Biochemistry

Najaf Polytechnic Collage

Biochemistry: introduction
1st Lecture

Assistant lecturer. Hayder Abed

Biochemistry or biological chemistry

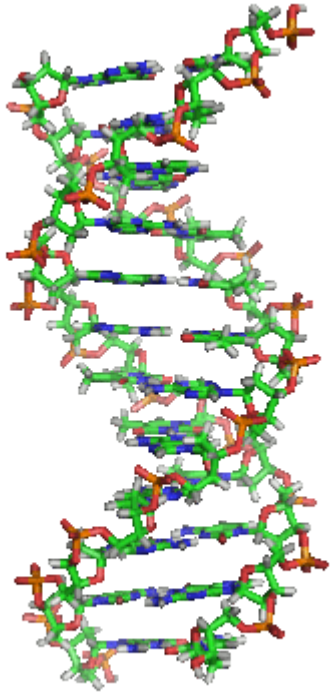
I. OVERVIEW

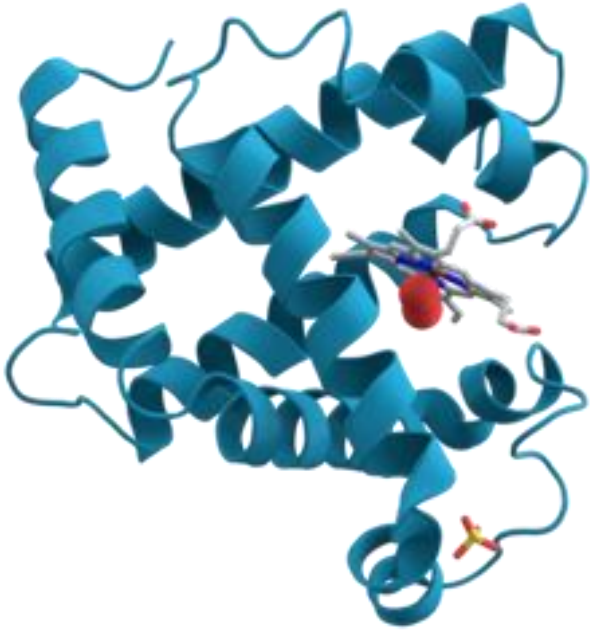
Biochemistry, or **biological chemistry** (distinct from chemical biology), is the study of chemical processes within and relating to living organisms

II. History

The term "biochemistry" was first used when Vinzenz Kletzinsky (1826–1882) had his "Compendium der Biochemie" printed in Vienna in 1858; it derived from a combination of biology and chemistry. In 1877,

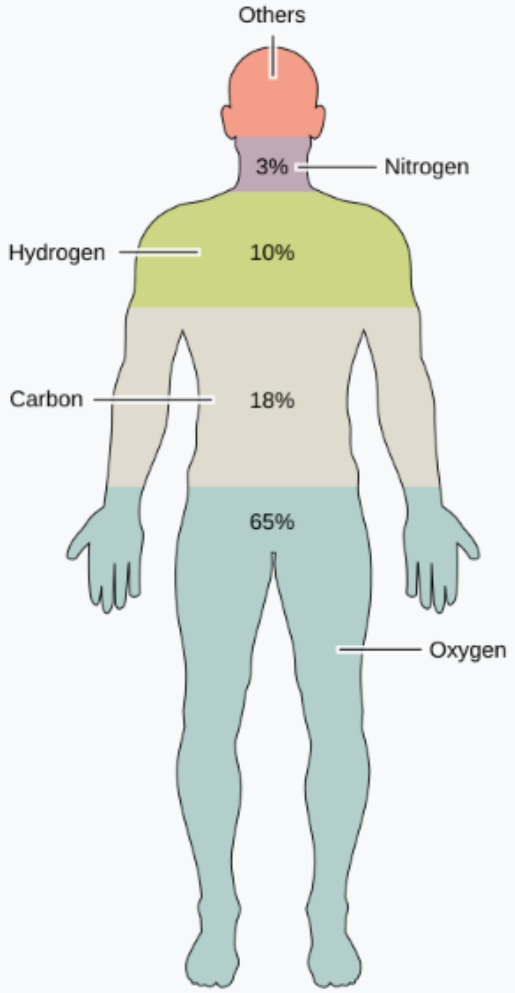






chemical elements of life

I. Elements



Element	Symbol	percent mass	percent atoms
Oxygen	O	65.0	24.0
Carbon	C	18.5	12.0
Hydrogen	H	9.5	62.0
Nitrogen	N	2.6	1.1
Calcium	Ca	1.3	0.22
Phosphorus	P	0.6	0.22
Sulfur	S	0.3	0.038
Potassium	K	0.2	0.03
Sodium	Na	0.2	0.037
Chlorine	Cl	0.2	0.024
Magnesium	Mg	0.1	0.015
All others		< 0.1	< 0.3

About 99% of the mass of the human body is made up of six elements: O, C, N, Ca, and P.
Only about 0.85% is composed of another five elements: K, S, Na, Cl, & Mg

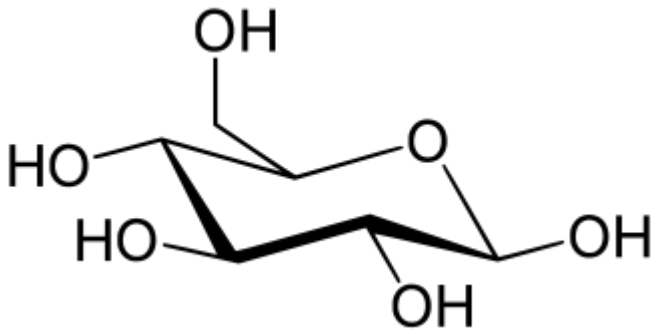
chemical Biomolecules of life

II. Biomolecules

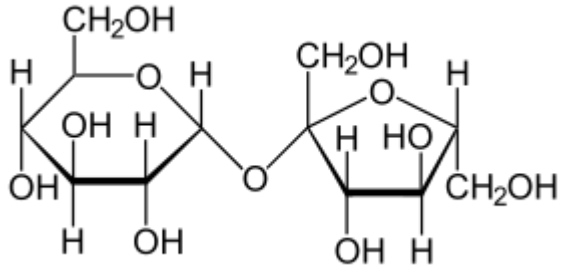
The 4 main classes of molecules in biochemistry (often called biomolecules) are carbohydrates, lipids, proteins, and nucleic acids

III. Carbohydrate

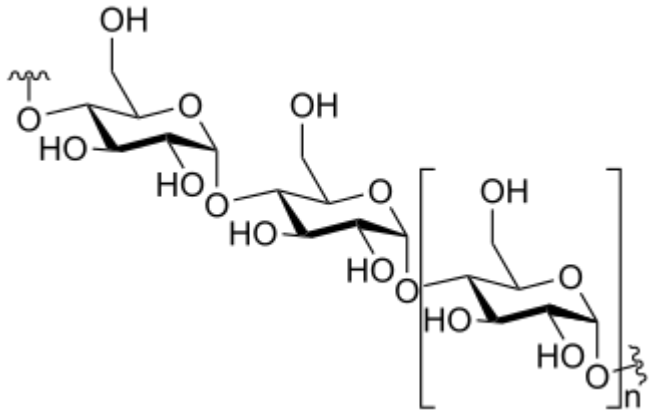
Two of the main functions of carbohydrates are energy storage and providing structure. One of the common sugars known as glucose is a carbohydrate, but not all carbohydrates are sugars.



monosaccharide



sucrose (glucose + fructose),



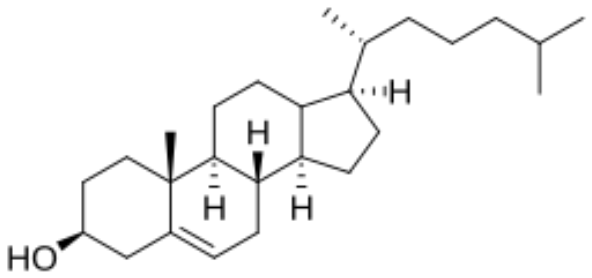
Amylose, a polysaccharide

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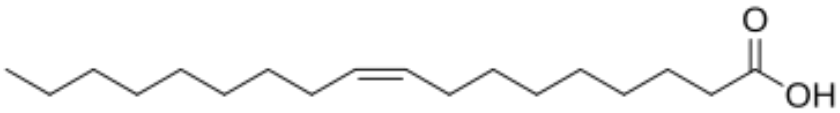
IV. Lipids

Lipids comprise a diverse range of molecules and to some extent is a catchall for relatively water-insoluble or nonpolar compounds of biological origin, including waxes, fatty acids,

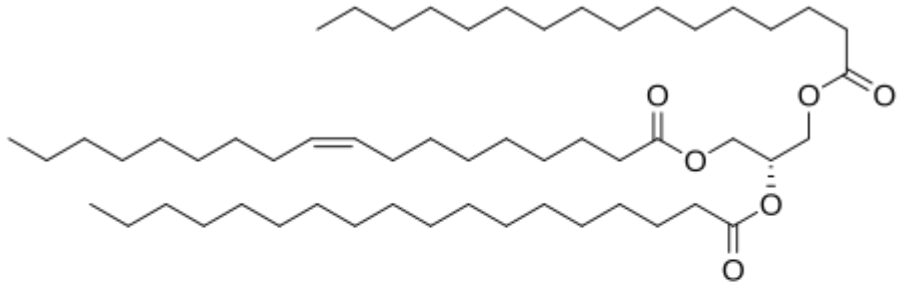
fatty-acid derived phospholipids, sphingolipids, glycolipids, and terpenoids (e.g., retinoids and steroids). Some lipids are linear, open-chain aliphatic molecules, while others have ring structures.



