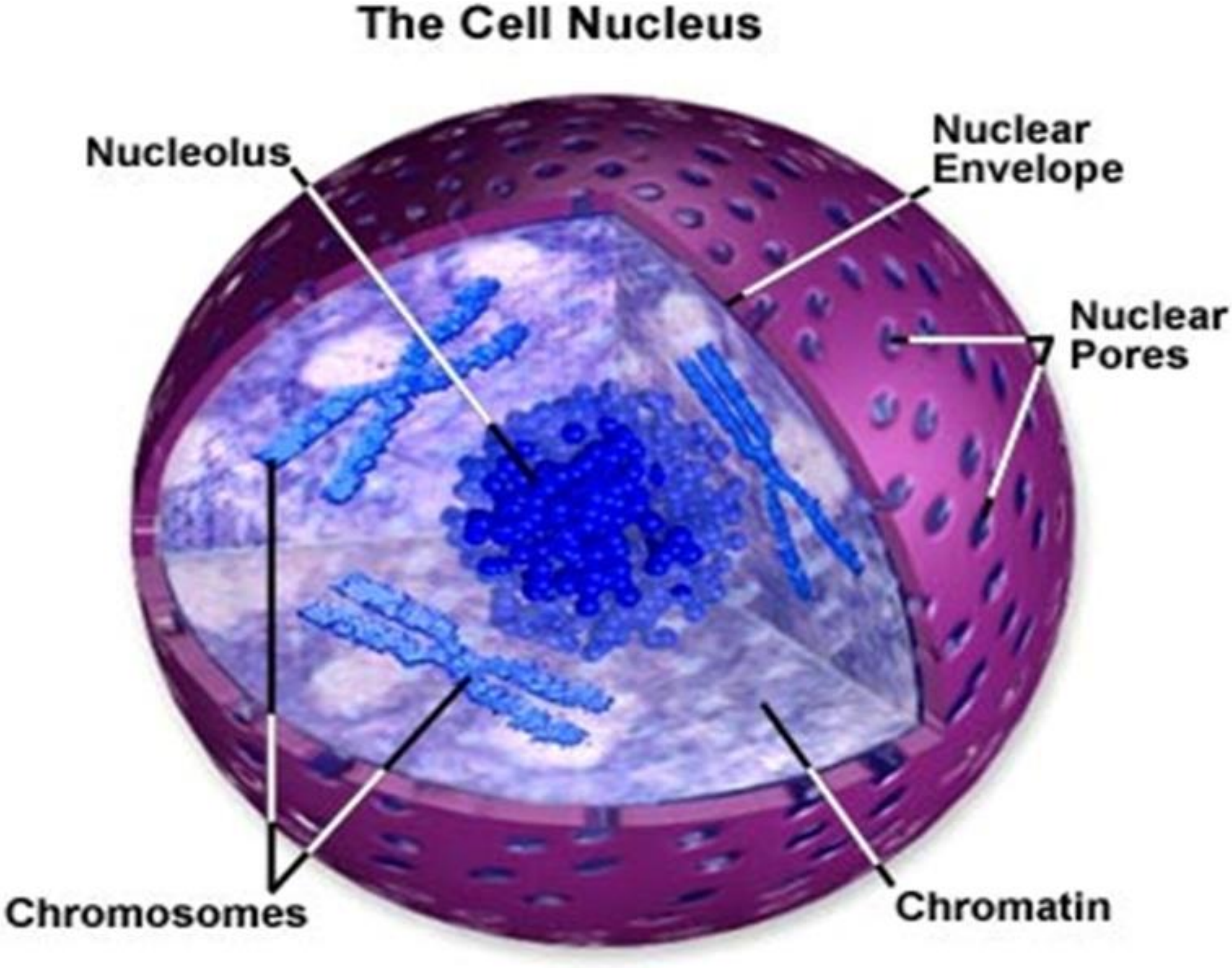
- Surrounds (boundary of) the cell and decides what comes in and out
- Semi-permeable: allows nutrients in and waste products out
- Made of a phospholipid bilayer
- Also called **Plasma Membrane**
- holds the shape of the cell
- Protects the cell

- **Factory Part:**
    - Gates or Doors
- **Found in**:
    - Plant cells
    - Animal cells
    - Prokaryotic cells



✓Nucleus

- Control center of the cell
- Stores DNA (chromosomes) which contains the coded instructions for making proteins which are the molecules that do “everything”.
- Surrounded by the nuclear membrane (Nuclear envelope).
- Pores let material in and out
- Also contains the Nucleolus, which makes ribosomes
- Usually one per cell (red blood cells do not have **nuclei**.)
- Usually the easiest organelle to see under a microscope
- **Factory Part:**
  - Manager’s Office
- Found in:
  - Plant cells and Animal cells


The Cell Nucleus
Nucleolus
Nuclear Envelope
Nuclear Pores
Chromosomes
Chromatin

✓Chromatin in the Nucleus

- The thread-like material in the nucleus is called **chromatin** which is DNA wrapped around protein.
- Usually looks like this but as a cell prepares to divide, chromatin condenses to form **chromosomes**.

✓Nucleolus

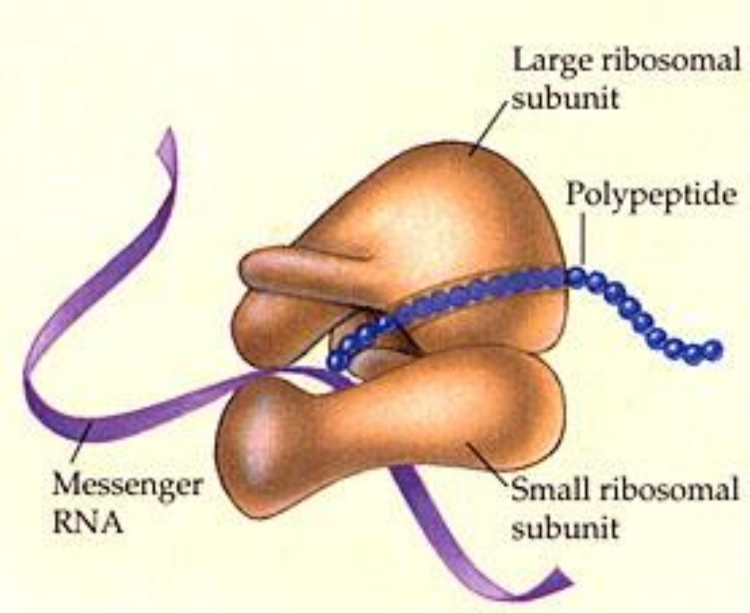
- Small dense region within the nucleus
- The assembly of ribosomes begins here

Ribosome

- Smallest organelle
- NOT surrounded by a membrane
- Proteins are assembled by ribosomes, following instructions from DNA.
- Ribosomes are found attached to rough endoplasmic reticulum or floating free in cytoplasm

Produced in a part of the nucleus called the nucleolus

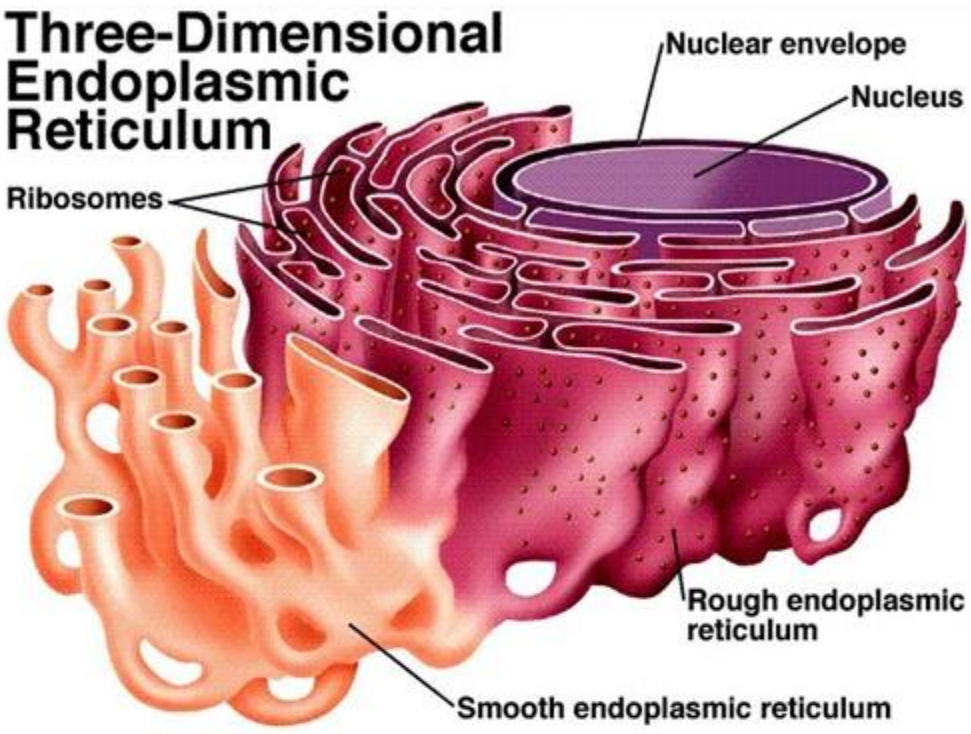
- Two Types:
  - Free ribosomes: float free in cytosol
  - Bound ribosomes: attached to rough ER



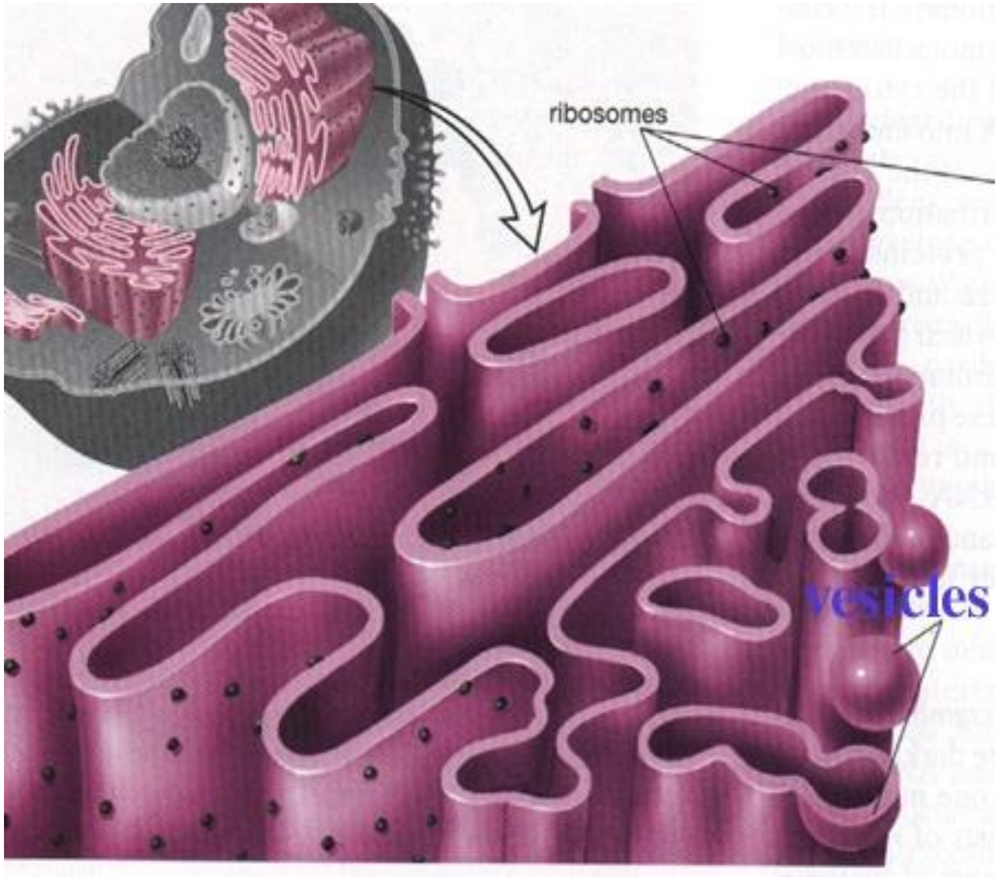
- **Factory Part:**
  - **Machines**
- **Found in:**
  - **Plant cells**
  - **Animal cells**
  - **Prokaryotic cells**

Endoplasmic Reticulum (ER)

- **Two Types:**
- **Rough ER:** covered with ribosomes; site of protein synthesis
- **Smooth ER:** no ribosomes; it makes hormones & lipids

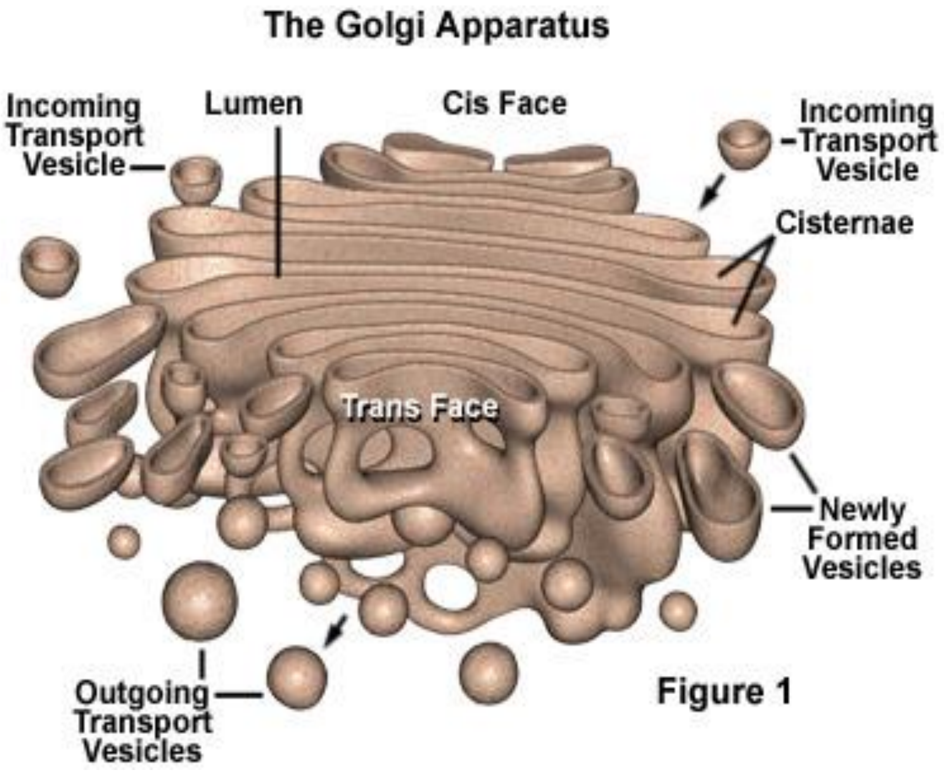


- The internal membrane system of the cell.
- Connected to the nuclear membrane.
- Assembles lipid components of the cell membrane, proteins and other materials for export from the cell.
- **Factory Part:**
  - Conveyor Belts
- Found in:
  - Plant cells
  - Animal cells

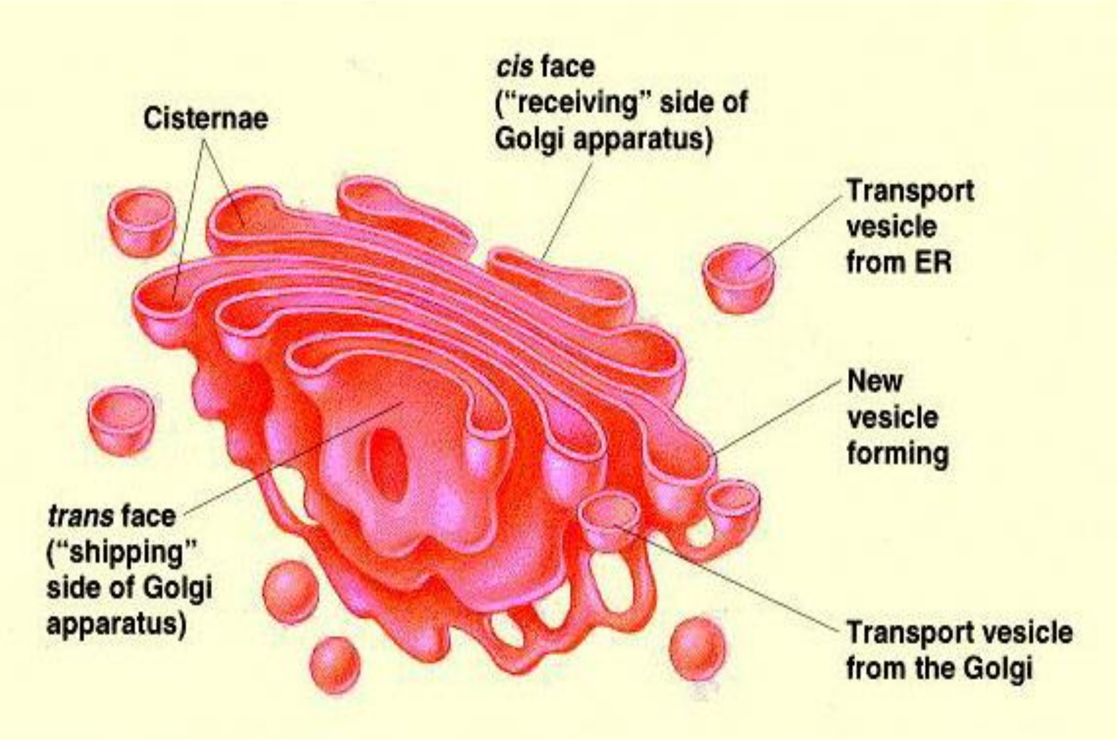


Golgi Apparatus

- Delivery system of the cell.
- Collects, modifies, and packages molecules in the cell
- Distributes and transports molecules in vesicles



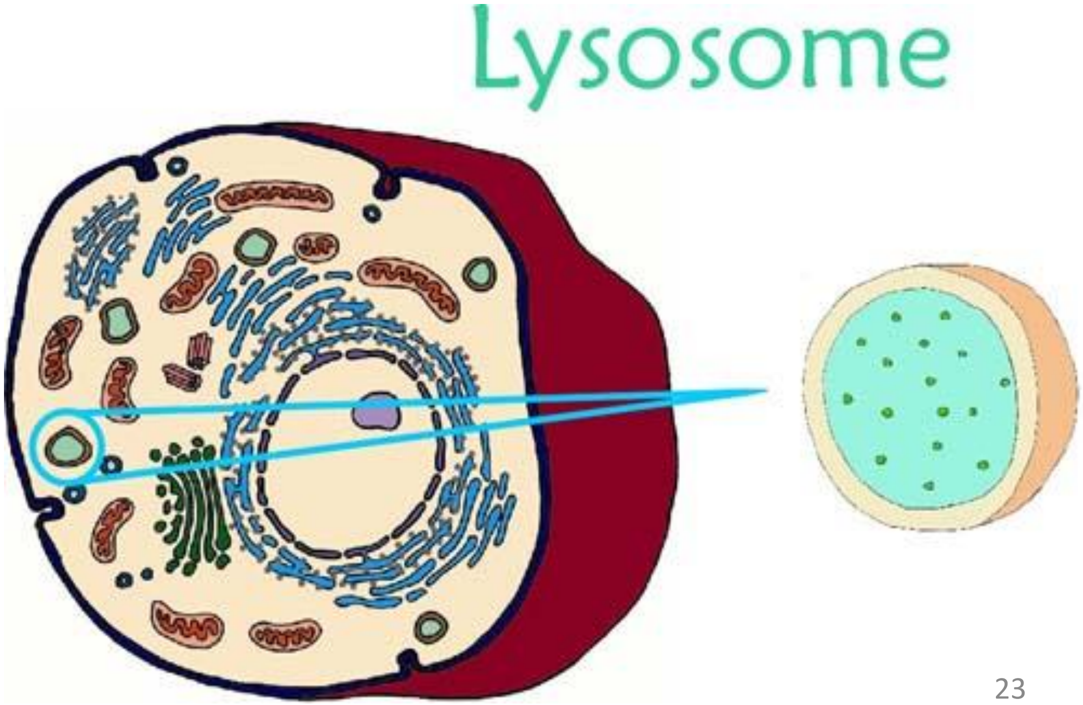
- **Factory Part:**
  - **Post office or Mail Room**
- **Found in:**
  - **Plant cells**
  - **Animal cells**



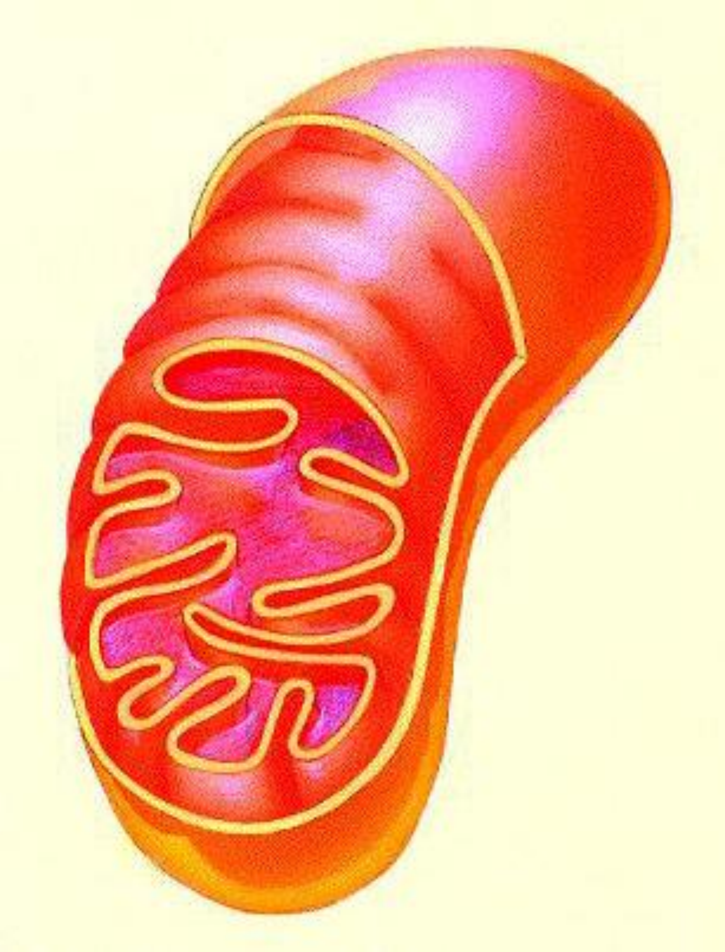
Lysosomes

- Clean-up crew (sometimes called cannibals)
- Membrane-bound sacks filled with enzymes that break down lipids, carbohydrates and proteins from food into smaller molecules that the cell can use.
- Trash Disposal of the cell
- Contain digestive enzymes that break down waste.

Factory Part:
    Janitors
Found in:
    Plant cells
    Animal cells



Mitochondria (singular = mitochondrion)



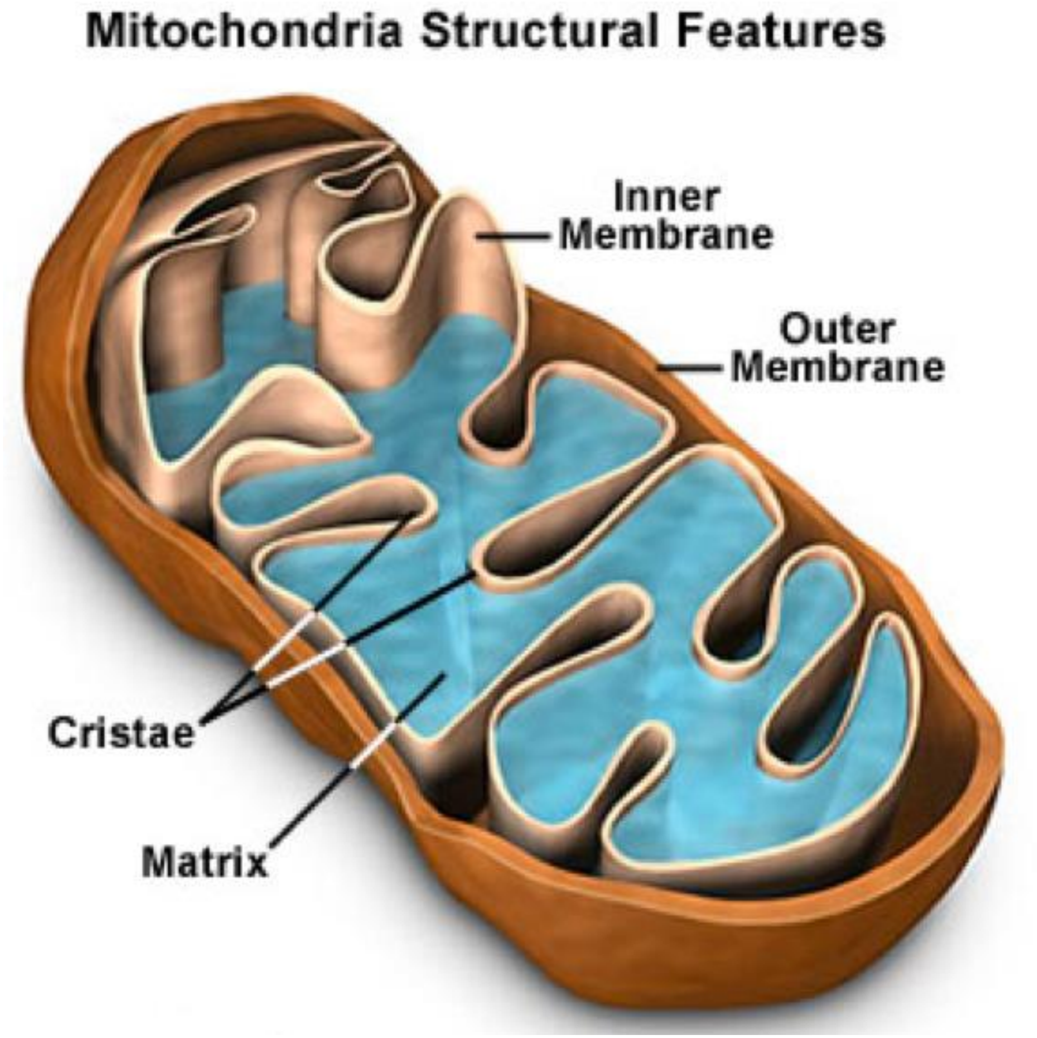
- “Powerhouse of the cell”
- Convert the chemical energy from food into energy that can be used by the cell.
- Enclosed by two membranes---an outer one and another that is folded up inside the mitochondrion
- Cellular respiration occurs here to release energy for the cell to use
- Has its own strand of DNA.
- Our mitochondria are inherited from our mothers via the eggs cell.

- **Sugar + Oxygen → Carbon dioxide + Water + ATP**

ATP = Adenosine triphosphate

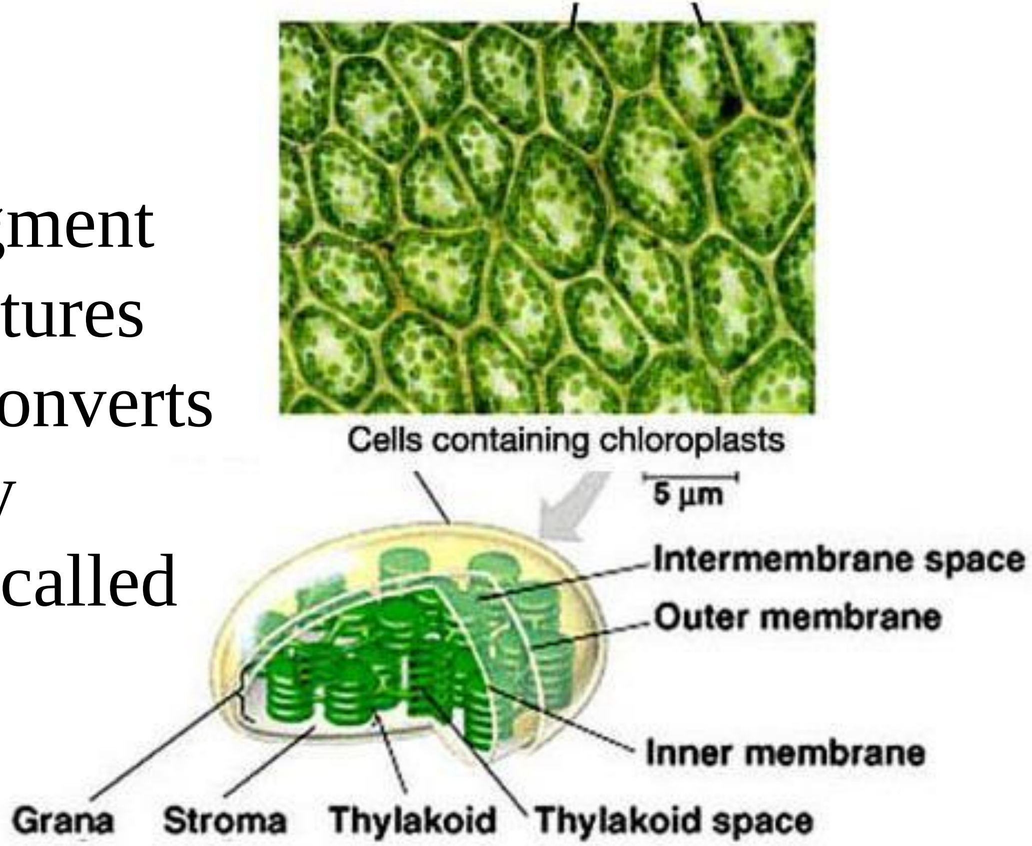
- **Factory Part:**
  - **Power Plant / Electrical Room**

- **Found in:**
  - **Plant cells**
  - **Animal cells**



Chloroplast

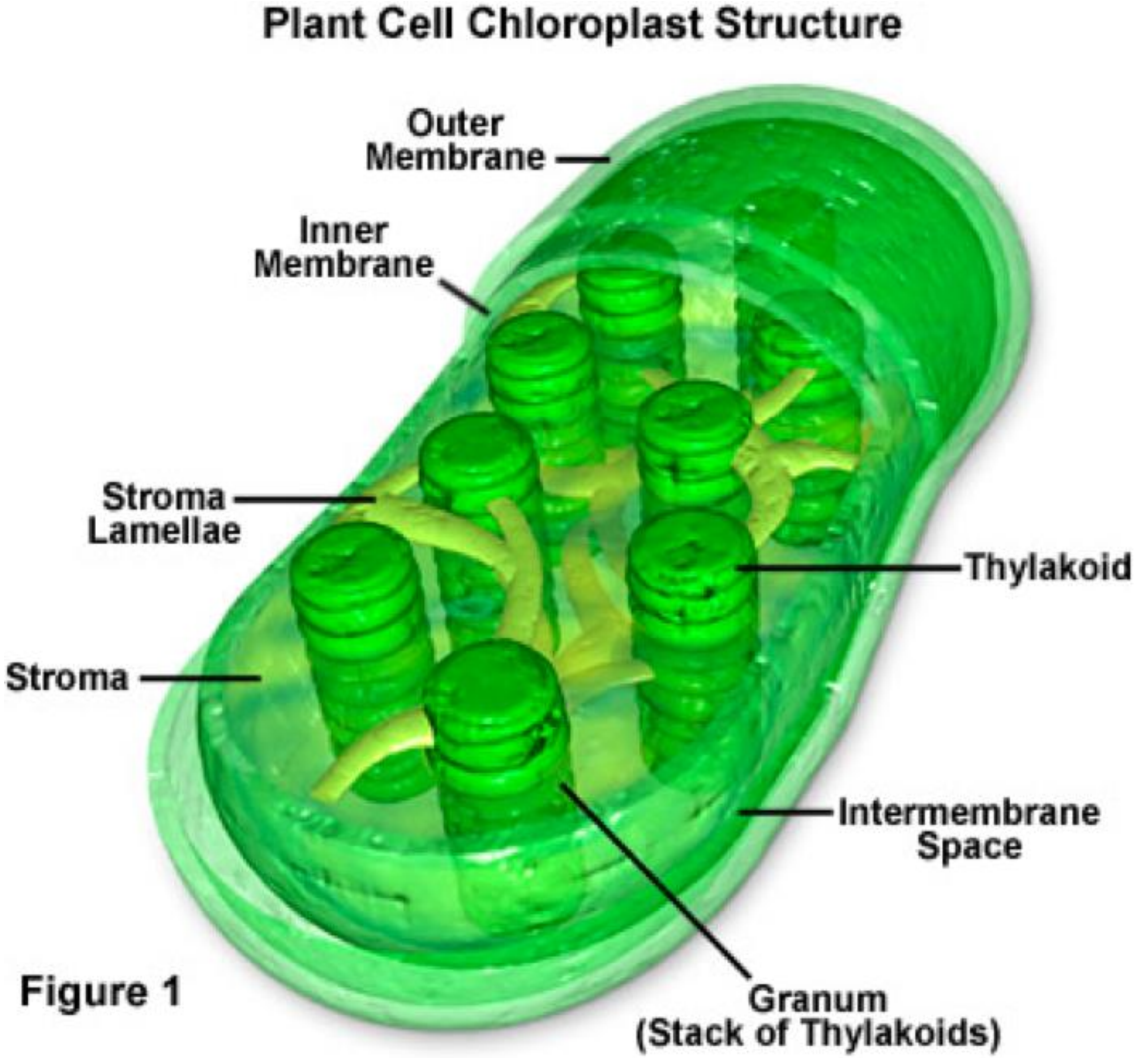
- Found in plant cells
- Contains the green pigment chlorophyll which captures the sun’s energy and converts it into chemical energy (glucose) in a process called **photosynthesis.**



Sunlight + Carbon Dioxide + Water → Sugar + Oxygen

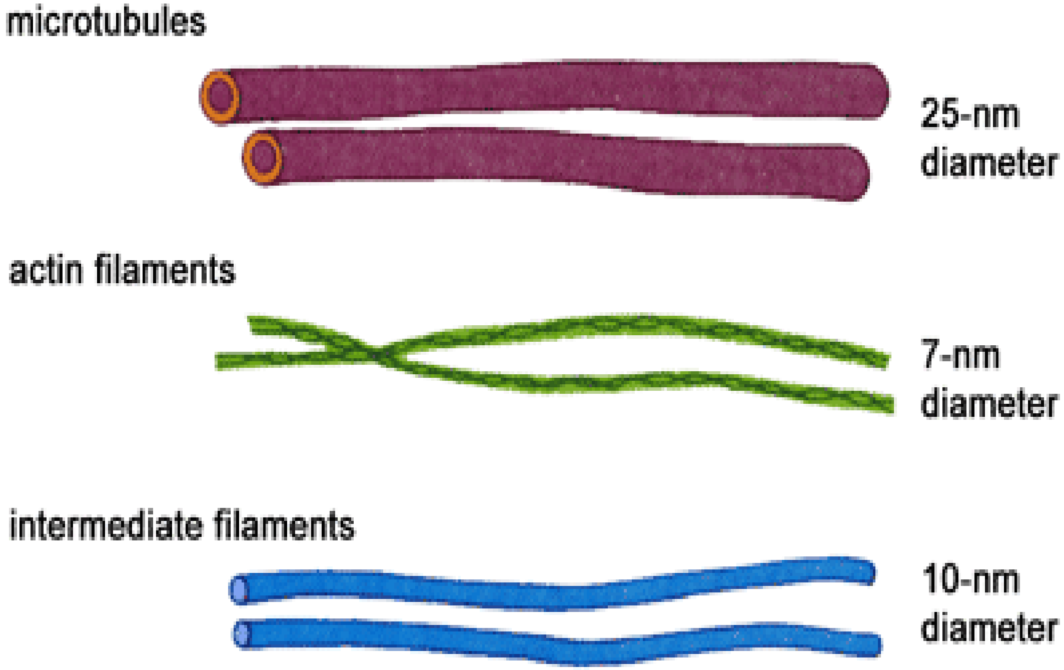
- **Factory Part:**
  - Solar Powered Energy Panels

- **Found in:**
  - Plant cells



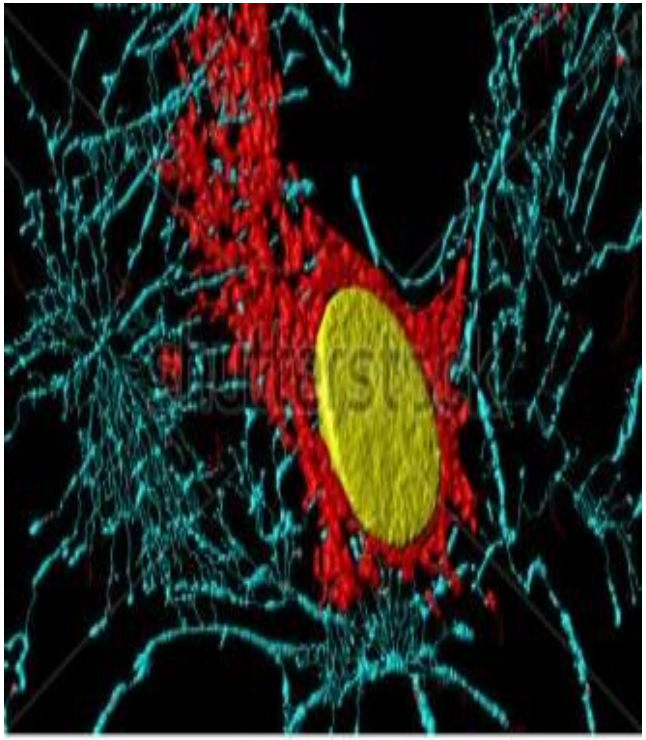
Cytoskeleton

- A network of protein filaments/tubes that helps the cell maintain its shape and which helps move materials around the cell.
- Acts as **skeleton** and **muscle**
- Provides shape and structure



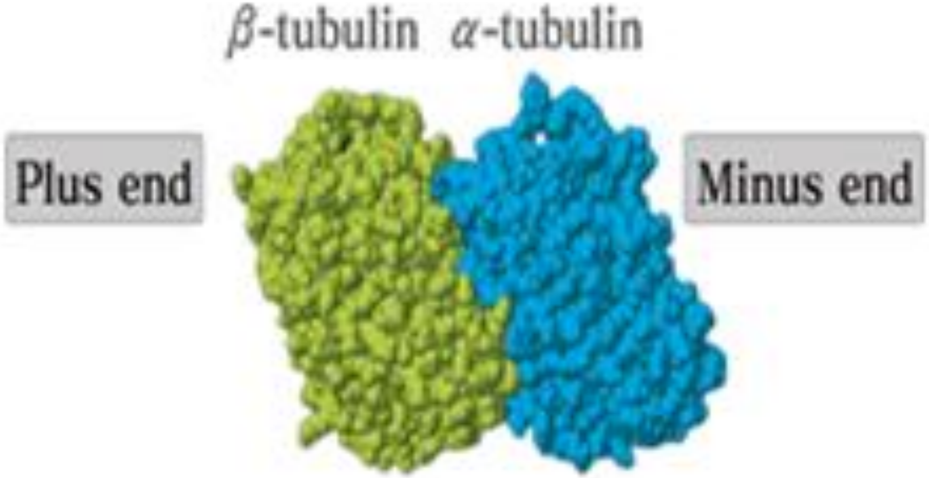
Microfilaments (1 type of cytoskeleton)

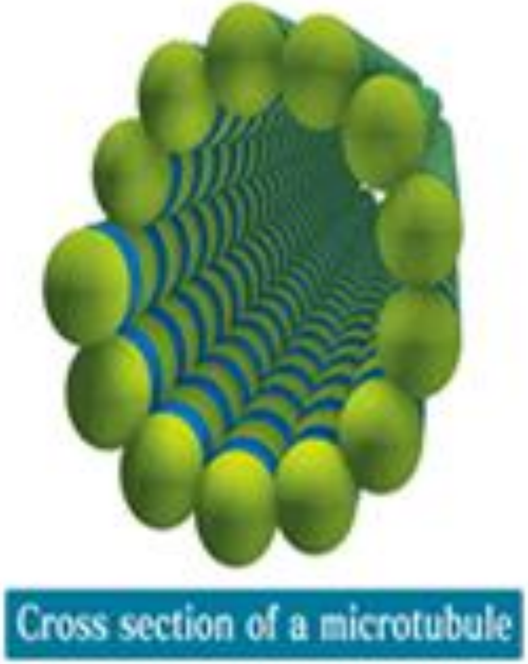
- Thread-like structures
- Made of a protein called **actin**
- Make a tough, flexible framework that supports the cell.
- May also help the cell move by assembling and disassembling.

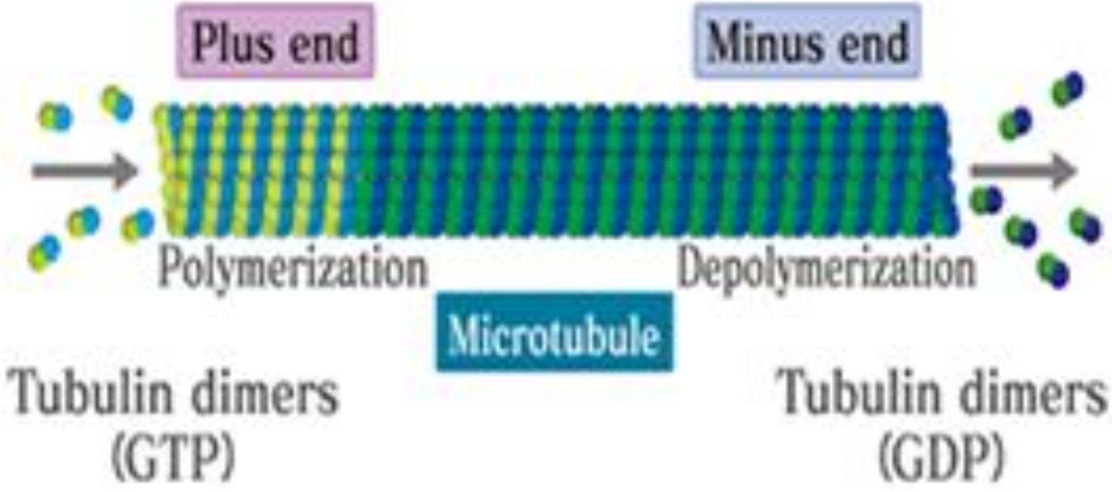


Microtubules (another type of microskeleton)

- Hollow structures made of proteins known as tubulins
- Perform different functions in different cells:
  - Critical to maintaining shape of some cells
  - Form centrioles (animal cells only)
  - Build projections from cell’s surface such as flagella and cilia that enable some cells to “swim”
  - Some cells have them arranged so that they can be used to produce controlled movements of the cell.