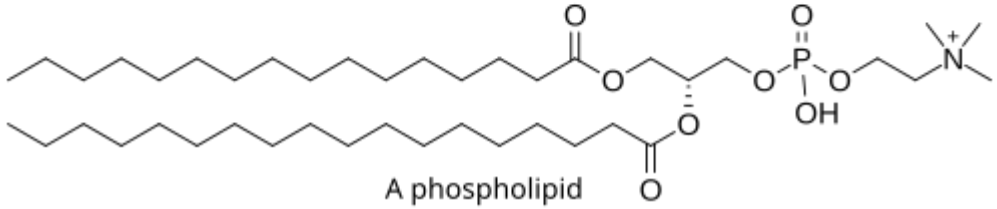
Cholesterol



A free fatty acid



A triglyceride

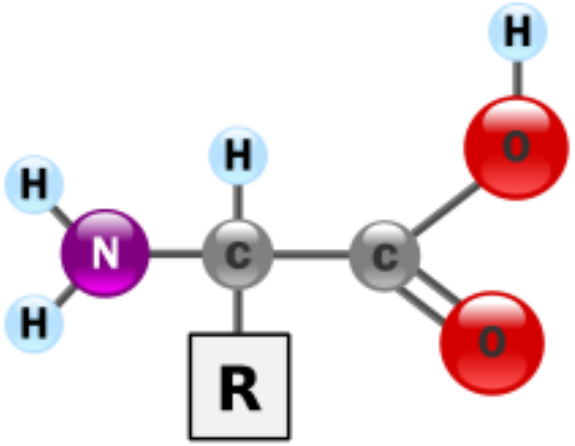


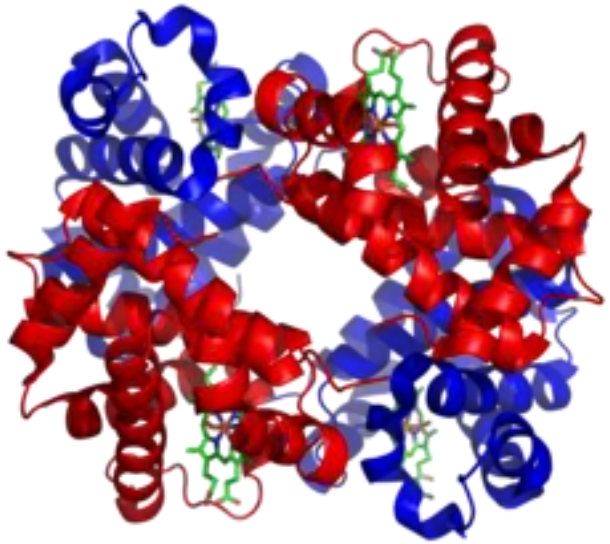
A phospholipid

chemical Biomolecules of life

V. Proteins

Proteins are very large molecules—macro-biopolymers—made from monomers called amino acids. An amino acid consists of an alpha carbon atom attached to an amino group, $–NH_2$, a carboxylic acid group, –COOH (although these exist as $–NH_3^+$ and $–COO^–$ under physiologic conditions), a simple hydrogen atom, and a side chain commonly denoted as "–R"

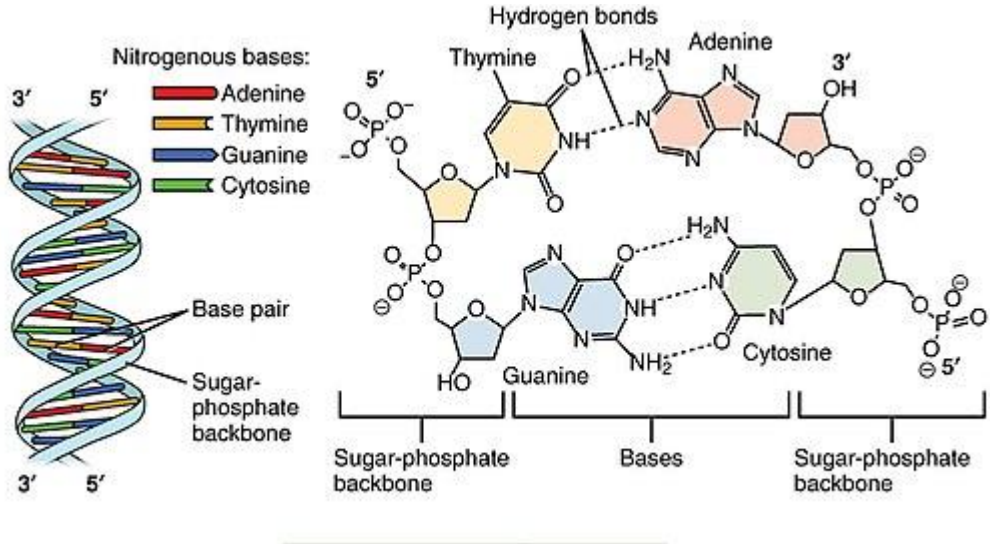


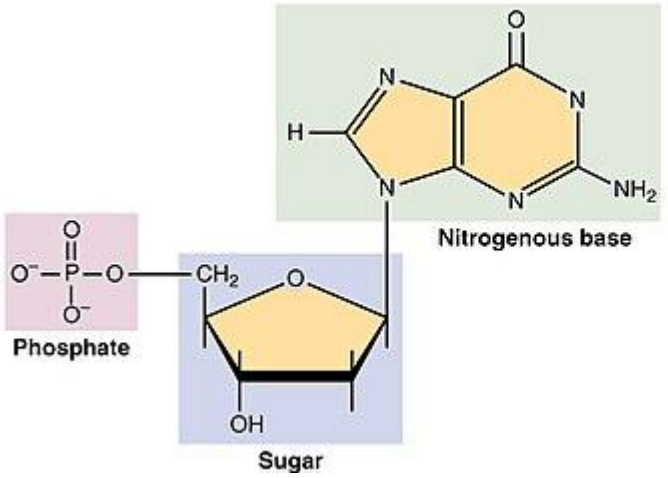


chemical Biomolecules of life

VI. Nucleic acids

Nucleic acids, so-called because of their prevalence in cellular nuclei, is the generic name of the family of biopolymers. They are complex, high-molecular-weight biochemical macromolecules that can convey genetic information in all living cells and viruses





Biochemistry

Najaf Polytechnic Collage

Carbohydrates
2nd Lecture

Assistant lecturer. Hayder Abed

Introduction to Carbohydrates

I. OVERVIEW

Carbohydrates are the most abundant organic molecules in nature. They have a wide range of functions, including providing a significant fraction of the dietary calories for most organisms, acting as a storage form of energy in the body, and serving as cell membrane components that mediate some forms of intercellular communication. Carbohydrates also serve as a structural component of many organisms, including the cell walls of bacteria, the exoskeleton of many insects, and the fibrous cellulose of plants. The empiric formula for many of the simpler carbohydrates is $(CH_2O)_n$, hence the name “hydrate of carbon.”





A- Monosaccharides

II. CLASSIFICATION AND STRUCTURE OF CARBOHYDRATES

Monosaccharides (simple sugars) can be classified according to the number of carbon atoms they contain. Examples of some mono-saccharides commonly found in humans are listed in Figure 7.1. Carbohydrates with an aldehyde as their most oxidized functional group are called aldoses, whereas those with a keto as their most oxidized functional group are called ketoses (Figure 7.2). For example, glyceraldehyde is an aldose, whereas dihydroxyacetone is a ketose. Carbohydrates that have a free carbonyl group have the suffix–ose. [Note: Ketoses (with some exceptions, for example, fructose) have an additional two letters in their suffix: –ulose, for example, xylulose.]