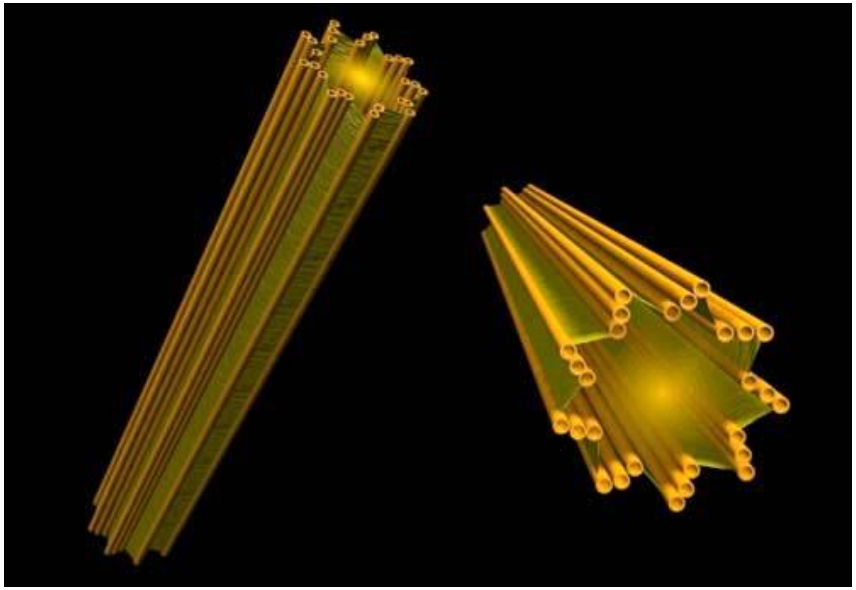

β-tubulin
α-tubulin
Plus end
Minus end


Cross section of a microtubule


Plus end
Minus end
Polymerization
Depolymerization
Microtubule
Tubulin dimers
(GTP)
Tubulin dimers
(GDP)

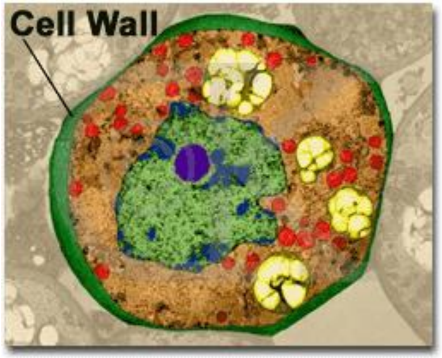
Centrioles

- Aid in cell division
- Found in pairs in animal cells
- Made of microtubules



Cell Wall

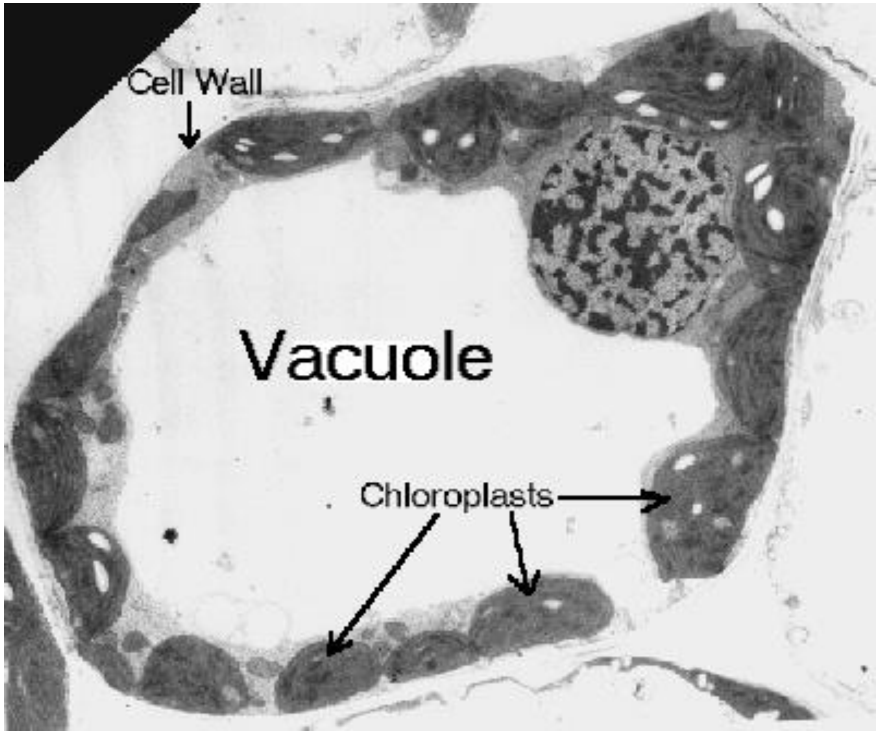
- Rigid, protective barrier (maintains cell shape)
- Found in plant and bacterial cells
- Located **outside** of the cell membrane
- Made of cellulose (Carbohydrate fiber)



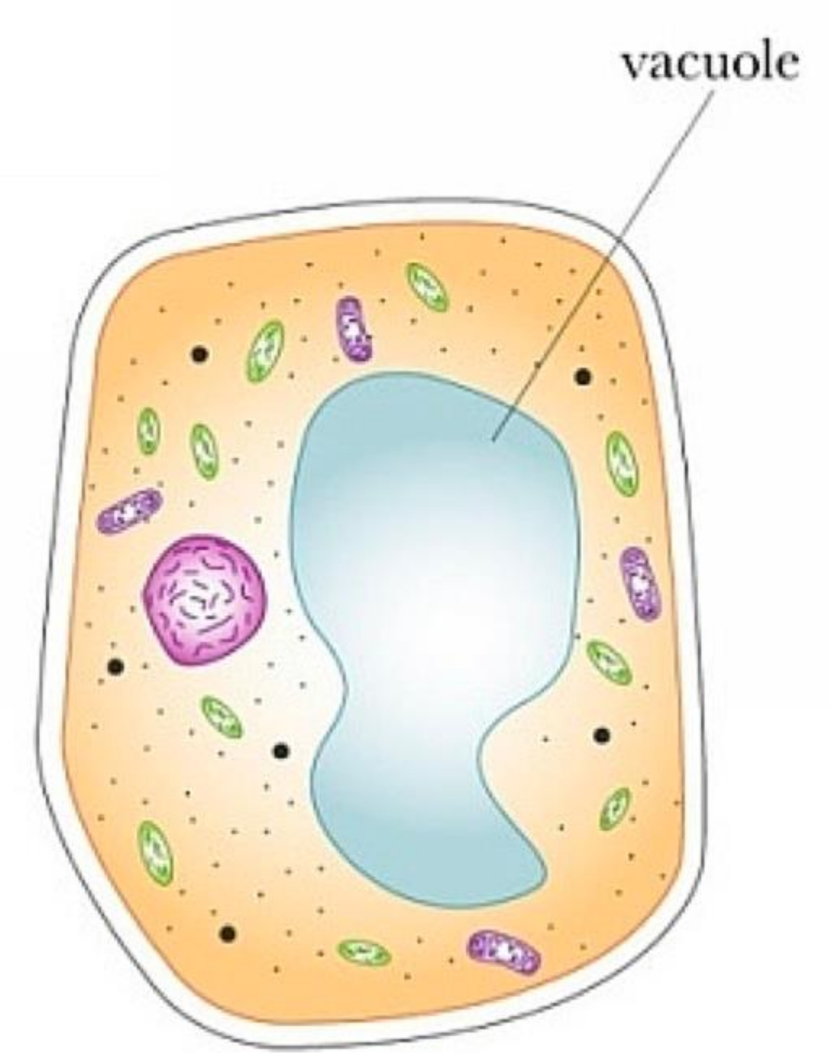
- **Factory Part:**
  - Factory Gates
- **Found in**:
  - Plant cells
  - Some Prokaryote cells

Vacuoles

- Large <u>central</u> vacuole usually in plant cells
- Many smaller vacuoles in animal cells
- Storage container for water, food, enzymes, wastes, etc
- Supports cell shape in plants



- **Factory Part:**
  - Storage room
- **Found in:**
  - Plant cells
  - Animal cells (smaller)



Chapter -2-

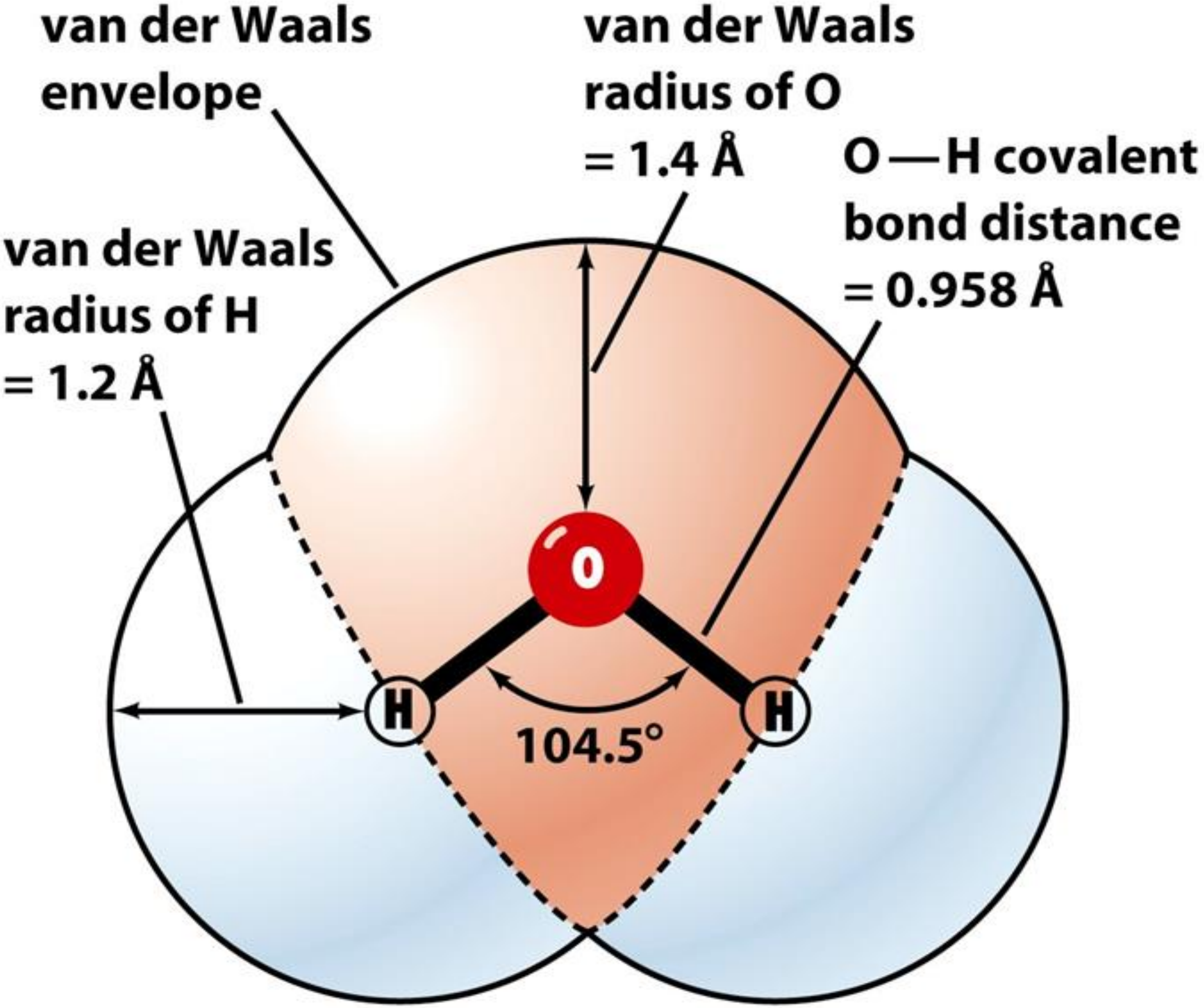
Water, pH and Buffer

2.1. Introduction

- Water is a major component of cells & the most abundant substance in living systems, making up 70% or more of the weight of most organisms.
- The attractive forces between water molecules and the slight tendency of water to ionize are of crucial importance to the structure and function of biomolecules.
- The water molecule and its ionization products, H^+ and OH^-, profoundly influence the structure and properties of all cellular components, including proteins, nucleic acids and lipids.

- The **non-covalent** interactions responsible for the strength and specificity of “recognition” among biomolecules are decisively influenced by the solvent properties of water, including its ability to form **hydrogen bonds** with itself and with solutes.
- Hydrogen bonds between water molecules provide the cohesive forces that make water a liquid at room temperature and that favor the extreme ordering of molecules that is typical of crystalline water (ice).
- Polar biomolecules dissolve readily in water because they can replace water-water interactions with more energetically favorable water-solute interactions.

- Hydrogen bonds, ionic bonds and van der Waals interactions are individually weak, but collectively they have a very significant influence on the three-dimensional structures of proteins, nucleic acids, polysaccharides, and membrane lipids.
- Water has a higher melting point, boiling point, and heat of vaporization than most other common solvents.
- These **unusual properties** are a consequence of attractions between adjacent water molecules that give liquid water great internal cohesion.
- look at the electron structure of the H_2O molecule reveals the cause of these intermolecular attractions.


van der Waals envelope
van der Waals radius of O = 1.4 Å
O — H covalent bond distance = 0.958 Å
van der Waals radius of H = 1.2 Å
O
H
H
104.5°

- The geometry of the molecule is dictated by the shapes of the outer electron orbitals of the oxygen atom, which are similar to the *sp3 bonding orbitals of carbon*.
- These orbitals describe a rough tetrahedral, with a hydrogen atom at each of two corners and unshared electron pairs at the other two corners
- The H-O-H bond angle is 104.5^0, slightly less than the 109.5^0 of a perfect tetrahedral because of crowding by the nonbonding orbitals of the oxygen atom.
- The oxygen nucleus attracts electrons more strongly than does the hydrogen nucleus (a proton); that is, oxygen is more electronegative.

- The sharing of electrons between H and O is therefore unequal; the electrons are more often in the vicinity of the oxygen atom than of the hydrogen.
- The result of this unequal electron sharing is two electric dipoles in the water molecule, one along each of the H-O bonds; each hydrogen bears a partial positive charge and the oxygen atom bears a partial negative charge equal to the sum of the two partial positives.
- As a result, there is an electrostatic attraction between the oxygen atom of one water molecule and the hydrogen of another called a **hydrogen bond.**
- *Hydrogen bonds are relatively weak.*

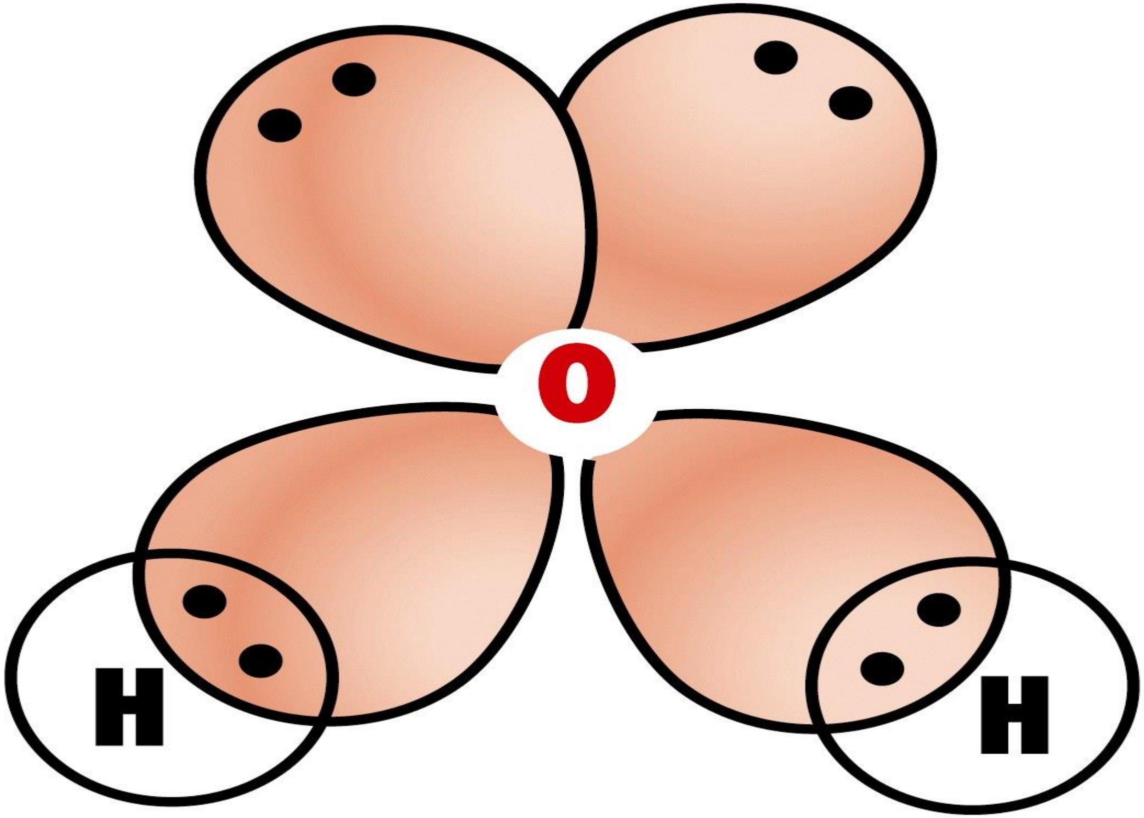


Figure 2-1b Fundamentals of Biochemistry, 2/e

- Each hydrogen atom of a water molecule shares an electron pair with the central oxygen atom.

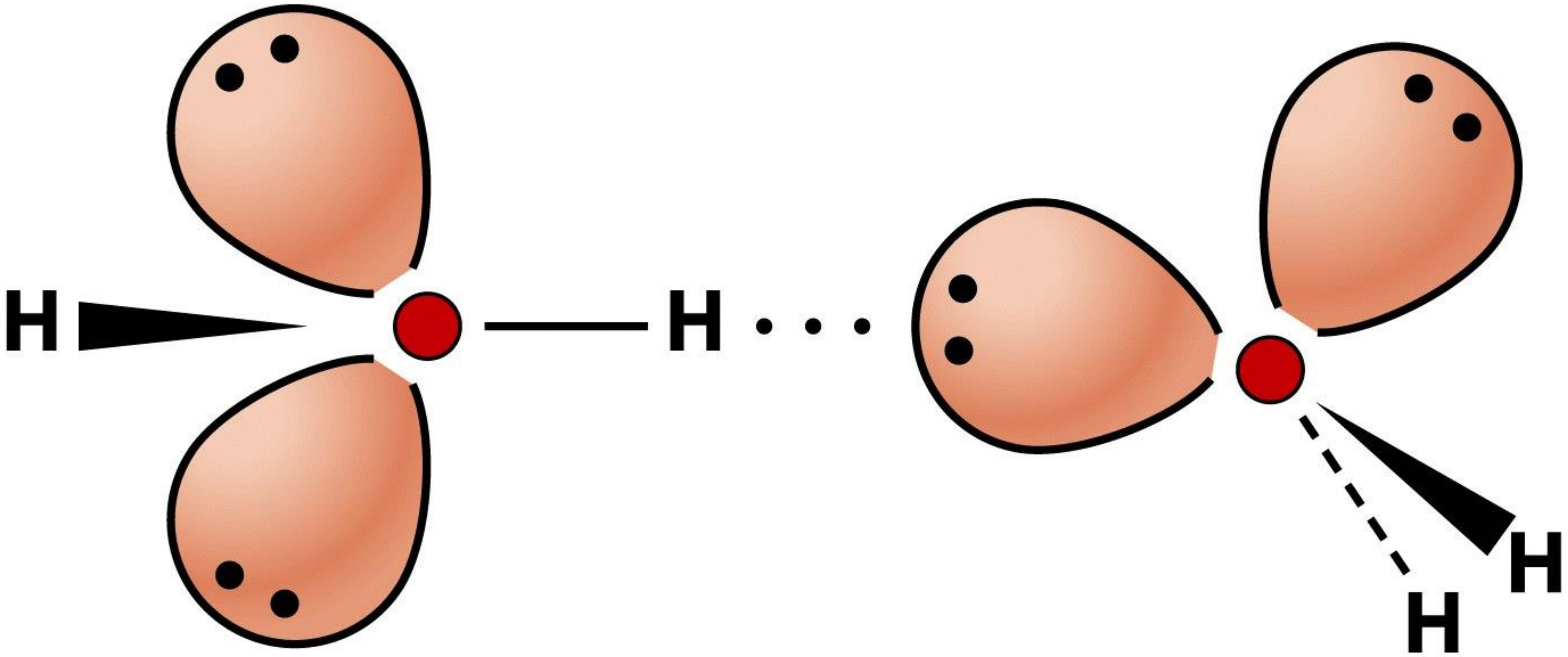


Figure 2-2 Fundamentals of Biochemistry, 2/e

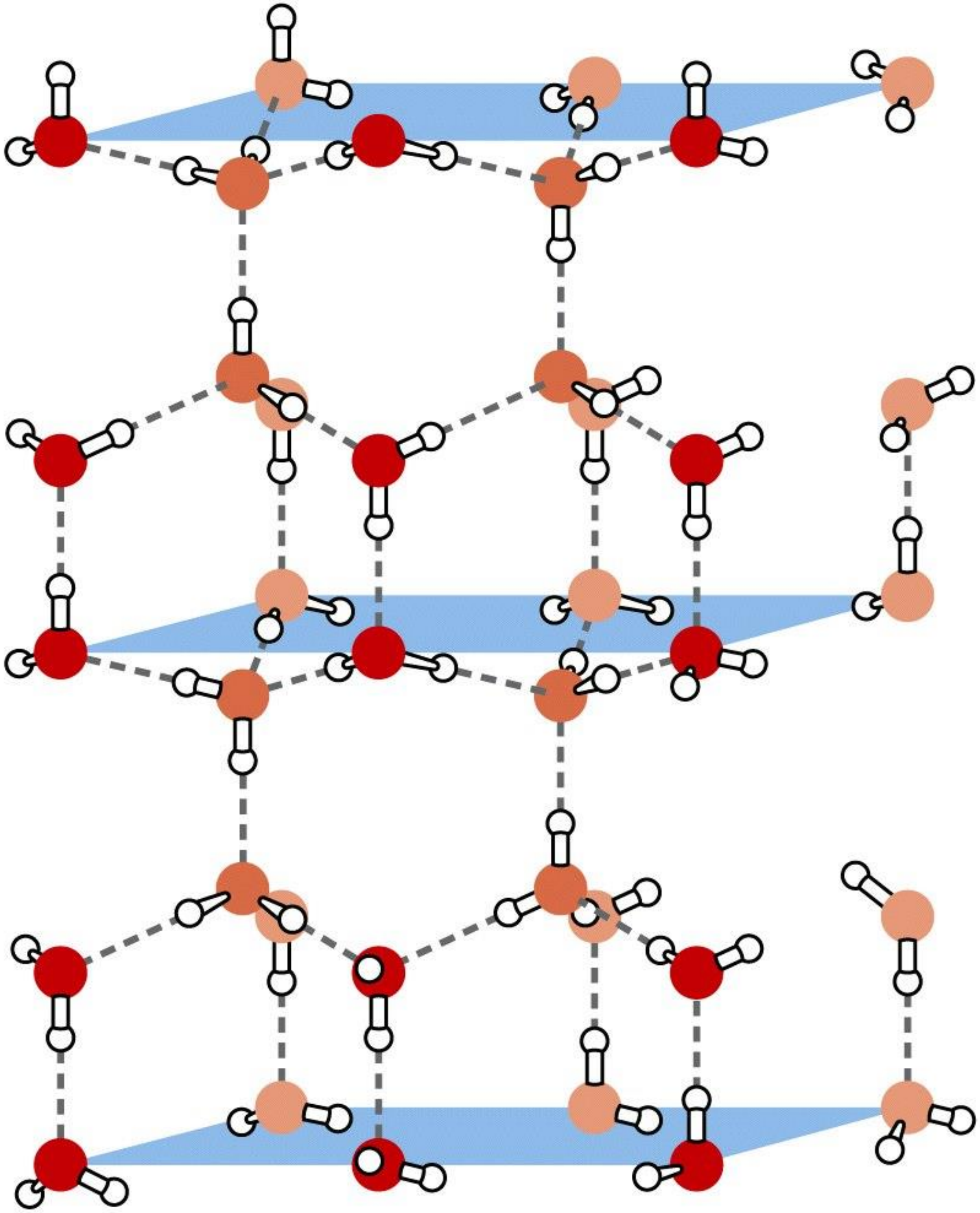


Figure 2-3 Fundamentals of Biochemistry, 2/e
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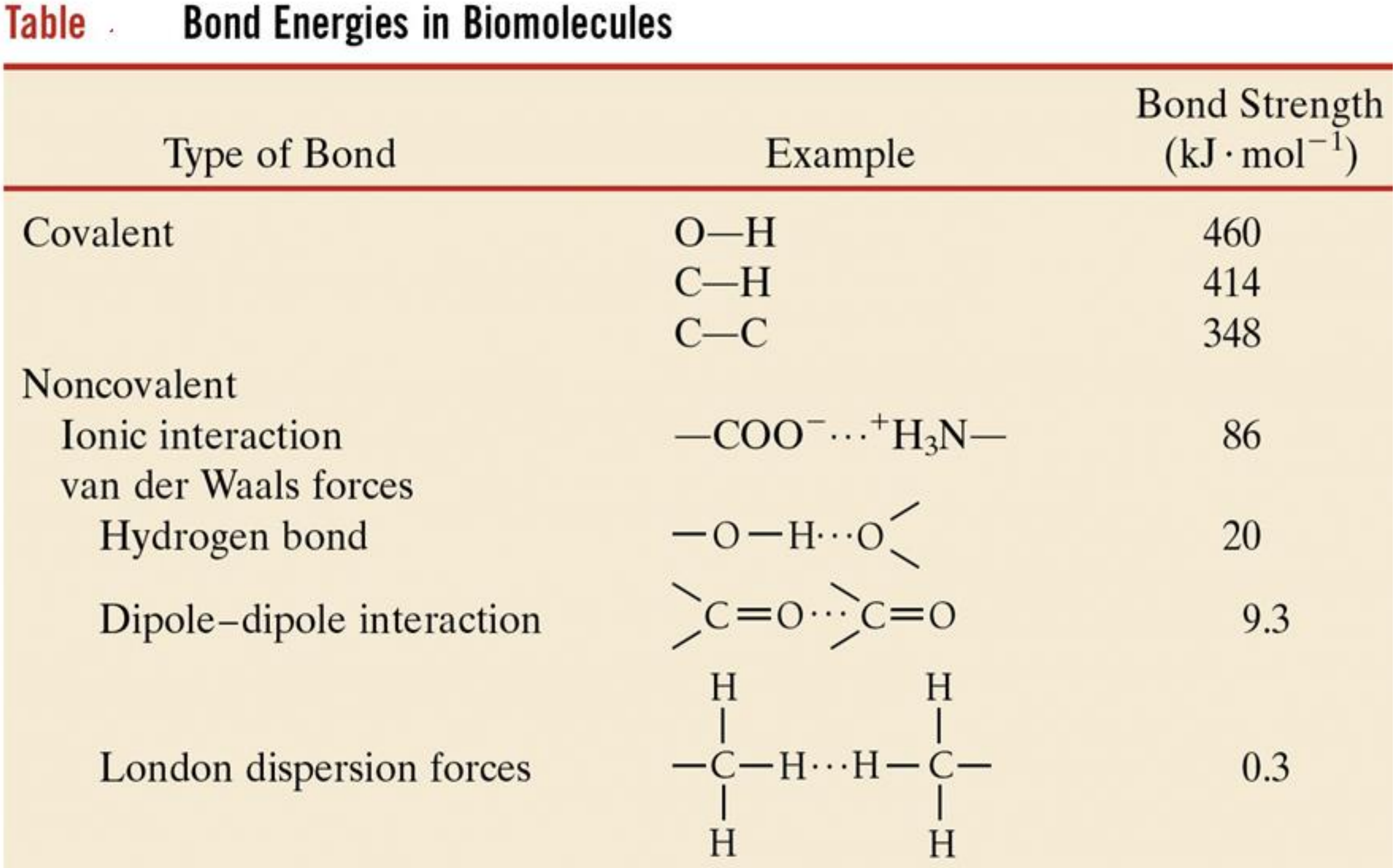

Table . **Bond Energies in Biomolecules**

Type of Bond	Example	Bond Strength ($kJ \cdot mol^{-1}$)
Covalent	O—H	460
	C—H	414
	C—C	348
Noncovalent		
Ionic interaction	$-COO^{-}\cdots{}^{+}H_3N-$	86
van der Waals forces		
Hydrogen bond	$-O-H\cdots O<$	20
Dipole–dipole interaction	$>C=O\cdots >C=O$	9.3
London dispersion forces	$-\overset{H}{\underset{H}{C}}-H\cdots H-\overset{H}{\underset{H}{C}}-$	0.3

- Water is a polar solvent. It readily dissolves most biomolecules, which are generally charged or polar compounds; compounds that dissolve easily in water are **hydrophilic (Greek, “water-loving”).**
- In contrast, nonpolar solvents such as chloroform and benzene are poor solvents for polar biomolecules but easily dissolve those that are **hydrophobic—nonpolar molecules** such as lipids and waxes.
- Water dissolves salts such as NaCl by hydrating and stabilizing the Na and Cl ions, weakening the electrostatic interactions between them and thus counteracting their tendency to associate in a crystalline lattice

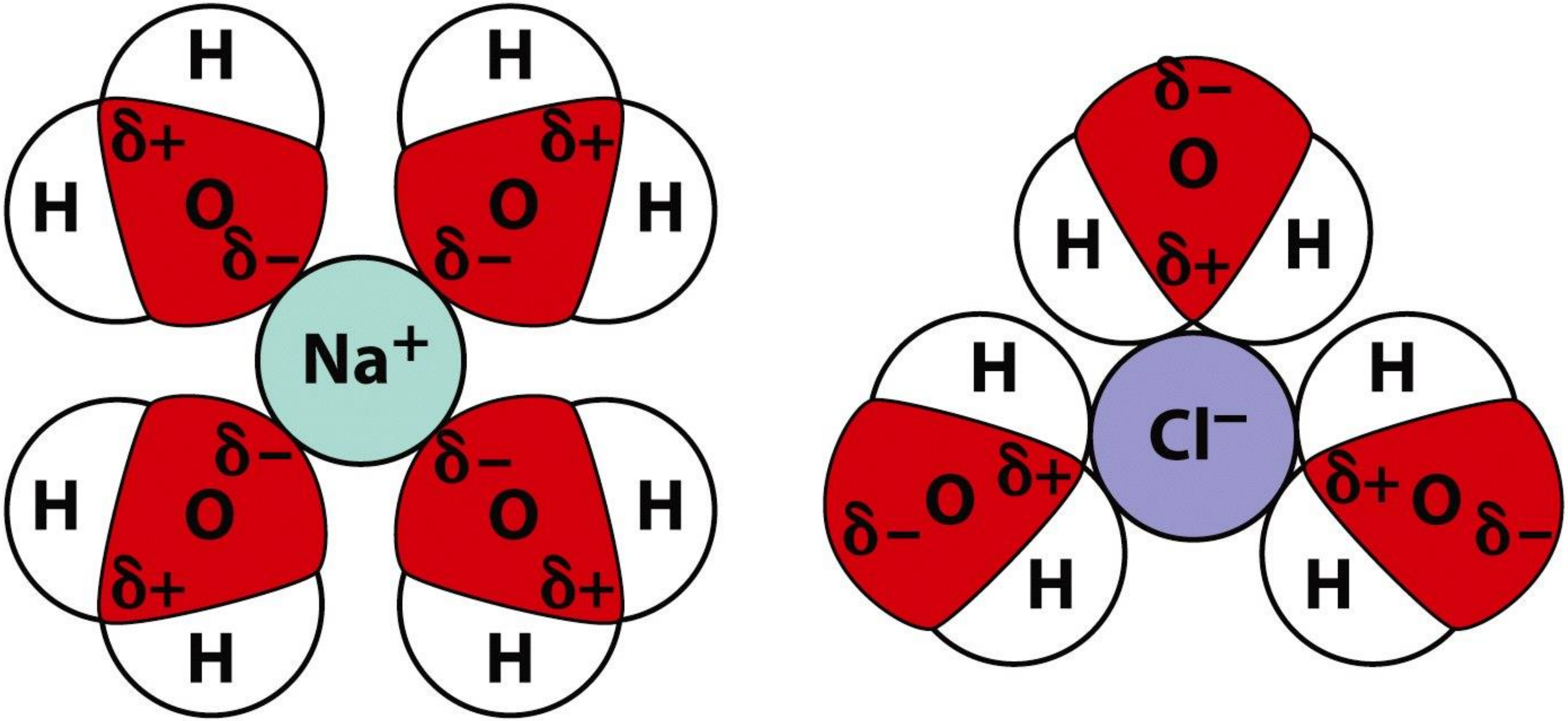

Figure 2-6 Fundamentals of Biochemistry, 2/e

Water Forms Hydrogen Bonds with Polar Solutes

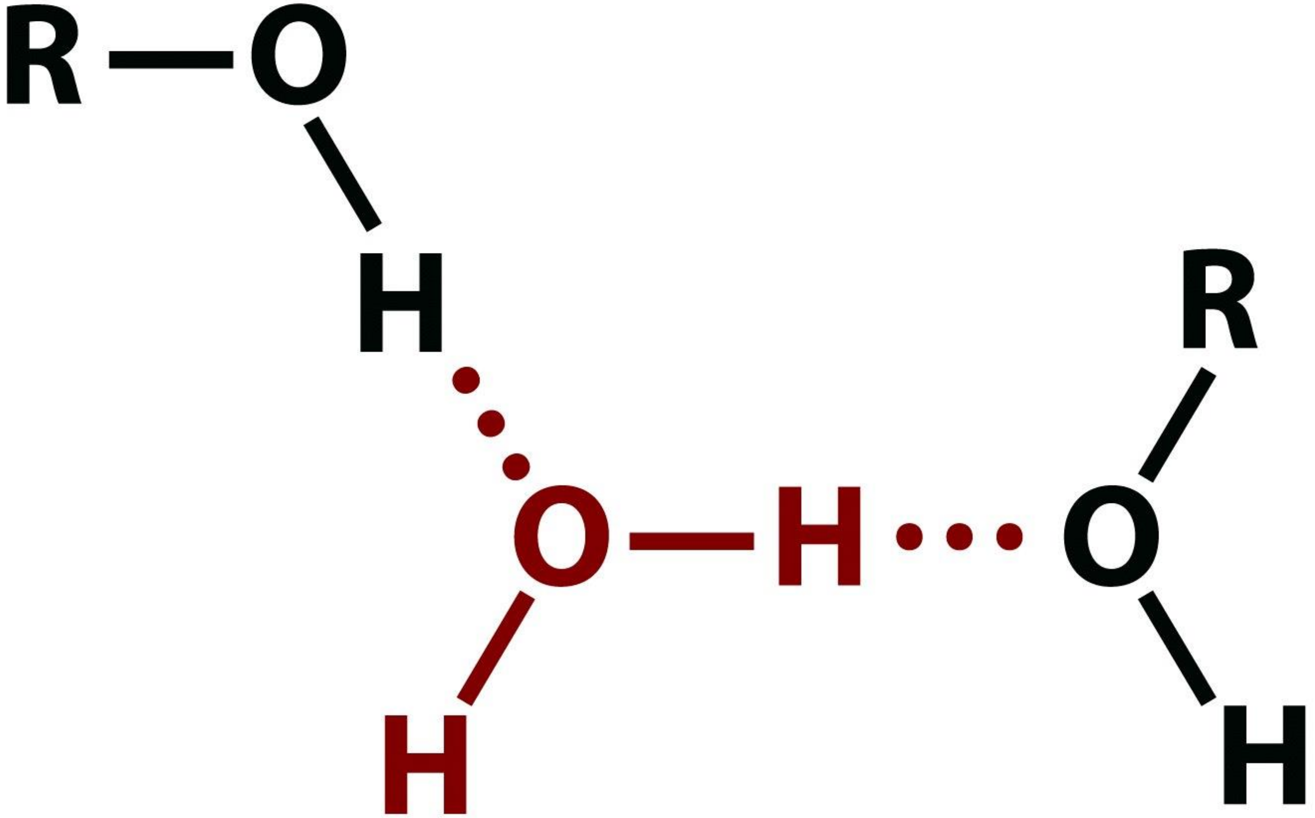

Figure 2-7a Fundamentals of Biochemistry, 2/e

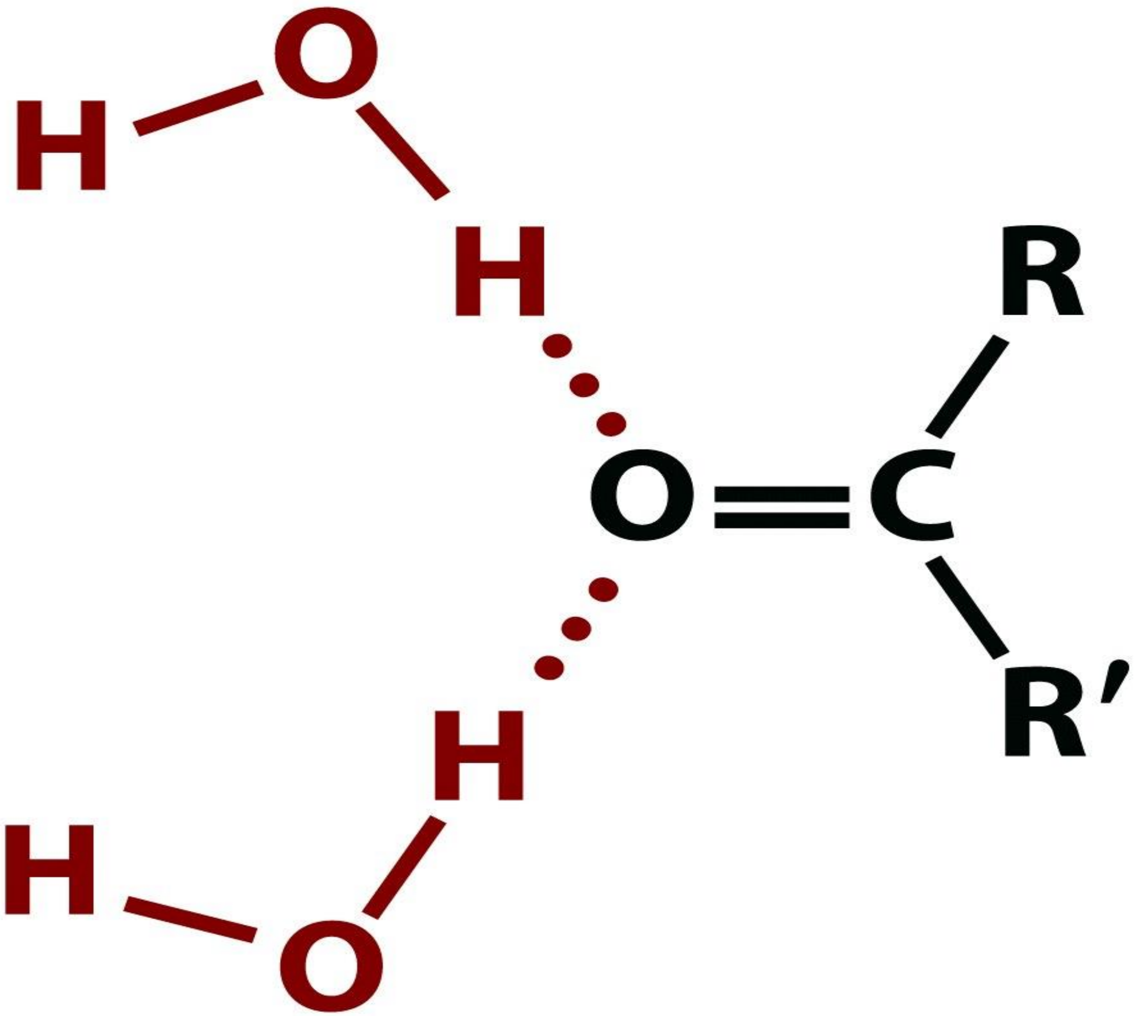

Figure 2-7b Fundamentals of Biochemistry, 2/e
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2.2. Unusual properties of Water

- **Water has**

➢ the highest boiling point by over 100° C (H_2S ~ -61°)

➢ the highest dielectric constant ε (~80)= preventing of substances from intraction among themselves by another substance.

➢ a solid density lower than the liquid (~9%).

➢ a high viscosity , high polarity, a high surface tension

➢ Cohesion properties: the attraction between water molecules to each other through Hydrogen bonds

- So, Most of water's properties come from its polarity

And its *hydrogen bonding ability*

  - Directionality → Structure (even in liquid state)
  - Acts as both donor and acceptor

2.3 Role of water in biological system

Role of water is both the solvent in which metabolic reactions occur and a reactant in many biochemical processes, including hydrolysis, condensation, and oxidation-reduction reactions

2.4 Colligative properties

The properties which depends only on the concentration of the **solute** or the **solvent** and do not depend on their chemical nature. **Colligative properties includes**;

- Lowering of the vapor pressure ,Elevation of the bp
- Lowering of freezing point and Osmotic pressure

2.5 Hydronium ion and pH

Pure water ionizes slightly, forming equal numbers of H^+ ions (hydronium ions, H_3O^+) and hydroxide ions, OH^-.

The ion product of water, *K*w, is the basis for the **pH scale**. It is a convenient means of designating the concentration of H^+ (and thus of OH^-) in any aqueous solution in the range between 1.0 M H^+ and 1.0 M OH^-.

The term **pH** is defined by the expression

$$PH = log\frac{1}{H^+} = -\log[H^+]$$

The greater the acidity of a solution, the lower its pH.

The dissociation constant (*K*a) weak acid or base is;

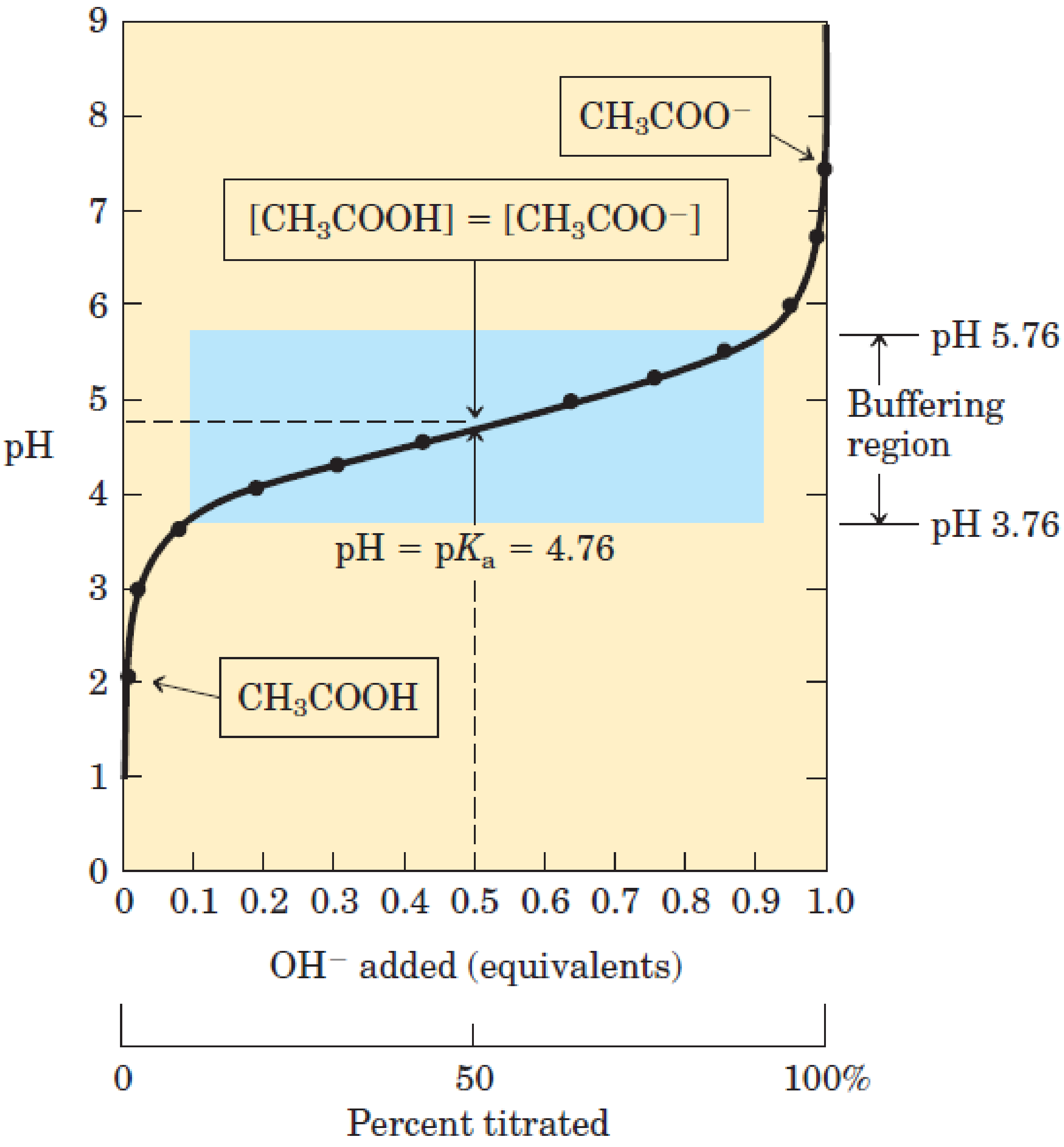
$$K_{eq} = \frac{[A^-][H^+]}{[HA]} = K_{eq}$$

Haslelbalch Equation

2.6 Physiological Buffers and buffering agent

- Almost every biological process is pH dependent; a small change in pH produces a large change in the rate of the process.
- Constancy of pH is achieved primarily by biological buffers which is a mixtures of weak acids and their conjugate bases. Or buffer system consists of a weak acid (the proton donor) and its conjugate base (the proton acceptor).
- **Buffers** are aqueous systems that tend to resist changes in pH when small amounts of acid (H^+) or base (OH^-) are added.
- In cells and tissues, phosphate and bicarbonate buffer systems maintain intracellular and extracellular fluids at their optimum (physiological) pH, which is usually close to pH 7 at which enzymes work optimally at this pH.

The titration curve of acetic acid. After addition of each increment of NaOH to the acetic acid solution, the pH of the mixture is measured.