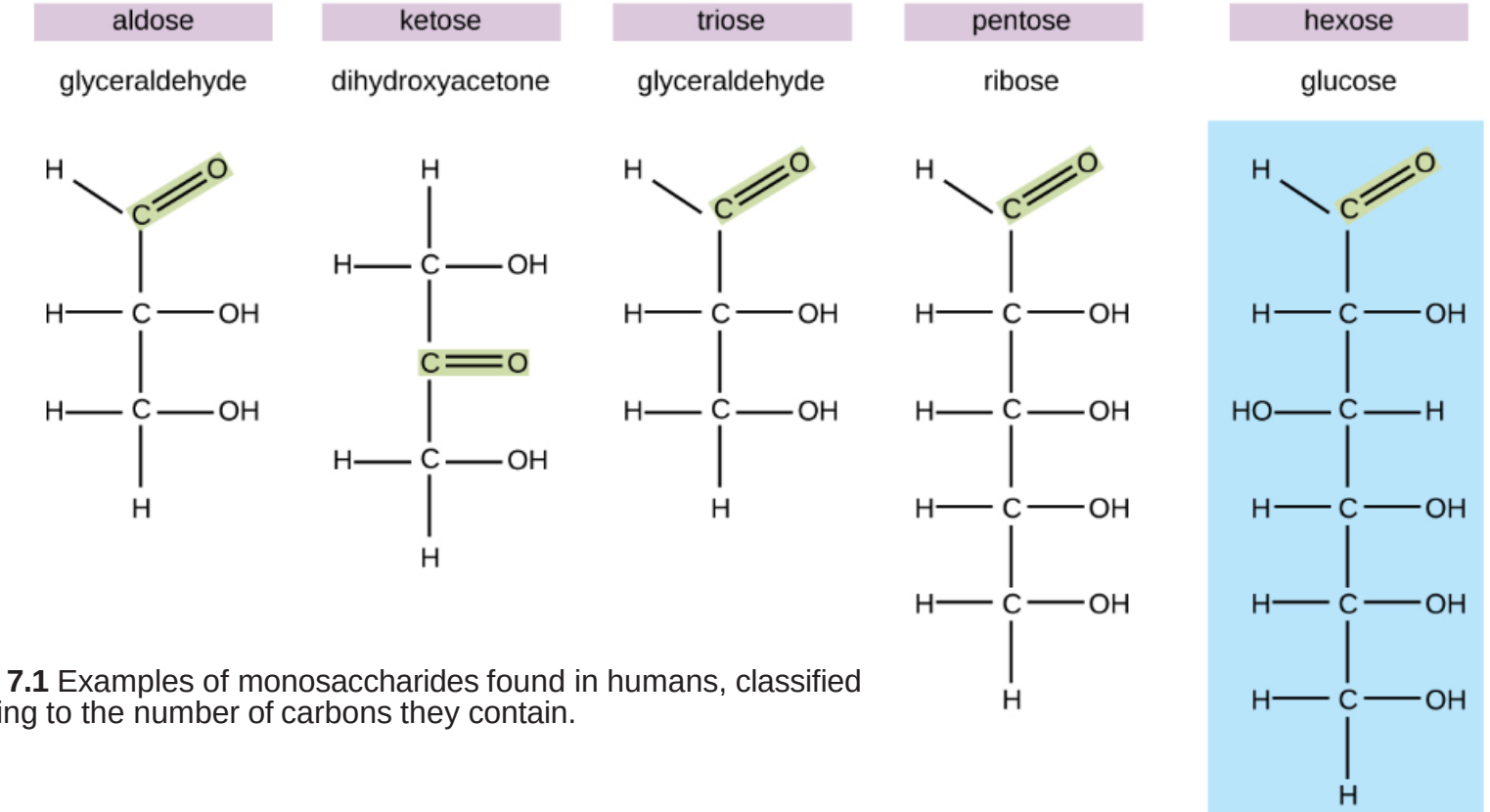


Figure 7.1 Examples of monosaccharides found in humans, classified according to the number of carbons they contain.

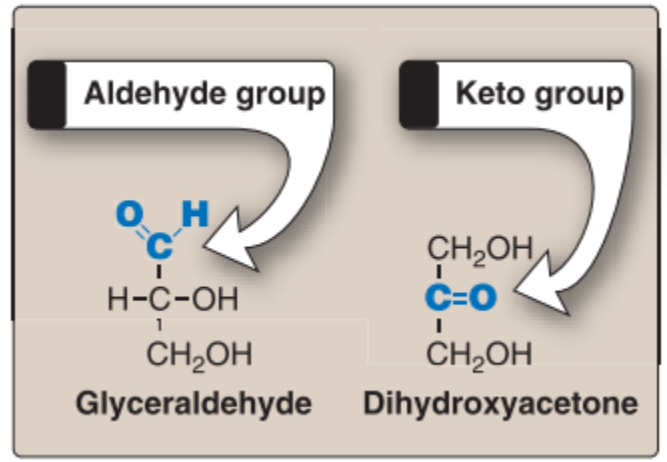


Figure 7.2 (a)Examples of an aldose (A) and a ketose (B) sugar.

Carbohydrates

A second comparison can be made when looking at glucose, galactose, and fructose. All three are hexoses; however, there is a major structural difference between glucose and galactose versus fructose: the carbon that contains the carbonyl (C=O). In glucose and galactose, the carbonyl group is on the C1 carbon, forming an aldehyde group. In fructose, the carbonyl group is on the C2 carbon, forming a ketone group. The former sugars are called aldoses based on the aldehyde group that is formed; the latter is designated as a ketose based on the ketone group. Again, this difference gives fructose different chemical and structural properties from those of the related aldoses, glucose, and galactose, even though fructose, glucose, and galactose all have the same chemical composition: $C_6H_{12}O_6$.

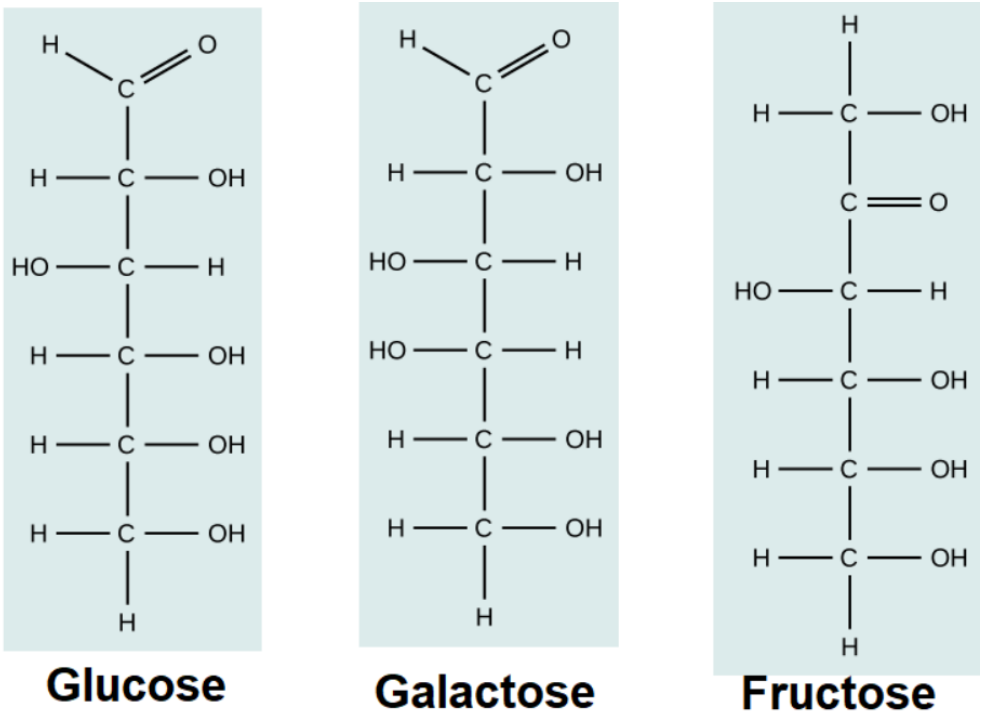


Figure 7.2 (b) Examples of an aldose (A) and a ketose (B) sugar.

Carbohydrates

B-Disaccharides

Monosaccharides can be linked by glycosidic bonds to create larger structures (Figure 7.3). Disaccharides contain two monosaccharide units, oligosaccharides contain from three to about ten monosaccharide units, whereas polysaccharides contain more than ten monosaccharide units, and can be hundreds of sugar units in length. Common disaccharides are the grain sugar maltose, made of two glucose molecules; the milk sugar lactose, made of one galactose and one glucose molecule; and the table sugar sucrose, made of one glucose and one fructose molecule