Regulation of pH

- Direct relation of the production and retention of acids and bases.
- When pH deviates from normal, the following systems kick in to minimize pH change:
  - Kidneys will respond within hours/days.
  - Respiratory Center and Lungs responds within minutes
  - Buffer system responds within seconds.
    - Found in all body fluids
    - Weak acids good buffers since they can tilt a reaction in the other direction
    - Strong acids are poor buffers because they make the system more acid

- **First line of defense against pH shift**
  - **Chemical buffer system**
    - **Bicarbonate buffer system**
    - **Phosphate buffer system**
    - **Protein buffer system**
- **Second line of defense against pH shift**
  - **Physiological buffers**
    - **Respiratory mechanism (CO_2 excretion)**
    - **Renal mechanism (H^+ excretion)**

Buffer Solutions

- A buffer is defined as a solution of two or more chemical compounds that prevent marked changes in H^+ ion concentration when either an acid or base is added to solution.
- Most buffers are mixtures of a weak acid and /or a weak base and its conjugate base/ acid respectively.
- Maintaining the pH of blood and other fluids within narrow limits is accomplished through the use of **buffers**.
- If $OH^–$ is added to a buffer solution, the pH increases only slightly; the acid component of the buffer neutralizes the added $OH^–$.
- If H^+ is added to a buffer solution, the pH decreases only slightly; the base component of the buffer neutralizes the added H^+.

Buffers in the Body: Acidosis and Alkalosis

- Each of the fluids in our bodies has a pH range suited to its function.
- Blood plasma and the interstitial fluid surrounding cells have a slightly basic pH with a normal range of 7.35–7.45.
- The reactions and equilibria that take place throughout the body are very sensitive to pH—variations of even a few tenths of a pH unit can produce severe symptoms.
- Maintaining the pH of blood serum is accomplished by the carbonic acid-bicarbonate buffer system.

- The bicarbonate buffer system is intimately related to the elimination of CO_2.
- ***Respiratory acidosis*** can be caused by a decrease in respiration, which leads to a buildup of excess CO_2 in the blood and a corresponding decrease in pH.
- ***Metabolic acidosis*** results from an excess of other acids in the blood that reduce the bicarbonate concentration.
- Increased breathing can remove too much CO_2 from the blood, causing *respiratory alkalosis.*
- The pH falls **(acidosis)** as bicarbonate decreases (increases CO_2) in relation to carbonic acid.
- The pH rises **(alkalosis)** as bicarbonate increases (decreases CO_2) in relation to carbonic acid.

Blood Buffer Systems

- Why do we need them?
  - If the acids produced in the body from the catabolism of food and other cellular processes are not removed or buffered, the body's pH would drop.
  - Significant drops in pH interferes with cell enzyme systems.
- Four Major Buffer Systems
  - Protein Buffer systems
  - Hemoglobin Buffer system
  - Phosphate Buffer system
  - Bicarbonate-carbonic acid Buffer system
  - Note: Buffer systems do not prevent pH change but rather minimize the pH change.

- **Protein Buffer System**
  - Originates from amino acids
    - ALBUMIN- primary protein due to high concentration in plasma
  - Buffer has both hydrogen ions and carbon dioxide
- **Hemoglobin Buffer System**
  - Roles
    - Binds CO_2
    - Binds and transports hydrogen and oxygen
    - Participates in the chloride shift
    - Maintains blood pH as hemoglobin changes from oxyhemoglobin to deoxyhemoglobin

- **Phosphate Buffer System**
  - Has a major role in the elimination of H^+ via the kidney.
    - Assists in the exchange of sodium for hydrogen
    - It participates in the following reaction
      - $HPO_4^{-2} + H^+ \longleftrightarrow H_2PO^-$
  - Essential within the erythrocytes
- **Bicarbonate/carbonic acid buffer system**
  - Function almost instantaneously
  - Cells that are utilizing O_2, produce CO_2, which builds up. Thus, more CO_2 is found in the tissue cells than in nearby blood cells. This results in a pressure (pCO_2).
  - Diffusion occurs, the CO_2 leaves the tissue through the interstitial fluid into the capillary blood

Bicarbonate/carbonic acid buffer system

- How is CO_2 transported?
  - 5-8% transported in dissolved form
  - A small amount of the CO_2 combines directly with the hemoglobin to form carbaminohemoglobin
  - 92-95% of CO_2 will enter the RBC, and under the following reaction
    - $CO_2 + H_2O \longleftrightarrow H^+ + HCO_3^-$
  - Once bicarbonate formed, exchanged for chloride

Physiologic Buffer Systems

- **Lungs/respiratory**
  - – Quickest way to respond, takes minutes to hours to correct pH
  - – Eliminate **volatile** respiratory acids such as CO_2
  - – Doesn't affect fixed acids like lactic acid
  - – Body pH can be adjusted by changing rate and depth of breathing "blowing off"
  - – Provide O_2 to cells and remove CO_2

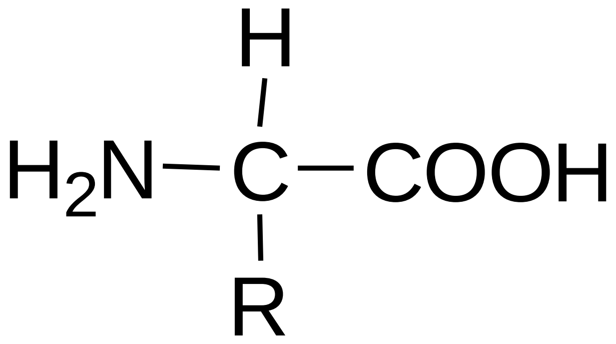
Physiologic Buffer Systems

- **Kidney/Metabolic**
  - Can eliminate large amounts of acid
  - Can excrete base as well
  - Can take several hours to days to correct pH
  - Most effective regulator of pH
  - If kidney fails, pH balance fails

Chapter -3- Proteins

Before going to study proteins let as see about amino acids.

- **3.1. Amino acids (a.a)** are organic molecules with carboxyl and amino groups.
- They are building blocks of proteins.
  - **Structures of amino acids**



$$H_2N-\overset{\displaystyle H}{\underset{\displaystyle R}{C}}-COOH$$

  - NH_2 – Group, which is **basic** ends of amino acid
  - COOH - Group, which is **acidic** end of amino acid
  - R–Group – which is may be **acidic, basic or neutral**

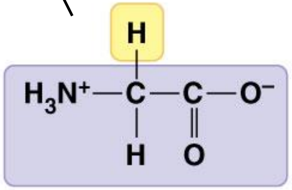
✓ There are 700 a.a. Among 700 a.a, 20 amino acids are made proteins.

✓ Among 20 a.a,19 amino acids are alpha amino acids but proline is secondary amino acid.

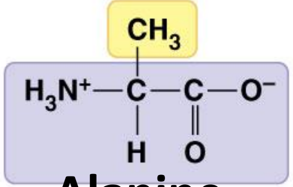
- Amino acids differ in their properties due to differing side chains (R) groups
- Amino acids have different properties that are well-suited to carry out a variety of biological functions i.e
- Capacity to polymerize
- Useful acid-base properties
- Varied physical properties
- Varied chemical functionality

The 20 amino acids of proteins classification.

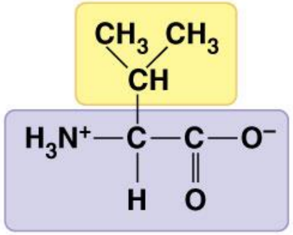
Nonpolar side chains(R) = hydrophobic side chain



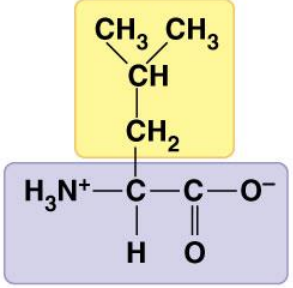
Glycine
(Gly or G)



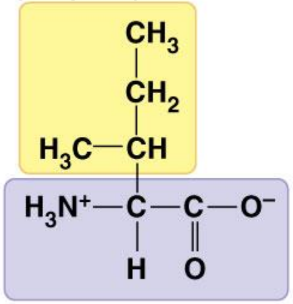
Alanine
(Ala or A)



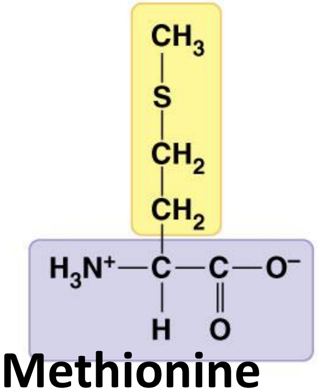
Valine
(Val or V)



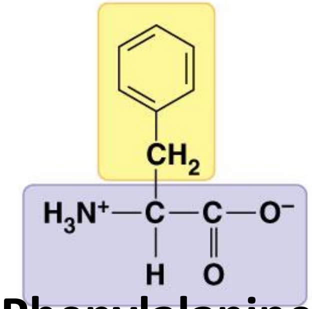
Leucine
(Leu or L)



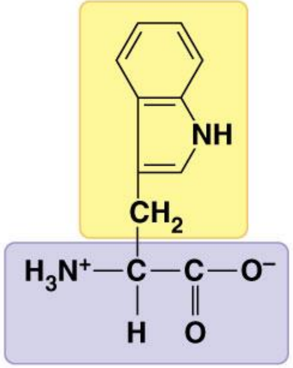
Isoleucine
(Ile or I)



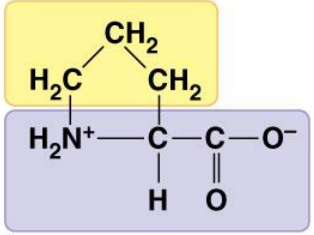
Methionine
(Met or M)



Phenylalanine
(Phe or F)



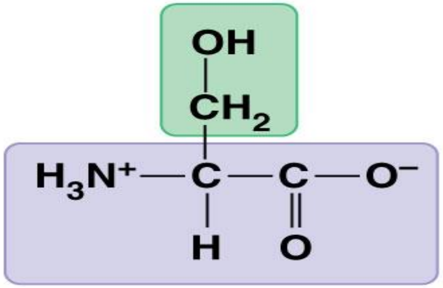
Tryptophan
(Trp or W)



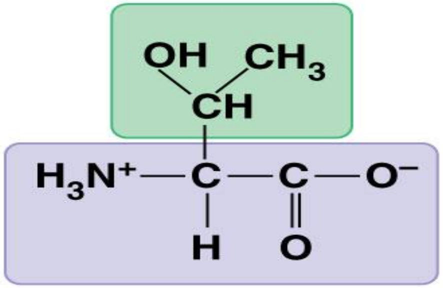
Proline
(Pro or P)

Each of these amino acids has a nonpolar side chain that does not bind or give off protons, or participate in hydrogen or ionic bonds

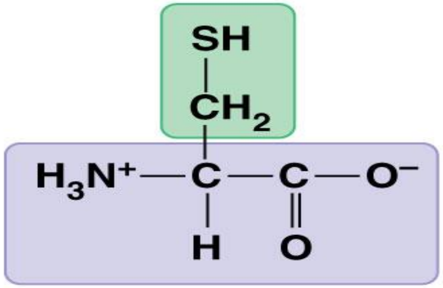
Polar side chains(R); hydrophilic



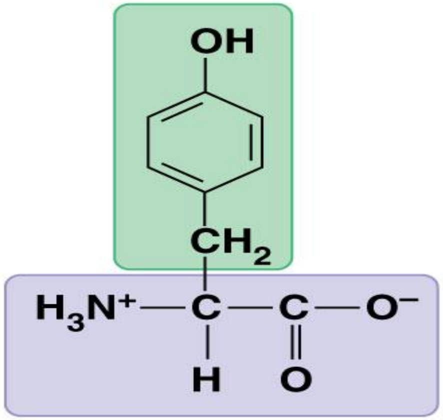
Serine
(Ser or S)



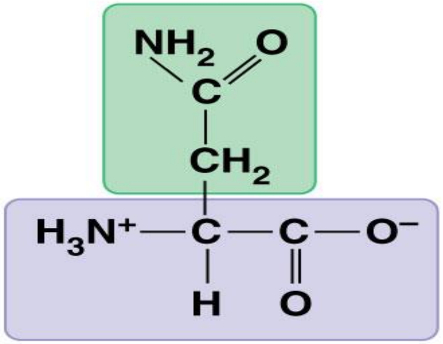
Threonine
(Thr or T)



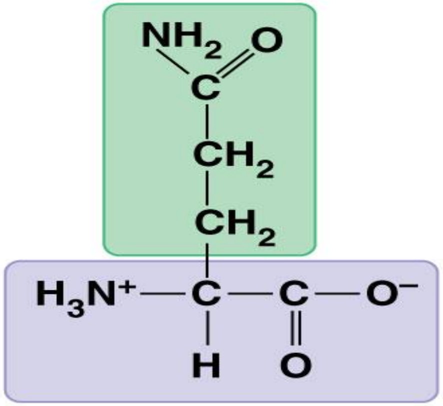
Cysteine
(Cys or C)



Tyrosine
(Tyr or Y)



Asparagine
(Asn or N)

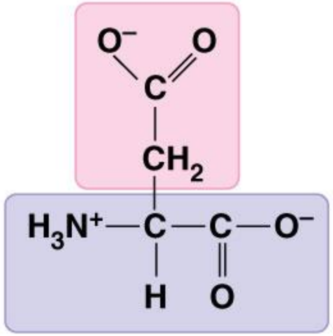


Glutamine
(Gln or Q)

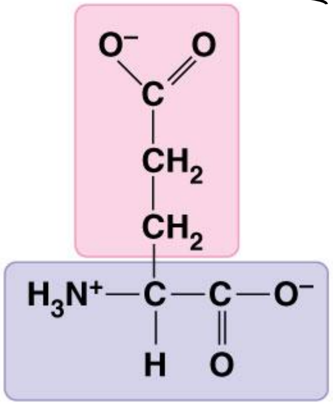
These amino acids have zero net charge at neutral pH, although the side chains of cysteine and tyrosine can lose a proton at an alkaline pH

Electrically charged side chains (R); hydrophilic

Acidic (negatively Charged R group)

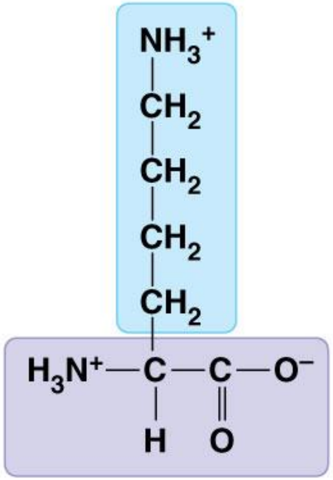


Aspartic acid (Asp or D)

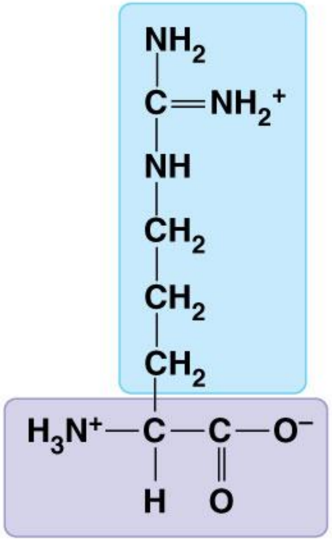


Glutamic acid (Glu or E)

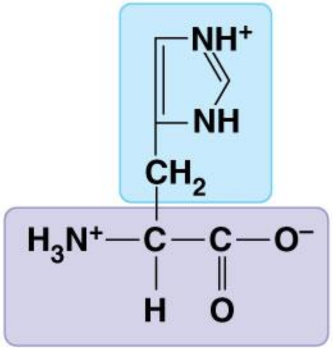
Basic (positively charged R Group)



Lysine (Lys or K)



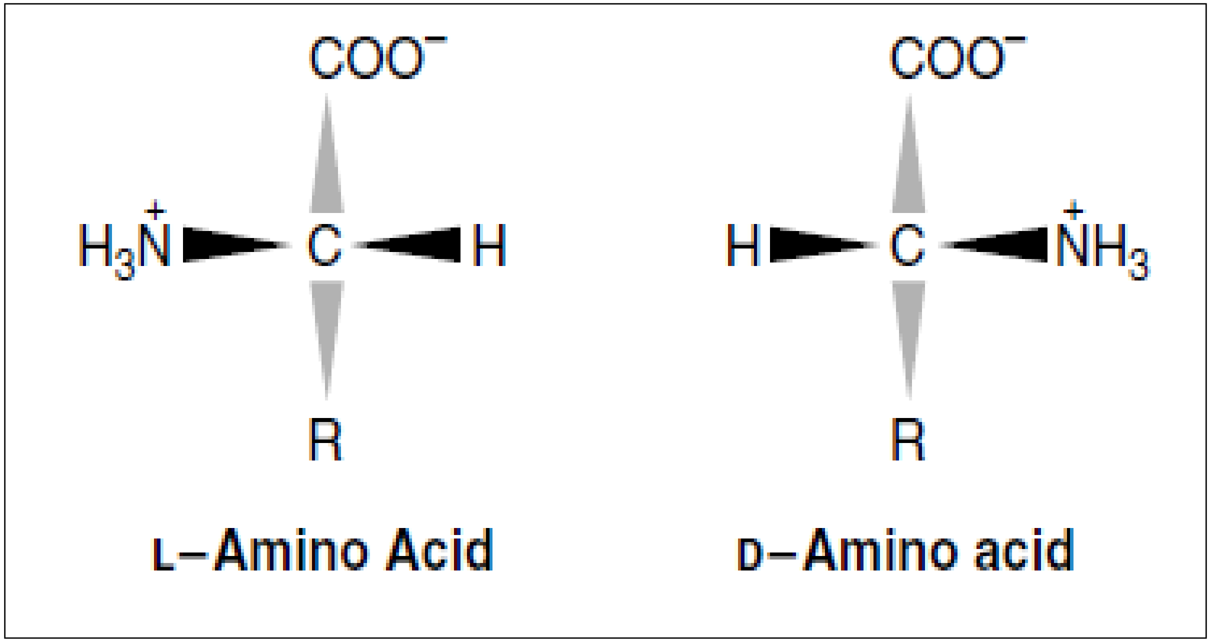
Arginine (Arg or R)



Histidine (His or H)

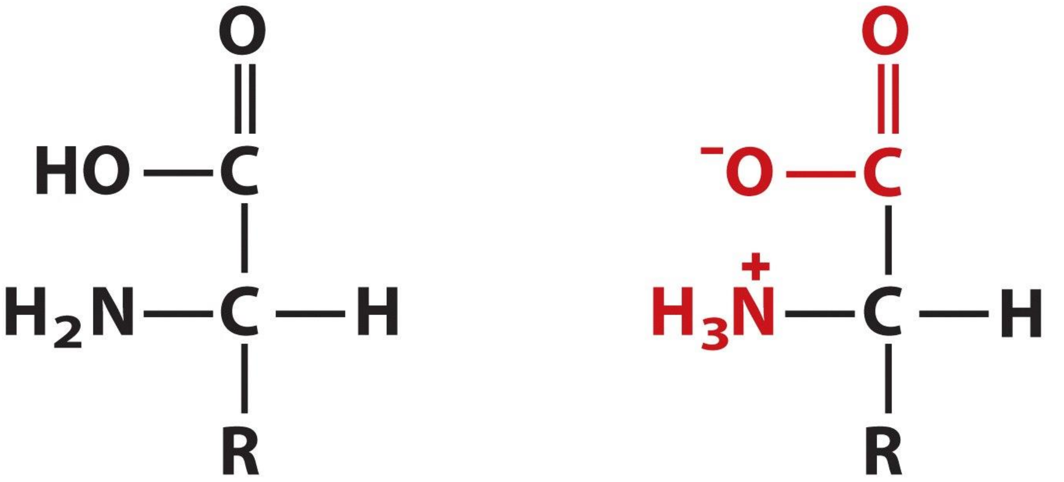
Optical Properties of Amino Acids

- The α-carbon of a.a. is attached to four different chemical groups is a chiral or optically active carbon atom, **Glycine** is the exception which is achiral.
- amino acids exist in two forms, D and L that are mirror images of each other.
- All amino acids found in proteins are the L-onfiguration.



“Zwitter” Ions:

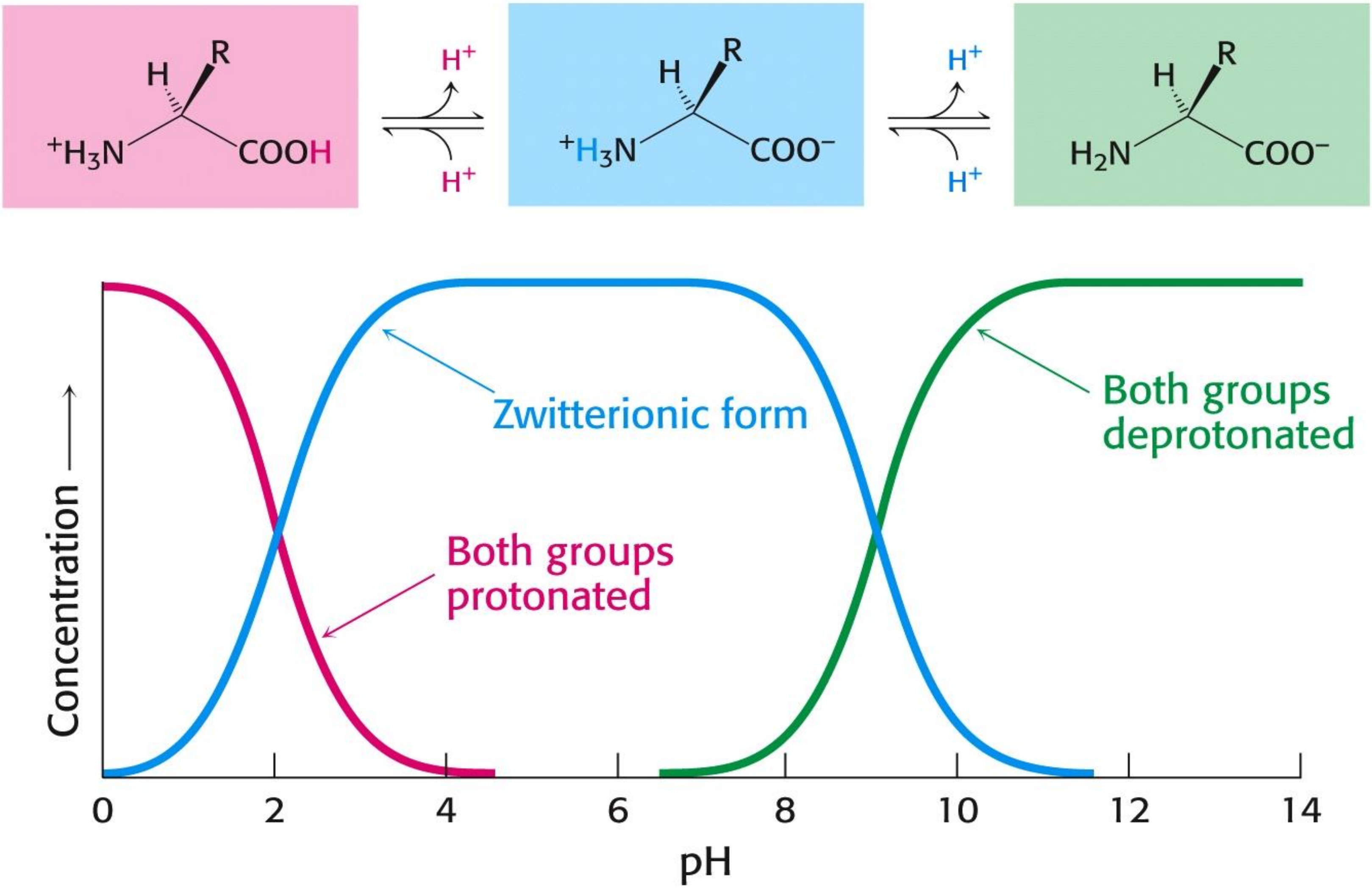
- Ions bearing two charges were named zwitter ions by German scientists; the name still applies today, especially for amino acids at **neutral pH=7**:
- Zwitter” ions have amphoteric behavior, act as acids and bases & zero charge at isoelectric PH.



Nonionic form

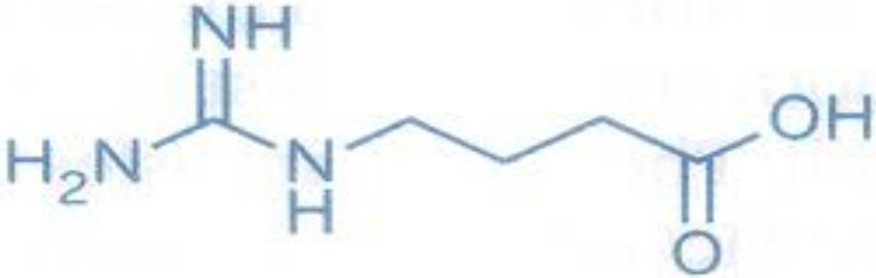
Zwitterionic form

- Even though both acids and amines are present in the same molecule, they mostly behave as though they were separate entities.



Toxic Amino Acids

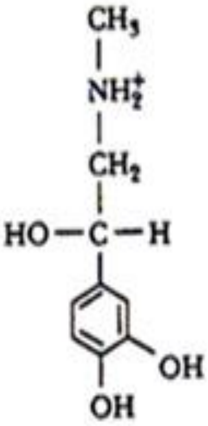
New toxic amino acids



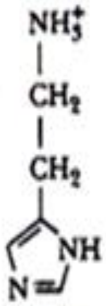
γ-Guanidinobutyric acid

Non Protein Amino Acids

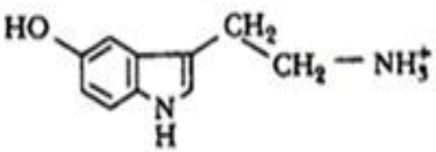
- You don’t have to know the structures, but do have to know that these are important metabolites. Some are antibiotics. Some are hormones and some are important immune modulators.



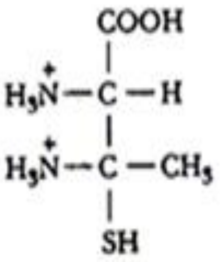
Epinephrine



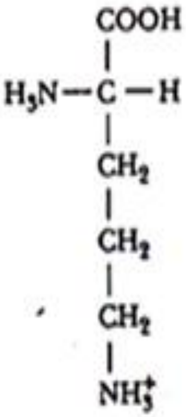
Histamine



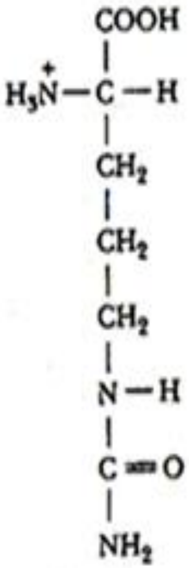
Serotonin



Penicillamine



Ornithine



Citrulline

Nutritional classification alpha (α) amino acids

- **1- Essential amino acids:** These amino acids can’t be formed in the body and so, it is essential to be taken in diet. Their deficiency affects growth, health and protein synthesis.
- **2- Semiessential amino acids:** These are formed in the body but not in sufficient amount for body requirements especially in children.
- Summary of essential and semiessential amino acids:
- V= valine i= isoleucine l= lysine l= leucine
- A = arginine* H= histidine* M= methionine
- T= tryptophan Th= threonine P= phenyl alanine
- *= **arginine** and **histidine** are semiessential
- **3- Non essential amino acids:** These are the rest of amino acids that are formed in the body in amount enough for adults and children. They are the remaining 10 amino acids.

Chemical properties of amino acids:

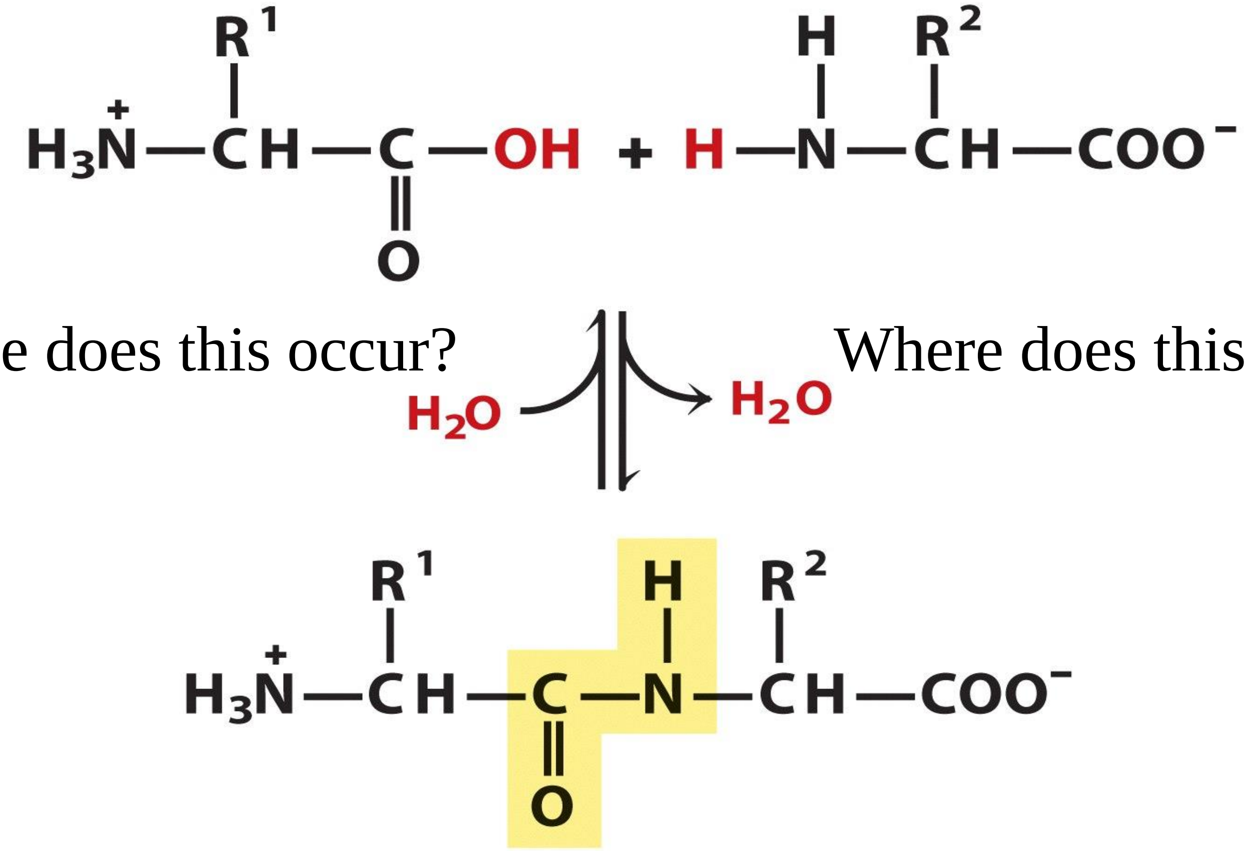
1- Reactions due to COOH group:

- Salt formation with alkalis, ester formation with alcohols, amide formation with amines and decarboxylation.

2- Reactions due to NH_2 group: deamination and reaction with ninhydrin reagent.

- Ninhydrin reagent reacts with amino group of amino acid yielding blue colored product. The intensity of blue color indicates quantity of amino acids present.

Peptide Bond Formation



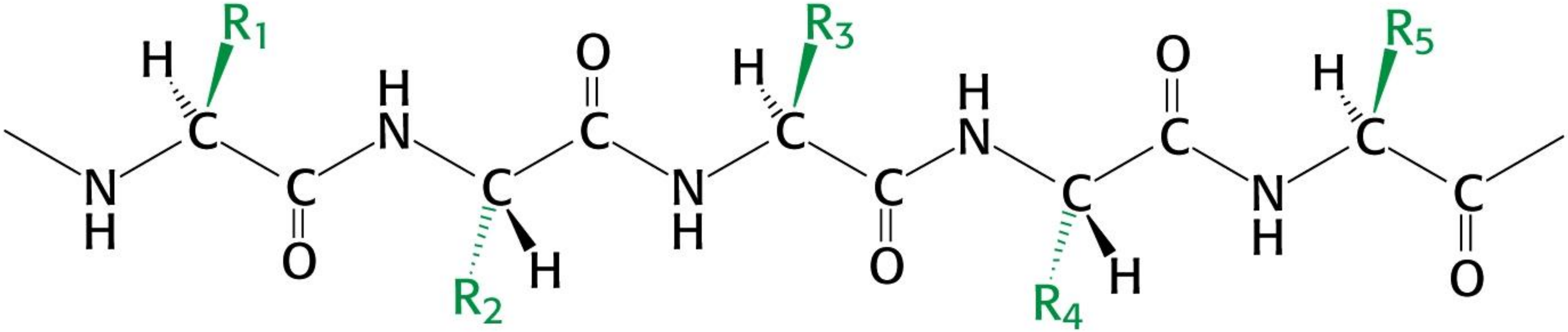
$$H_3\overset{+}{N}-CH(R^1)-C(=O)-OH + H-NH-CH(R^2)-COO^- \rightleftharpoons H_3\overset{+}{N}-CH(R^1)-C(=O)-NH-CH(R^2)-COO^- + H_2O$$

Where does this occur?

Where does this occur?

- Peptide bond formation (dehydration) occurs on the **ribosome**. Peptide bond breaking is the key to protein digestion **(small intestine)** and in the **cytoplasm** of every living cell as protein turnover.
- Note that the peptide bond is **trans**.

- Copolymer of amino acids:
  - α“polypeptide”



Amino acid polymers of ≤50 amino acids are called

“polypeptides, peptides, oligopeptides, etc.”

Amino acids polymer of >50 amino acids are called “proteins.”

- Peptides are classified according to the number of amino acids linked together as dipeptides, tripeptides, tetrapeptides,etc.(Higher peptides)

3. 2. Proteins

- *Proteins are polymers of amino acids and t*ermed polypeptides
- Elements in protein are C,H,O,N &S
- Proteins are large, complex biological molecules that serve diverse functional and structural roles within cells.
- Proteins are biological workhorses that carry out most of the functions within the cell.
- Proteins are synthesized during the translation process.

- Proteins have four basic levels of structure. However, proteins must fold correctly in order to function properly.
- Proteins are composed of amino acids that are covalently linked by peptide bonds.
- Proteins are polypeptide molecules that contain many peptide subunits

3.3.Classification of proteins

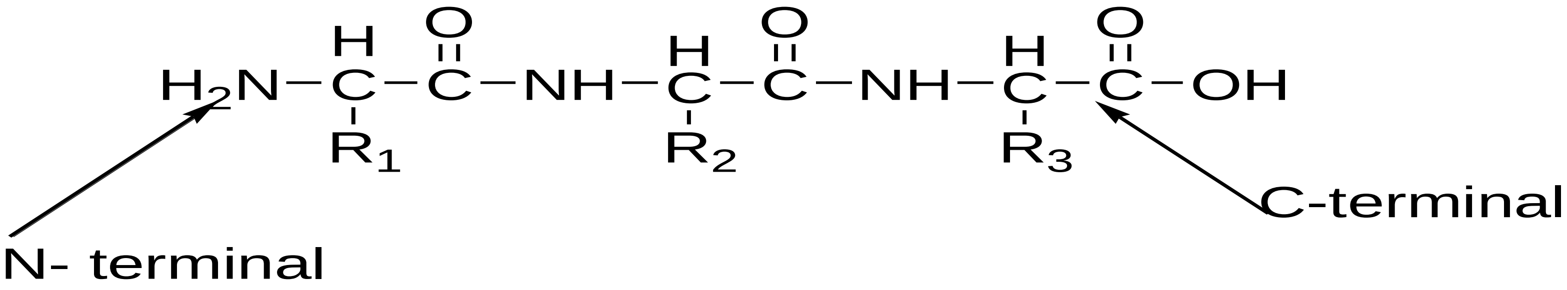
- Classified in many ways some common once like based on Structure; composition; Shape; Nutritional Value; Solubility& Function.

I. Classification of proteins based on Structure

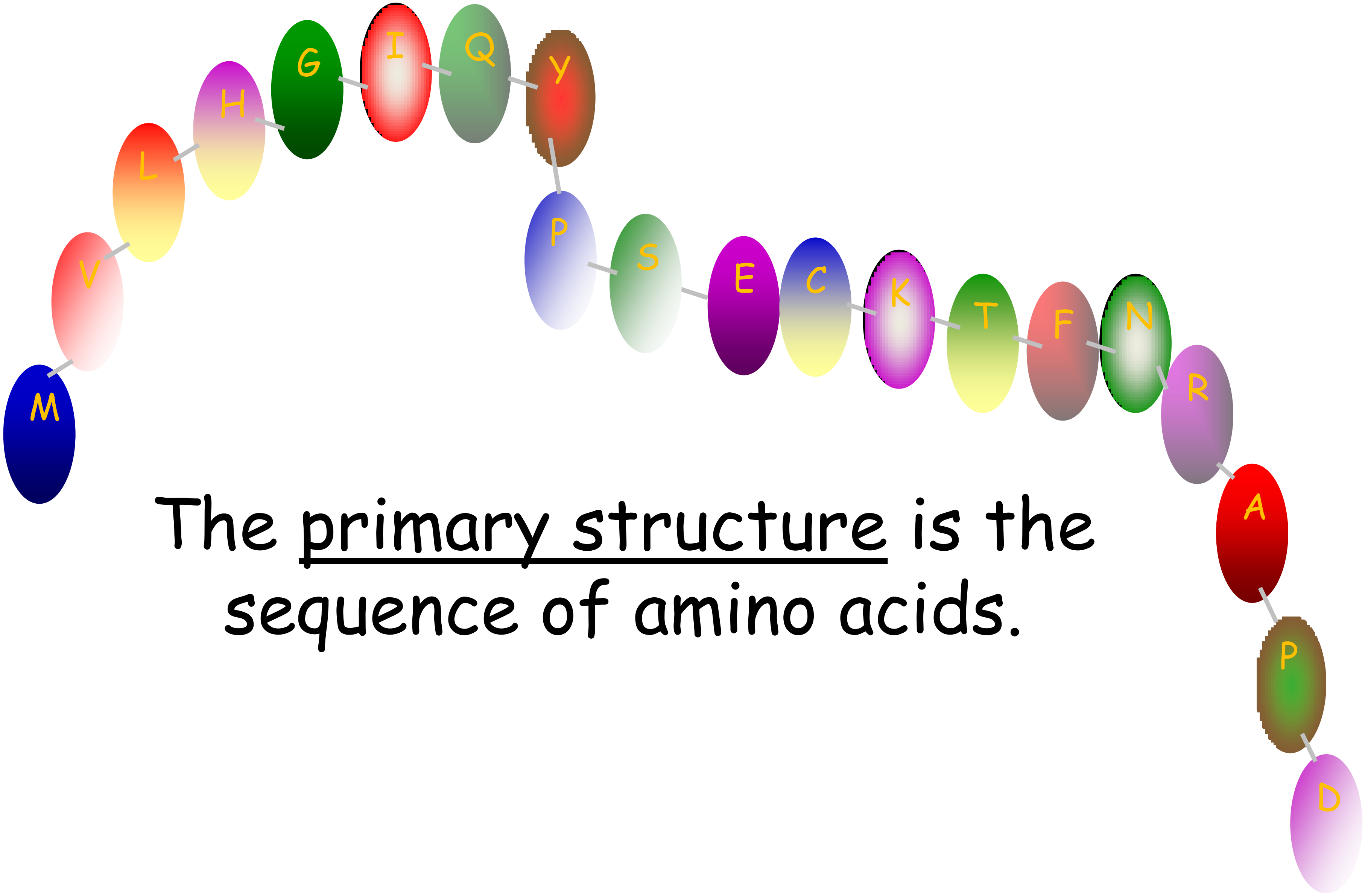
There are four types of protein structures

1. Primary Structure of Proteins

The linear sequence of amino acids linked together covalently is primary structure of proteins



$$H_2N-\underset{R_1}{\overset{H}{C}}-\overset{O}{\overset{\|}{C}}-NH-\underset{R_2}{\overset{H}{C}}-\overset{O}{\overset{\|}{C}}-NH-\underset{R_3}{\overset{H}{C}}-\overset{O}{\overset{\|}{C}}-OH$$



The primary structure is the sequence of amino acids.

2. Secondary Structure of Proteins

- The configurationally relation ship between residues which are about 3-4 amino acids apart in the linear sequences.

Or refers to the arrangement in space of the atoms in the backbone of the polypeptide chain.

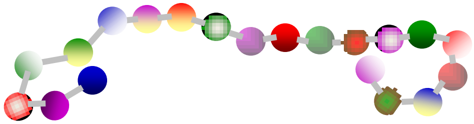
- **Side chain groups are not included** at the level of secondary structure.

- Forces stabilizing the secondary structure – hydrogen bonds (non- covalent) of the peptide bond atoms.

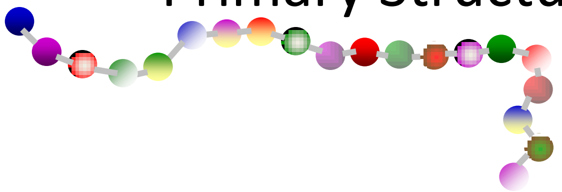
- common types of secondary structures. **α-Helix & β-sheet**

The secondary structure is primarily composed of alpha helix and beta-pleated sheets.

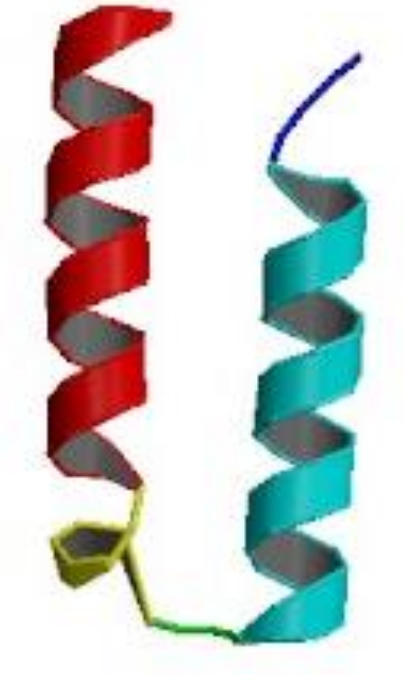
Folding Back and Coiling



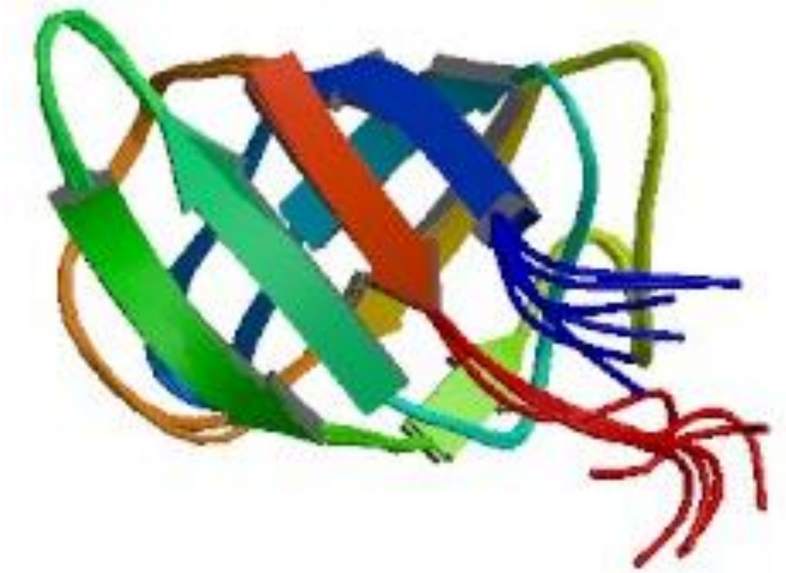
Primary Structure



Alpha Helix



Beta-Pleated Sheet

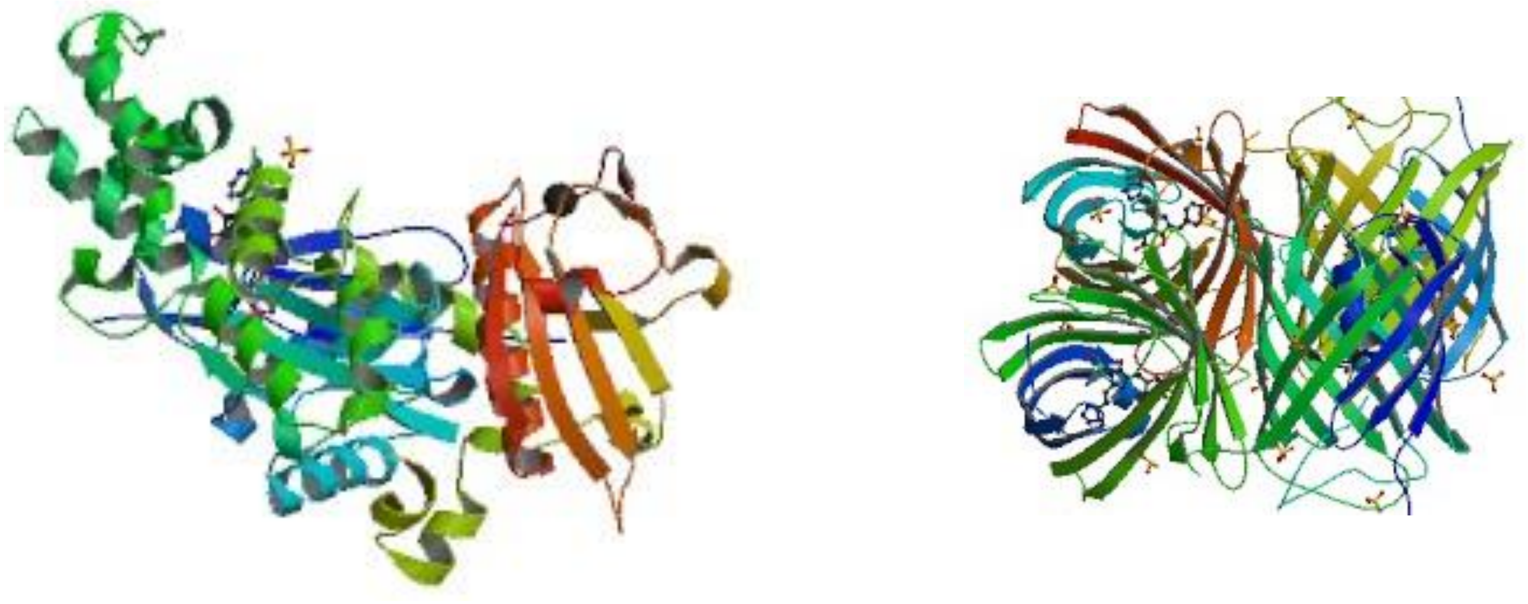


3. Tertiary Structure of Proteins

- The primary structure of polypeptide chain determines its tertiary structure.
- It refers to the folding of domains.
- Domains are a fundamental functional and three dimensional structure units of the polypeptides.
- Poly peptide chains greater than 200 amino acids in length generally consists of two or more domains.
- The interactions in the tertiary structure are stabilized by:
  - *Disulphide bond*
  - *Hydrophobic interaction*
  - *Hydrogen bonding*
  - *Ionic interactions*

The tertiary structure is the protein’s 3D shape.