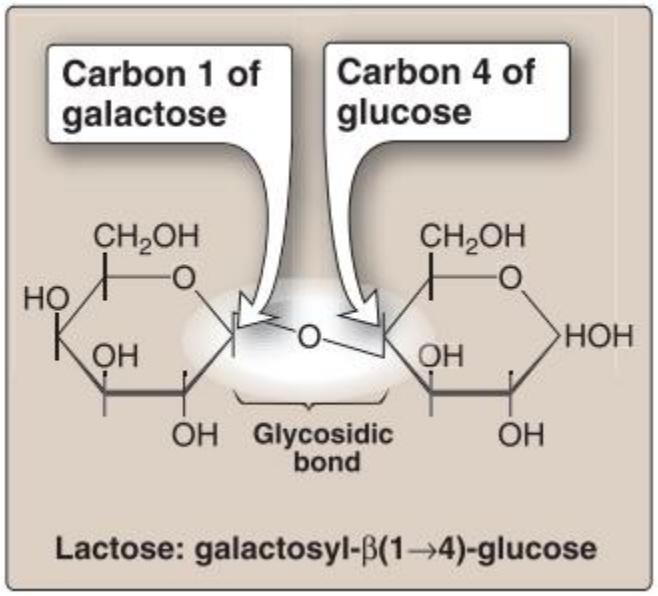
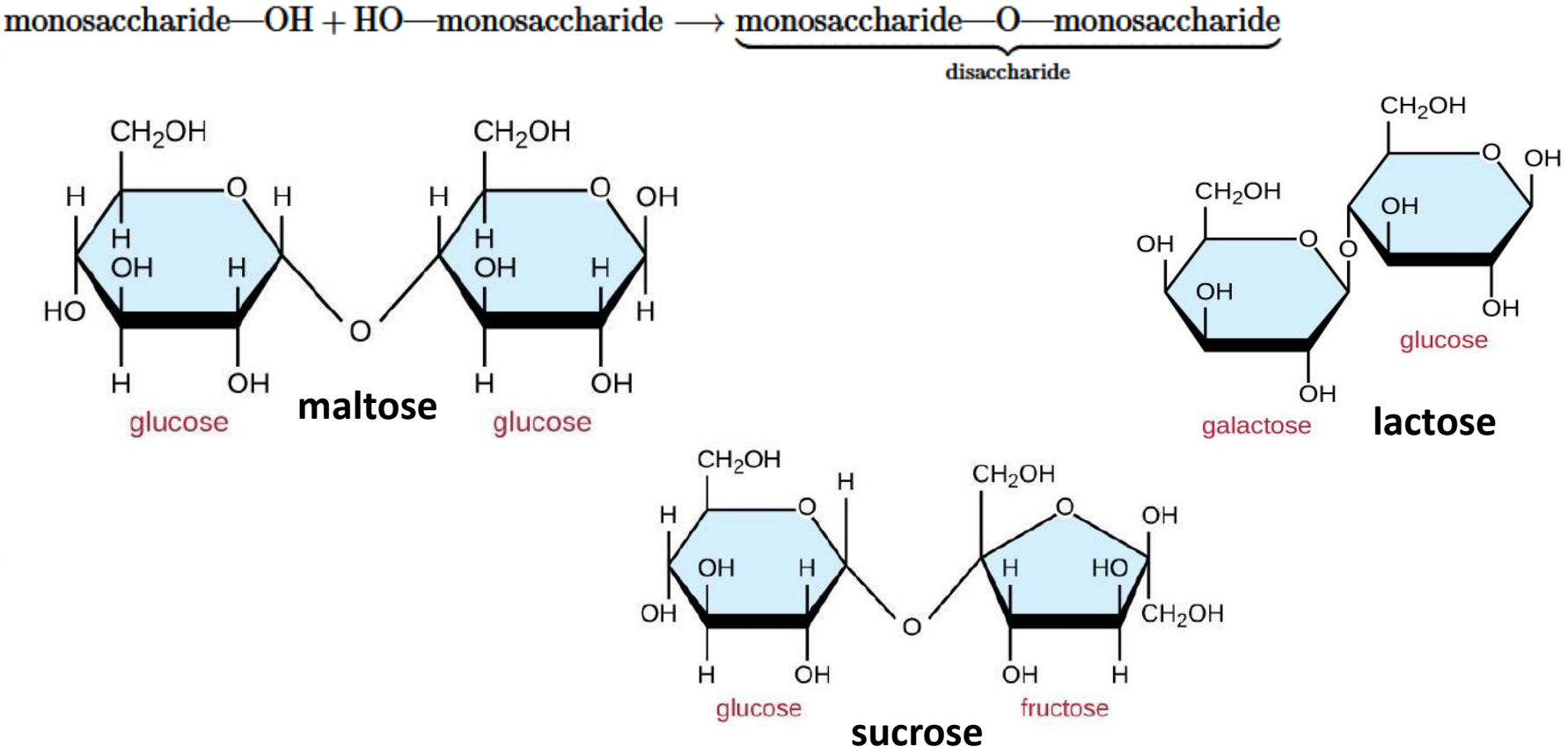


Figure 7.3 A glycosidic bond between two hexoses producing a disaccharide.

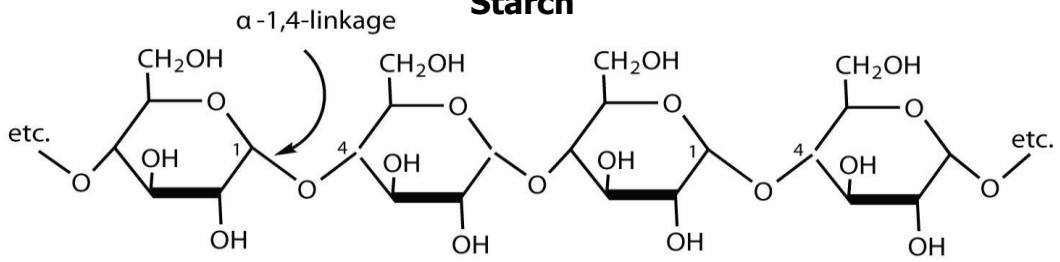


Carbohydrates

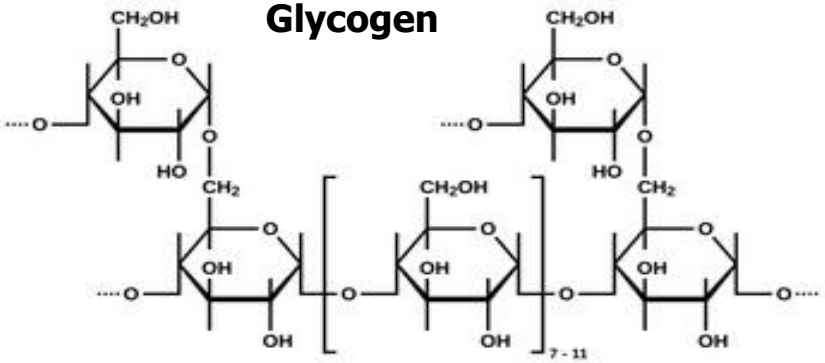
C- Polysaccharides,

Polysaccharides, also called glycans, are large polymers composed of hundreds of monosaccharide monomers. Unlike monosaccharides and disaccharides, polysaccharides are not sweet and, in general, they are not soluble in water. Like disaccharides, the monomeric units of polysaccharides are linked together by glycosidic bonds Polysaccharides are very diverse in their structure. Three of the most biologically important polysaccharides starch, glycogen, and cellulose are all composed of repetitive glucose units, although they differ in their structure. Cellulose consists of a linear chain of glucose molecules and is a common structural component of cell walls in plants and other organisms. Glycogen and starch are branched polymers; glycogen is the primary energy-storage molecule in animals and bacteria, whereas plants primarily store energy in starch. The orientation of the glycosidic linkages in these three polymers is different as well and, as a consequence, linear and branched macromolecules have different properties.

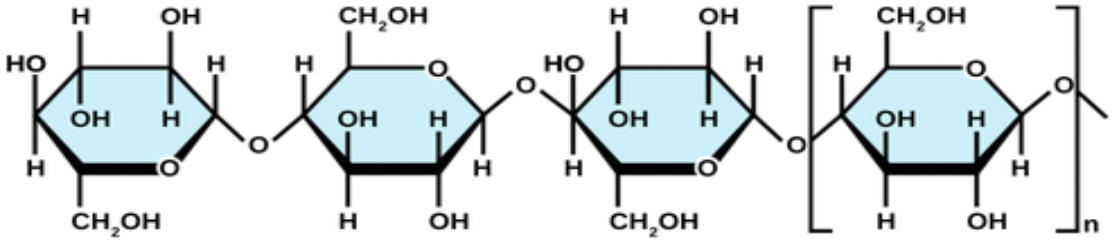
Starch



Glycogen



Cellulose



Carbohydrates

Compounds that have the same chemical formula but have different structures are called isomers. For example, fructose, glucose, man-nose, and galactose are all isomers of each other, having the same chemical formula, $C_6H_{12}O_6$. Carbohydrate isomers that differ in configuration around only one specific carbon atom (with the exception of the carbonyl carbon, see "anomers" below) are defined as epimers of each other. For example, glucose and galactose are C-4 epimers their structures differ only in the position of the –OH group at carbon 4. [Note: The carbons in sugars are numbered beginning at the end that contains the carbonyl carbon that is, the aldehyde or keto group (Figure 7.4).] Glucose and mannose are C-2 epimers. However, galactose and mannose are NOT epimers—they differ in the position of –OH groups at two carbons (2 and 4) and are, therefore, defined only as isomers (see Figure 7.4).

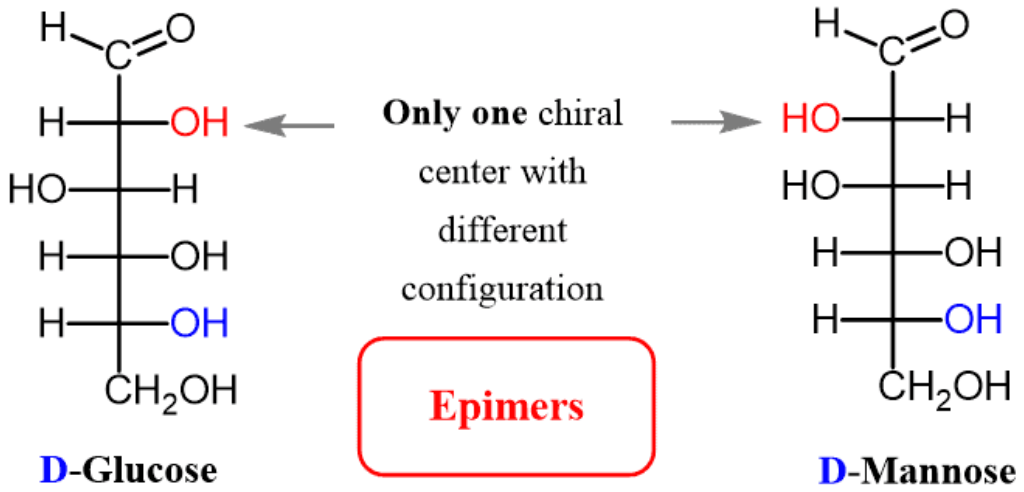


Figure 7.4 C-2 and C-4 epimers and an isomer of glucose.

E. Enantiomers

A special type of isomerism is found in the pairs of structures that are mirror images of each other. These mirror images are called enantiomers, and the two members of the pair are designated as a D- and an L-sugar (Figure 7.5). The vast majority of the sugars in humans are D-sugars. In the D isomeric form, the –OH group on the asymmetric carbon (a carbon linked to four different atoms or groups) farthest from the carbonyl carbon is on the right, whereas in the L-isomer it is on the left. Enzymes known as racemases are able to interconvert D- and L-isomers.

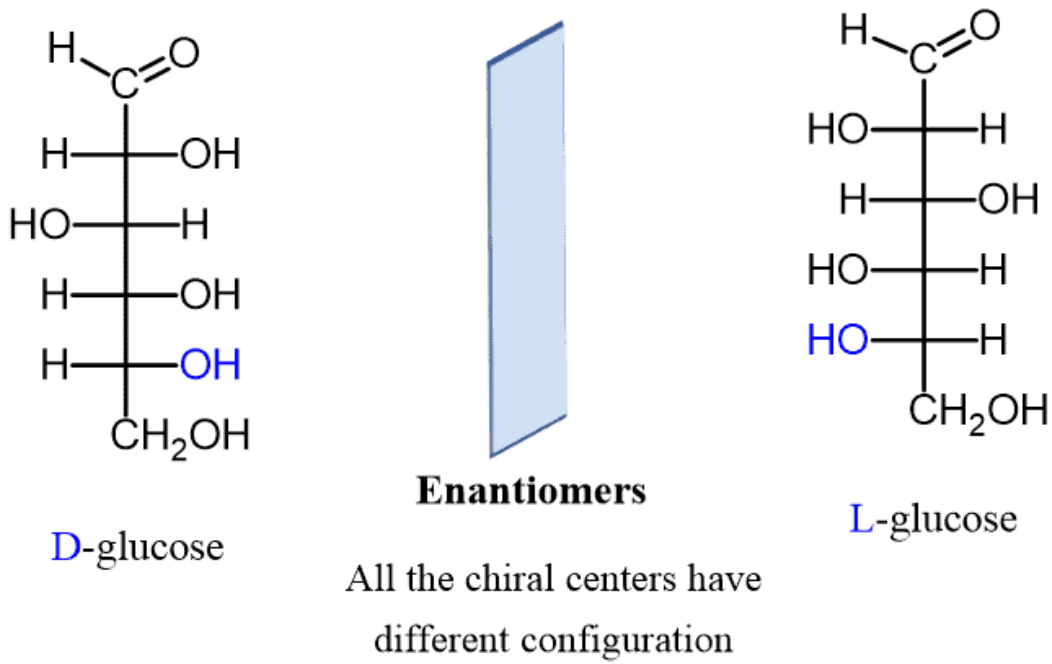
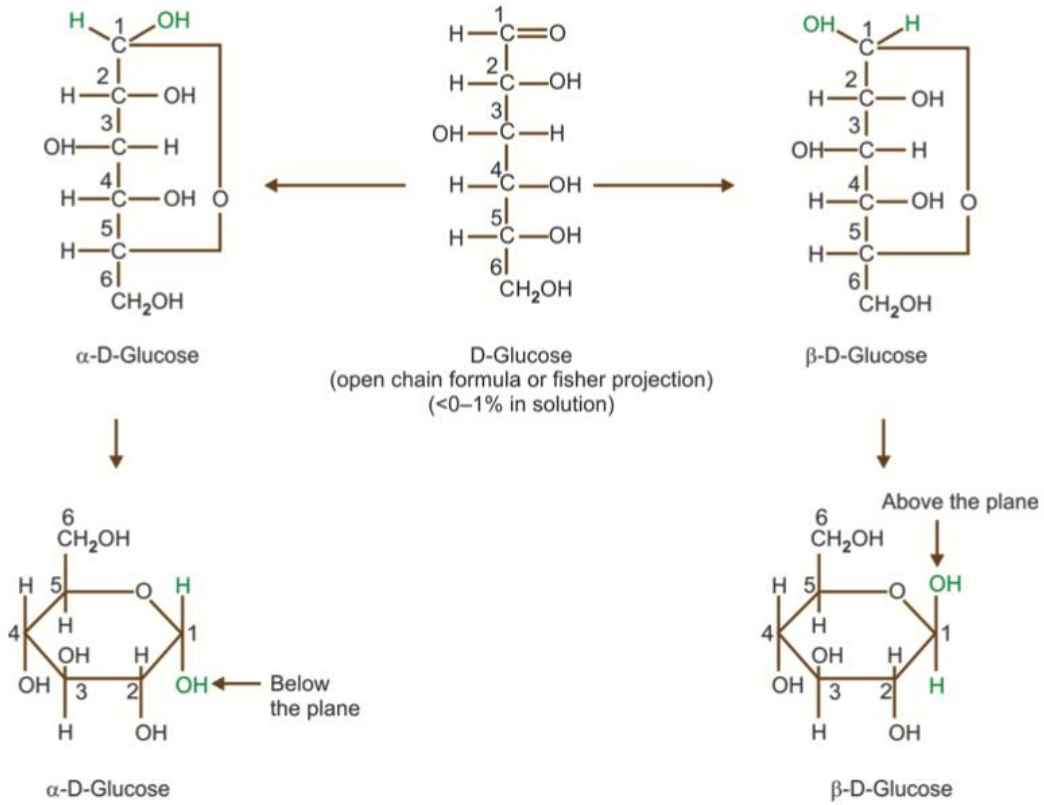


Figure 7.5 Enantiomers (mirror images) of glucose.

Carbohydrates

F. Cyclization of monosaccharides

Less than 1% of each of the monosaccharides with five or more carbons exists in the open-chain (acyclic) form. Rather, they are predominantly found in a ring (cyclic) form, in which the aldehyde (or keto) group has reacted with an alcohol group on the same sugar, making the carbonyl carbon (carbon 1 for an aldose or carbon 2 for a ketose) asymmetric. [Note: Pyranose refers to a six-membered ring consisting of five carbons and one oxygen, for example, gluco-pyranose, whereas furanose denotes a five membered ring with four carbons and one oxygen.]



Carbohydrate Metabolism

During digestion, carbohydrates are broken down into simple, soluble sugars that can be transported across the intestinal wall into the circulatory system to be transported throughout the body. Carbohydrate digestion begins in the mouth with the action of **salivary amylase** on starches and ends with monosaccharides being absorbed across the epithelium of the small intestine. Once the absorbed monosaccharides are transported to the tissues, the process of **cellular respiration** begins (Figure 1). This section will focus first on glycolysis, a process where the monosaccharide glucose is oxidized, releasing the energy stored in its bonds to produce ATP.