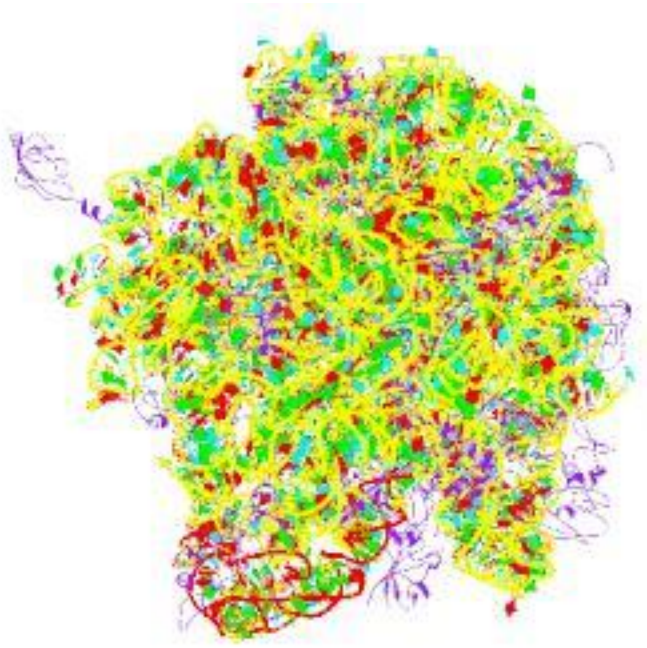
Includes the three-dimensional arrangement of all atoms in the protein, including the atoms in the side chains and any prosthetic groups (ones other than amino acids)

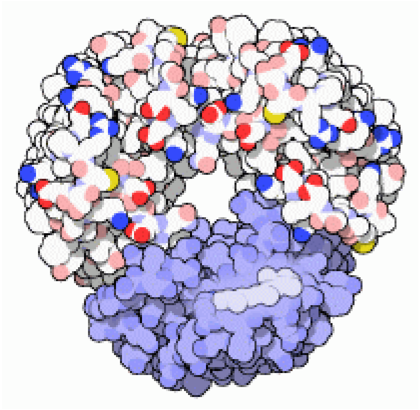


4. Quaternary Structure of Proteins

- Many proteins consists of single polypeptide chain are defined as monomeric proteins, however other consists of two or more poly peptide chains it may structurally identical or totally unrelated. The arrangement of these sub unit is called quaternary structure.
- All forces are responsible for quaternary structures.
- Each sub units can function independently or cooperate each other.

The quaternary structure is the **assembly of folded subunits.**





II. Classification of Proteins based on composition

a/ Simple proteins (build from amino acids only)

b/ Conjugated Proteins(**protein and nonprotein combination)**

c/ Derived Proteins

III. Classification Based on Shape

a/ Globular Proteins: based mostly on an α-helix is **hemoglobin** but based mostly on a β-pleated sheet is the **immunoglobulin,** antibody molecule.

- Globular proteins are spherically shaped, compact, water soluble, most of soluble in the cytosol or in the lipid phase of biological membranes.
- They are primary agents of biological actions: like enzymes, transport molecules, hormones, membrane-bound receptors, immunoglobulins.

B/ Fibrous proteins – have relatively low water solubility, higher amount of the secondary structure elongated, “rodlike” shape, high tensile strength, unusual covalent cross-links. Fibrous proteins are generally insoluble in the **cytosol**.

- They have mechanical and structural functions, provide mechanical support, a structural matrix, to individual cells and tissues of the mammalian organisms.

IV. Classification Based on Nutritional Value

- **Nutritionally rich proteins/ complete proteins/**

  Contain all essential amino acids.

  These proteins in the diet will grow the individual satisfactorily. e.g. casein in milk

- **Incomplete proteins**

  They lack one essential amino acid, can’t promote body growth and they sustain body weight of individual.

- **Poor proteins**

  They lack many essential amino acids, can’t promote body growth, and they can’t sustain even the original body weight.

V. Classification based on Solubility

Albumins: Soluble in water and salt solution

Globulins: Sparingly soluble in water but soluble in salt solutions

Prolamines: Soluble in 70-80% EtOH but insoluble in water and absolute EtOH

Histones: Soluble in salt solutions

Scleroproteins: Insoluble in water or salt solution

Function or Uses of proteins

- Catalytic proteins - enzymes
- Structural proteins - collagen, elastin, keratin
- Contractile proteins - myosine, actin, flagellar
- Transport proteins – hemoglobine, myoglobine
- Regulatory proteins – hormones, insulin
- Genetic proteins - histone
- Protective proteins – immunoglobins

3.4. Structure and Function of Myoglobin and Hemoglobin

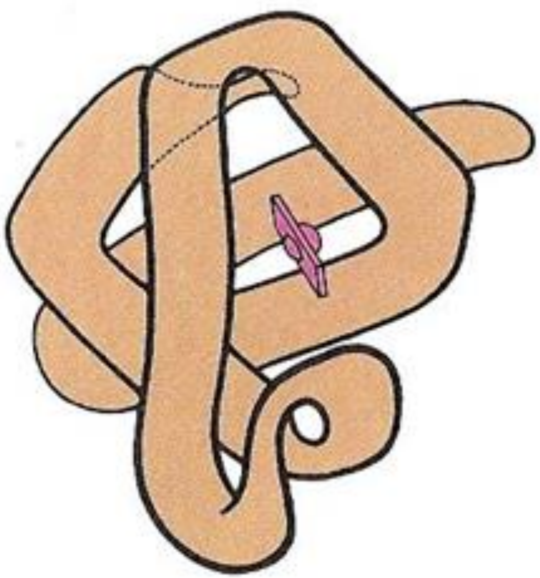
Myoglobin

- It is protein present in heart and skeleton muscle.
- It functions as reservoir of oxygen and an oxygen carrier that increase the rate of transport oxygen with the muscle cell.
- It consists **single poly peptide chain** that is structurally similar to the individual subunit polypeptide chains of the hemoglobin molecules.
- It’s structure is secondary structure, α-helix.
- Eighty (80%) of its poly peptide chain folded in to eight stretches of α- helix.
- All the non-polar amino acids are found in the interior part of its structure , and the polar/charged/ amino acids are found on the surface.

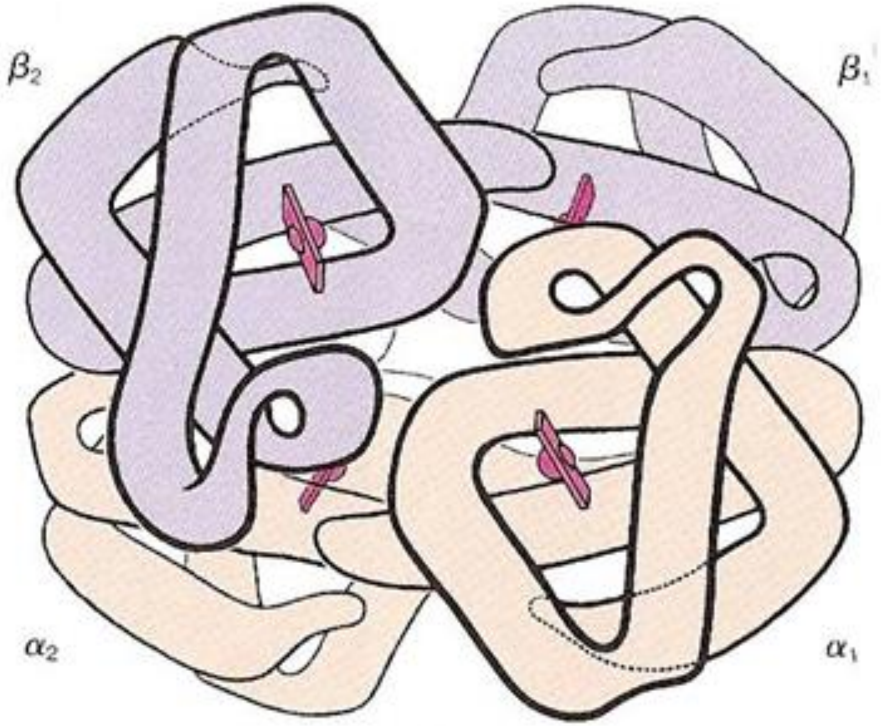
Hemoglobin

- It is exclusively found in **red blood** cells.
- It’s main function is transport oxygen from the lung to the capillaries of the tissue.
- Hemoglobin A (HaA) the major hemoglobin in adult, its composed four poly peptide chains, two α- helix and two β-chains held together by non- covalent interaction.
- The oxygen binding properties of hemoglobin are regulated by interaction with allosteric effectors.
- Hemoglobin has quaternary structure.
- It can be bind **four oxygen molecules** one at each of its four heme groups, where as mygolbin can bind only **one molecule of oxygen.**
- Hemoglobin has less oxygen affinity than myoglobin

Myoglobin and hemoglobin Structure



Myoglobin



Hemoglobin

Myoglobin: **one polypeptide chain**

Hemoglobin: 4 polypeptide chains – 4 subunits

3.5 Denaturation of Proteins

- It is unfolding or disorganization of protein’s secondary and tertiary structures.
- Denaturation agent are heat, organic solvents, mechanical mixing, strong acids and bases and ions of heavy metals such as lead and mercury.
- In some extent denatured proteins may reverse to the original native structure when the denaturating agent is removed.
- How ever in most cases proteins are denatured permanently.

Chapter -4- Enzymes

4.1 Definition of Enzymes

- Enzymes are biological catalysts that promote and speed up chemical reactions without themselves being altered (consumed) in the process.
- They do not change the equilibrium, just reduce the time required to reach equilibrium.
- They increase or accelerate the rate of a reaction (10^6-10^{12}) by a millions fold by lowering the activation energy barrier.
- *They determine the patterns of transformations for chemicals, as well as forms of energy in the living organisms.*
- Most enzymes are Proteins (tertiary and quaternary structures).

Common features for enzymes and inorganic catalysts

1. Catalyze only thermodynamically possible reactions
2. Are not used or changed during the reaction.
3. Don’t change the position of equilibrium and direction of the reaction
4. Usually act by forming a temporary complex with the reactant, thus stabilizing the transition state

Specific features of enzymes

1. Accelerate reactions in much higher degree than inorganic catalysts
2. Specificity of action
3. Sensitivity to temperature
4. Sensitivity to pH

Naming of Enzymes:

✓The name of an enzyme in many cases end in –***ase***

For example, *sucrase* catalyzes the hydrolysis of sucrose

✓The name describes the function of the enzyme

For example, *oxidases* catalyze oxidation reactions

✓Sometimes common names are used, particularly for the digestion enzymes such as *pepsin*, *trypsin*, and *rennin*.

✓Some names describe both the substrate and the function

For example; *alcohol dehydrogenase* (oxidation of ethanol)

- Urease (hydrolysis of urea)

- Transaminase (transfer amino group from one molecule to another).
- RNA polymerase (formation of RNA by polymerization).
- Lactase catalyze the hydrolysis of a disaccharide lactose

$$C_{12}H_{22}O_{11} + H_2O \rightarrow \quad 2C_6H_{12}O_6$$

- 25% of human population have no lactase-do not metabolize lactose
- Solution- add lactase to milk

Major Classes of Enzyme

Enzymes are classified into six functional classes by the International Union of Biochemists (I.U.B.) based on the types of reactions that they Catalyze. This makes up the first number of the enzyme identity.

1. Oxidoreductase: oxidation-reduction reaction.

2. Transferase: transfer of intact functional group.

3. Hydrolase: hydrolysis (addition or removal of water).

4. Lyase: Cleavage of a C-C or C-N or C-O bond. Removal (or addition) of water across double bond.

5. Isomerase: Isomerization (L ⟷ D ,cis ⟷ trans ,CHO ⟷ C=O)

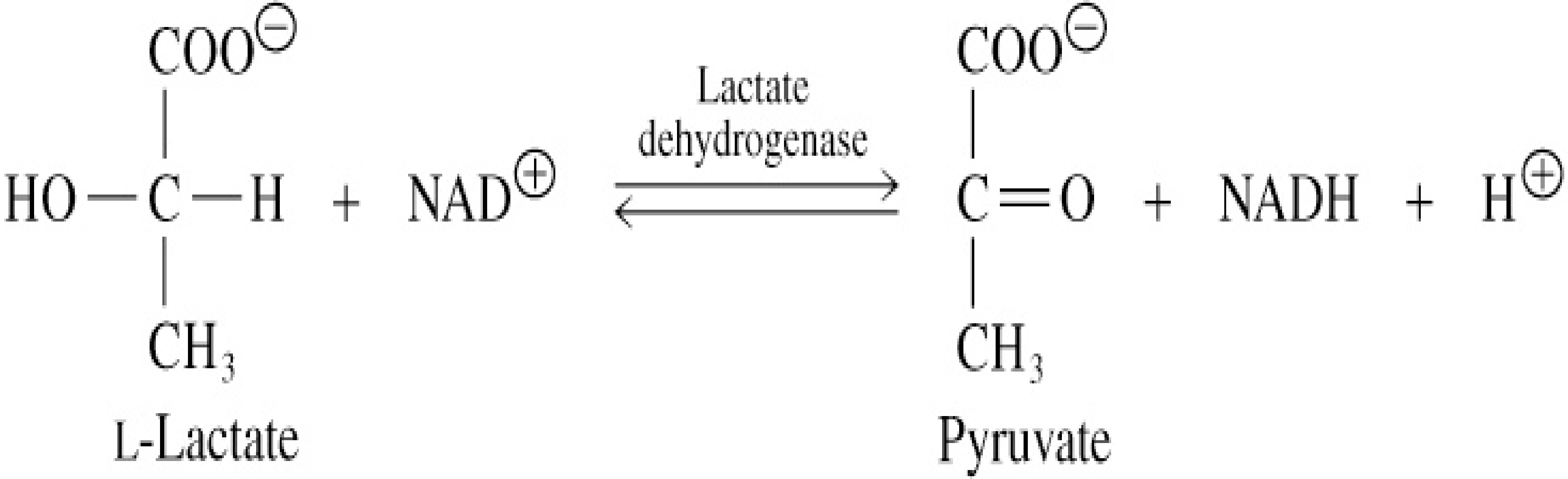
6. Ligase: Joining of two molecules requiring energy from ATP.

1. Oxidoreductases

- Biochemical Activity:
  - Catalyse Oxidation/Reduction Reactions act on many chemical groupings to add or remove hydrogen atoms.
- Examples:
  - Lactate dehydrogenase
  - Glucose Oxidase
  - Peroxidase
  - Catalase
  - Phenylalanine hydroxylase

Oxidoreductases

- Catalyze oxidation-reduction reactions



$$\mathrm{HO{-}\overset{\overset{\textstyle COO^{\ominus}}{|}}{\underset{\underset{\textstyle CH_3}{|}}{C}}{-}H} + \mathrm{NAD^{\oplus}} \xrightleftharpoons[]{\text{Lactate dehydrogenase}} \mathrm{\overset{\overset{\textstyle COO^{\ominus}}{|}}{\underset{\underset{\textstyle CH_3}{|}}{C}}{=}O} + \mathrm{NADH} + \mathrm{H^{\oplus}}$$

-oxidases

- peroxidases

- dehydrogenases

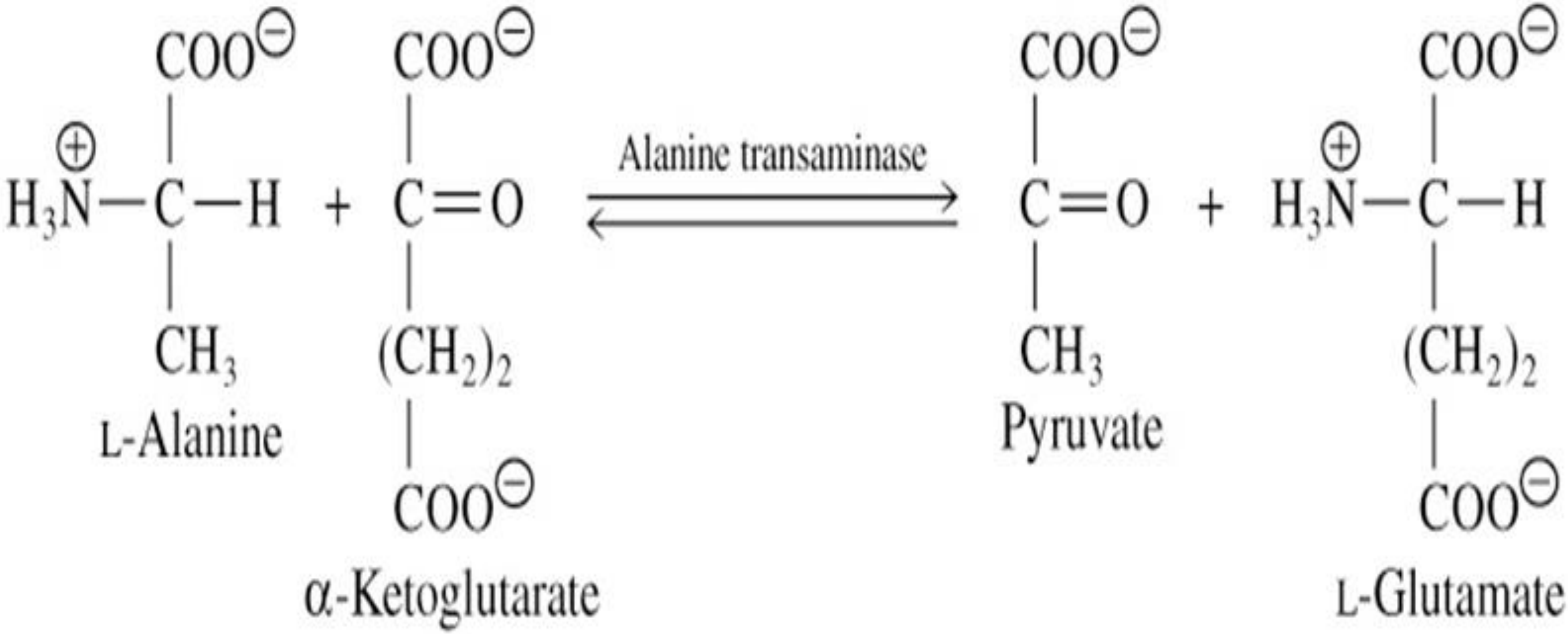
Note: NAD = nicotinamide adenine dinucleotide

2. Transferases

- Kinases are specialized transferases that regulate metabolism by transferring phosphate from ATP to other molecules.

- **Biochemical Activity:**
  - Transfer a functional groups (e.g. methyl or phosphate) between donor and acceptor molecules.
- Examples:
  - Transaminases (ALT & AST)
  - Phosphotransferases (Kinases)
  - Transmethylases
  - Transpeptidases
  - Transacylases

- Catalyze group transfer reactions

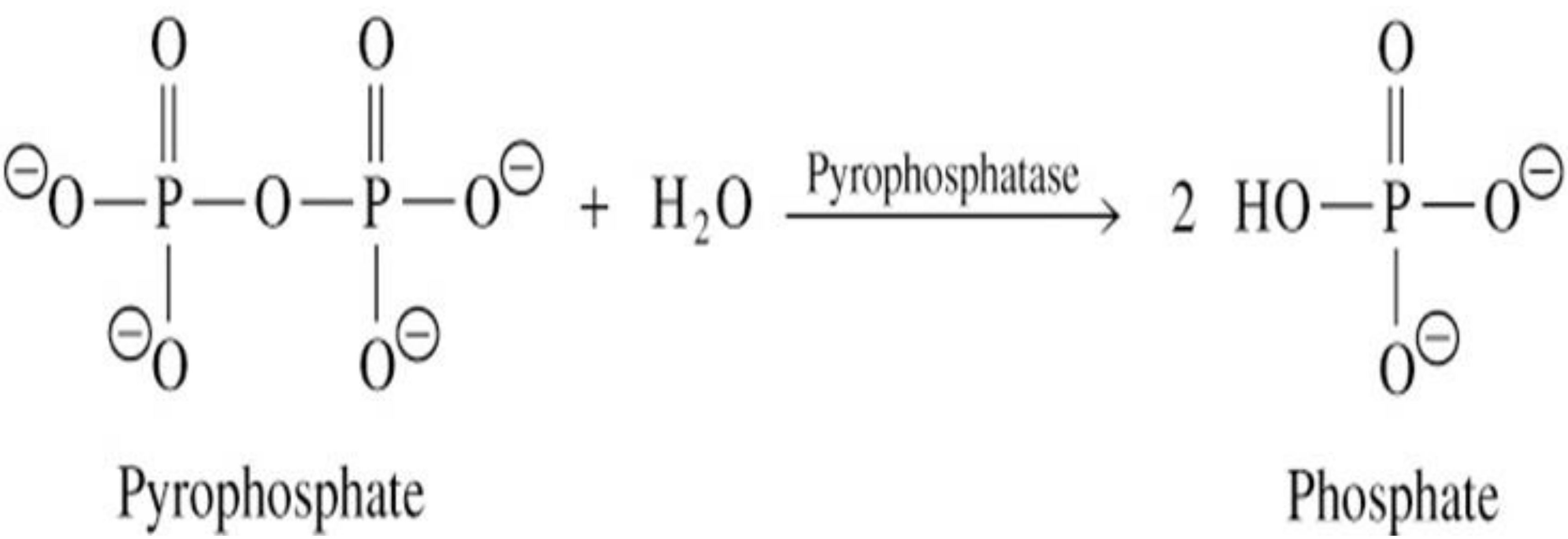


$$\mathrm{H_3\overset{\oplus}{N}}-\underset{\mathrm{CH_3}}{\overset{\mathrm{COO^{\ominus}}}{\mathrm{C}}}-\mathrm{H} + \underset{\substack{\mathrm{(CH_2)_2} \\ \mathrm{COO^{\ominus}}}}{\overset{\mathrm{COO^{\ominus}}}{\mathrm{C}}}=\mathrm{O} \xrightleftharpoons{\text{Alanine transaminase}} \underset{\mathrm{CH_3}}{\overset{\mathrm{COO^{\ominus}}}{\mathrm{C}}}=\mathrm{O} + \mathrm{H_3\overset{\oplus}{N}}-\underset{\substack{\mathrm{(CH_2)_2} \\ \mathrm{COO^{\ominus}}}}{\overset{\mathrm{COO^{\ominus}}}{\mathrm{C}}}-\mathrm{H}$$

3. Hydrolases

- **Biochemical Activity:**
  - Catalyse the hydrolysis of various bonds Add water across a bond.
- Examples:
  - Protein hydrolyzing enzymes (Peptidases).
  - Carbohydrases (Amylase, Maltase, Lactase).
  - Lipid hydrolyzing enzymes (Lipase).
  - Deaminases.
  - Phosphatases.

- Catalyze hydrolysis reactions where water is the acceptor of the transferred group.

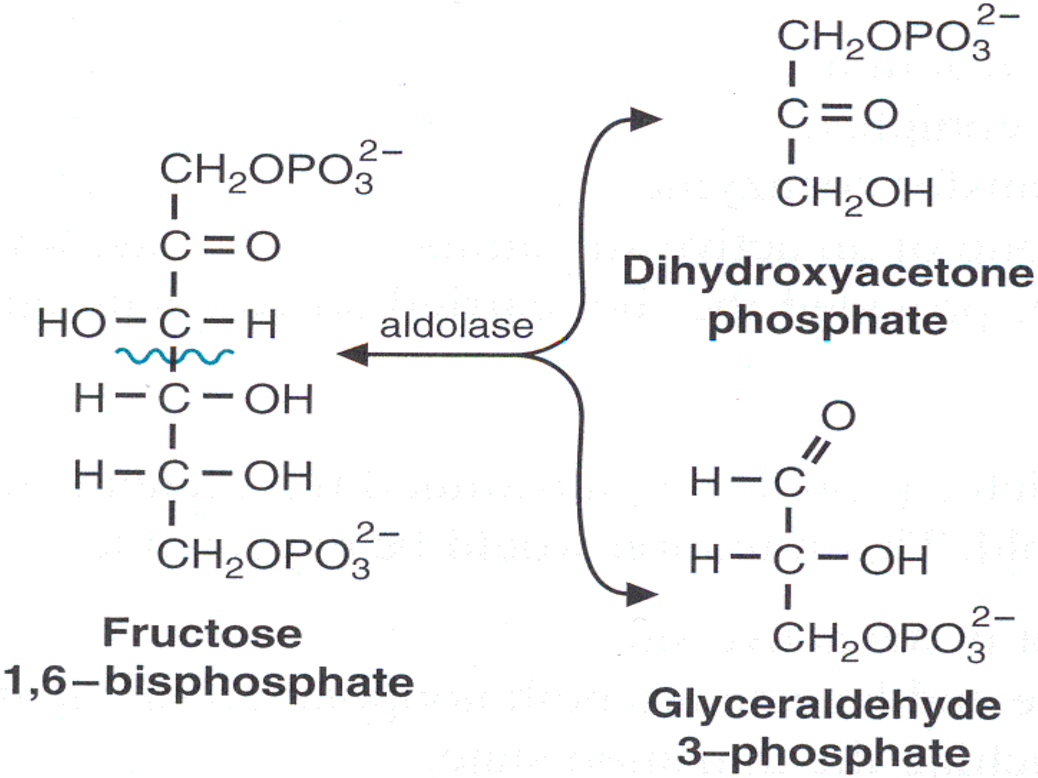


- esterases
- peptidases
- glycosidases

4. Lyases

- **Biochemical Activity:**
  - Cleave various bonds by means other than hydrolysis and oxidation.
  - Add Water, Ammonia or Carbon dioxide across double bonds, or remove these elements to produce double bonds.
- Examples:
  - Fumarase.
  - Carbonic anhydrase.

Lyases

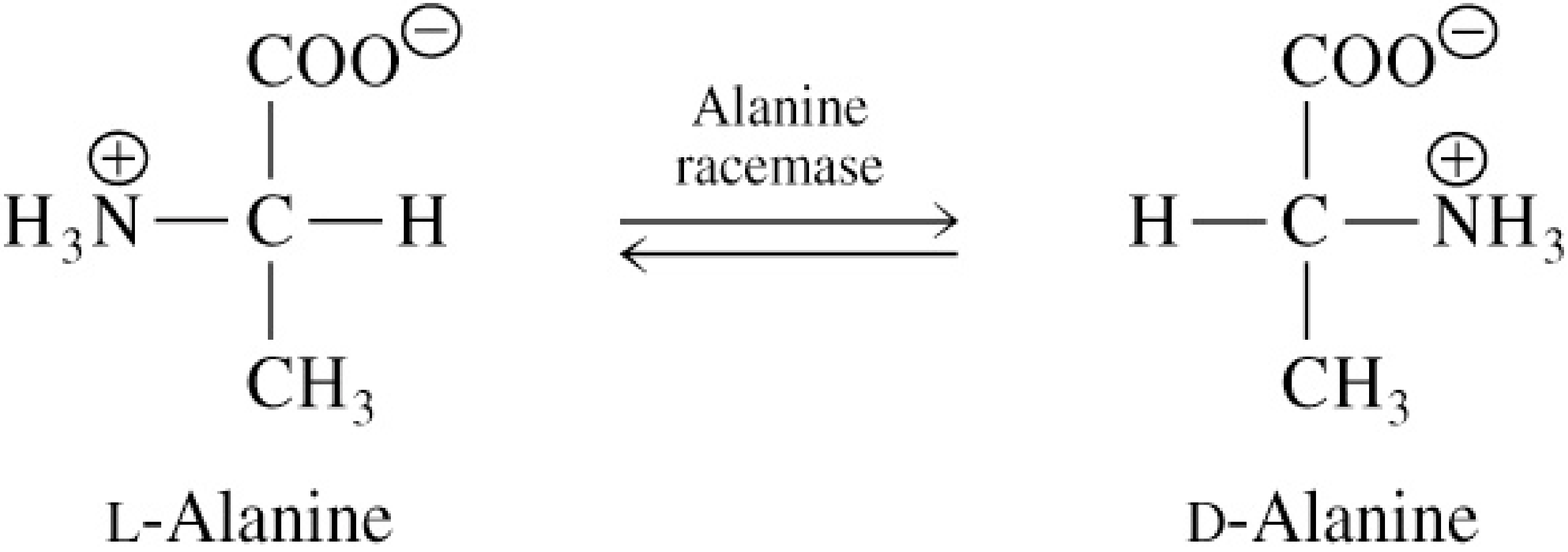

Fructose 1,6–bisphosphate
aldolase
Dihydroxyacetone phosphate
Glyceraldehyde 3–phosphate

5. Isomerases

- **Isomerases** are a general class of enzymes which convert a molecule from one isomer to another. The general form of such a reaction is as follows:
- **A–B → B–A**

- **Biochemical Activity:**
  - Catalyse isomerization changes within a single molecule.
  - Carry out many kinds of isomerization:
    - L to D isomerizations.
    - Mutase reactions (Shifts of chemical groups).
- Examples:
  - Isomerase.
  - Mutase.

- Catalyze isomerization reactions

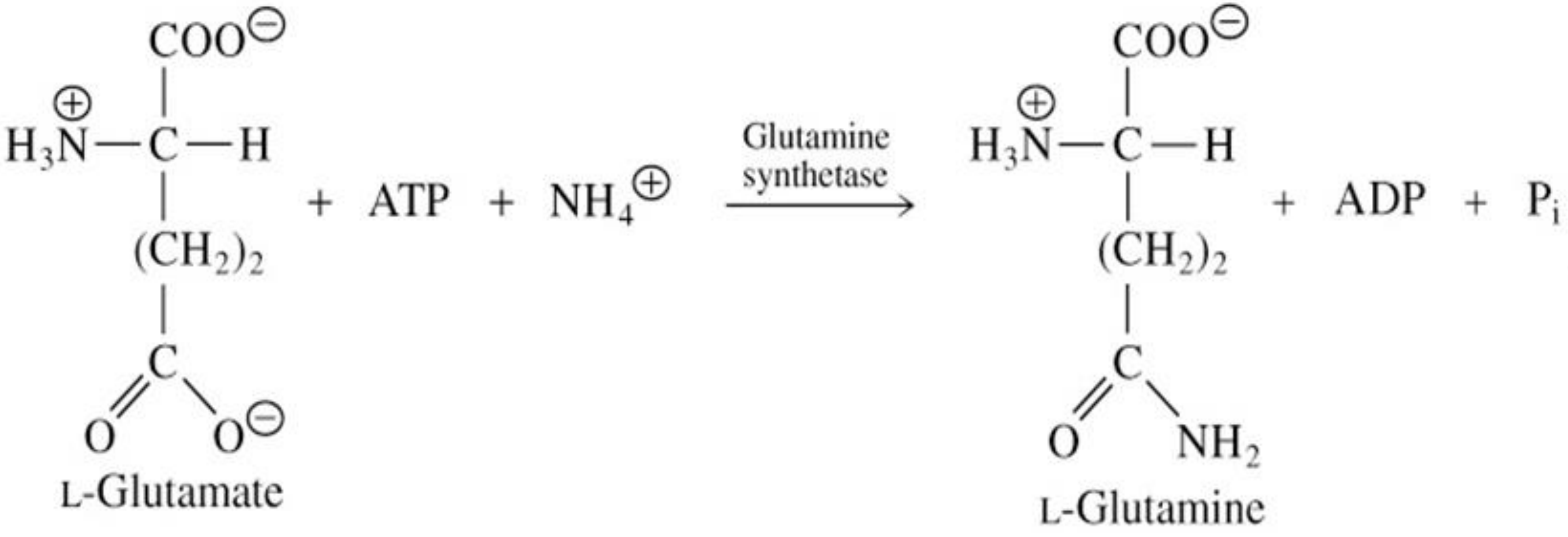


6. Ligases

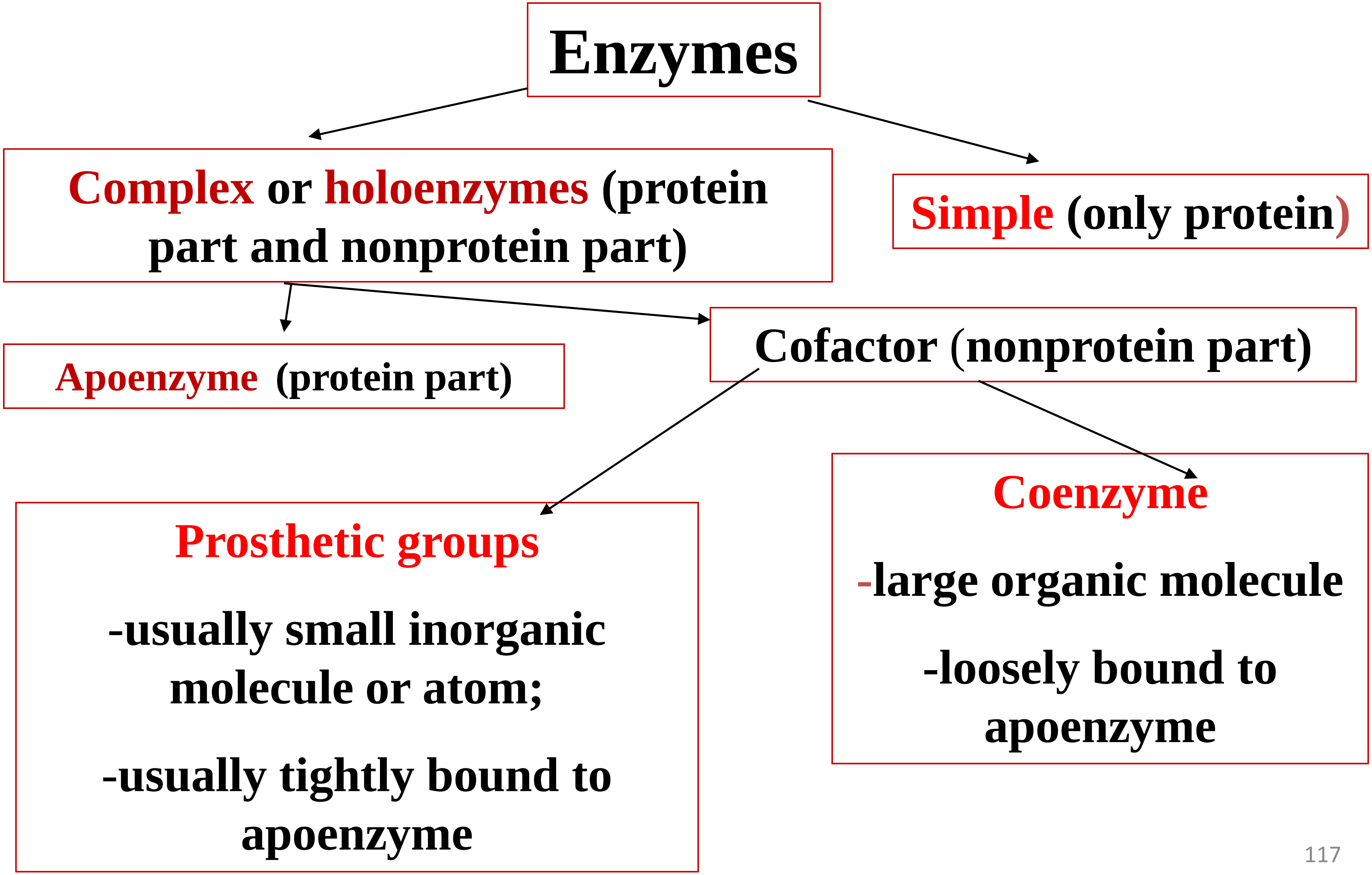
- **Biochemical Activity:**
  - Join two molecules with covalent bonds Catalyse reactions in which two chemical groups are joined (or ligated) with the use of energy from ATP.
- Examples:
  - Acetyl~CoA Carboxylase
  - Glutamine synthetase

Ligases (synthetases)

- Catalyze ligation, or joining of two substrates
- Require chemical energy (e.g. ATP)



Structure of enzymes



Enzymes

Complex or **holoenzymes** (protein part and nonprotein part)

Simple (only protein)

Apoenzyme (protein part)

Cofactor (nonprotein part)

Prosthetic groups

-usually small inorganic molecule or atom;

-usually tightly bound to apoenzyme

Coenzyme

-large organic molecule

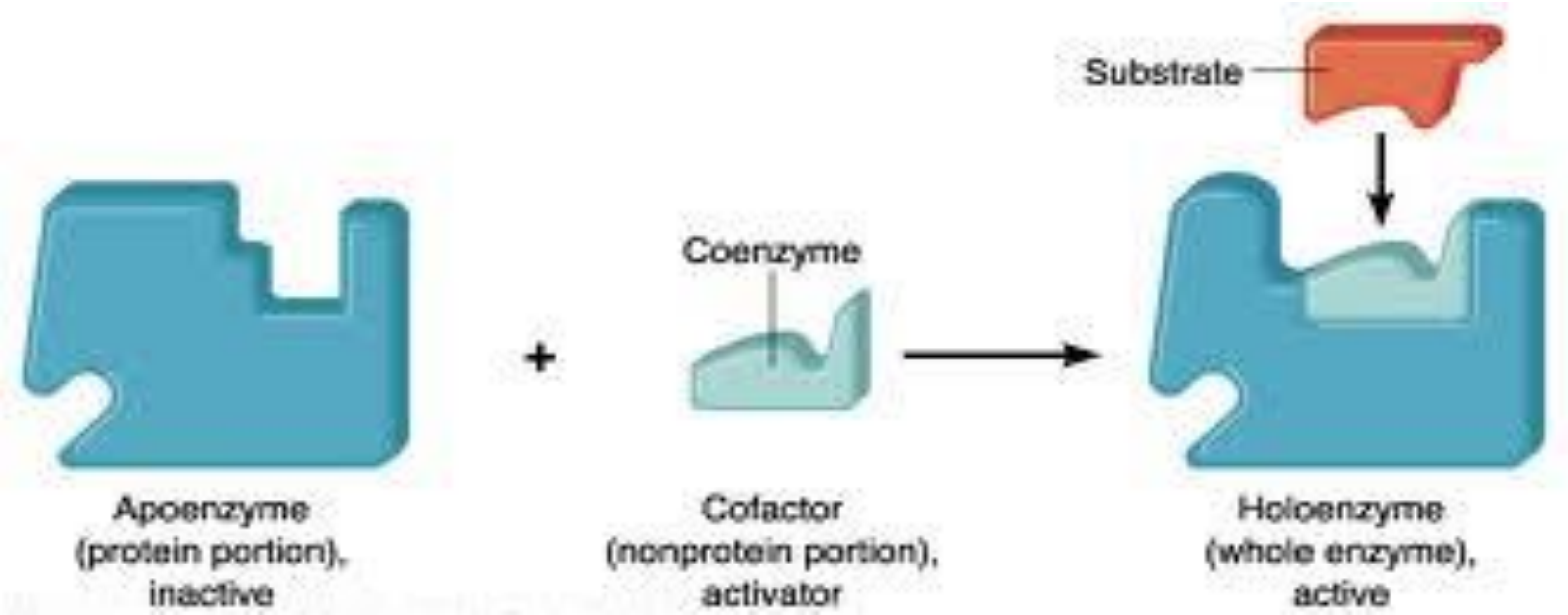
-loosely bound to apoenzyme

Active Site of enzyemes

- The area on the enzyme where the substrate or substrates attach to is called the **active site**.
- Enzymes are usually very large proteins and the active site is just a small region of the enzyme molecule.

✓ **Apoenzyme:** The enzyme with its protein moiety is termed as apoenzyme and it is inactive.

✓ **Holoenzyme** is an active enzyme with its non protein component.



✓**Cofactor** is a non-protein chemical compound that is bound (either tightly or loosely) to an enzyme and is required for catalysis.

Types of Cofactors:

– Coenzymes &Prosthetic groups.

Coenzyme

The non-protein component, loosely bound to apoenzyme by non-covalent bond.

Examples : vitamins or compound derived from vitamins.

Prosthetic group

The non-protein component, tightly bound to the apoenzyme by covalent bonds is called a Prosthetic group.

Four distinct types of enzyme specificity

1.Absolute specificity - the enzyme will catalyze only **one reaction.**

2. Group specificity - the enzyme will act only on molecules that have specific **functional groups**, such as amino, phosphate and methyl groups.

3. Linkage specificity - the enzyme will act on a particular type of **chemical bond** regardless of the rest of the molecular structure.

4. Stereochemical specificity - the enzyme will act on a particular **steric or optical isomer**.

Exceptions – Isoenzymes (Different enzymes catalyzing the same reaction)

Note: More than 2000 enzymes found in our body.

Activation energy or Energy of Activation:

All chemical reactions require some amount of energy to get them started. OR

- It is First push to start reaction. This energy is called activation energy.

General Mechanism of Action of Enzymes

- An enzyme provides an alternative pathway for the conversion of the substrates to the products, thus lowers the activation energy and speeds up the reaction

They do not affect the reaction equilibrium.

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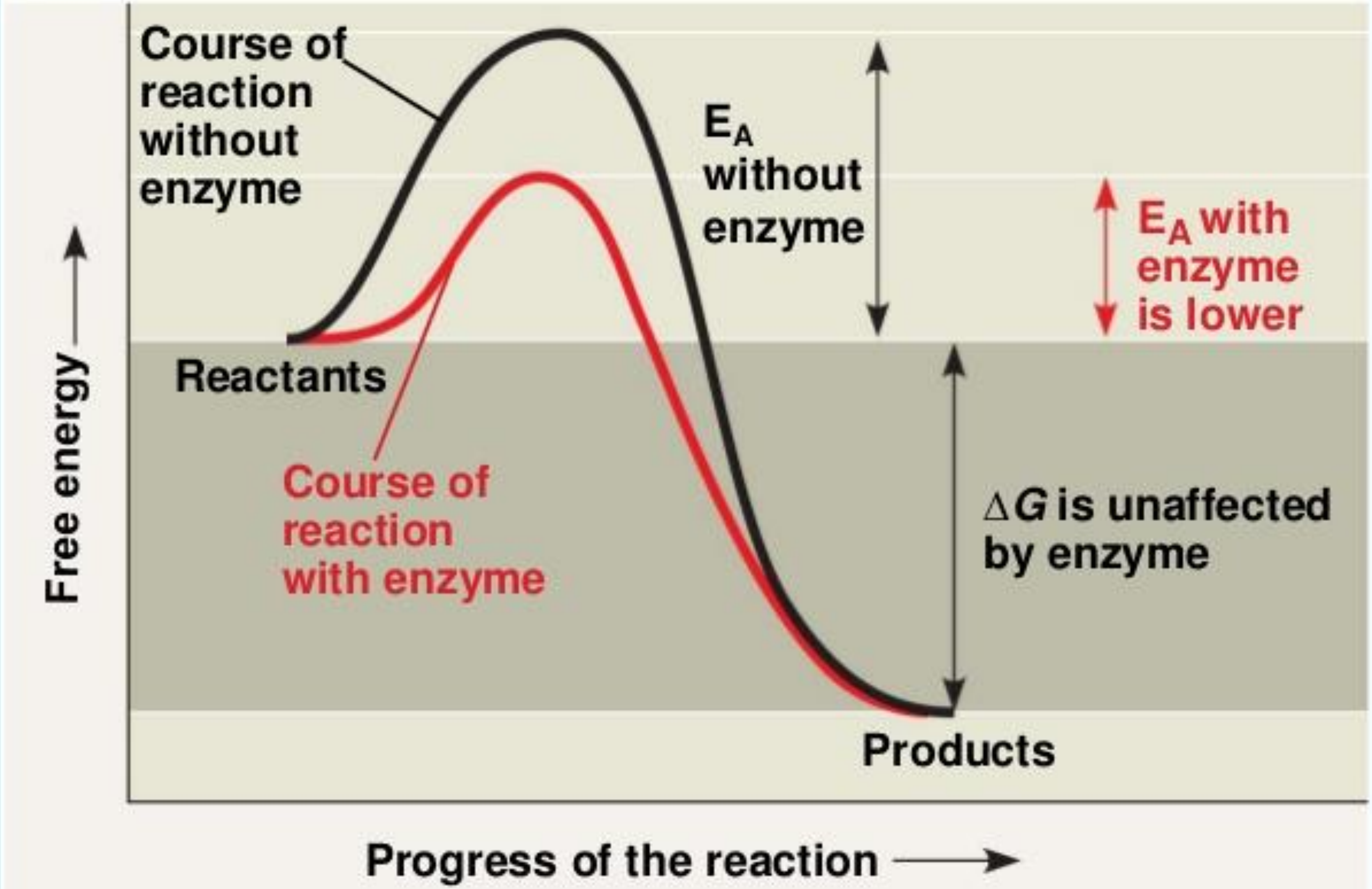

Course of reaction without enzyme
E_A without enzyme
E_A with enzyme is lower
Free energy
Reactants
Course of reaction with enzyme
ΔG is unaffected by enzyme
Products
Progress of the reaction

Enzyme-Substrate Interactions:

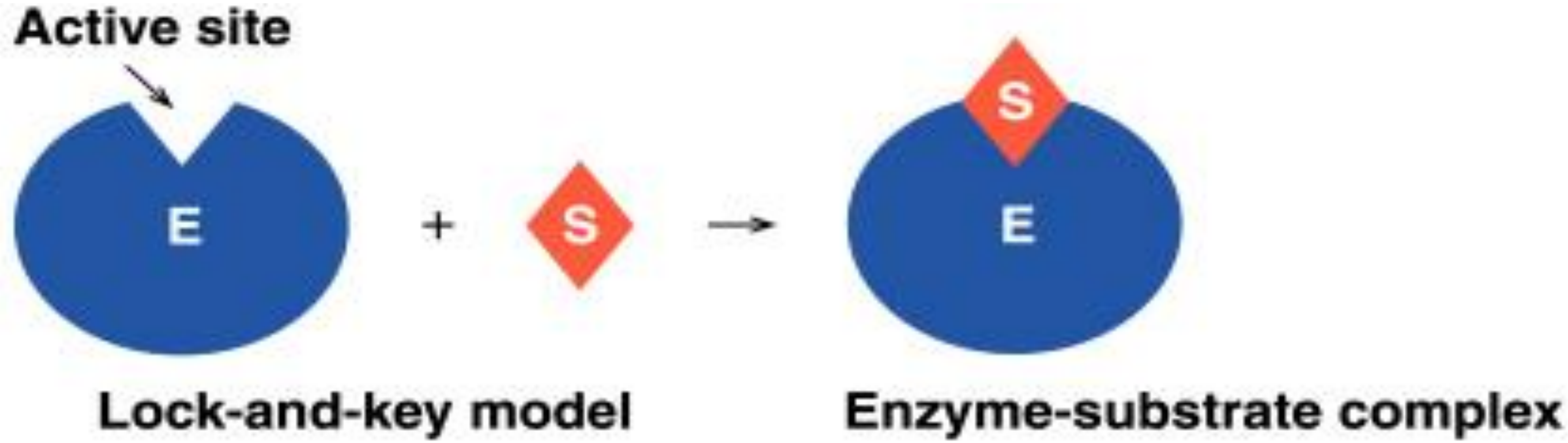
Formation of Enzyme substrate complex can be by:

- –Lock-and-Key Model & Induced Fit Model

In the **lock-and-key model** of enzyme action:

- - the active site has a rigid shape
- - only substrates with the matching shape can fit
- - the substrate is a key that fits the lock of the active site

This is an older model, however, and does not work for all enzymes.

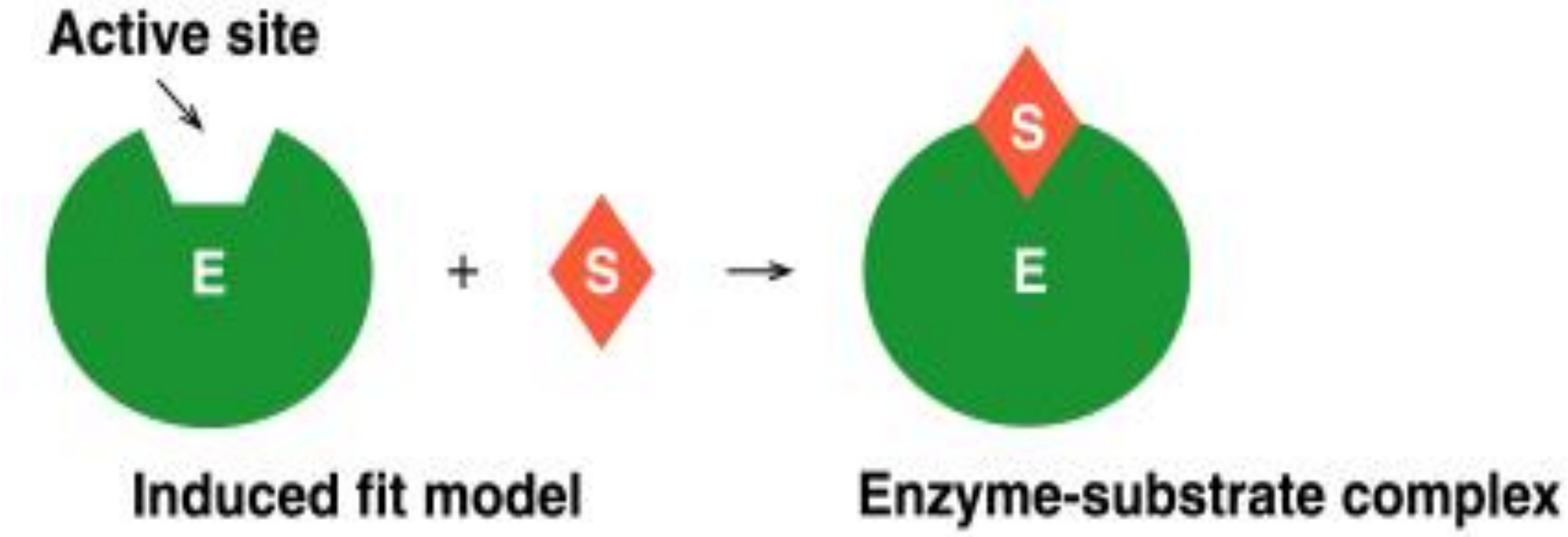


- In the **induced-fit model** of enzyme action:

  - the active site is flexible, not rigid

  - the shapes of the enzyme, active site, and substrate adjust to maximumize the fit, which improves catalysis.

  - there is a greater range of substrate specificity
- This model is more consistent with a wider range of enzymes



Enzyme Catalyzed Reactions

- When a substrate (S) fits properly in an active site, an **enzyme-substrate (ES) complex** is formed.

  $$E + S \leftrightarrows ES$$

- Within the active site of the ES complex, the reaction occurs to convert substrate to product (P):

  $$ES \rightarrow E + P$$

- The products are then released, allowing another substrate molecule to bind the enzyme.

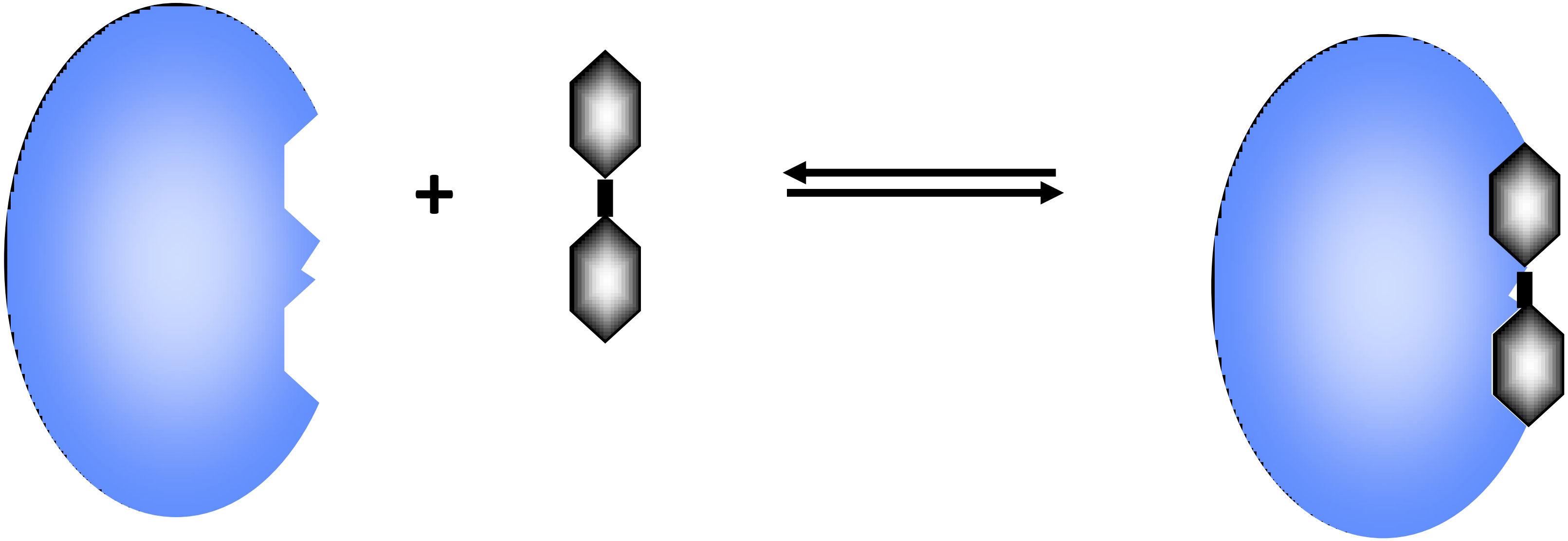
  \- this cycle can be repeated millions (or even more) times per minute.

- The overall reaction for the conversion of substrate to product can be written as follows:

  $$E + S \leftrightarrows ES \rightarrow E + P$$

Enzyme-substrate complex

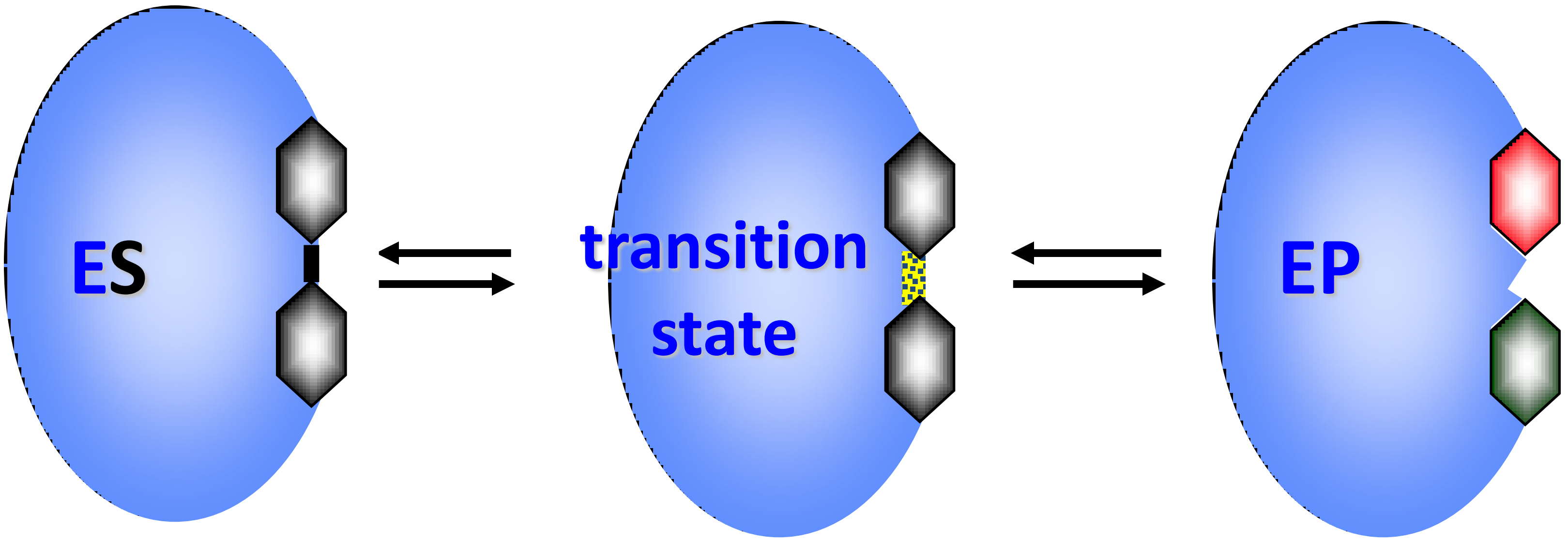
- Step 1:
- Enzyme and substrate combine to form complex
- E + S $\rightleftharpoons$ ES
- Enzyme Substrate Complex



Enzyme-product complex

- Step 2:
- An enzyme-product complex is formed.

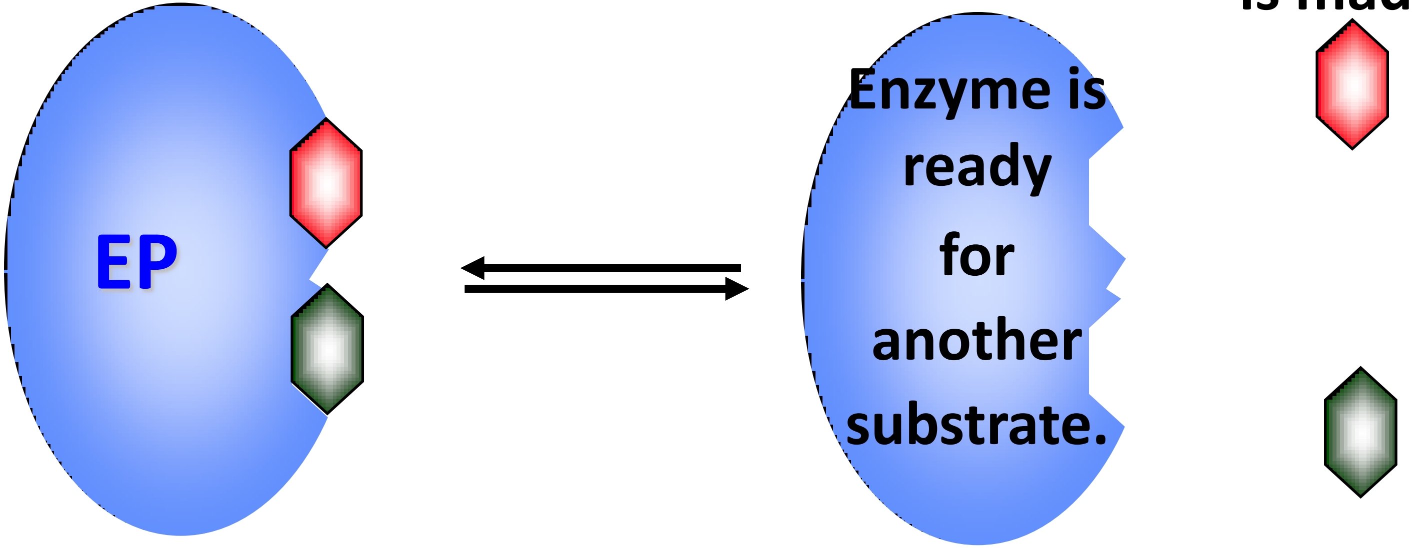
- ES ⇌ EP



Product

- The enzyme and product separate

- $EP \rightleftharpoons E + P$



The product is made

EP

Enzyme is ready for another substrate.

What Affects Enzyme Activity?

- **Three factors:**
  1. **Environmental Conditions**
  2. **Cofactors and Coenzymes**
  3. **Enzyme Inhibitors**

1. Environmental Conditions

I. Extreme Temperature are the most dangerous

- high temps may denature (unfold) the enzyme.

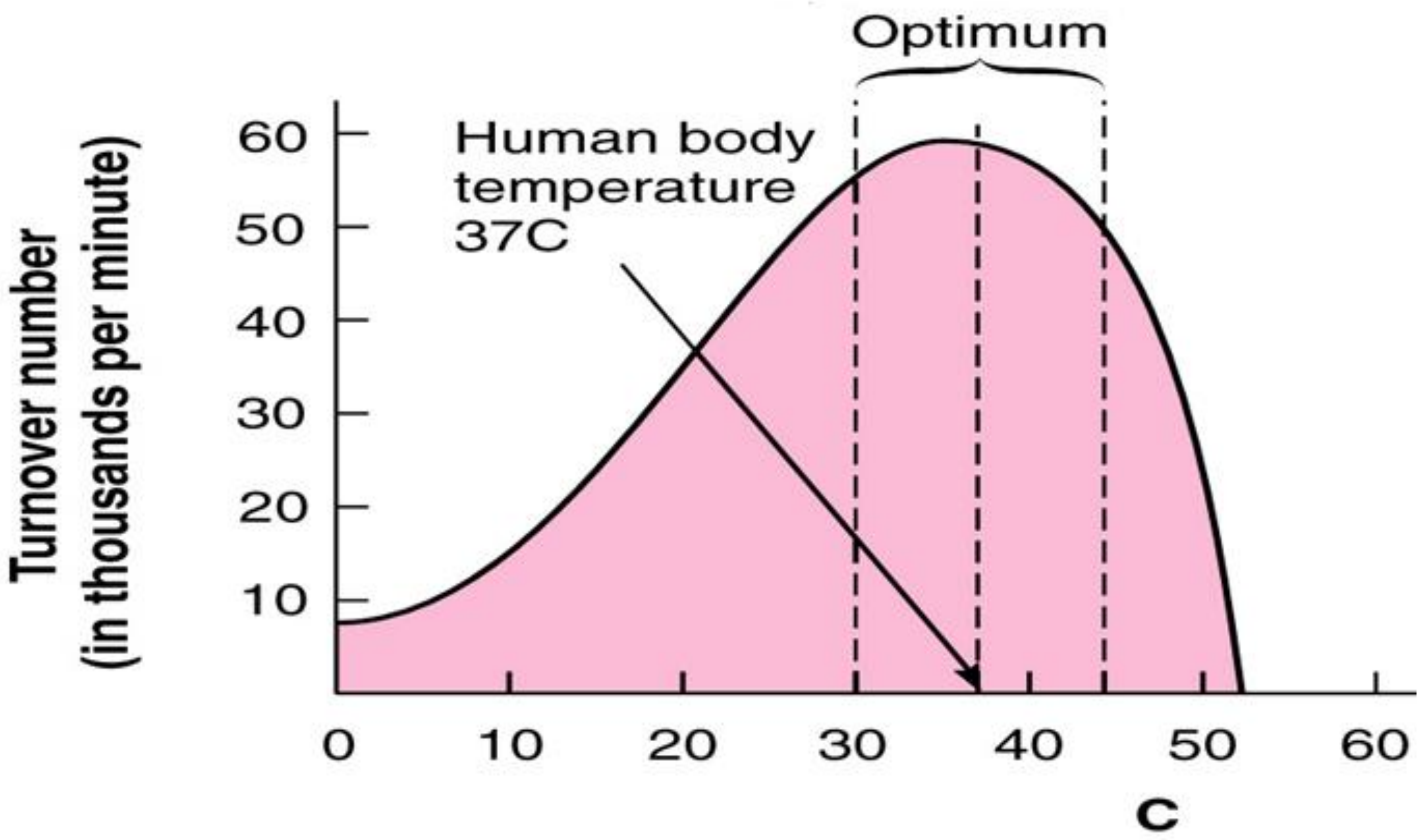
II. pH (most like 6 - 8 pH near neutral)

III. substrate concentration .

I. Temperature: The reaction velocity increase with temperature until a peak velocity is reached. This increase is a result of the increased number of molecules having sufficient energy to pass over the energy barrier and form the product of the reaction. Further elevation of the temperature results in decrease in reaction velocity as a result of temperature-induced called **denaturation** of enzyme.

Environmental factors

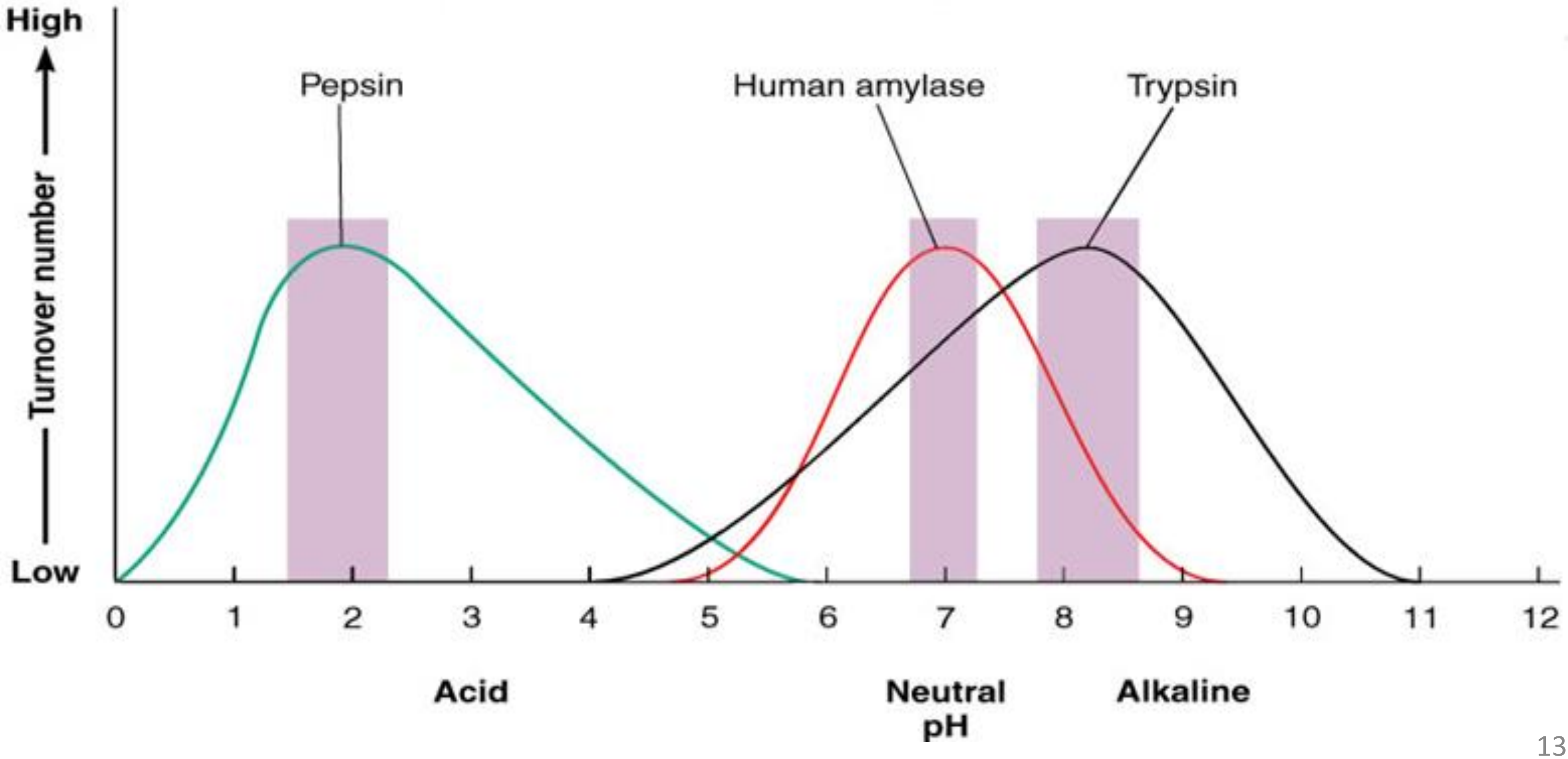
- ***Optimum temperature*** The temp at which enzymatic reaction occur fastest.



Environmental factors

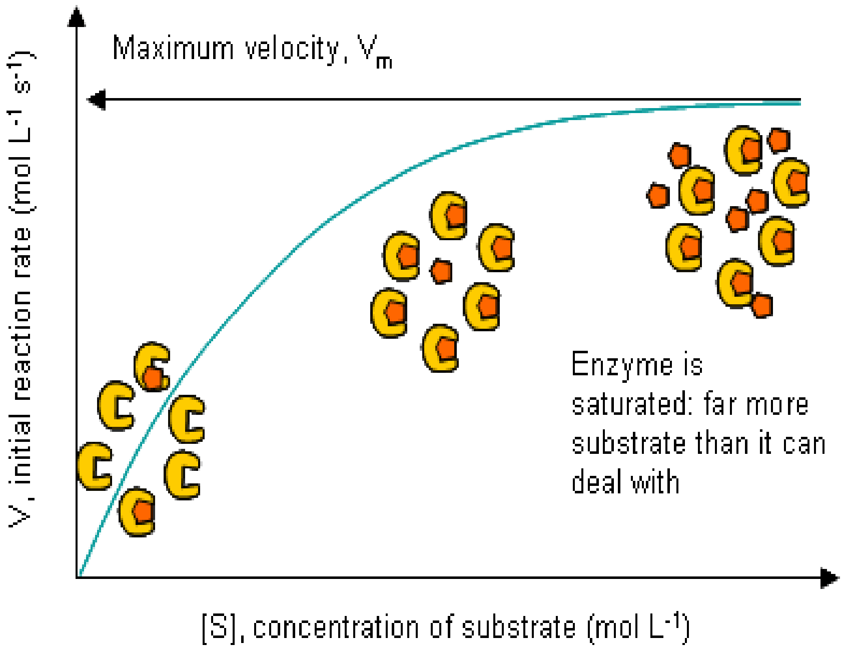
II. pH also affects the rate of enzyme-substrate complexes.

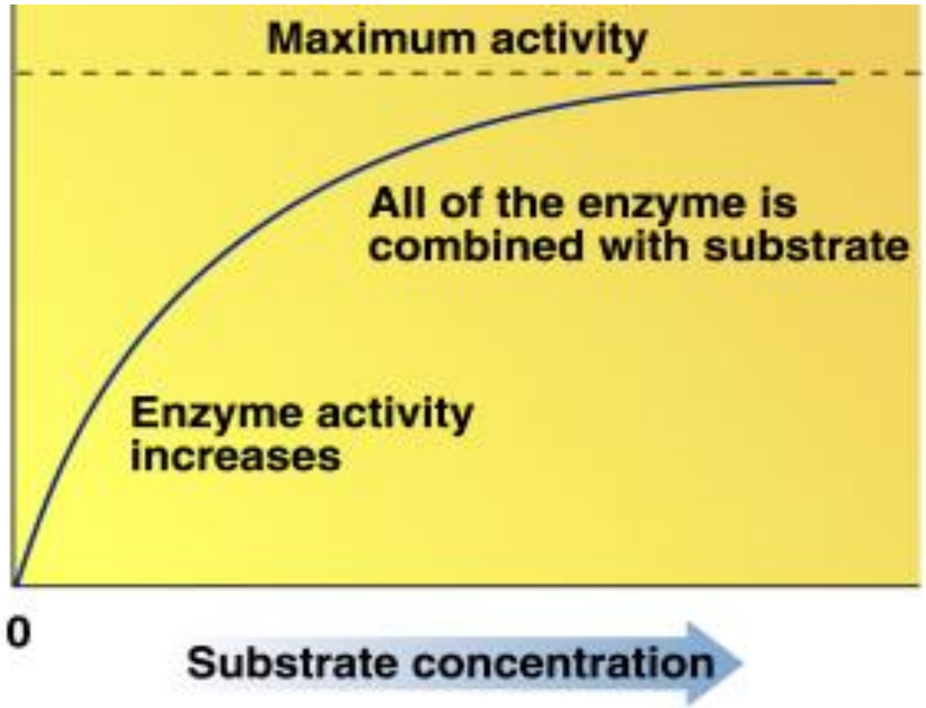
- Most enzymes have an optimum pH of around 7 (neutral)
  - However, some prefer acidic or basic conditions



III. Substrate Concentration and Reaction Rate

- The rate of reaction increases as substrate concentration increases (at constant enzyme concentration)
- Maximum activity occurs when the enzyme is saturated (when all enzymes are binding substrate**)**





2. Cofactors and Coenzymes

- Many enzymes require a coenzyme or cofactor for activity.
- In the absence of the appropriate cofactor apoenzyme typically does not show biological activity.

Apoenzyme	+ Coenzyme	→ Holoenzyme
(inactive)	(activator)	(active)

- Coenzymes (organic molecule) are derived from vitamins and act as co-substrates and are converted into products.

- Coenzymes and cofactors alter the conformation around the active site of the enzyme.
- Cofactors: are metal ions such as Cu, Mg, Mn, Fe, Ca, Zn, Mo etc.
- Also called prosthetic groups.
- are not usually converted to products.
- Inorganic substances (zinc, iron) and vitamins (respectively) are sometimes need for proper enzymatic activity.
- Example: Iron must be present in the quaternary structure-hemoglobin in order for it to pick up oxygen.

3. Enzyme inhibition

✓In a tissue and cell different chemical agents (**metabolites, substrate analogs, toxins, drugs, metal complexes** etc) can inhibit the enzyme activity. **Two types of inhibitors:**

Reversible and irreversible inhibitors

Inhibitor (I) binds to an enzyme and prevents the formation of ES complex or breakdown it to E + P

Reversible inhibitors – after combining with enzyme (EI complex is formed) can **rapidly dissociate**. Enzyme is inactive only when bound to inhibitor.

EI complex is held together by weak, noncovalent interaction.

Three basic types of reversible inhibition:

Competitive, Noncompetitive, Uncompetitive

1. Competitive Reversible inhibition

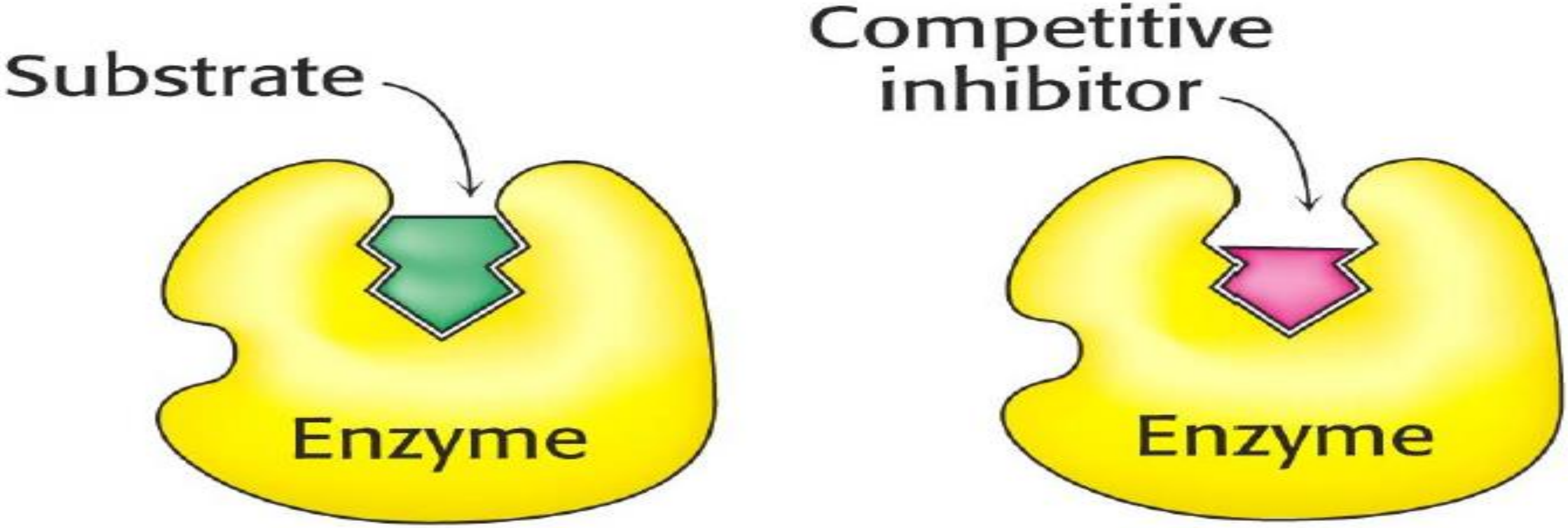
- Inhibitor has a structure similar to the substrate thus can bind to the same active site.

- The enzyme cannot differentiate between the two compounds.

- When inhibitor binds, prevents the substrate from binding.

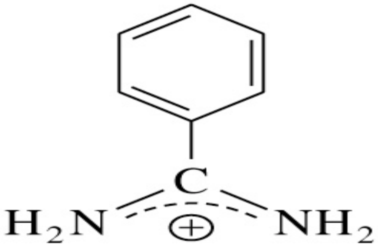
- Inhibitor can be released by increasing substrate concentration.

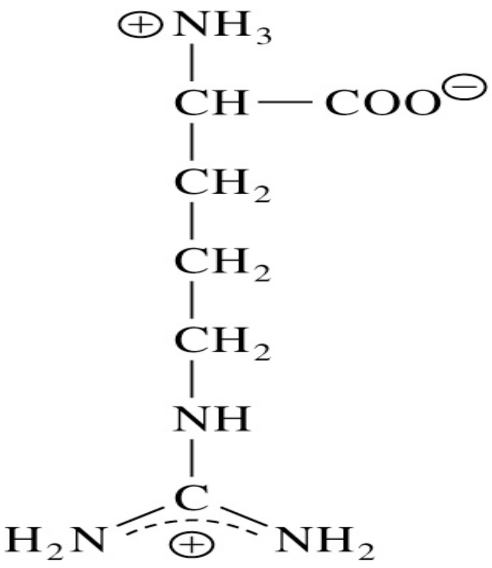
Competitive inhibition



Example of competitive inhibition

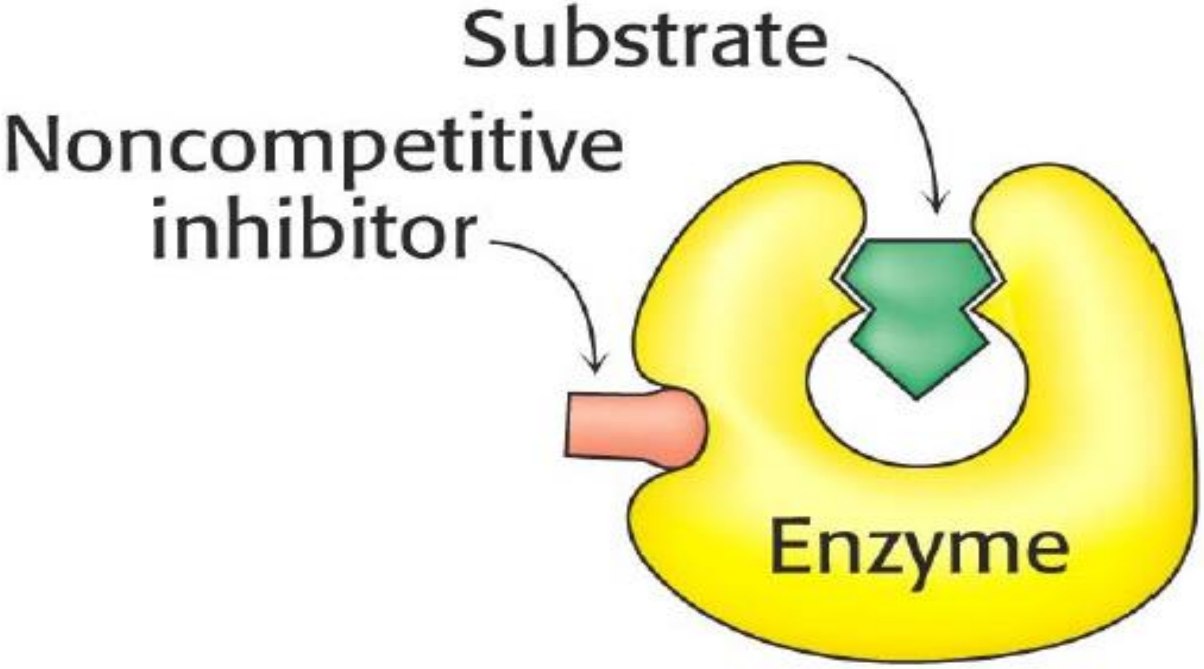
Benzamidine competes with arginine for binding to trypsin


Benzamidine


Arginine

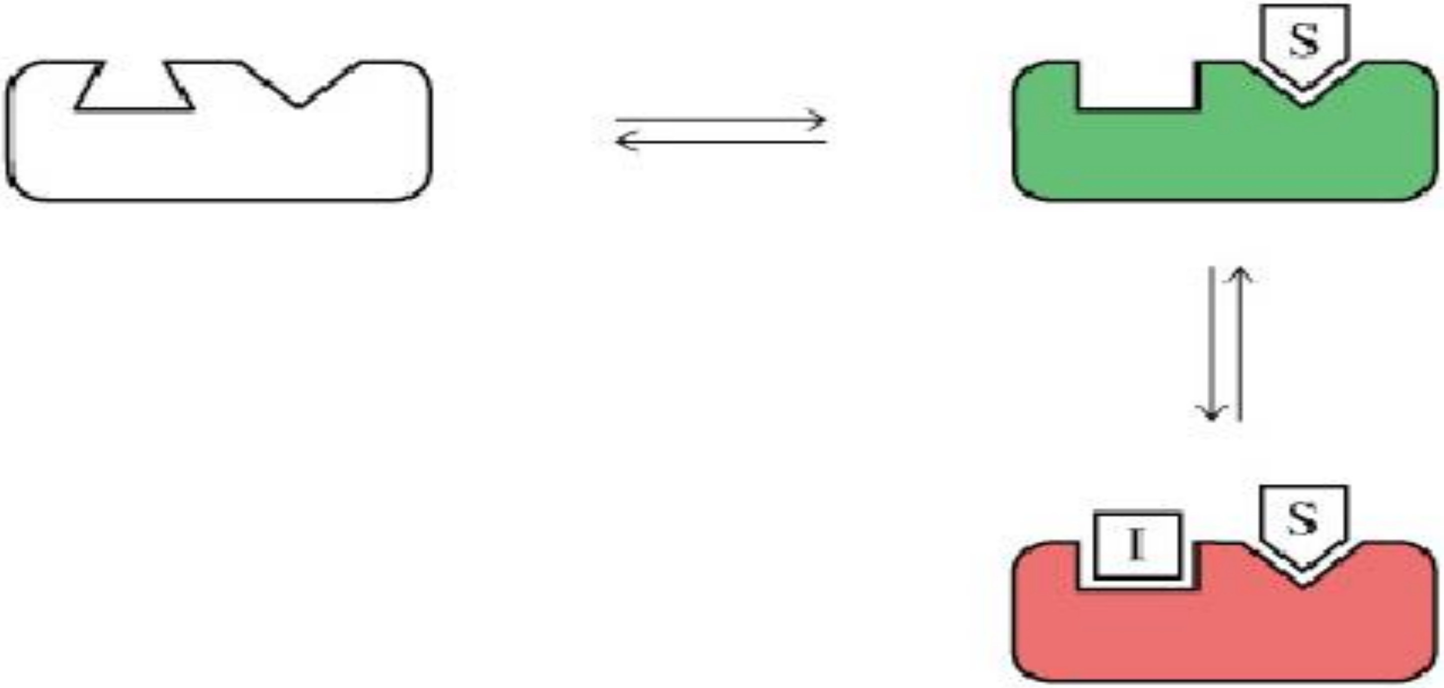
2. Noncompetitive inhibition

- Binds to an enzyme site different from the active site.
- Inhibitor and substrate can bind enzyme at the same time.
- Cannot be overcome by increasing the substrate concentration



3. Uncompetitive inhibition

- Uncompetitive inhibitors bind to ES not to free E.
- This type of inhibition usually only occurs in multi substrate reactions.



Irreversible Enzyme Inhibition

Very slow dissociation of EI complex.

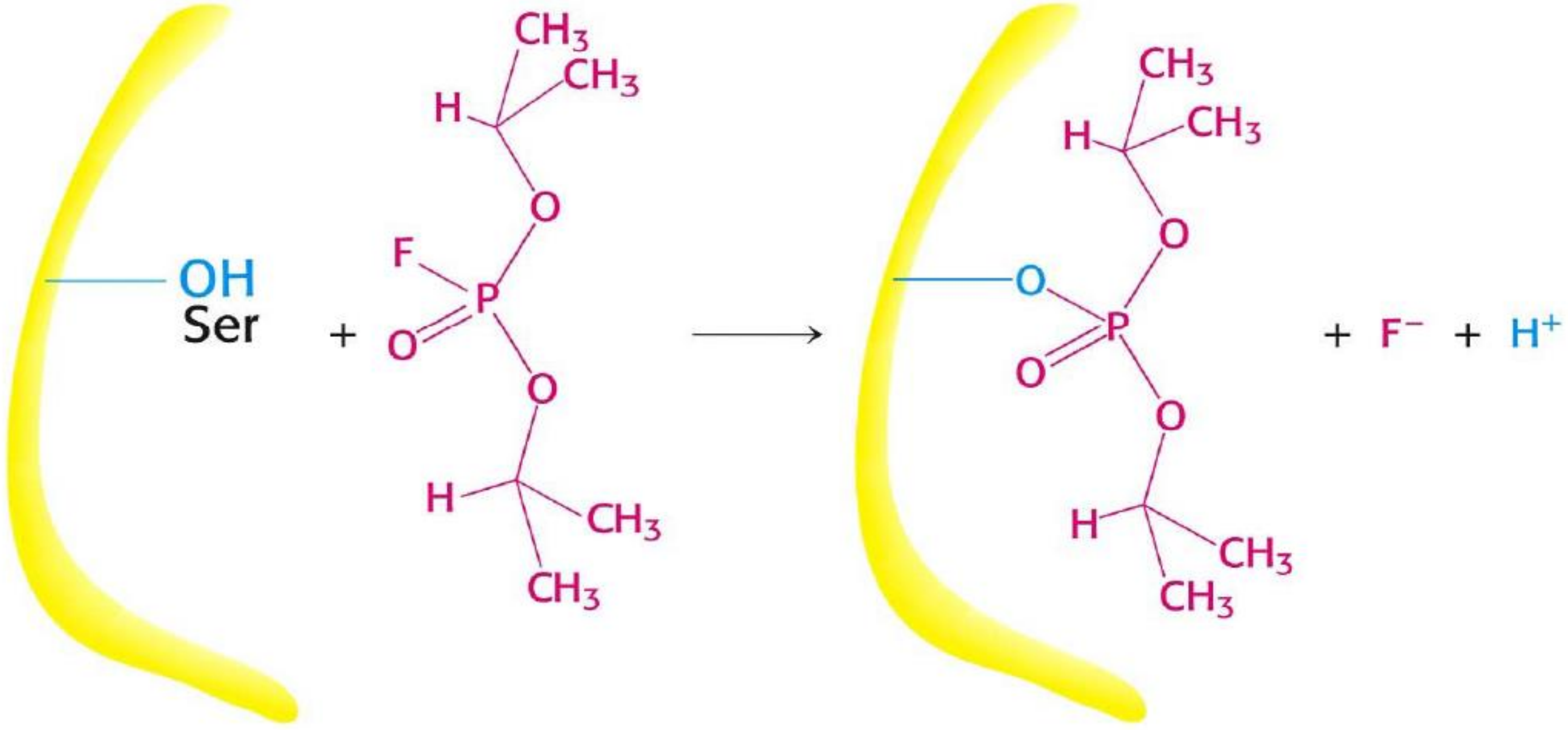
Tightly bound through covalent or noncovalent interactions.