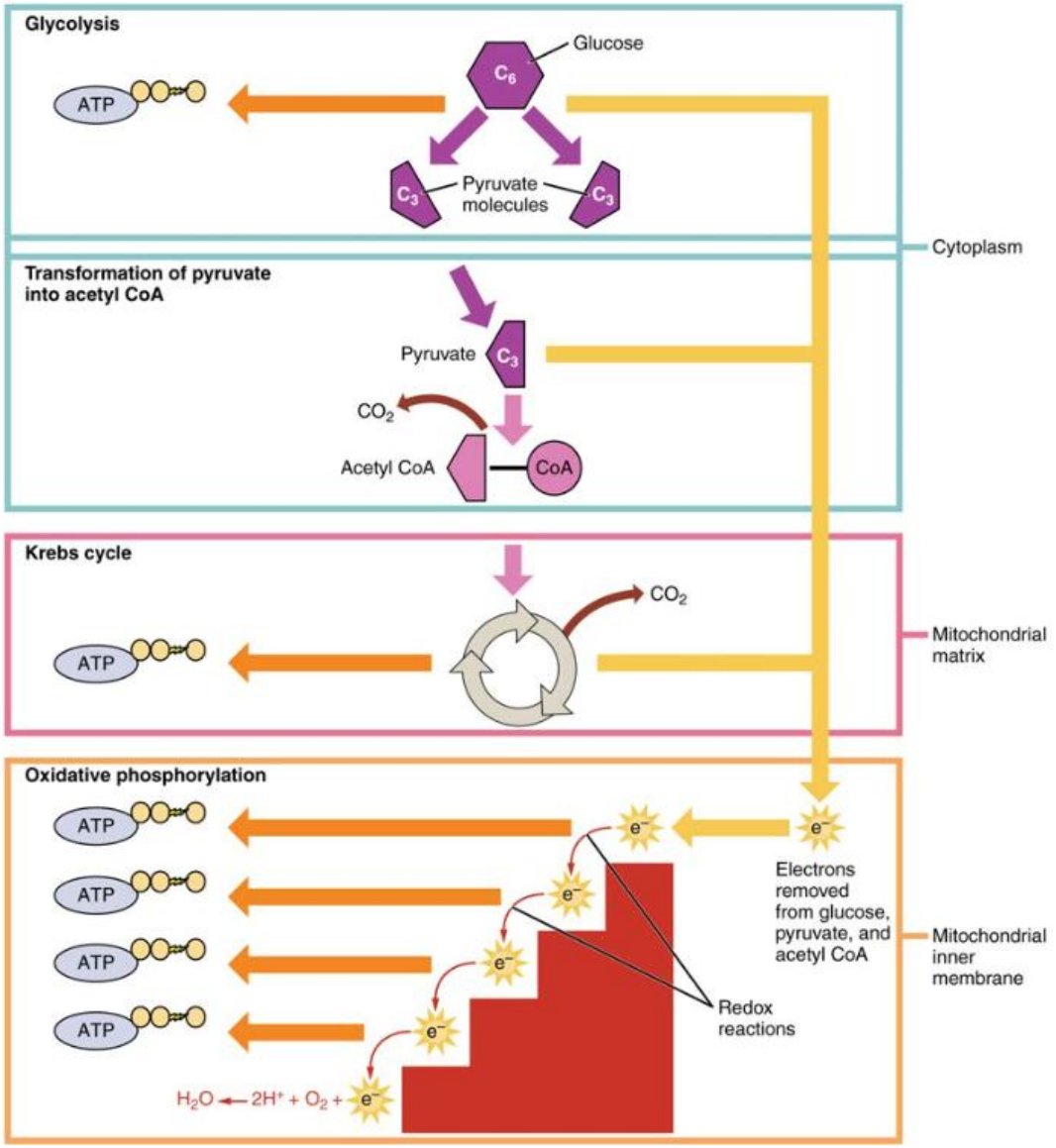
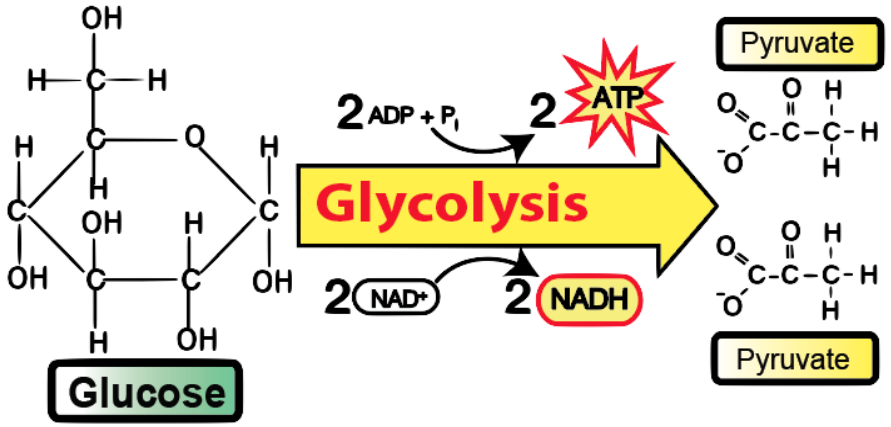
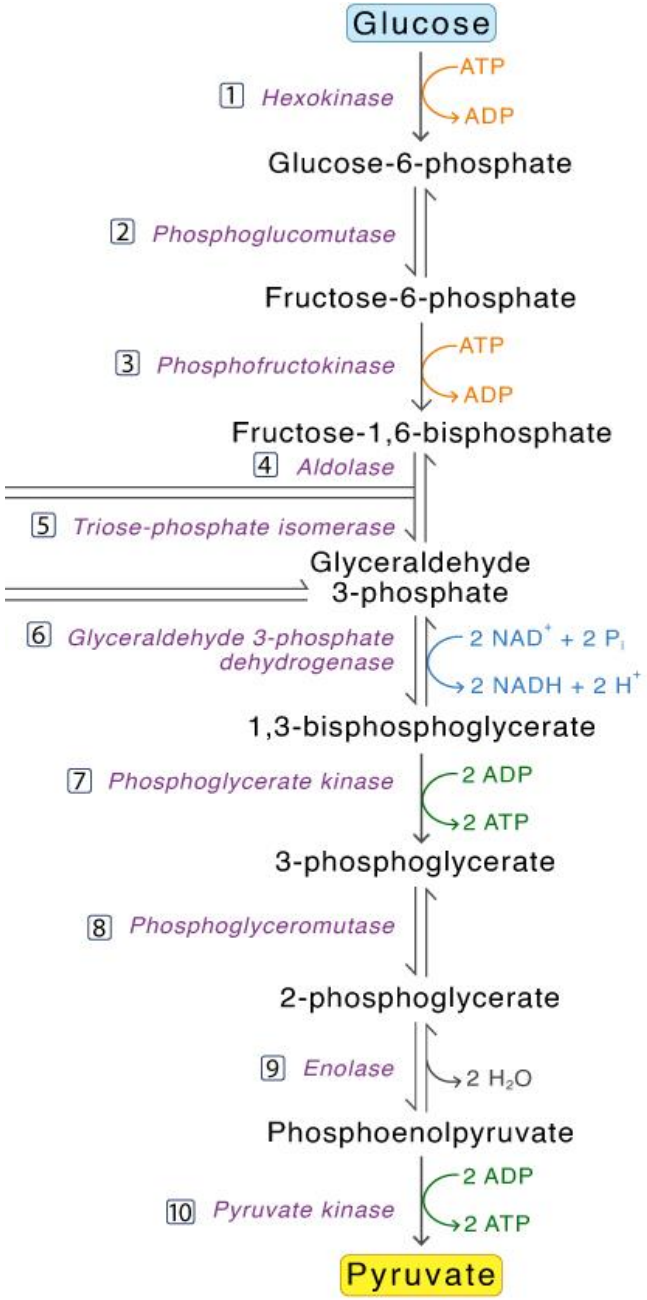


Figure 1. Cellular respiration oxidizes glucose molecules through glycolysis, the Krebs cycle, and oxidative phosphorylation to produce ATP.

Glycolysis

The glycolytic pathway is employed by all tissues for the breakdown of glucose to provide energy (in the form of ATP) and intermediates for other metabolic pathways. Glycolysis is at the hub of carbohydrate metabolism because virtually all sugars—whether arising from the diet or from catabolic reactions in the body—can ultimately be converted to glucose. Pyruvate is the end product of glycolysis in cells with mitochondria and an adequate supply of oxygen. This series of ten reactions is called aerobic glycolysis because oxygen is required to re-oxidize the NADH formed during the oxidation of glyceraldehyde 3-phosphate. Aerobic glycolysis sets the stage for the oxidative decarboxylation of pyruvate to acetyl CoA, a major fuel of the TCA (or citric acid) cycle. Alternatively, pyruvate is reduced to lactate as NADH is oxidized to NAD^+.





Glycolysis Steps

Step 1: In the first step, a phosphate group from ATP gets transferred to the glucose molecule present in the cell cytoplasm, producing glucose-6-phosphate. This step is catalyzed by the enzyme hexokinase.

Step 2: Next, the glucose-6-phosphate gets converted into its isomer, fructose-6-phosphate by the action of phosphoglucomutase.

Step 3: Another phosphate group gets transferred from ATP to fructose-6-phosphate to produce fructose-1,6-bisphosphate, under the influence of phosphofructokinase.

Step 4: In this step, the enzyme aldolase acts on the fructose-1,6-bisphosphate and splits it into dihydroxyacetone phosphate (DHAP) and glyceraldehyde 3-phosphate. These two three-carbon molecules are isomers of each other. Out of them, only glyceraldehyde-3-phosphate can directly continue through the next steps of glycolysis

Step 5: As DHAP cannot directly take part in the consecutive steps of the process, it gets converted into its isomer glyceraldehyde-3-phosphate by the enzyme triose-phosphate isomerase.

Glycolysis Steps

Step 6: Next, the enzyme glyceraldehyde 3-phosphate dehydrogenase (GAPDH) adds a phosphate from the cytosol to the glyceraldehyde 3-phosphate to form 1,3-bisphosphoglycerate. The same enzyme also dehydrogenates glyceraldehyde 3-phosphate by transferring one of its hydrogen (H^+) molecules to the oxidizing agent NAD^+ to form NADH and H^+. The two molecules of glyceraldehyde 3-phosphate, one formed directly and one after the interconversion, both undergo this process of phosphorylation and dehydrogenation.

Step 7: After this, the 1,3-bisphosphoglycerate donates one of its phosphate groups to ADP, making a molecule of ATP and turning into 3-phosphoglycerate (3 PGA) in the process. As there are two molecules of 1,3-bisphosphoglycerate, the reaction yields two 3 PGA, and 2 ATPs

Step 8: 3-phosphoglycerate gets converted into its isomer, 2-phosphoglycerate by the action of phosphoglyceromutase.

Step 9: In this step, the enzyme enolase acts on 2-phosphoglycerate and removes a molecule of water from it, thus producing phosphoenolpyruvate (PEP).

Step 10: As PEP is an unstable molecule, it loses one of its phosphate group in this step. The lost phosphate group gets to ADP under the influence of the enzyme pyruvate kinase. This step yields 2 molecules of pyruvate and 2 ATPs in the end. As this pyruvate enters the next phase of cellular respiration, it is considered as the end product of glycolysis.

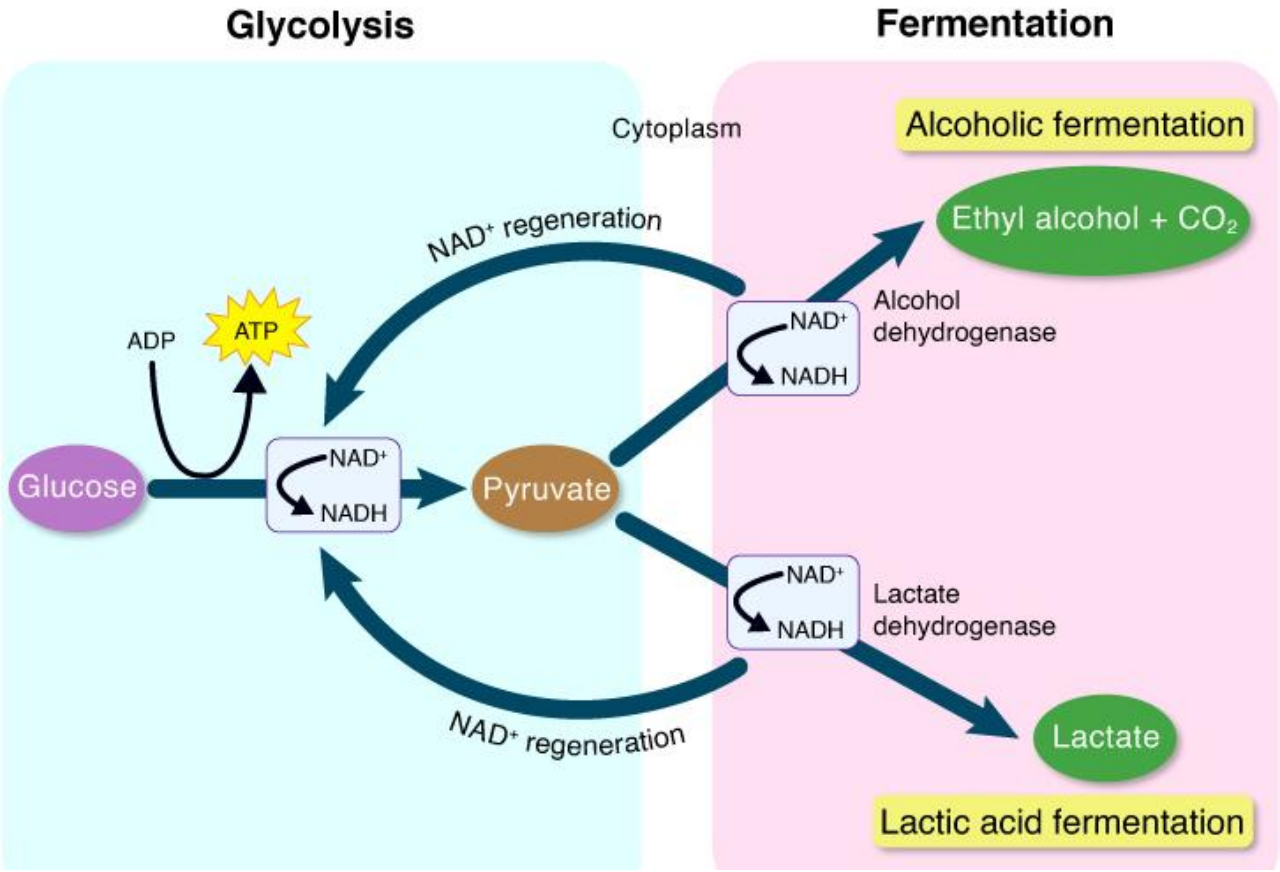
Anaerobic Respiration

What is Anaerobic Respiration and Where Does it Occur

The term ‘anaerobic’ stands for ‘absence of air or free oxygen.’ Accordingly, anaerobic respiration is a type of cellular respiration, in which stored energy of glucose gets converted into biochemical energy coins, ATP without free oxygen. Many microorganisms rely on this process to produce energy when there is a lack of oxygen. These include prokaryotes, like bacteria and Archaea, and eukaryotes, such as plants and animals.

What Happens During Anaerobic Cellular Respiration

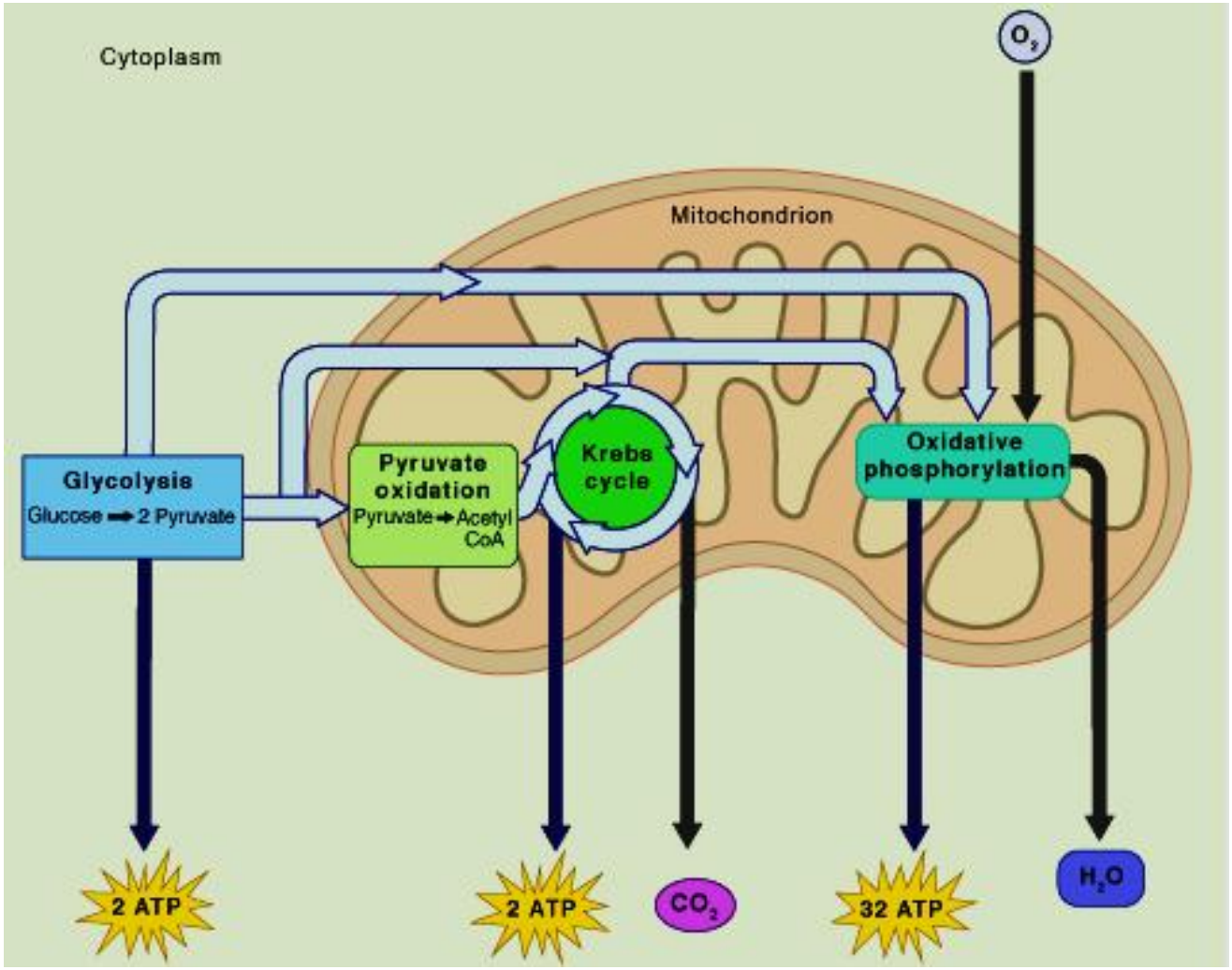
Similar to aerobic respiration, anaerobic respiration also starts with glycolysis by converting glucose into pyruvate. However, the pyruvate does not further enter the mitochondria to complete aerobic respiration due to the absence of oxygen. Instead, it follows a different pathway altogether and gets converted into a different by products (Ethyl alcohol + CO_2 + Lactate)



Aerobic Respiration

What are Aerobic and Anaerobic Respiration

Aerobic respiration is the process through which cells break down the glucose molecule to convert its stored biochemical energy into energy-coin Adenosine triphosphate (ATP) in the presence of oxygen. This type of respiration is the primary energy-yielding process of all living beings, providing all the energy to maintain life.