Irreversible inhibitors

- ***group-specific reagents***
- ***substrate analogs***
- ***suicide inhibitors***

1. Group-specific reagents

-react with specific R groups of amino acids



Acetylcholin-esterase

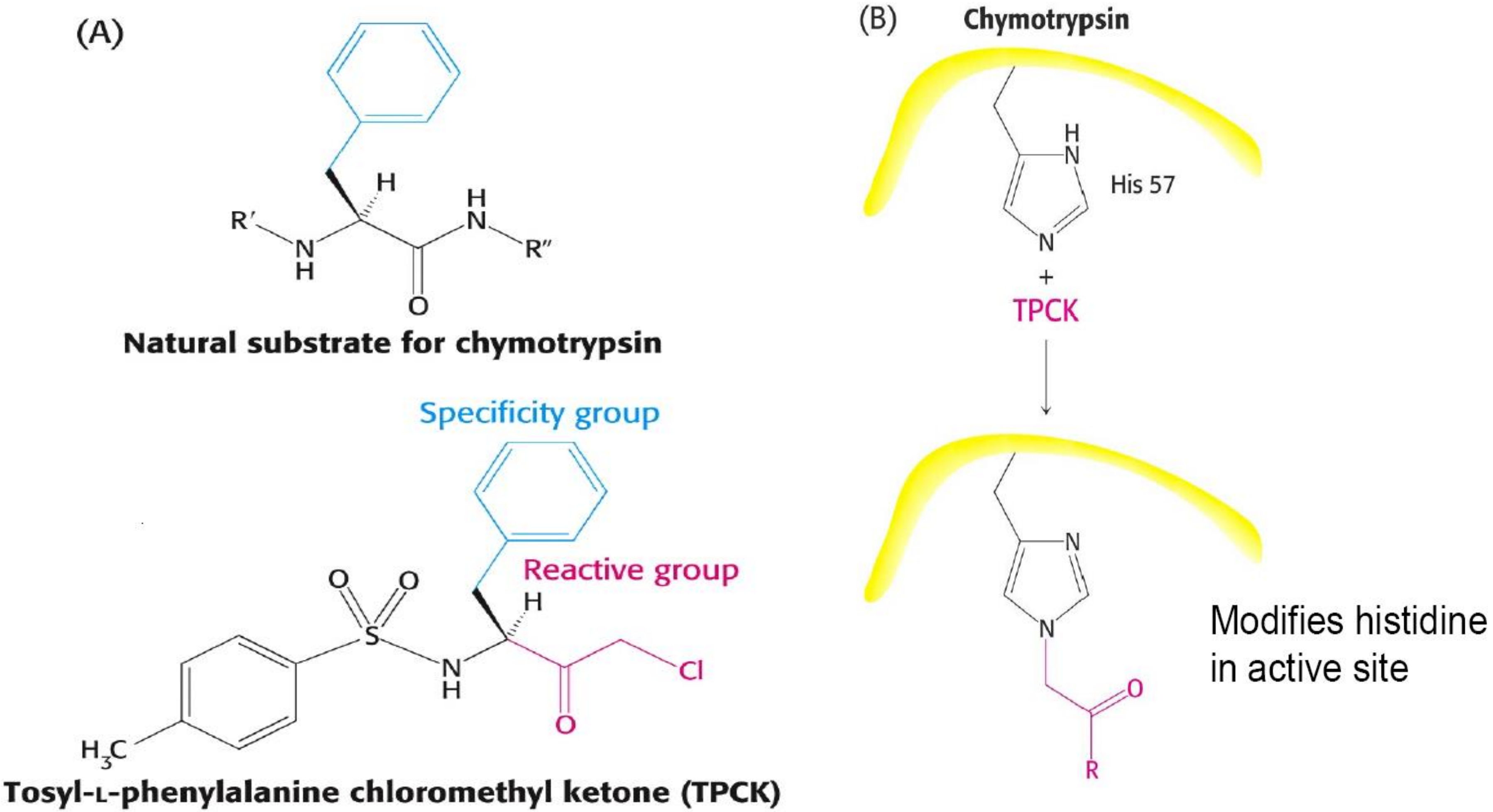
DIPF
diisopropylphosphofluoridate

Inactivated enzyme

2.Substrate analogs

-structurally similar to the substrate for the enzyme.

-covalently modify active site residues.



Natural substrate for chymotrypsin

Tosyl-L-phenylalanine chloromethyl ketone (TPCK)

Modifies histidine in active site

3.Suicide inhibitors

- Inhibitor binds as a substrate and is initially processed by the normal catalytic mechanism.

- It then generates a chemically reactive intermediate that inactivates the enzyme through covalent modification.

- Suicide because enzyme participates in its own irreversible inhibition.

Regulation of enzyme activity

Methods of regulation of enzyme activity

- **Allosteric control**
- **Reversible covalent modification**
- **Isozymes (isoenzymes)**
- **Proteolytic activation**

Allosteric enzymes

Allosteric enzymes have a second regulatory site (allosteric site) distinct from the active site

Allosteric enzymes contain more than one polypeptide chain (have quaternary structure).

Allosteric modulators bind noncovalently to allosteric site and regulate enzyme activity via conformational changes.

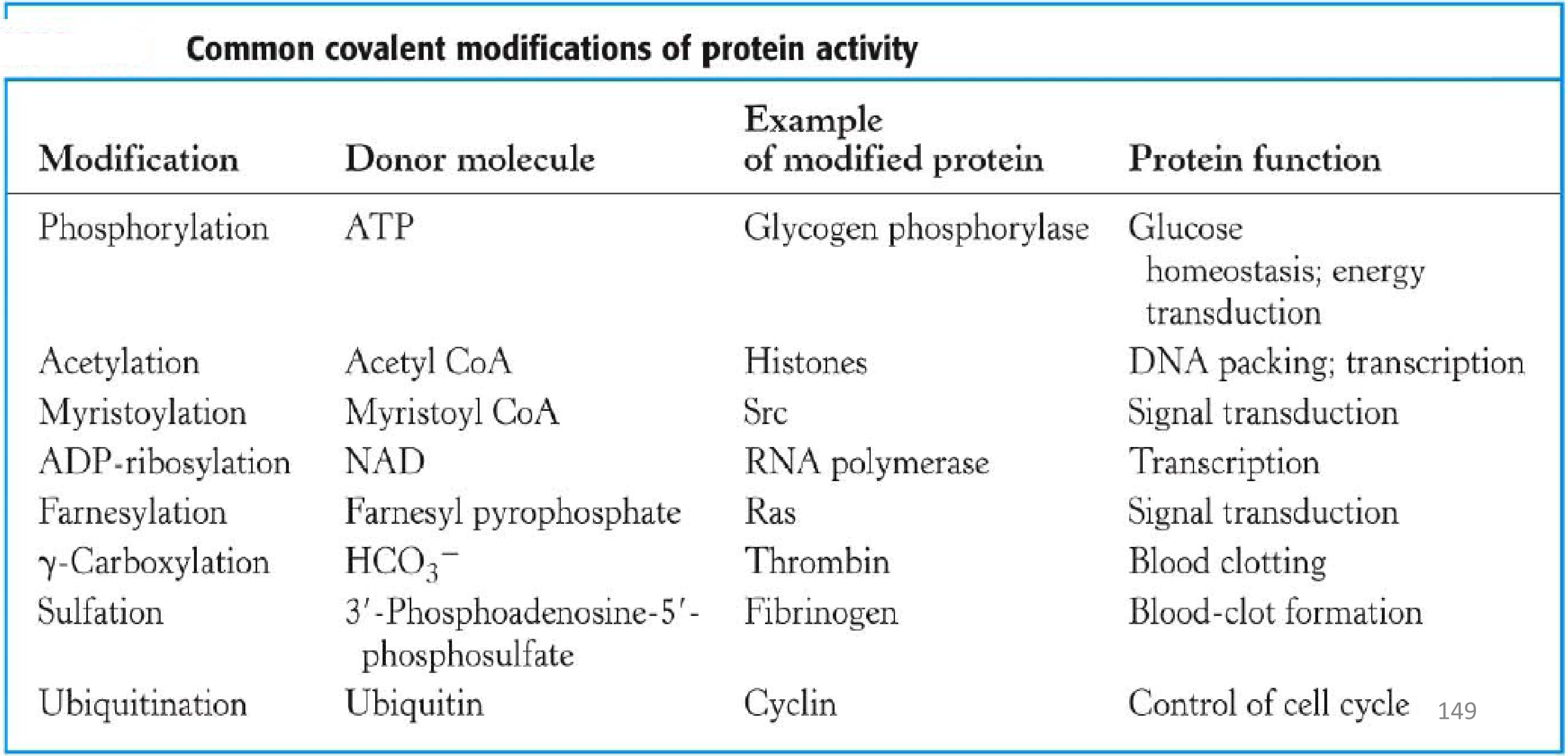
2 types of modulators (inhibitors or activators)

- ***Negative modulator (inhibitor)***
  - binds to the allosteric site and inhibits the action of the enzyme.
  - usually it is the end product of a biosynthetic pathway
  - end-product (feedback) inhibition.

- ***Positive modulator (activator)***
  - binds to the allosteric site and stimulates activity.
  - usually it is the substrate of the reaction.

Regulation of enzyme activity by covalent modification

Covalent attachment of a molecule to an amino acid side chain of a protein can modify activity of enzyme

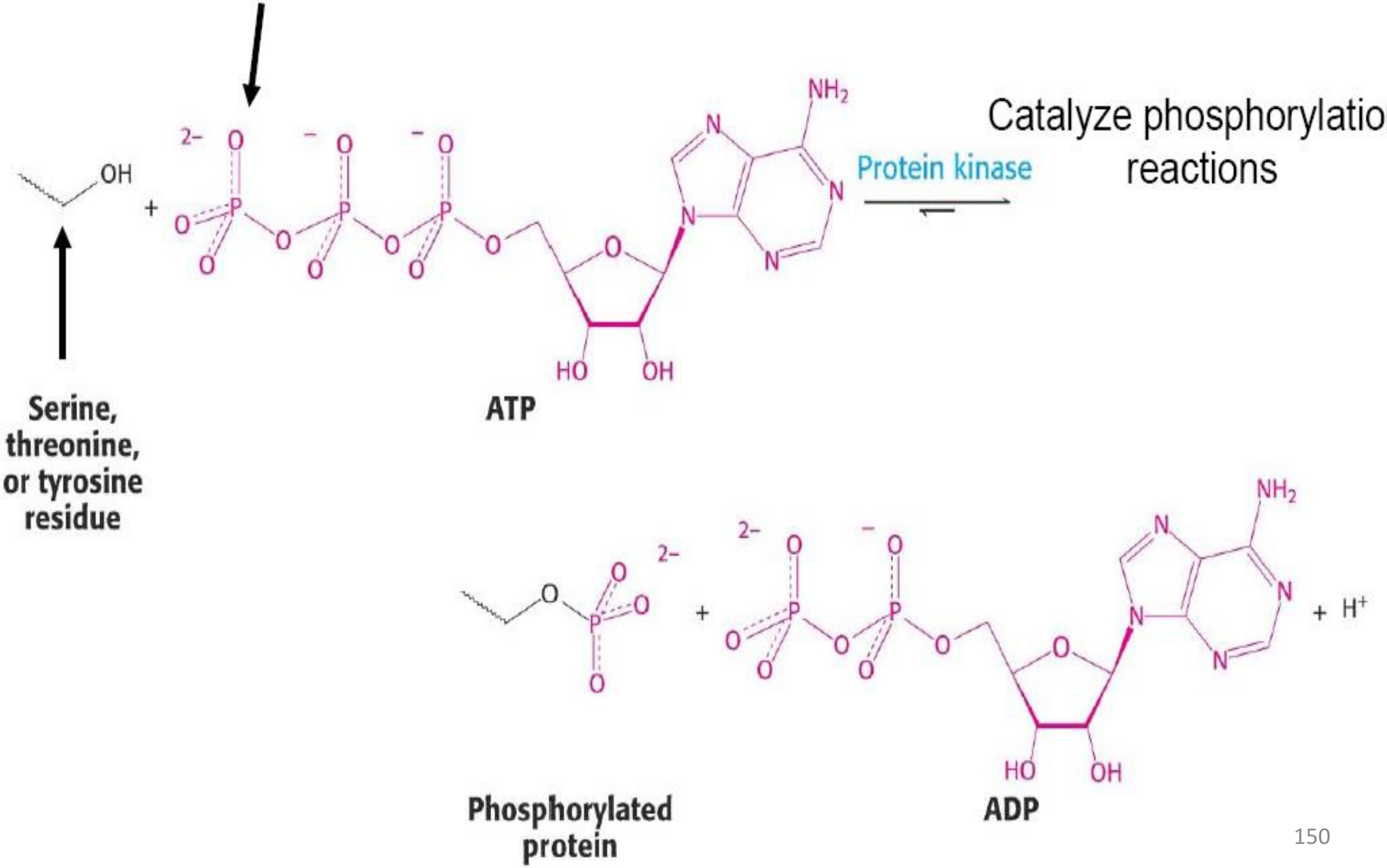


Common covalent modifications of protein activity

Modification	Donor molecule	Example of modified protein	Protein function
Phosphorylation	ATP	Glycogen phosphorylase	Glucose homeostasis; energy transduction
Acetylation	Acetyl CoA	Histones	DNA packing; transcription
Myristoylation	Myristoyl CoA	Src	Signal transduction
ADP-ribosylation	NAD	RNA polymerase	Transcription
Farnesylation	Farnesyl pyrophosphate	Ras	Signal transduction
γ-Carboxylation	HCO_3^-	Thrombin	Blood clotting
Sulfation	3′-Phosphoadenosine-5′-phosphosulfate	Fibrinogen	Blood-clot formation
Ubiquitination	Ubiquitin	Cyclin	Control of cell cycle

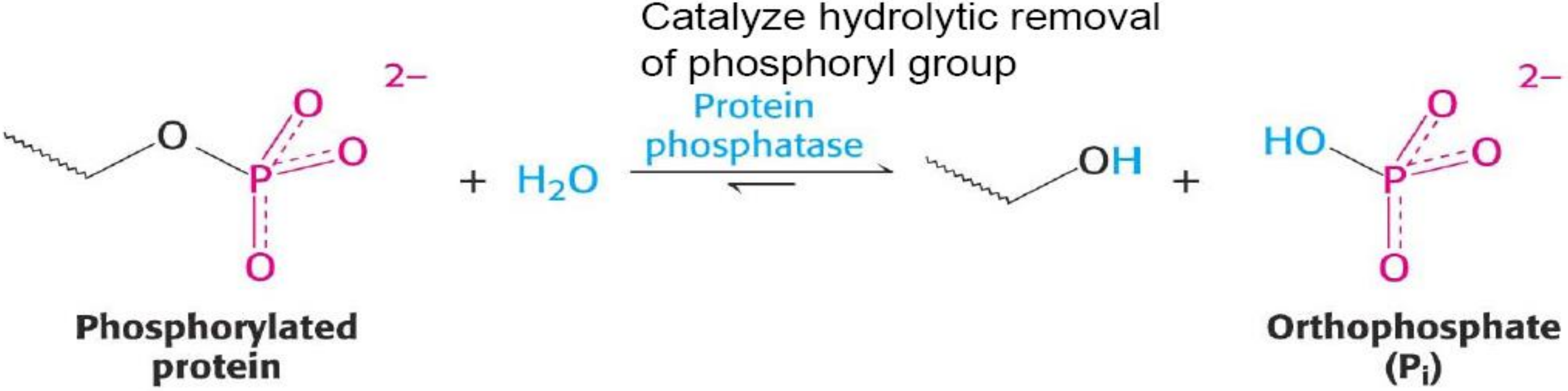
Phosphorylation reaction

Terminal γ phosphoryl group



Catalyze phosphorylation reactions

Dephosphorylation reaction



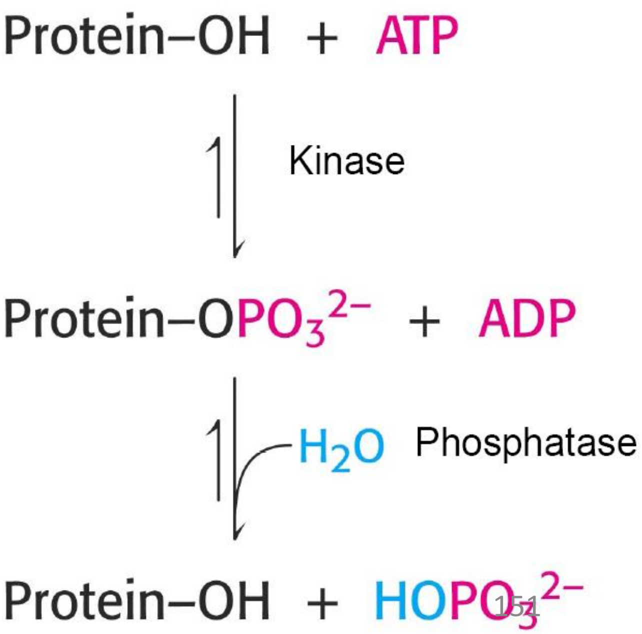
Catalyze hydrolytic removal of phosphoryl group

Not reverse reactions

Usually phosphorylated enzymes are active, but there are exceptions (glycogen synthase)

Enzymes taking part in phospho-rylation are called **protein kinases**

Enzymes taking part in dephosphorylation are called **phosphatases**



Protein–OH + ATP

Kinase

Protein–OPO_3^{2-} + ADP

H_2O Phosphatase

Protein–OH + $HOPO_3^{2-}$

Isoenzymes (isozymes)

Some metabolic processes are regulated by enzymes that exist in different molecular forms – **isoenzymes.**

Isoenzymes - multiple forms of an enzyme which differ in amino acid sequence but catalyze the same reaction.

Isoenzymes can differ in:
- *kinetics*,
- *regulatory properties*,
- the form of ***coenzyme*** they prefer and
- *distribution* in cell and tissues

Example: ***lactate dehydrogenase (LDH)***

$$\text{Lactate} + \text{NAD}^+ \rightleftharpoons \text{pyruvate} + \text{NADH} + \text{H}^+$$

Lactate dehydrogenase – tetramer (four subunits) composed of two types of polypeptide chains, **M** and **H**

There are **5 Isozymes** of LDH:

- **H_4 – heart**
- **HM_3**
- **H_2M_2**
- **H_3M**
- **M_4 – liver, muscle**

- **H_4**: highest affinity; best in aerobic environment
- **M_4**: lowest affinity; best in anaerobic environment

Isoenzymes are important for diagnosis of different diseases.

Activation by proteolytic cleavage

- Many enzymes are synthesized as **inactive precursors** (**zymogens**) that are activated by proteolytic cleavage

- Proteolytic activation only occurs once in the life of an enzyme molecule

Examples of specific proteolysis

- Digestive enzymes
  - Synthesized as zymogens in stomach and pancreas
- Blood clotting enzymes
  - Cascade of proteolytic activations
- Protein hormones
  - Proinsulin to insulin by removal of a peptide

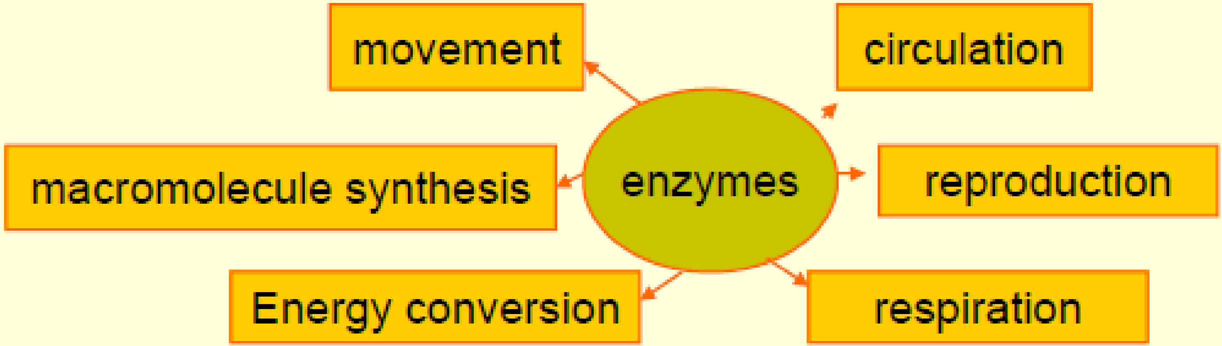
Multienzyme Complexes and Multifunctional Enzymes

- **Multienzyme complexes** - different enzymes that catalyze sequential reactions in the same pathway are bound together.
- **Multifunctional enzymes** - different activities may be found on a single, multifunctional polypeptide chain.

How importance

- Living procedures →based on reaction
- Catalyst→essential to accelerate reactions
- Enzymes→ biologic catalysts

- Without them→ NO LIFE (KNOWN)



Chapter -5- Carbohydrates

✓ What are carbohydrates?

- Compounds containing C, H and O
- General formula: $C_x(H_2O)_x$
- All have C=O and -OH functional groups.
- Carbohydrates also called sacharides and Produced by plants during photosynthesis.

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

➢ After eating plant foods, humans convert the carbohydrates into glucose.

Sources of Carbohydrates

Classifications carbohydrates

based on **Number of unit sugars**, **Location of C=O** **and Size of base carbon chain**

Classifications based on **number of sugar** units in total chain.

I. Monosaccharides - single sugar unit

II. Disaccharides - two sugar units

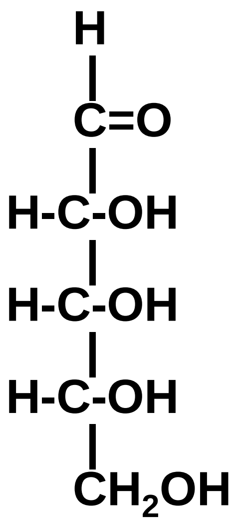
III. Oligosaccharides - 3 to 10 sugar units

IV. Polysaccharides - more than 10 units

- Chaining relies on ‘bridging’ of oxygen atoms is called O-glycoside bonds

I. Monosaccharides

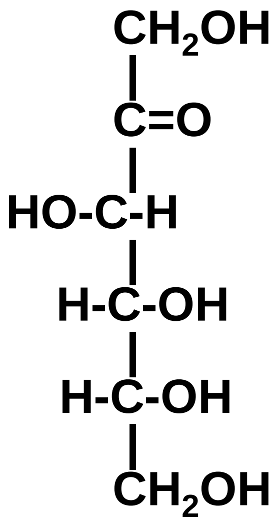
- Based on location of C=O (Aldose or ketose)



$$\begin{array}{l} \quad\;\mathrm{H} \\ \quad\;\;| \\ \quad\;\mathrm{C{=}O} \\ \quad\;\;| \\ \mathrm{H{-}C{-}OH} \\ \quad\;\;| \\ \mathrm{H{-}C{-}OH} \\ \quad\;\;| \\ \mathrm{H{-}C{-}OH} \\ \quad\;\;| \\ \quad\;\mathrm{CH_2OH} \end{array}$$

Aldose

- aldehyde C=O

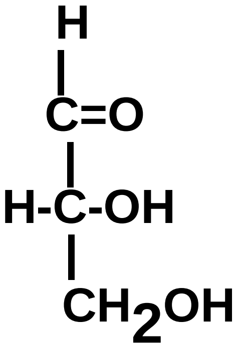


$$\begin{array}{l} \quad\;\mathrm{CH_2OH} \\ \quad\;\;| \\ \quad\;\mathrm{C{=}O} \\ \quad\;\;| \\ \mathrm{HO{-}C{-}H} \\ \quad\;\;| \\ \mathrm{H{-}C{-}OH} \\ \quad\;\;| \\ \mathrm{H{-}C{-}OH} \\ \quad\;\;| \\ \quad\;\mathrm{CH_2OH} \end{array}$$

Ketose

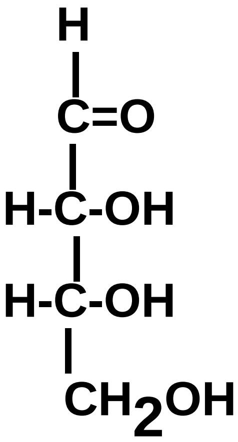
- ketone C=O

- Based on Number of carbon atoms in the chain



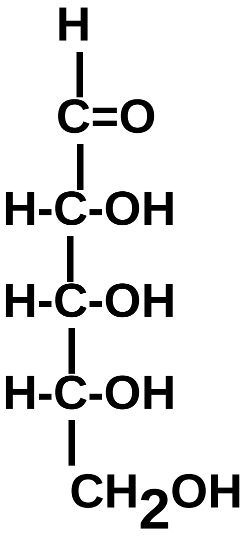
$$\begin{array}{c} H \\ | \\ C{=}O \\ | \\ H{-}C{-}OH \\ | \\ CH_2OH \end{array}$$

triose



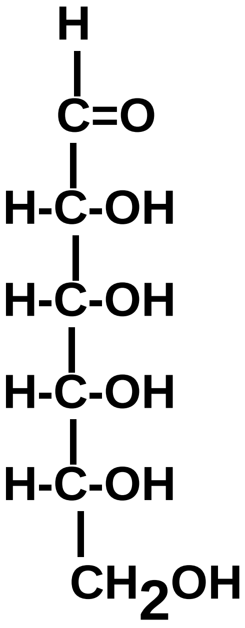
$$\begin{array}{c} H \\ | \\ C{=}O \\ | \\ H{-}C{-}OH \\ | \\ H{-}C{-}OH \\ | \\ CH_2OH \end{array}$$

tetrose



$$\begin{array}{c} H \\ | \\ C{=}O \\ | \\ H{-}C{-}OH \\ | \\ H{-}C{-}OH \\ | \\ H{-}C{-}OH \\ | \\ CH_2OH \end{array}$$

pentose

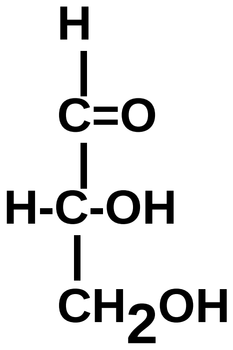


$$\begin{array}{c} H \\ | \\ C{=}O \\ | \\ H{-}C{-}OH \\ | \\ H{-}C{-}OH \\ | \\ H{-}C{-}OH \\ | \\ H{-}C{-}OH \\ | \\ CH_2OH \end{array}$$

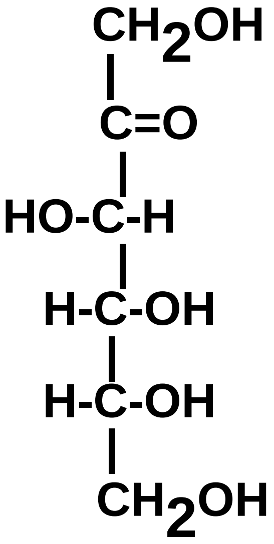
hexose

Can be either aldose or ketose sugar.

Examples



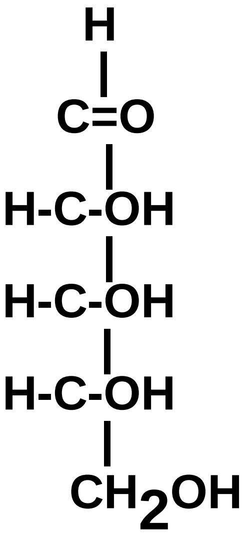
$$\begin{array}{c} \mathrm{H} \\ | \\ \mathrm{C{=}O} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$



$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{C{=}O} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

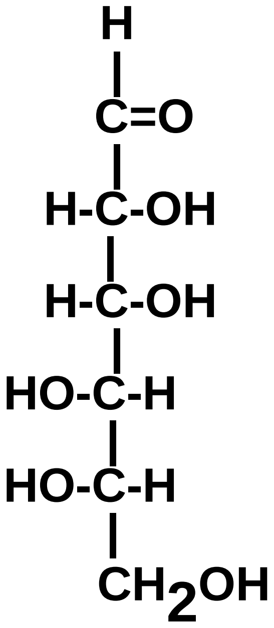
D-glyceraldehyde	D-fructose
triose	hexose
aldose	ketose
aldotriose sugar	ketohexose sugar

Examples



$$\begin{array}{c} H \\ | \\ C{=}O \\ | \\ H{-}C{-}OH \\ | \\ H{-}C{-}OH \\ | \\ H{-}C{-}OH \\ | \\ CH_2OH \end{array}$$

D-ribose
pentose, aldose
aldopentose sugar



$$\begin{array}{c} H \\ | \\ C{=}O \\ | \\ H{-}C{-}OH \\ | \\ H{-}C{-}OH \\ | \\ HO{-}C{-}H \\ | \\ HO{-}C{-}H \\ | \\ CH_2OH \end{array}$$

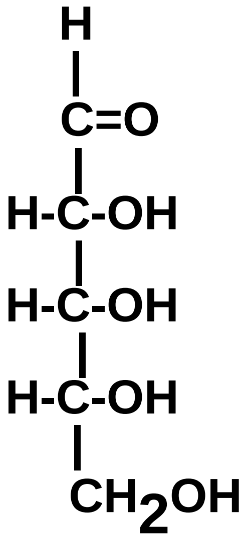
L-mannose
hexose, aldose
aldohexose sugar

Some important monosaccharides

D-glyceraldehyde	Simplest sugar
D-glucose	Most important in diet
D-fructose	Sweetest of all sugars
D-galactose	Part of milk sugar
D-ribose	Used in RNA

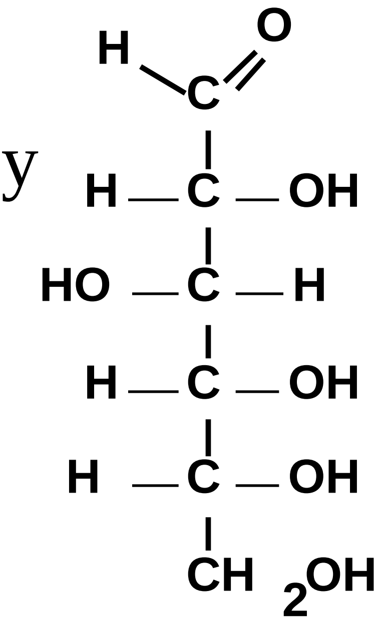
Note: D-ribose is an important sugar used in genetic material. This sugar is not used as energy source but is a part of the backbone of RNA.

- When the C-2 OH is removed, the sugar becomes deoxyribose which is used in the backbone of DNA.



D-glucose

- Glucose is an **aldohexose** sugar.
- Common names include **dextrose, grape sugar, blood sugar.**
- Most abundant organic compound found in **nature**.
- **Brain cells**, and the **growing embryo** only utilize glucose as a source of energy.
- Energy source for **cells** in the body.
- Building block of **disaccharide**s and **polysachharides**
- It is the sugar present in **blood.**

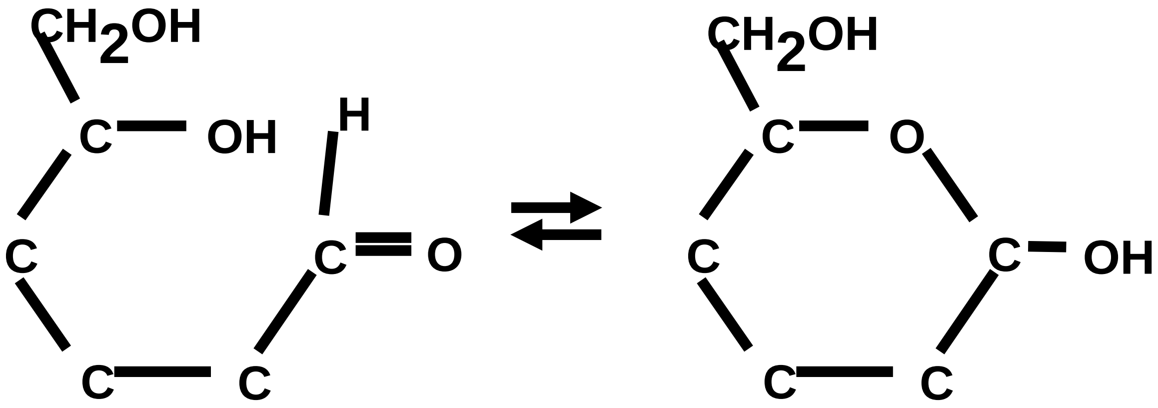


Dietary sources: fruits, vegetables(in the form of starch), honey

Carbohydrates in cyclic structures

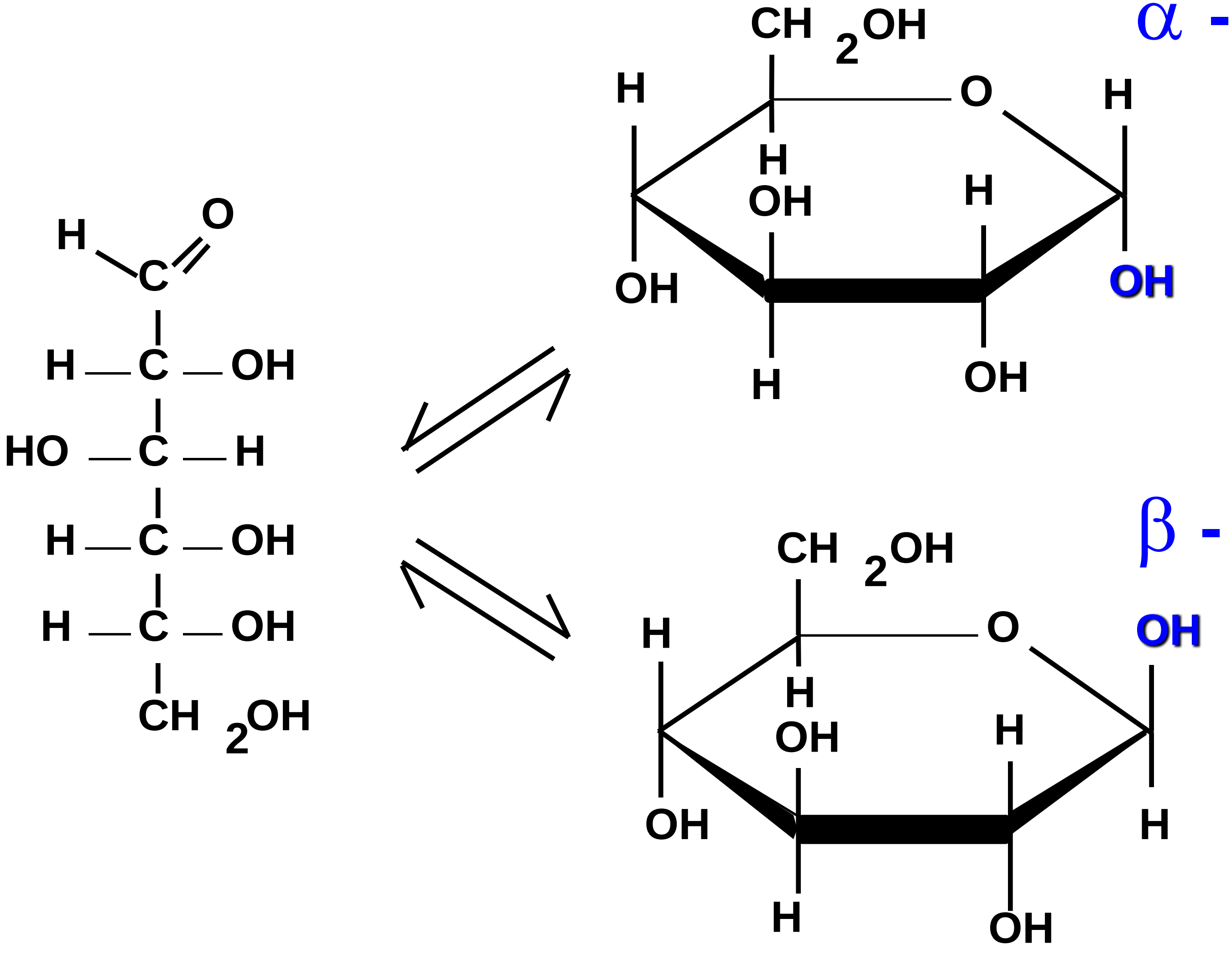
- sugars form rings. For many sugars, its the most common form.
- **hemiacetal** - forms from alcohol and aldehyde
- **hemiketal** - forms from alcohol and ketone

Intramolecular cyclization



- The -OH group that forms can be above or below the ring resulting two forms is called α or β anomers .
- α - OH group is down compared to CH_2OH (trans).
- β - OH group is up compared to CH_2OH (cis).
- The α and β forms are in equilibrium. So, one form can convert to the other is called mutarotation.

Cyclization of D-glucose

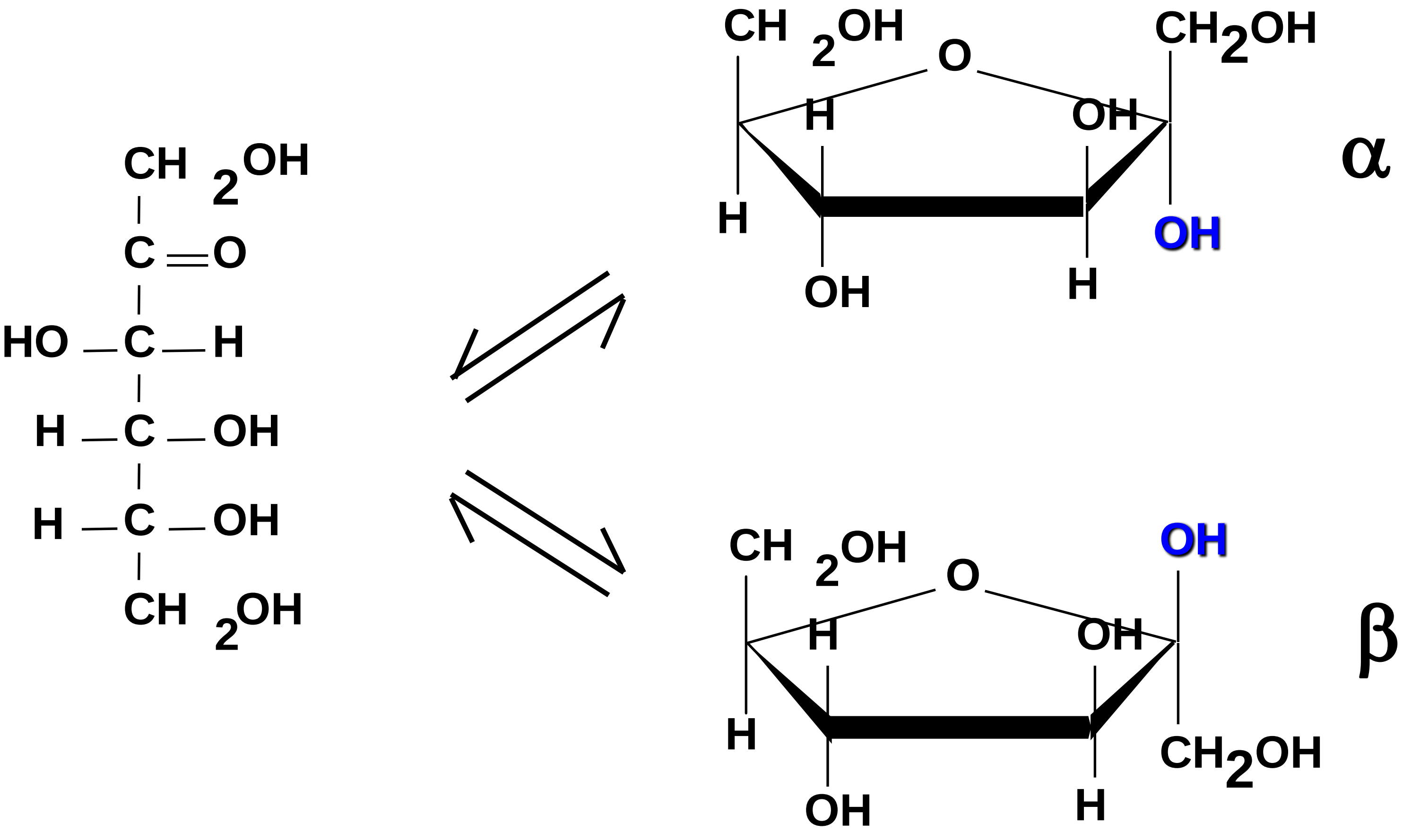


α -D - glucose

β - D - glucose

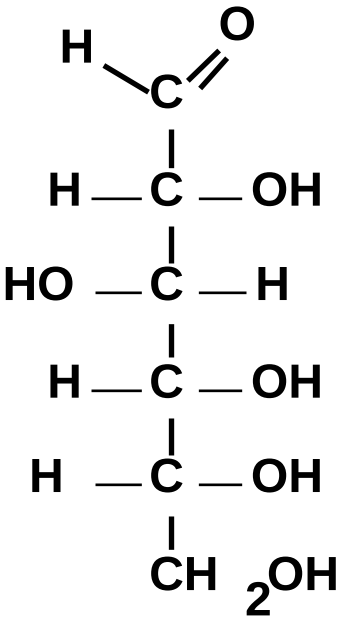
Cyclization of D-fructose

- This can also happen to ketose sugars.

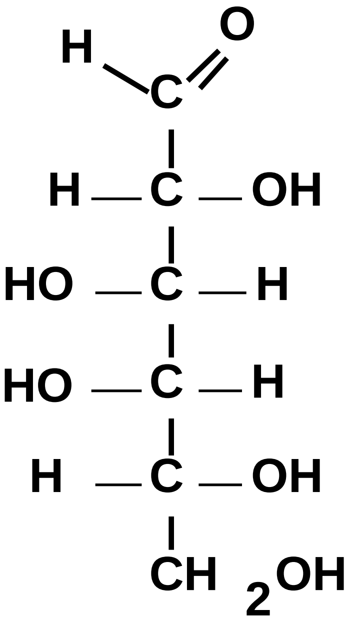


D-glucose vs. D-galactose

D-glucose



D-galactose



Can you find a difference? Your body can!

You can’t digest galactose - it must be converted to glucose first.

Reactions of glucose and other monosaccharides

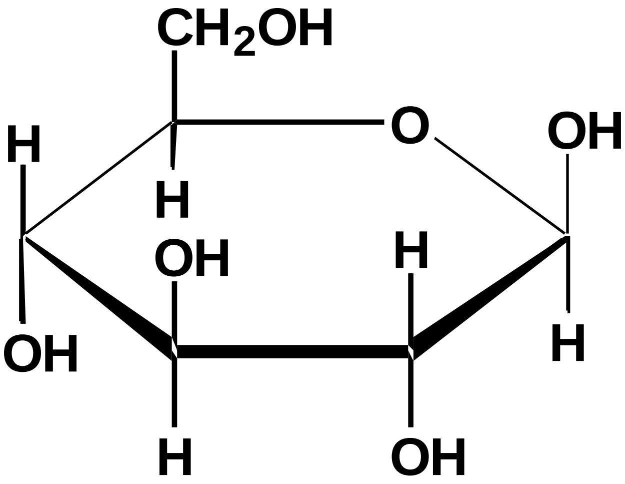
- Oxidation-Reduction. Required for their complete metabolic breakdown.
- Esterification. Production of phosphate esters.
- Amino derivatives. Used to produce structural components and glycoprotein.
- Glycoside formation. Linkage of monosaccharides to form polysaccharides.

More Monosaccharide Derivatives are:

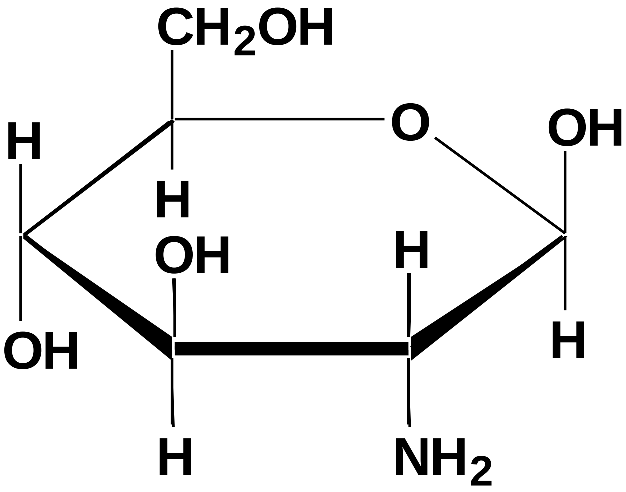
- **Sugar alcohols**: mild reduction of sugars
- **Deoxy sugars**: constituents of DNA, etc.
- **Sugar esters**: phosphate esters like ATP
- **Amino sugars**: contain an amino group in place of a hydroxyl group
- **Acetals, ketals and glycosides:** basis for oligo- and poly-saccharides

Amino derivatives

- The replacement of a hydroxyl group on a carbohydrate results in an amino sugar.



β-D-glucose



β-D-2-aminoglucose
(glucosamine)

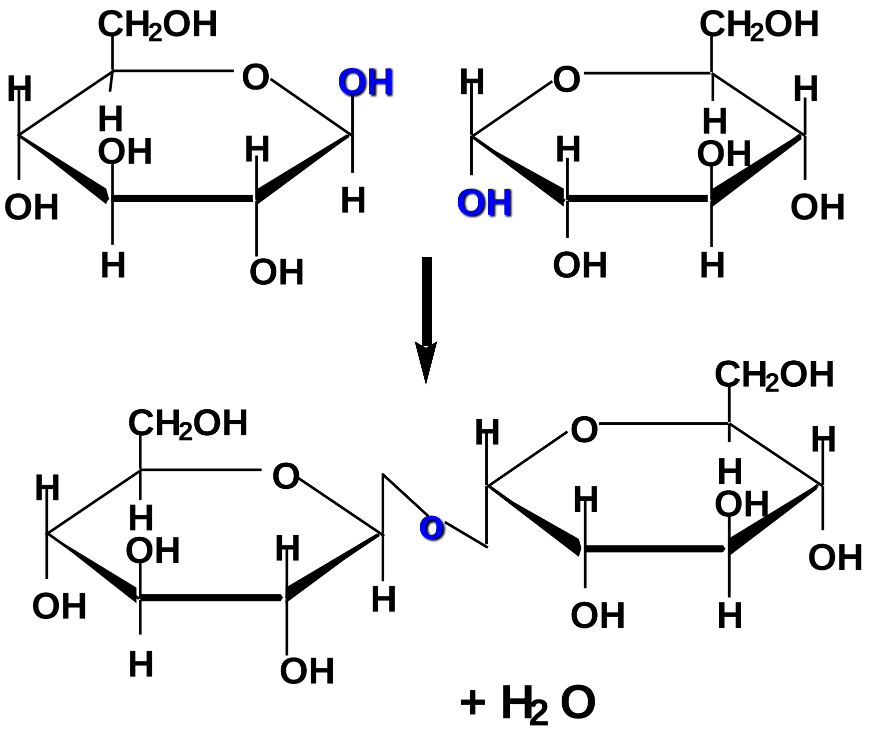
Amino derivatives

- Uses for amino sugars.
- Structural components of bacterial cell walls.
- As a component of chitin, a polymer found in the exoskeleton of insects.
- A major structural unit of chondroitin sulfate - a component of cartilage.
- Component of glycoprotein and glycolipids.

2.Disaccharides

Non Reducing : aldehyde or ketone group of the sugar isn't freely involved in bond formation.

2. Reducing : aldehyde or ketnoe group involved in bond formation.



- glycosidic bond
- sugar -O- sugar
- oxygen bridge

Glycosidic bonds

- Are two types based on the position of the C-1 OH

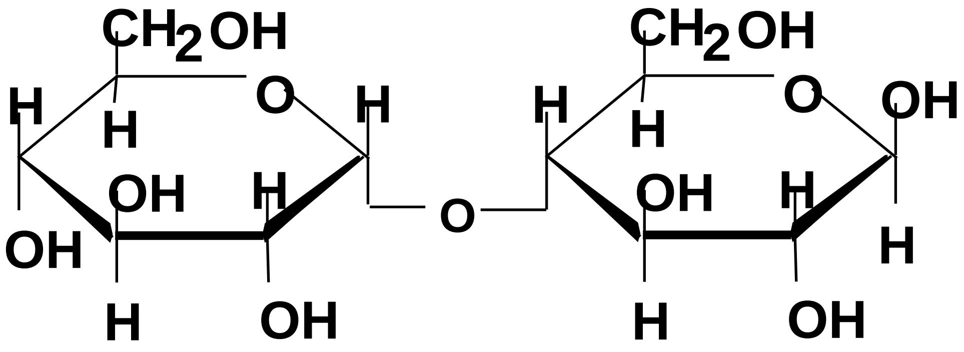
α-glycosidic bond

- linkage between a C-1 **α** OH and C-4 OH

β– glycosidic bond

- linkage between a C-1 β OH and C-4 OH

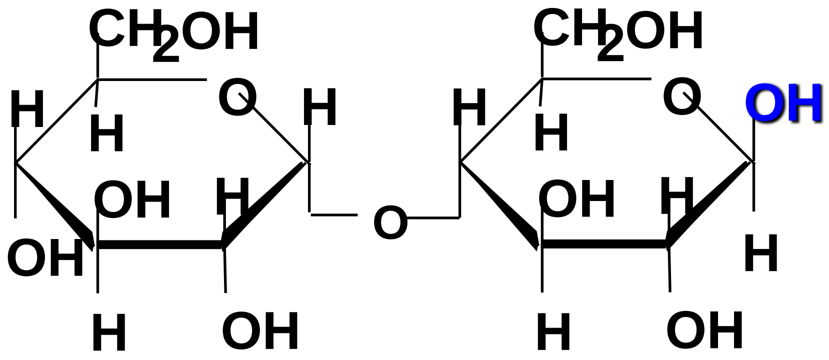
- **β-Maltose:** **Malt sugar.** Not common in nature except in germinating grains.



α-D-glucose β-D-glucose

α-D-glucose and β-D-glucose, α (1 → 4) linkage.

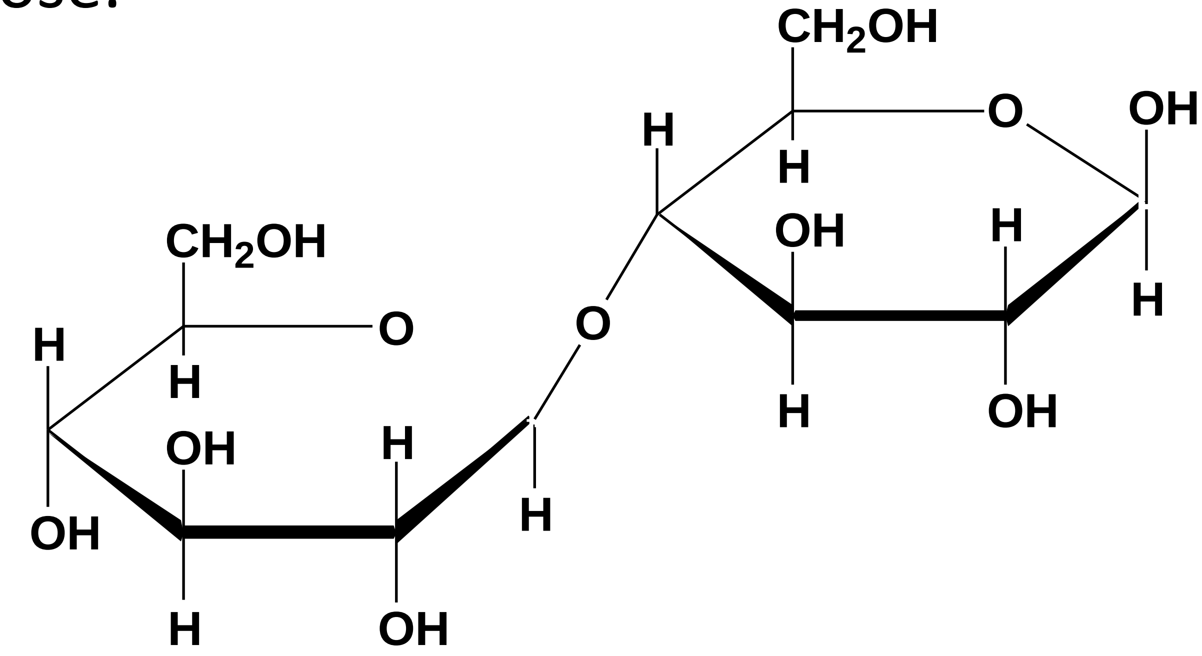
- maltose referred to as β-maltose because the unreacted C-1 on β-D-glucose is in the β position.



- **Uses for β-maltose**
- Ingredient in infant formulas.
- Production of beer.
- Flavoring - fresh baked aroma.
- It is hydrolyzed the in body by:
  - $\text{maltose} + H_2O \xrightarrow{\textbf{maltase}} 2\ \text{glucose}$

Cellobiose

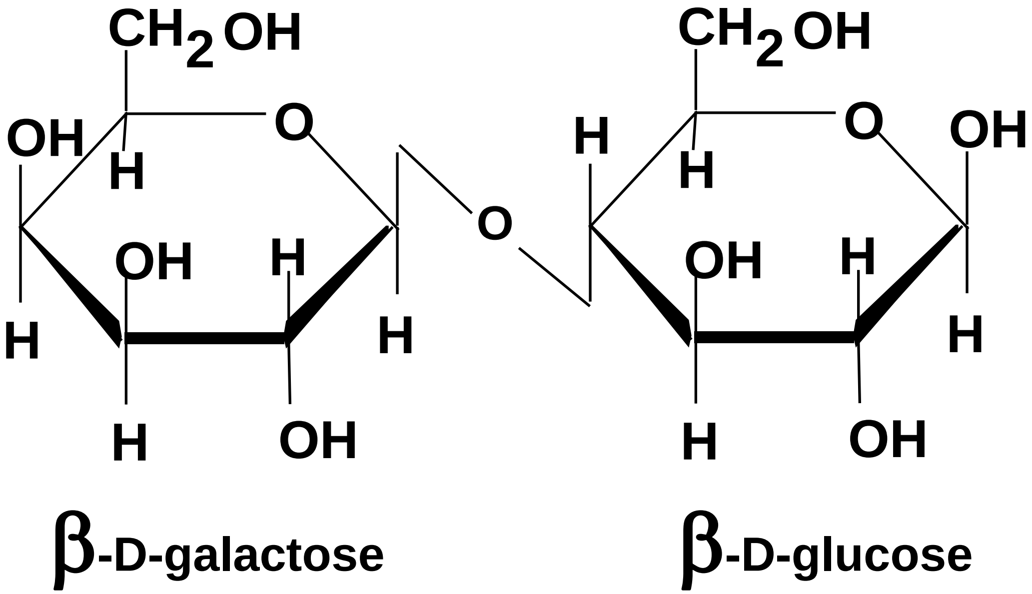
- Like maltose, it is composed of two molecules of D-glucose - but with a β (1 ⟶ 4) linkage.
- The difference in the linkage results in cellobiose being unusable b/c we lack an enzyme that can hydrolyze cellobiose.



Lactose (**r**educing)

- **Milk sugar** - dimer of β-D-galactose and either the α or β - D-glucose.

- **β-Lactose**



β (1 ⟶ 4) linkage, β disaccharide.

- **Lactase** is an enzyme required to hydrolyze lactose.

Lactose intolerance

Lack or insufficient amount of the enzyme.

- Due to the absence of the enzyme lactase,
- Undigested lactose leads to bacterial fermentation in colon and generation of gases.
- These products cause diarrhea, bloat and pain in the gut.
- **Gut is alimentary canal:** the whole of the alimentary canal in people and animals, from the mouth to the anus, or the lower part of intestine, from the stomach to the anus

- We can’t directly use galactose. It must be converted to a form of glucose.
- Galactosemia
- **excess of milk-sugar constituent:** a genetic disorder causing the absence of an enzyme necessary for the breakdown (conversion) of galactose in milk to glucose.
- Build up of galactose or a metabolite like dulcitol (galactitol) causes toxic effects.
- Can lead to retardation, cataract, death.

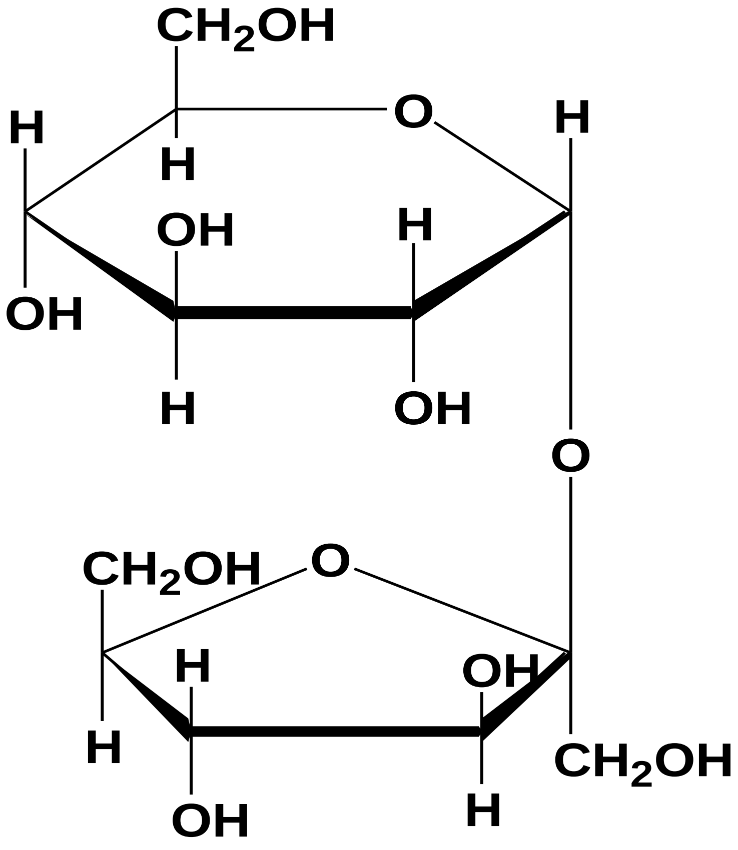
Cataract: **eye disease:** an eye disease in which the lens becomes covered in an opaque film that affects sight, eventually causing total loss of sight.

Sucrose (non reducing) common table sugar:

Also known as *cane sugar or beet sugar*.

Only one isomer present in solution & Easily crystallized.

- Table sugar - most common sugar in all plants.
- Sugar cane and beet, are up to 20% by mass sucrose.
- Disaccharide of α-glucose and β-fructose.



α (1 → 2) linkage

3. Oligosaccharides

- 3-10 monosaccharides: raffinose and stachyose
- Found in beans and legumes
- Not digested by the body
- Metabolized by bacteria in the large intestine
- Raffinose=galactose+glucose+fructose
- Stachyose=galactose+galactose+glucose+fructose
- Fructooligosaccharides, Cell membrane proteins contain oligosaccharides, The oligosaccharide units of glycoproteins are rich in **information** and are **functionally** important.

4. Polysaccharides (complex carbohydrates)

characteristics:

- ✓ polymers (MW from 200,000), White and amorphous products (glassy), not sweet, not reducing (do not give the typical aldose or ketose reactions), form colloidal solutions or suspensions.

Carbohydrate polymers are:

1. Storage Polysaccharides; Energy storage - starch and glycogen
2. Structural Polysaccharides

Used to provide protective walls or lubricative coating to cells – cellulose and mucopolysaccharides.

3. Structural Peptidoglycans; Bacterial cell walls

Polysaccharides may be one of two

Homoglycans (starch, cellulose, glycogen)

Heteroglycans (gums, mucopolysaccharides)

Starch

- Energy storage used by plants
- Long repeating chain of α-D-glucose
- Chains up to 4000 units

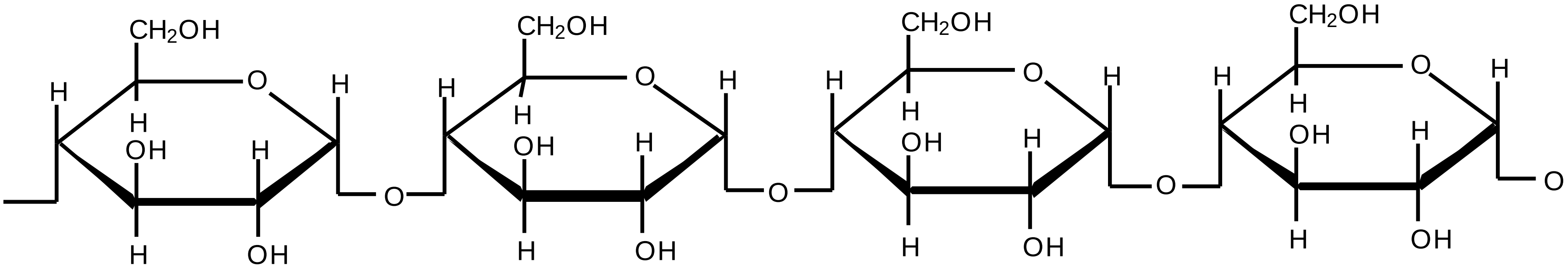
Two types of starch

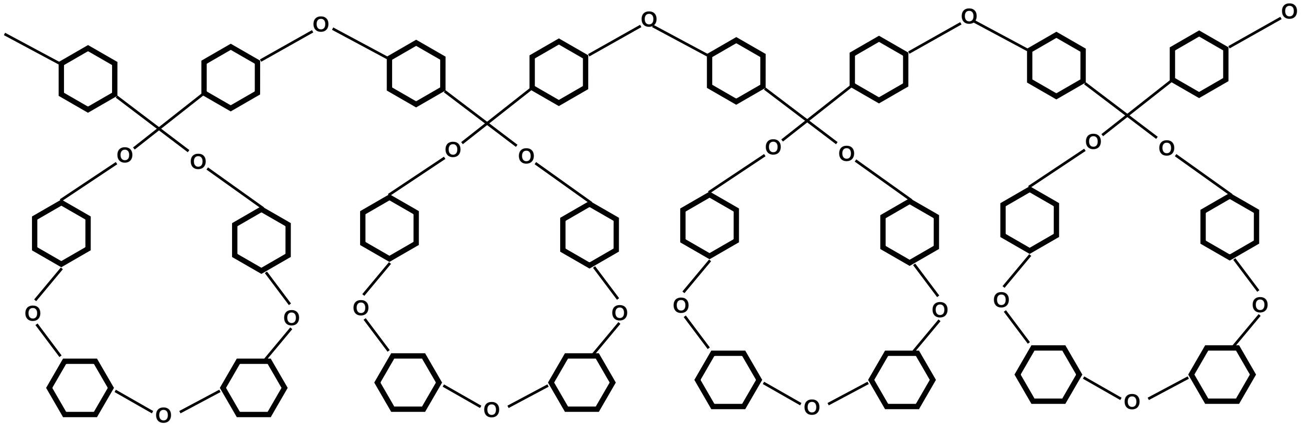
Amylose: straight chain, major form of starch

Amylopectin; branched structure

Amylose starch

- Straight chain that forms coils α (1 → 4) linkage. Most common type of starch.

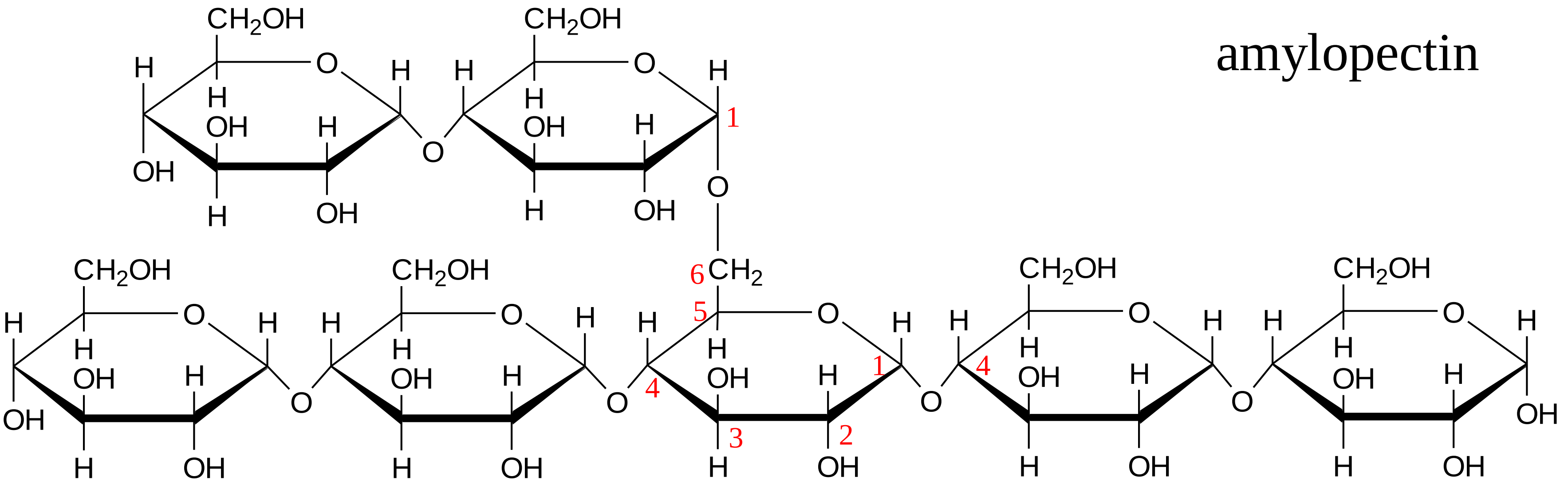




Amylopectin

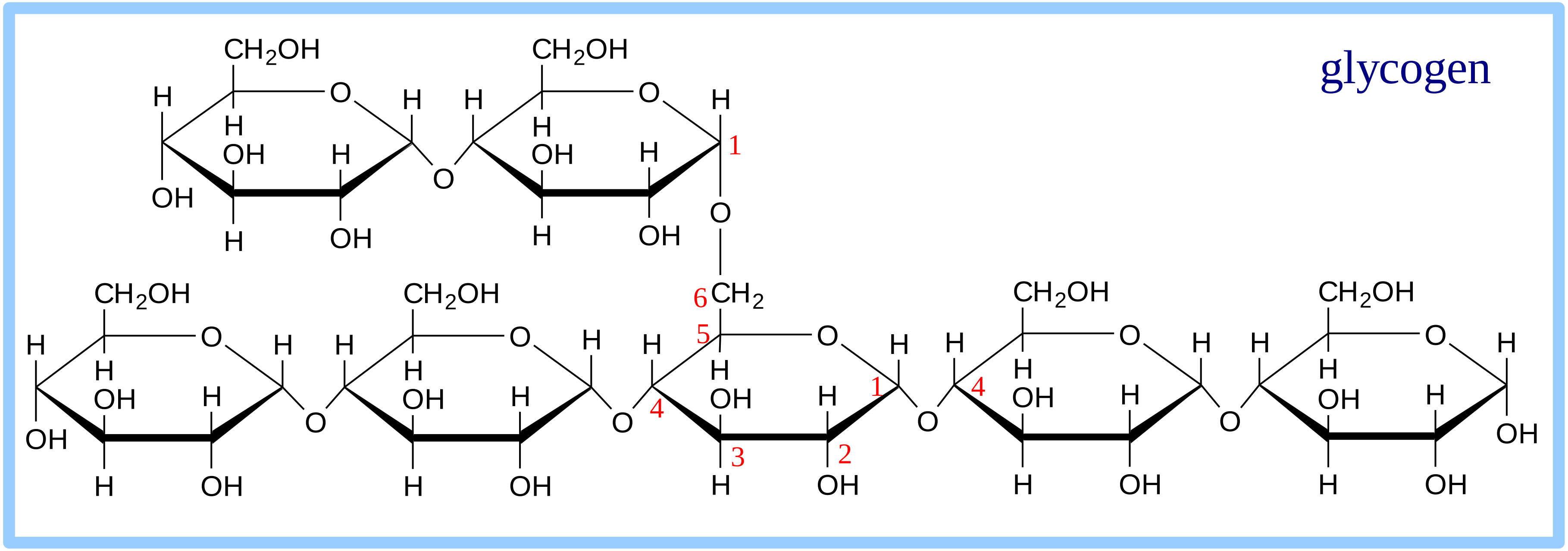
is a glucose polymer with mainly α(1→4) linkages, but it also has **branches** formed by α(1→6) linkages. Branches are generally longer than shown above.

The branches produce a compact structure & provide multiple chain ends at which enzymatic cleavage can occur.



Glycogen

- Energy Storage form of glucose in animals and humans.
- Stored in liver and muscles as granules.
- Similar in linkage & structure with amylopectin but differ due to presence of more α(1→6) branch.
- Have numerous alpha bonds.
- Found in liver (400 kcal) and muscles (1400 kcal)



Fiber

- Dietary fiber= fibers found naturally in foods.
- Functional fibers= fiber added to foods that has shown to provide health benefits.
- Total fiber= dietary fiber + functional fiber.

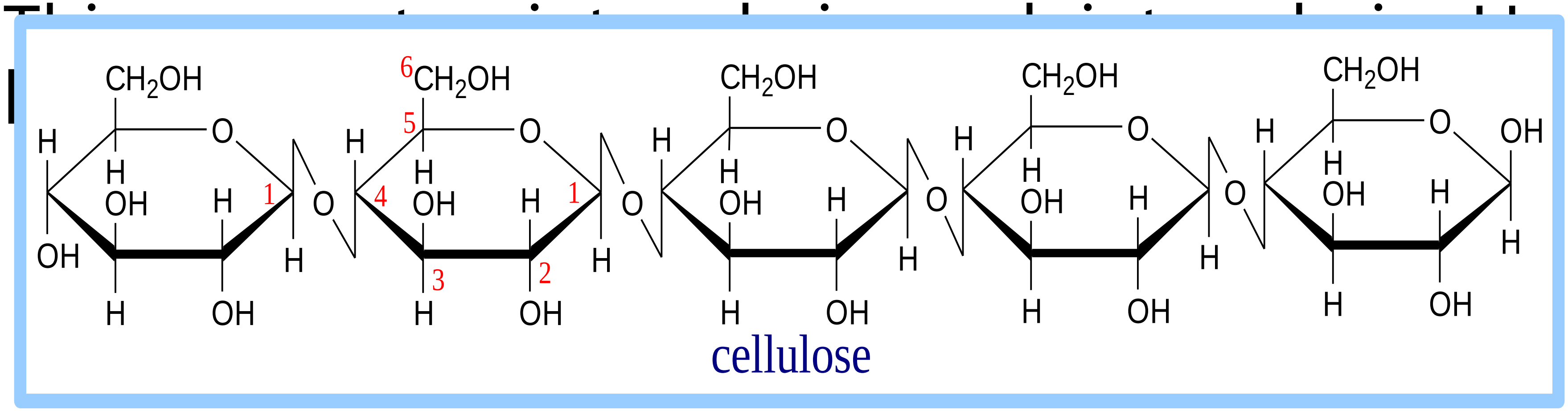
Chemical Composition of Fibers

- Contain beta bonds
- **Insoluble**: not fermented
  - Cellulose(carbohydrate)
  - Hemicellulose (carbohydrate)
  - Lignin (non carbohydrate)
- **Soluble**: 1.5-2.5 kcal/g
  - Gum, Pectin, Mucilage are carbohydrates

Cellulose

a major constituent of plant cell walls, consists of long linear chains of glucose with β(1→4) linkages.

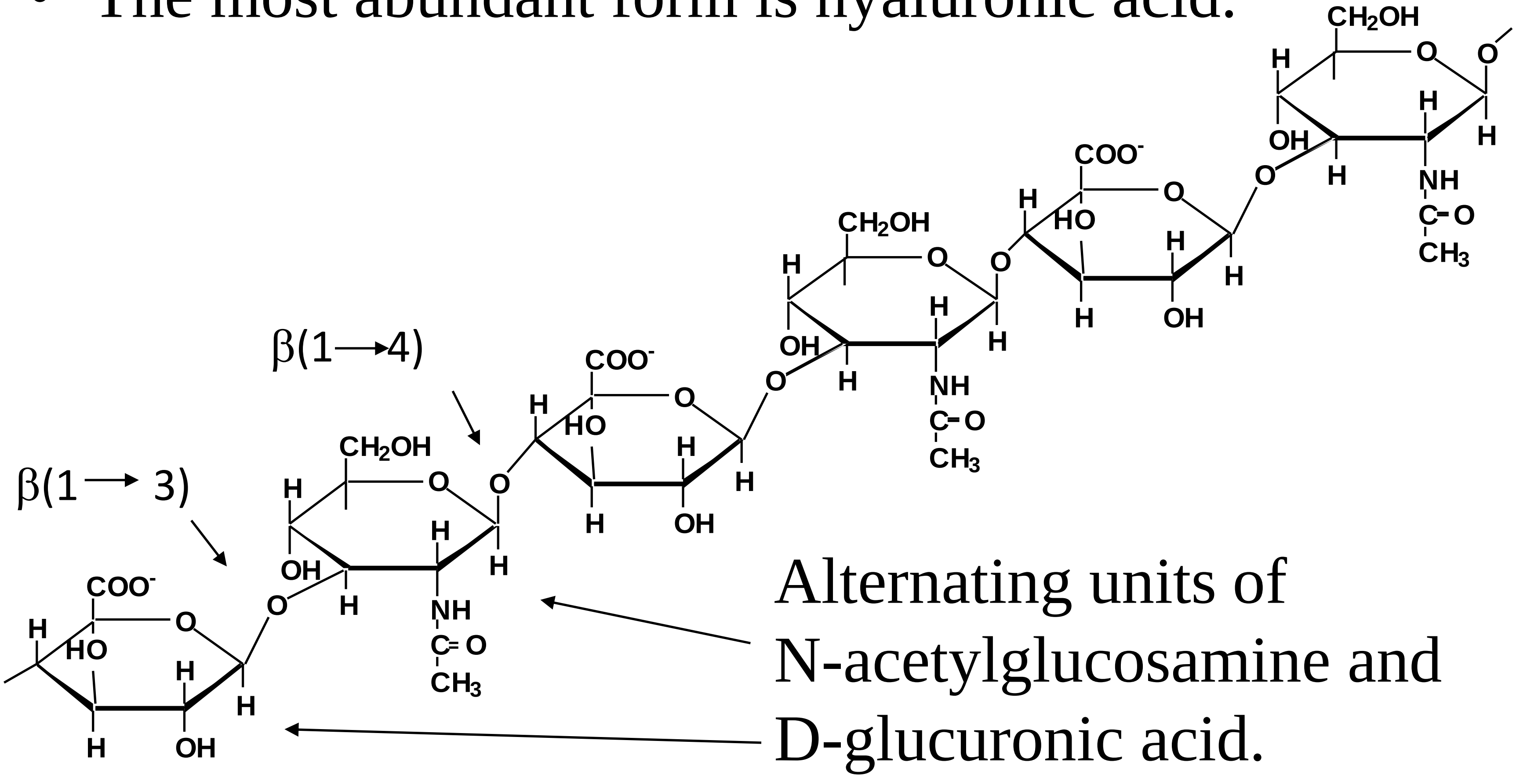
Every other glucose is flipped over, due to β linkages.



cellulose

Mucopolysaccharides

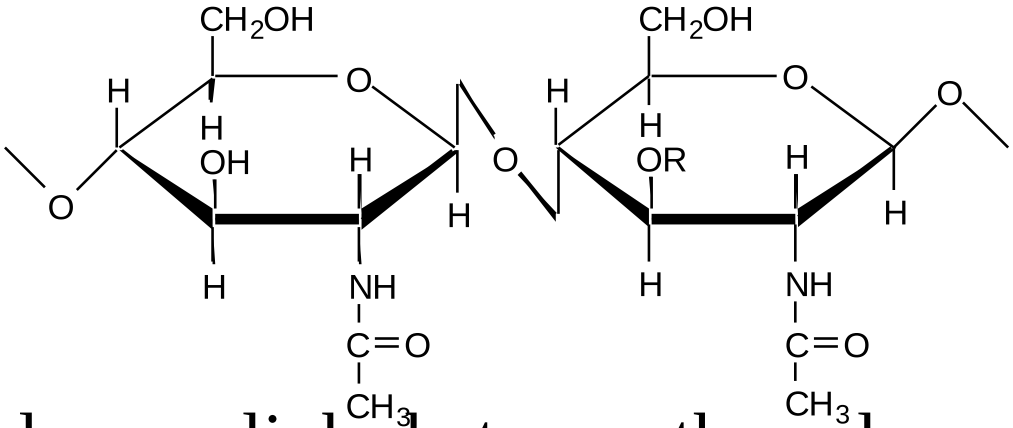
- These materials provide a thin, viscous, jelly-like coating to cells.
- The most abundant form is hyaluronic acid.



Alternating units of N-acetylglucosamine and D-glucuronic acid.

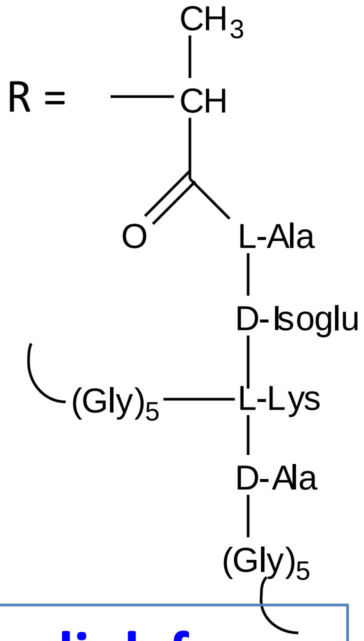
Structural peptidoglycans

- Bacterial cell walls are composed primarily of an unbranched polymer of alternating units of N-acetylglucosamine and N-acetylmuramic acid.



Peptide crosslinks between the polymer strands provide extra strength

- varies based on bacterium.



crosslink for *Staphylococcus aureus*

Glycoproteins

- Proteins that carry covalently bound carbohydrate units.
- They have many biological functions.

E.g. immunological protection, cell-cell recognition, blood clotting, host-pathogen interaction.

Glycoprotein structure

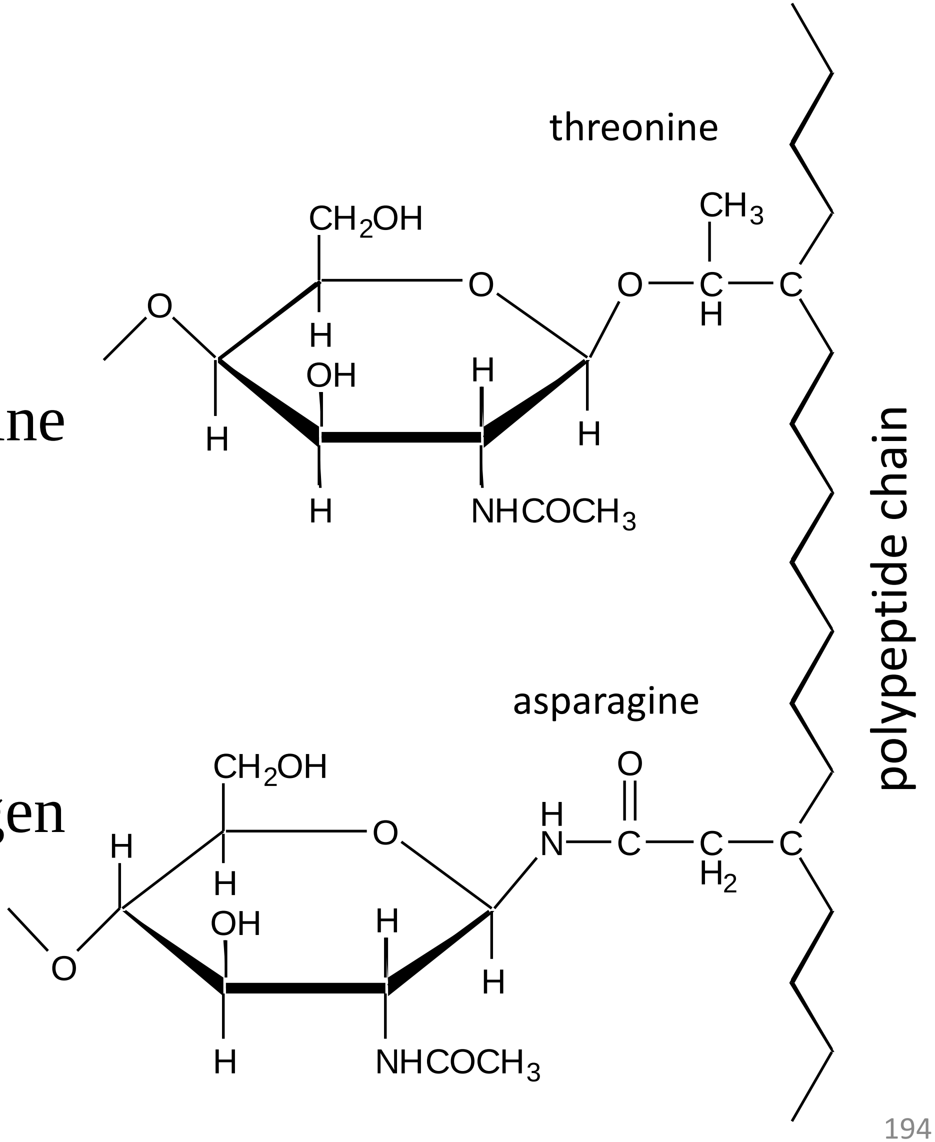
- Carbohydrates only account for 1-30% of the total weight of a glycoprotein.
- The most common mono saccharides found in Glycoprotein are:
    - Glucose, mannose, galactose, fucose, sialic acid N-acetylgalactosamine, N-acetylglucosamine

Glycoprotein structure

- Linking sugars to proteins.

- O-glycosidic bonds using hydroxyl groups of serine and threonine

- N-glycosidic bonds using side chain amide nitrogen of asparagine residue.



Functions of Carbohydrates

- Supplies energy
- Protein sparing
- Prevents ketosis (**overproduction of ketones).**
- Food sweeteners
  - Fructose
  - Sucrose
  - Glucose
  - Maltose
  - Galactose

Why is sugar added to foods?

- flavour enhancement
- provide texture and colour
- permits fermentation
- adds bulk
- acts as a preservative
- balance acidity

Functions of Dietary Fiber

- Promotes regularity and softer, larger stool
- Reduces hemorrhoids and diverticulitis
- Aids weight control
- Causes a filling of fullness
- Slows glucose absorption
- Decrease in colon cancer
- Reduces cholesterol absorption
- Reduces heart disease

Chapter-6- lipids

6.1 free Fatty Acids

- Fatty acids are aliphatic mono-carboxylic acids that are mostly obtained from the hydrolysis of natural fats and oils.
- Have a carboxyl group (-COOH) at one end and a methyl group (CH_3) at the other end.
- Have the general formula R-$(CH_2)_n$-COOH and with a few exception natural fatty acids have straight chain (a few exceptions have branched and heterocyclic chains). In this formula "n" is mostly an even number of carbon atoms (2-34) with a few exceptions that have an odd number.
- Fatty acids are classified according to several bases as follows:

According to presence or absence of double bonds fatty acids can be classified into **Saturated & unsaturated Fatty Acids**

- 6.1.1. Saturated Fatty Acids
- they have not double bonds with 2-24 or more carbons.
- They are solid at room temperature except if they are short chained.
- They may be even or odd number C.
- They have the molecular formula of, $C_nH_{2n+1}COOH$.

Eg. Butter, lard, coconut oil, palm oil, and fully hydrogenated vegetable oils, Poultry skin, whole milk

A-Short chain Saturated F.A. (2-10 carbon).

i-Short chain Saturated volatile F.A.(2-6 carbon).

ii- Short chain Saturated non volatile F.A.(7-10 carbon).

i-Volatile short-chain fatty acids:

- They are liquid in nature and contain (1-6) carbon atoms.
- water-soluble and volatile at room temperature, e.g., acetic, butyric, and caproic acids.
- Acetic F.A. (2C) CH_3-COOH.
- Butyric F.A. (4C) $CH_3-(CH_2)_2$-COOH.
- Caproic F.A. (6C) $CH_3-(CH_2)_4$-COOH.

ii-Non-volatile short-chain fatty acids:

- are solids at room temp. and contain 7-10 C atoms.
- are water-soluble & non-volatile at room tempreture include:

caprylic F.A (8 C) CH_3-$(CH_2)_6$-COOH

Capric F.A (10 C) CH_3-$(CH_2)_8$-COOH.

B-Long chain Saturated F.A.(more the10 carbon)

- They contain more than 10 carbon atoms.
- They occur in hydrogenated oils, animal fats, butter and coconut and palm oils.
- They are non-volatile and water-insoluble
- Include palmitic, stearic, and lignoceric F.A.
- palmitic(16C) CH_3-$(CH_2)_{14}$-COOH
- stearic (18 C) CH_3-$(CH_2)_{16}$-COOH
- lignoceric (24C) CH_3-$(CH_2)_{22}$-COOH

6.1.2. Unsaturated Fatty Acids

6.1.2.1. Mono-Unsaturated Fatty Acids

- Are only one double bond containing fatty acids; Therefore, two H atoms can be added
- Liquid at room temperature
  - Olive oil, canola oil, peanut oil
  - Other sources: avocado, almonds, cashews, pecans and sesame seeds.

1-Palmitoleic acid :

- It is found in all fats.
- It is $C16:1(\Delta^{9})$ i.e., has 16 carbons and one double bond located at carbon number 9 and involving carbon 10.

$$CH_3\text{-}(\ CH_2\ )_5CH\ = CH\text{-}(CH_2)_7 – COOH$$

2-Oleic acid

- Is the most common fatty acid in natural fats.
- It is $C18:1\Delta^9$, i.e., has 18 carbons and one double bond located at carbon number 9 and involving carbon 10.

CH_3-$(CH_2)_7$- CH=CH – $(CH_2)_7$-COOH

3-Nervonic acid

(Unsaturated lignoceric acid).

- It is found in cerebrosides.
- It is $C24:1\Delta^{15}$, i.e., has 24 carbons and one double bond located at carbon number 15 and involving carbon 16.

CH_3 – $(CH_2)_7$ CH= CH – $(CH_2)_{13}$- COOH

6.1.2.2-Polyunsaturated fatty acids:

Definition:

- They are essential fatty acids that can not be synthesized in the human body and must be taken in adequate amounts in the diet.
- They are required for normal growth and metabolism
- Source: vegetable oils such as corn oil, linseed oil, peanut oil, olive oil, cottonseed oil, soybean oil and many other plant oils, cod liver oil and animal fats.
- Deficiency: Their deficiency in the diet leads to nutrition deficiency disease.
- Its symptoms include: poor growth and health with susceptibility to infections, dermatitis, decreased capacity to reproduce, impaired transport of lipids, fatty liver, and lowered resistance to stress.

- Poly-Unsaturated Fatty Acids have two or more double bonds

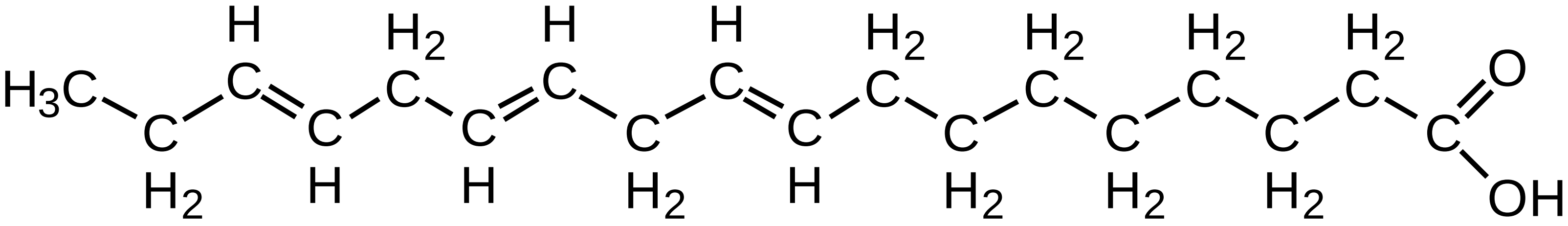
Eg. omega-3 and omega-6 fatty acids (essential fatty acids we must be found in diet b/c Tissues can not synthesize

- Linoleic acid: omega 6 fatty acid (2double bond)
- Linolenic acid & Arachidonic acid are omega 3 fatty acid (3double bond)
    - Arachidonic acid (Not found in plants) can be synthesized from linoleic acid in most mammals (except in cat)
        - *Essential nutrient in the diet of cats.*
        - so Arachidonic acid is not essential.
- Richest sources of poly-unsaturated fatty acids include:
    - Vegetable oils
        - Corn, sunflower, safflower, cotton seed oils

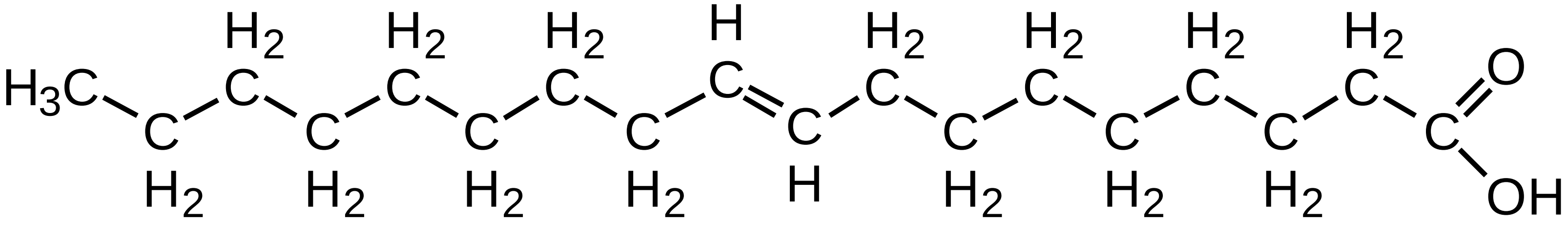
Fatty-acid Nomenclature

Omega system

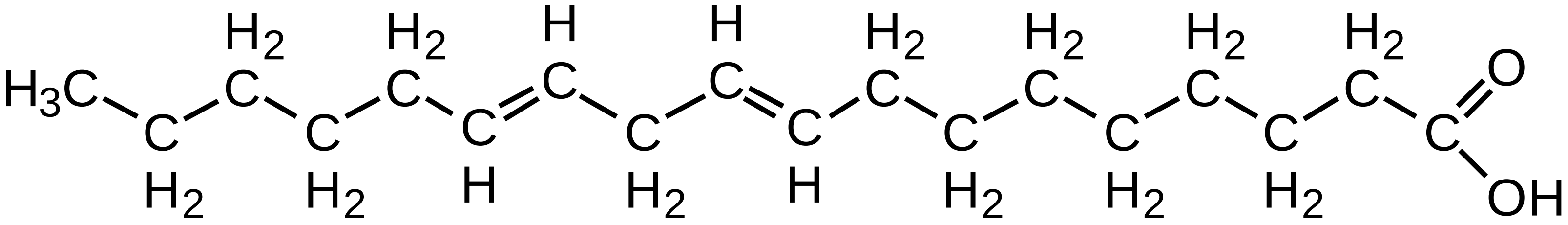
- Named according to the location of the *first* double bond from the non-carboxyl end (count from the methyl end)
  - Omega system (e.g., omega 3, ω3)
  - n–system (e.g., n–3)



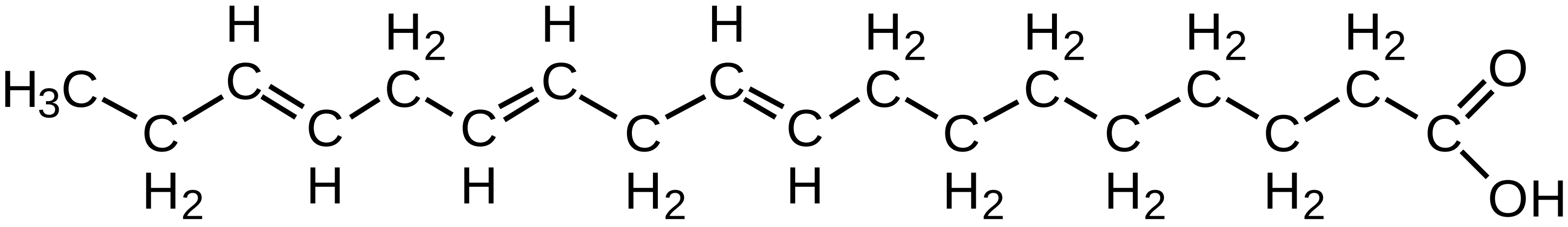
Fatty-acid Nomenclature



Omega 9 or n–9 fatty acid



Omega 6 or n–6 fatty acid



Omega 3 or n–3 fatty acid

- The common pattern in the location of double bonds;Δ^{9}, Δ^{12} and Δ^{15}.
- The double bonds of polyunsaturated fatty acids are almost never conjugated

$$–CH=CH-CH=CH-$$

but are separated by a methylene group

$$-CH=CH-CH_2-CH=CH-$$

- In nearly all naturally occurring unsaturated fatty acids, the double bonds are in the cis configuration
- Diets those have high in trans fatty acids correlate

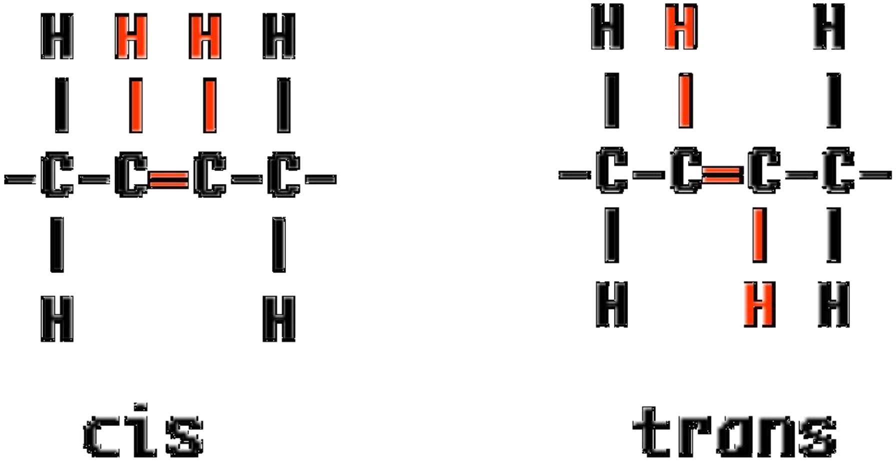
with increased blood levels of LDL (bad cholesterol) and decreased HDL (good cholesterol)

Acids	Carbons	Double bonds	Abbreviation	Source
Acetic	2	0	2:0	bacterial metabolism
Propionic	3	0	3:0	bacterial metabolism
Butyric	4	0	4:0	butterfat
Caproic	6	0	6:0	butterfat
Caprylic	8	0	8:0	coconut oil
Capric	10	0	10:0	coconut oil
Lauric	12	0	12:0	coconut oil
Myristic	14	0	14:0	palm kernel oil
Palmitic	16	0	16:0	palm oil
Palmitoleic	16	1	16:1	animal fats
Stearic	18	0	18:0	animal fats
Oleic	18	1	18:1	olive oil
Linoleic	18	2	18:2	grape seed oil
Linolenic	18	3	18:3	flaxseed (linseed) oil
Arachidonic	20	4	20:4	peanut oil, fish oil

Isomers of fatty acids

- Geometrical isomers due to double bond
  - Cis
    - occurs naturally
    - bend in acyl chain
  - Trans
    - Not as common
    - Found in hydrogenated oils
    - Results from bacterial synthesis
      - In fats in ruminants!!
    - Straight acyl chains

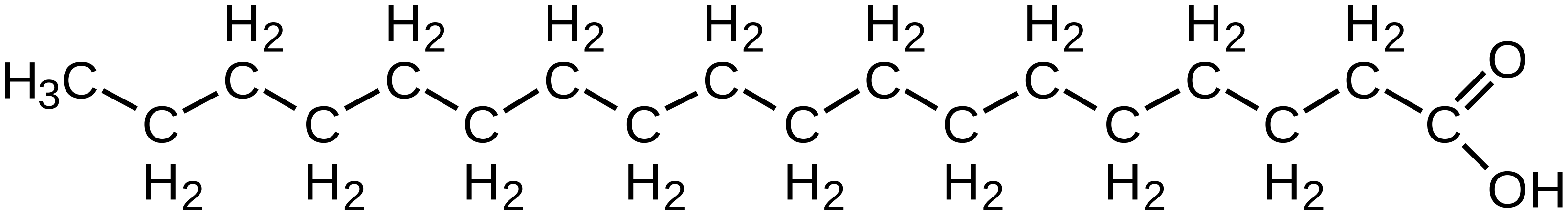
- Chain branching
  - Straight
    - Synthesized by mammals and plants
  - Branched
    - Synthesized by bacteria

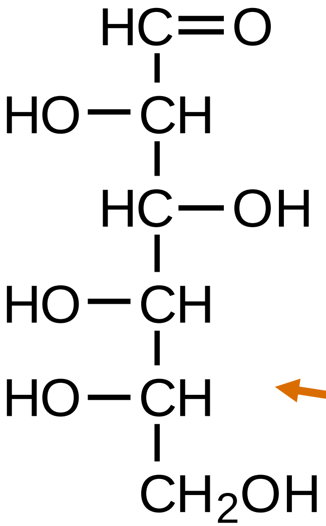


Traits of Fatty Acids

- Unsaturated fatty acids oxidize spontaneously in presence of oxygen
  - Auto-oxidation, peroxidation, rancidity
  - Free radicals formed
    - Reduce nutritional value of fats
  - Antioxidants prevent oxidation
    - Vitamins C and E, selenium
- Fatty acids form “soaps” with cations
  - Na & K soaps – water soluble
  - Ca & Mg soaps – not water soluble
    - Poorly digested

Fatty acid or Glucose more reduced?





More reduced state (more H bound to C)
⇒ More potential for oxidation

Less reduced state (more O bound to C)
⇒ Less potential for oxidation

Compared to carbohydrates, fatty acids contain more hydrogen molecules per unit of carbon, thus, they are in a more reduced form.

Carbohydrates are partially oxidized so they contain less potential energy (H+ and e-) per unit of carbon.

Function of Essential Fatty Acids

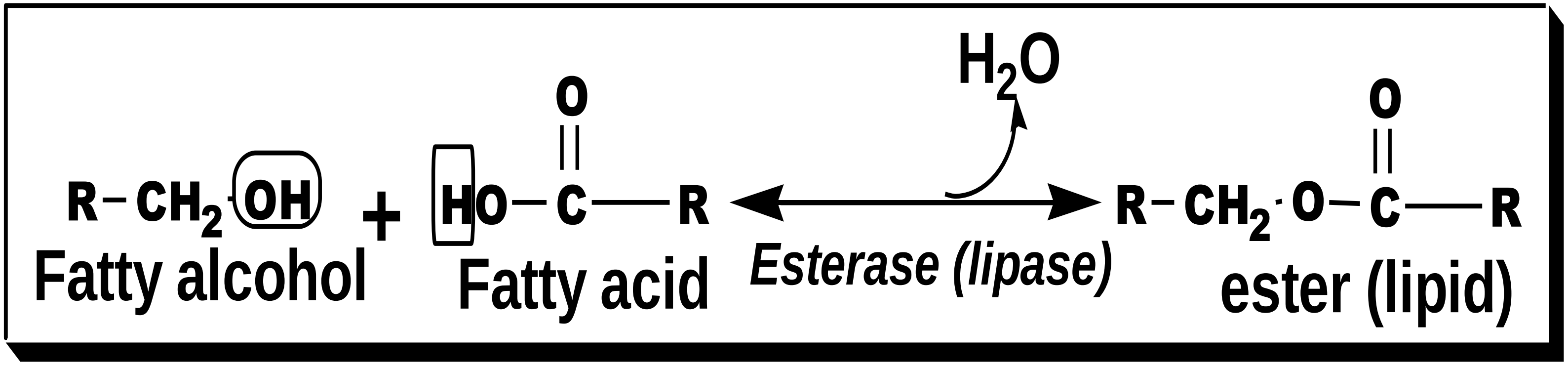
1. They are useful in the treatment of atherosclerosis by help transporting blood cholesterol and lowering it and transporting triglycerides.
2. The hormones are synthesized from them.
3. They enter in structure of all cellular and subcellular membranes and the transporting plasma phospholipids.
4. They are essential for skin integrity, normal growth and reproduction.
5. They have an important role in blood clotting (intrinsic factor).
6. Important in preventing and treating fatty liver.
7. Important role in health of the retina and vision.
8. They can be oxidized for energy production.

Functions of Essential Fatty Acids

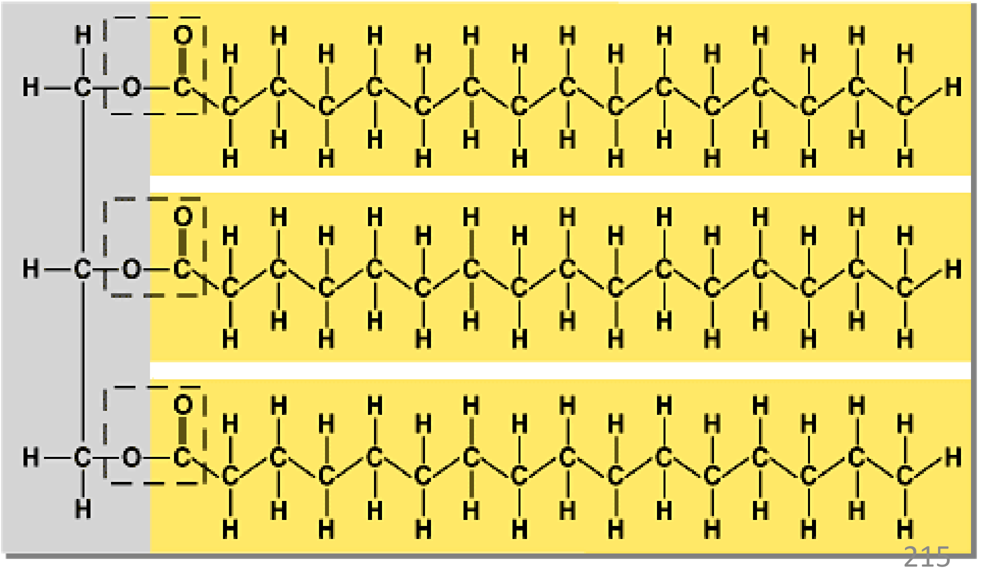
- A component of the phospholipids in cell membranes
- Precursor for prostaglandins: arachidonic acid
- Important metabolic regulator
  - Contraction of smooth muscle
  - Aggregation of platelets
  - Inflammation
- **Deficiency of essential fatty acid intakes:**
  - Growth retardation
  - Problems with reproduction
  - Skin lesions
  - Kidney and liver disorders

6.1 Definition of **Lipids**

- Lipids are organic compounds formed mainly from alcohol and fatty acids combined together by ester linkage.



- Lipids are the polymer of fatty acids.



- lipids have hydrophobic properties due to the aliphatic chain of fatty acids or simply fats.
- - Lipids are insoluble in water, but soluble in fat or organic solvents (ether, chloroform, benzene, acetone).
- - Lipids include **fats, oils, waxes** and related compounds.
- They are widely distributed in nature both in plants and in animals.

Biological Importance of Lipids:

1. They are more palatable and storable to unlimited amount compared to carbohydrates.
2. They have a high-energy value (25% of body needs) and they provide more energy per gram than carbohydrates and proteins but carbohydrates are the preferable source of energy.

3. They Supply the essential fatty acids that cannot be synthesized by the body.

4. Supply the body with fat-soluble vitamins (A, D, E and K).

5. They are important constituents of the nervous system.

6. Tissue fat is an essential constituent of cell membrane and nervous system. It is mainly phospholipids in nature that are not affected by starvation.

7-Stored lipids “depot fat” is stored in all human cells acts as:

- **A store of energy.**
- **A pad for the internal organs to protect them from outside shocks.**
- **A subcutaneous thermal insulator against loss of body heat.**

8-Lipoproteins, which are complex of **lipids** and **proteins**, are important cellular constituents that present both in the cellular and subcellular membranes.

9. **Cholesterol** enters in membrane structure and is used for synthesis of adrenal cortical hormones, vitamin D3 and bile acids.

10. Lipids provide bases for dealing with diseases such as obesity, atherosclerosis, lipid-storage diseases, essential fatty acid deficiency, respiratory distress syndrome.

Classification of Lipids

1. **Simple lipids (Fats & Waxes)**
2. **Compound or conjugated lipids**
3. **Derived Lipids**
4. **Lipid-associating substances**

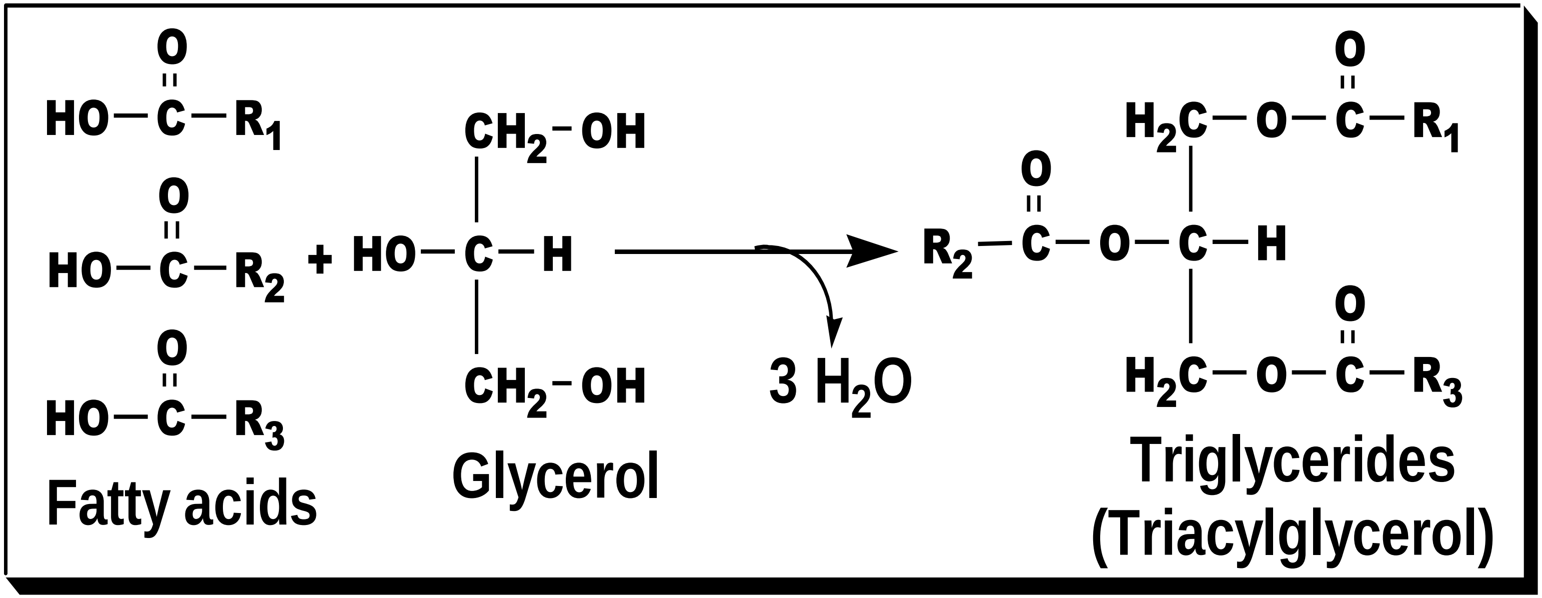
Simple Lipids: Neutral Fats and oils

Definition:

A triglyceride (TG, triacylglycerol, TAG, or triacylglyceride) is Composed of one glycerol molecule and three fatty acids connected by an ester bond (bond between an alcohol and and organic acid). It is the most common structure in dietary lipids.

- They are called neutral because they are uncharged due to absence of ionizable groups in it.
- The main difference between fats and oils is for oils being liquid at room temperature, whereas, fats are solids.
- The neutral fats are the most abundant lipids in nature. They constitute about 98% of the lipids of adipose tissue, 30% of plasma or liver lipids, less than 10% of erythrocyte lipids.

- They are esters of glycerol with various fatty acids. Since the 3 hydroxyl groups of glycerol are esterified, the neutral fats are also called “Triglycerides”.
- Esterification of glycerol with one molecule of fatty acid gives monoglyceride, and that with 2 molecules gives diglyceride and with 3 molecules gives triglyceride.



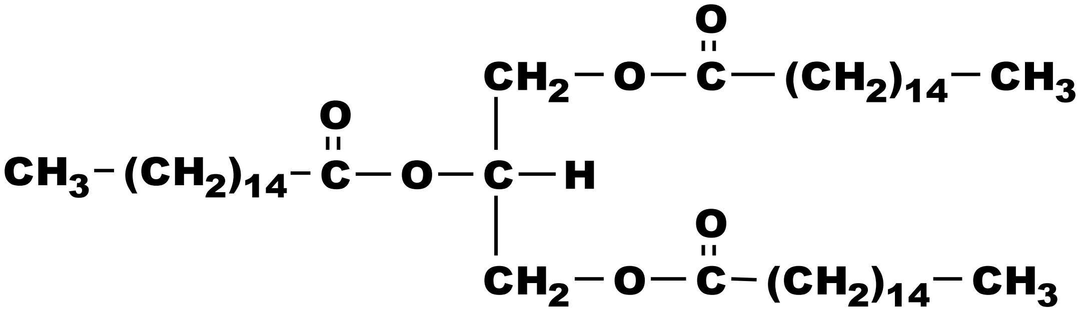
- Neutral fats and oils are **Simple Lipids.**
  - Monoacyl glycerols (monoglycerides)
  - Diacyl glycerols (diglycerides) (found in plant leaves)
  - Triacyl glycerols (triglycerides)
    - Triglycerides found in seeds and animal adipose tissue.
    - Lipid storage form
    - Most lipids consumed are triglycerides

Types of triglycerides

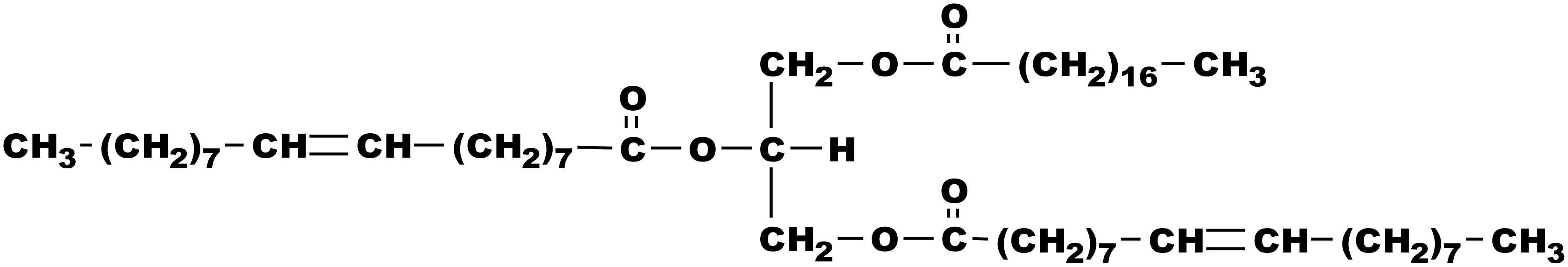
1-Simple triglycerides: If the three fatty acids connected to glycerol are of the same type the triglyceride is called simple triglyceride, e.g., tripalmitin.

2-Mixed triglycerides: if they are of different types, it is called mixed triglycerides, e.g., stearo-diolein and palmito-oleo-stearin.

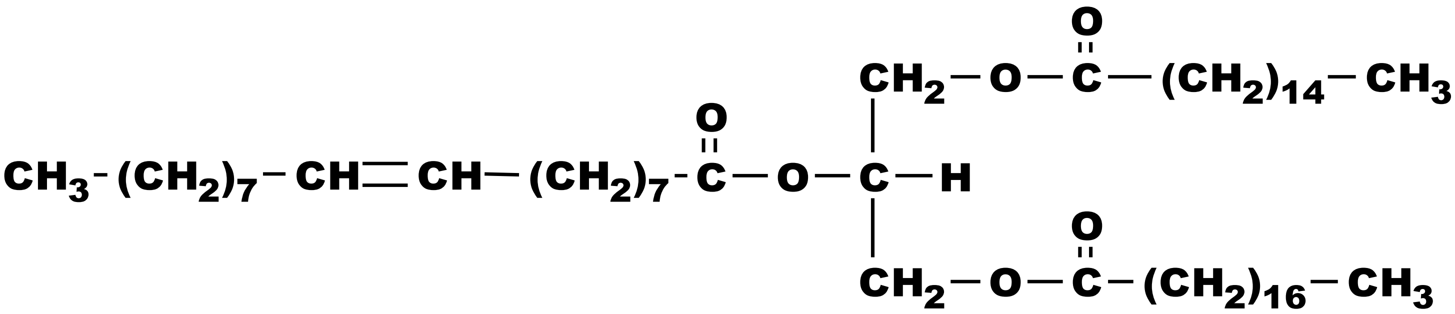
- Natural fats are mixtures of mixed triglycerides with a small amount of simple triglycerides.



Tripalmitin
(simple triacylglycerol)



1-Stearo-2,3-diolein
(mixed triacylglycerol)



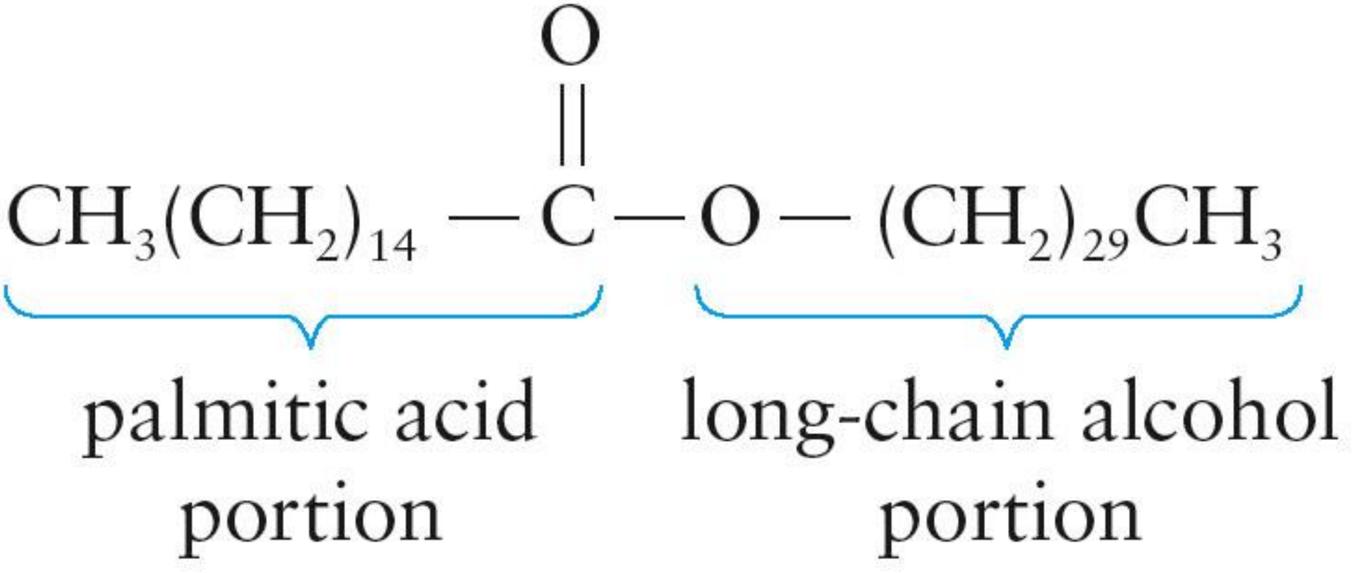
1-palmito-2-oleo-3-stearin
(mixed triacylglycerol)

Physical properties of fat and oils:

1. Freshly prepared fats and oils are colorless, odorless and tasteless. Any color, or taste is due to association with other foreign substances, e.g., the yellow color of body fat or milk fat is due to carotene pigments(cow milk).
2. Fats have specific gravity less than 1 and, therefore, they float on water.
3. Fats are insoluble in water, but soluble in organic solvents as ether and benzene.
4. Melting points of fats are usually low, but higher than the solidification point,

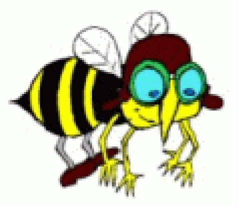
Waxes

- **Definition**: Waxes are solid simple lipids containing a monohydric alcohol (with a higher molecular weight than glycerol) esterified to long-chain fatty acids.
- Ester formed from a long chain carboxylic acid (fatty acid) and a long chain alcohol



$$\underbrace{CH_3(CH_2)_{14}-\overset{O}{\overset{\|}{C}}}_{\text{palmitic acid portion}}\underbrace{-O-(CH_2)_{29}CH_3}_{\text{long-chain alcohol portion}}$$

BEESWAX-Glands under the abdomen of bees secrete a wax, which they use to construct the honeycomb. The wax is recovered as a by-product when the honey is harvested and refined.



LANOLIN - The grease obtained from the wool of sheep during the cleaning or refining process is rich in wax


© Sean Fitzgerald

BIRD WAXES -Special glands of birds secrete waxes that consist largely of wax esters. The main purpose of the waxes is to give a water-proof layer to the feathers.

MARINE WAXES - Waxes appear to have a variety of functions in fish, from serving as an energy source to insulation and buoyancy.

PLANT WAXES -The wax provides protection from disease and insects, and helps the plants resist drought.

Differences between neutral lipids and waxes:

	Waxes	Neutral lipids
1.Digestibility:	Indigestible (not hydrolyzed by lipase).	Digestible (hydrolyzed by lipase).
2-Type of alcohol:	Long-chain monohydric alcohol + one fatty acid.	Glycerol (trihydric) + 3 fatty acids
3-Type of fatty acids:	Fatty acid mainly palmitic or stearic acid.	Long and short chain fatty acids.
4-Acrolein test:	Negative.	Positive.
5-Rancidability:	Never get rancid.	Rancidible.
6-Nature at room temperature.	Hard solid.	Soft solid or liquid.
7-Saponification	Nonsaponifiable.	Saponifiable.
8-Nutritive value:	No nutritive value.	Nutritive.
9-Example:	Bee & carnuba waxes.	Butter and vegetable oils.

Compound Lipids

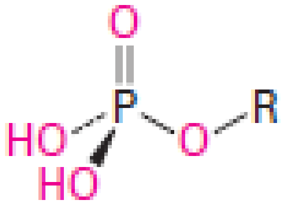
Definition:

- They are lipids that contain additional substances, e.g., sulfur, phosphorus, amino group, carbohydrate, or proteins beside fatty acid and alcohol.
- Compound or conjugated lipids are classified into the following types according to the nature of the additional group:

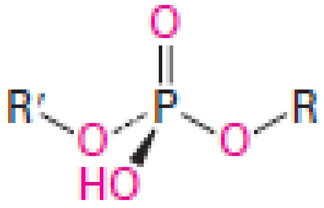
1. Phospholipids
2. Glycolipids.
3. Lipoproteins
4. Sulfolipids and amino lipids.

Phospholipids

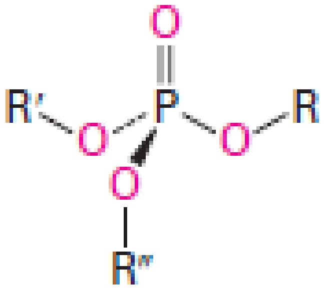
- Definition: Just as waxes, fats, and oils are esters of carboxylic acids, phospholipids are esters of phosphoric acid, H_3PO_4.
- Or Phospholipids or phosphatides are compound lipids, which contain phosphoric acid group in their structure.



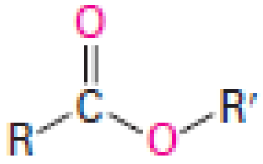
A phosphoric acid monoester



A phosphoric acid diester



A phosphoric acid triester



A carboxylic acid ester

Importance

1. The membranes bounding cells and subcellular organelles are composed mainly of phospholipids. Thus, the transfer of substances through these membranes is controlled by properties of phospholipids.

1. They are important components of the lipoprotein coat essential for secretion and transport of plasma lipoprotein complexes. Thus, they are lipotropic agents that prevent fatty liver.
2. Myelin sheath of nerves is rich with phospholipids.
3. Important in digestion and absorption of neutral lipids and excretion of cholesterol in the bile.
4. Important function in blood clotting and platelet aggregation.
5. They provide lung alveoli with surfactants that prevent its irreversible collapse.
6. Important role in signal transduction across the cell membrane.

7. Phospholipase A2 in snake venom hydrolyses membrane phospholipids into hemolytic lysolecithin or lysocephalin.

8. They are source of polyunsaturated fatty acids for synthesis of eicosanoids.

Sources: They are found in all plant and animal cells (Every animal and plant cell contains phospholipids), milk and egg-yolk in the form of lecithins. They are present in large amounts in the liver and brain as well as blood.

Structure: phospholipids are composed of:

1. Fatty acids (a saturated and an unsaturated fatty acid).
2. Nitrogenous base (choline, serine, threonine, or ethanolamine).
3. Phosphoric acid.
4. Fatty alcohols (glycerol, inositol or sphingosine).

Phospholipids are classified into 2 groups according to the type of the alcohol present into two types:

A-Glycerophospholipids: They are regarded as derivatives of phosphatidic acids that are the simplest type of phospholipids and include:

1. Phosphatidic acids.
2. Lecithins
3. Cephalins.
4. Plasmalogens.
5. Inositides.
6. Cardiolipin.

B-Sphingophospholipids: They contain sphingosine as an alcohol and are named Sphingomyelins.

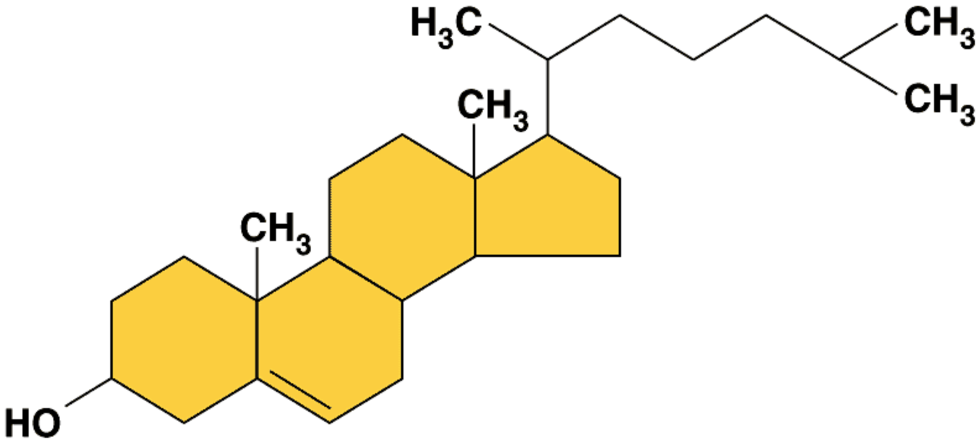
The two major lipids found in the blood are cholesterol and triglycerides.

Cholesterol

helps keep cell membranes fluid & flexible

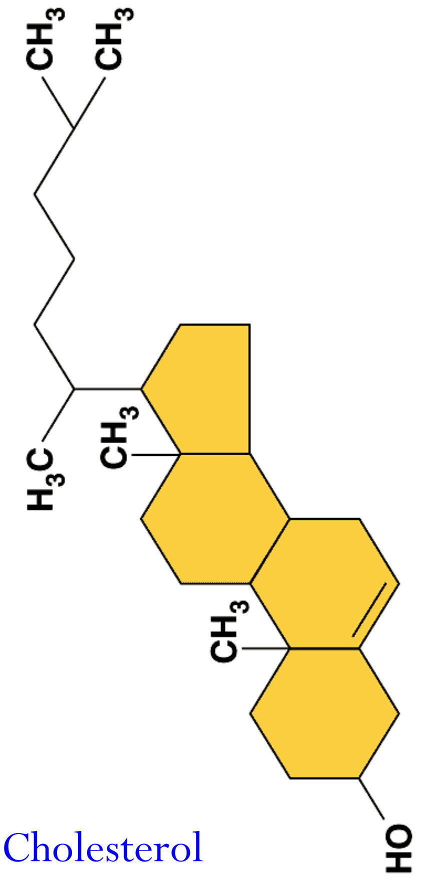
- Important cell component
- animal cell membranes- Structural
- precursor of all other steroids
- including vertebrate sex hormones

- high levels in blood may contribute to cardiovascular disease

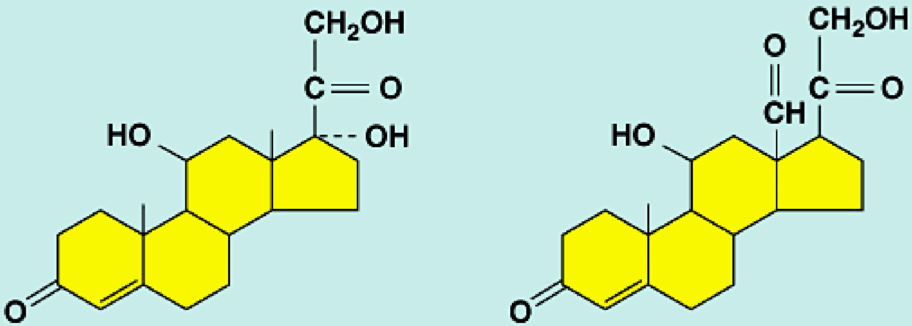


From Cholesterol → Sex Hormones

- What a big difference a few atoms can make!



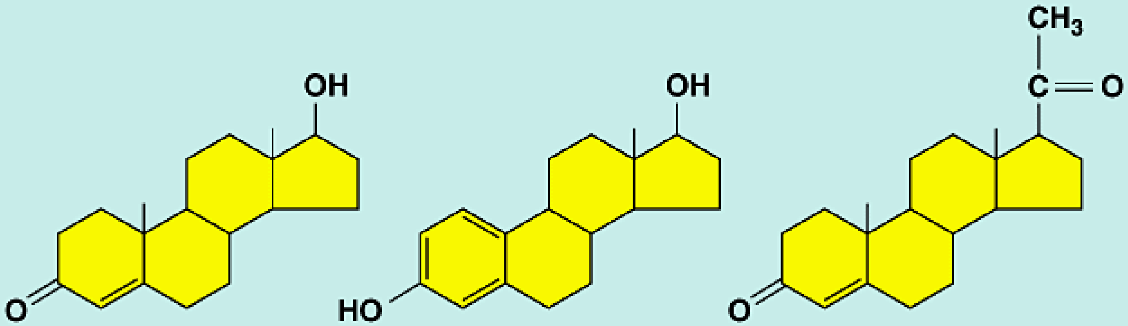
Cholesterol



Cortisol
(a glucocorticoid)

Aldosterone
(a mineralocorticoid)

(a) Steroid hormones made in adrenal cortex



Testosterone
(an androgen)

Estradiol
(an estrogen)

Progesterone
(a progestin)

(b) Steroid hormones made primarily in gonads

Sterols (Steroids) are;

- Cholesterol, ergosterol, bile acids
- Compounds with multi-ring structure
- Insoluble in water
- Present both in plant and animal foods but Major sterol is cholesterol

✓ cholesterol is found only in animal products (manufactured in liver)

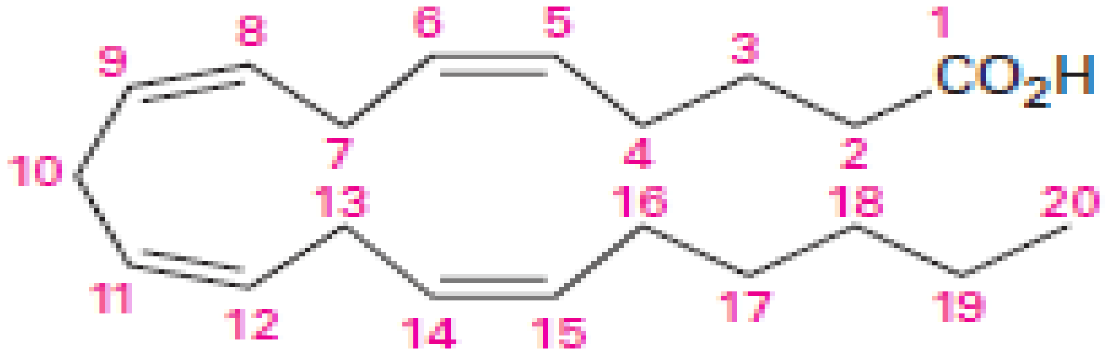
  - High content in organ meats and egg yolk

Prostaglandins

- The prostaglandins are a group of C_{20} lipids that contain a five-membered ring with two long side chains.

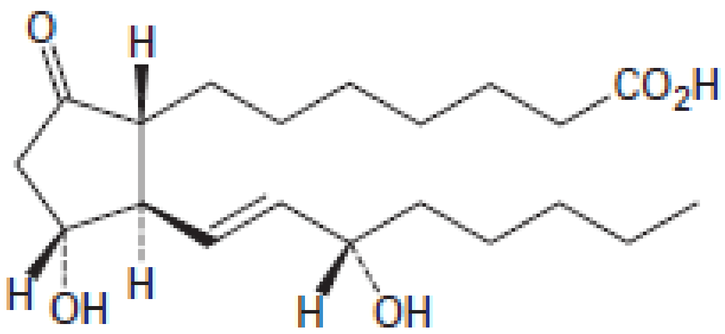
The several dozen known prostaglandins have an Extraordinarily wide range of biological effects. Among their many properties, they can lower blood pressure, affect blood platelet aggregation during clotting, lower gastric secretions, control inflammation, affect kidney function, affect reproductive systems, and stimulate uterine contractions during childbirth.

- Prostaglandins, together with related compounds called thromboxanes and leukotrienes, make up a class of compounds called **eicosanoids** because they are derived biologically from 5,8,11,14-eicosatetraenoic acid, or arachidonic acid.

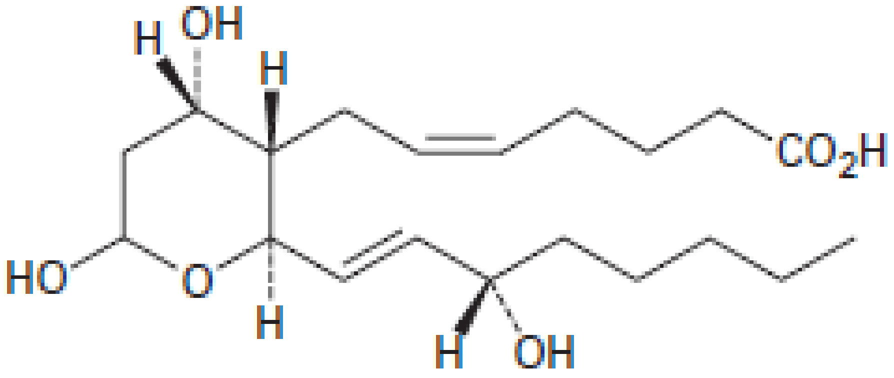


Arachidonic acid

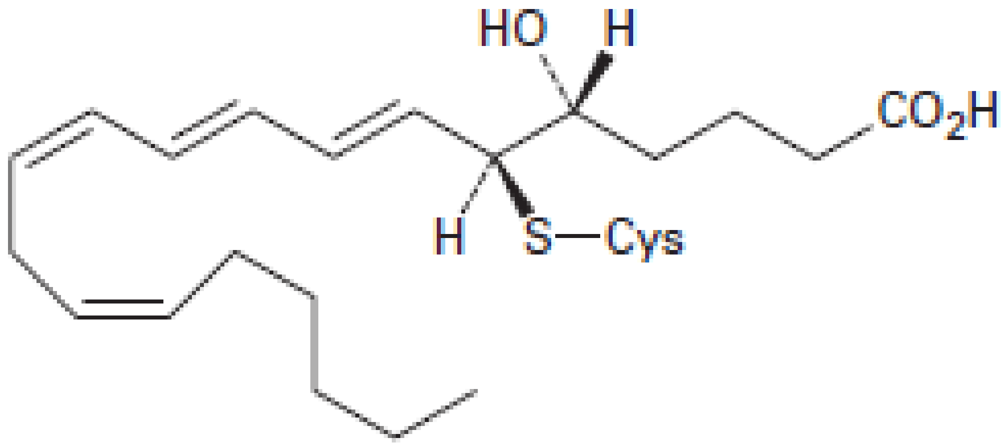
Prostaglandins (PG) have a cyclopentane ring with two long side chains; thromboxanes (TX) have a six-membered, oxygen-containing ring; and leukotrienes (LT) are acyclic.



Prostaglandin E_1 (PGE_1)



Thromboxane B_2 (TXB_2)



Leukotriene E_4 (LTE_4)

Functions and Properties Lipids

- Concentrated source of energy (9 kcal/gm)
- Energy reserve: any excess energy from carbohydrates, proteins and lipids are stored as triglycerides in adipose tissues.
- Provide insulation to the body from cold;
  - Maintain body temperature
- Mechanical insulation;
  - Protects vital organs

- Electrical insulation
  - Protects nerves, help conduct electro-chemical impulses (myelin sheath)
- Supply essential fatty acids (EFA)
  - Linoleic acid and linolenic acid
- Formation of cell membranes
  - Phospholipids, a type of fat necessary for the synthesis of every cell membrane (also glycoproteins and glycolipids)