Home work

Q.1. Can glycolysis occur without oxygen?

Q.2. Does glycolysis produce CO_2?

Q.3 Does glycolysis occur before Krebs cycle?

Q.4. Does glycolysis occur in all cells?

Q.5. Why is ATP required for glycolysis?

Q.6. Which is required for both anaerobic respiration and aerobic

Q7. Compare fermentation with anaerobic and aerobic respiration.

Biochemistry

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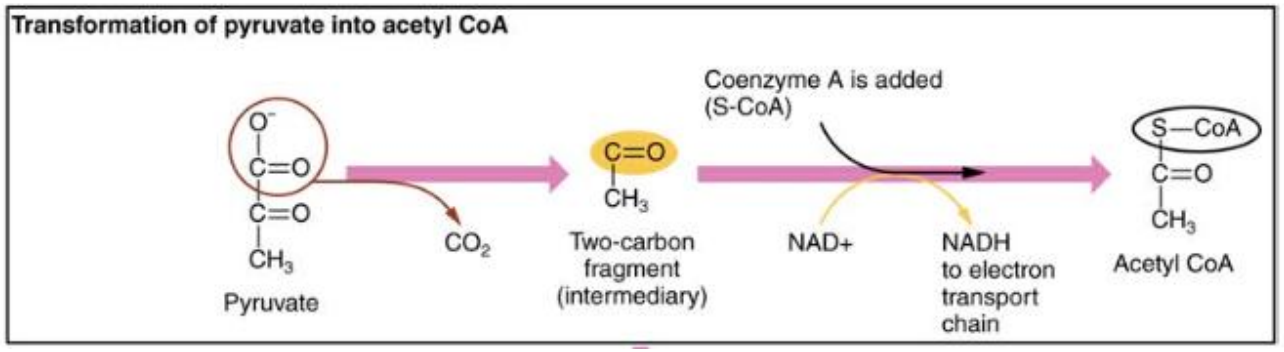
Carbohydrates
4nd Lecture

Assistant lecturer. Hayder Abed

Krebs Cycle/Citric Acid Cycle/Tricarboxylic Acid Cycle

The pyruvate molecules generated during glycolysis are transported across the mitochondrial membrane into the inner mitochondrial matrix, where they are metabolized by enzymes in a pathway called the **Krebs cycle** (Figure 1). The Krebs cycle is also commonly called the citric acid cycle or the tricarboxylic acid (TCA) cycle. During the Krebs cycle, high-energy molecules, including ATP, NADH, and FADH2, are created. NADH and FADH2 then pass electrons through the electron transport chain in the mitochondria to generate more ATP molecules.

Cytoplasm



Mitochondrial

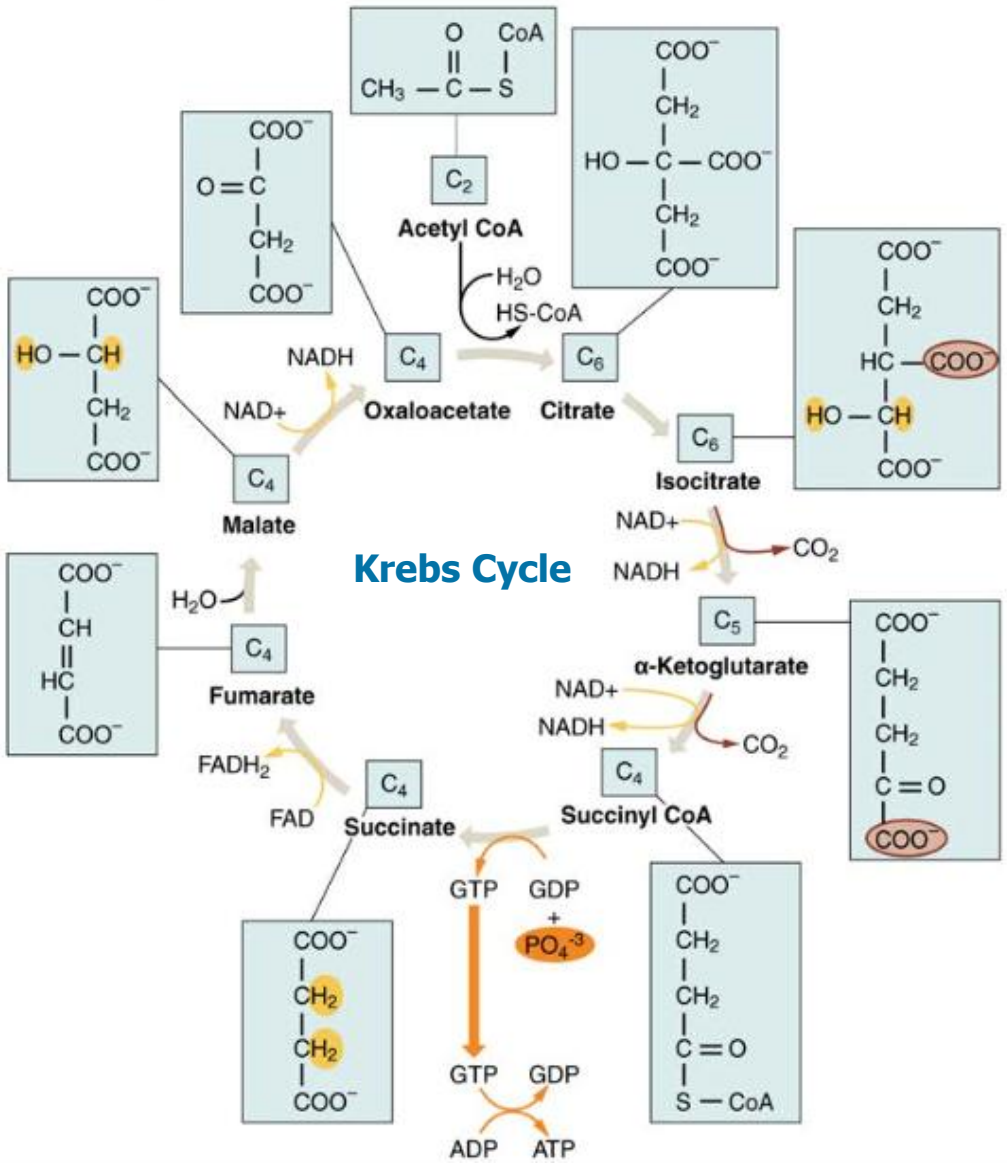


Figure 1. During the Krebs cycle.

Krebs Cycle Steps

The three-carbon pyruvate molecule generated during glycolysis moves from the cytoplasm into the mitochondrial matrix, where it is converted by the enzyme pyruvate dehydrogenase into a two-carbon **acetyl coenzyme A (acetyl CoA)** molecule. This reaction is an oxidative decarboxylation reaction. It converts the three-carbon pyruvate into a two-carbon acetyl CoA molecule, releasing carbon dioxide and transferring two electrons that combine with NAD+ to form NADH. Acetyl CoA enters the Krebs cycle by combining with a four-carbon molecule, oxaloacetate, to form the six-carbon molecule citrate, or citric acid, at the same time releasing the coenzyme A molecule.

The six-carbon citrate molecule is systematically converted to a five-carbon molecule and then a four-carbon molecule, ending with oxaloacetate, the beginning of the cycle. Along the way, each citrate molecule will produce one ATP, one FADH2, and three NADH. The FADH2 and NADH will enter the oxidative phosphorylation system located in the inner mitochondrial membrane. In addition, the Krebs cycle supplies the starting materials to process and break down proteins and fats.

To start the Krebs cycle, citrate synthase combines acetyl CoA and oxaloacetate to form a six-carbon citrate molecule; CoA is subsequently released and can combine with another pyruvate molecule to begin the cycle again. The aconitase enzyme converts citrate into isocitrate. In two successive steps of oxidative decarboxylation, two molecules of CO_2 and two NADH molecules are produced when isocitrate dehydrogenase converts isocitrate into the five-carbon α-ketoglutarate, which is then catalyzed and converted into the four-carbon succinyl CoA by α-ketoglutarate dehydrogenase.

The enzyme succinyl CoA dehydrogenase then converts succinyl CoA into succinate and forms the high-energy molecule GTP, which transfers its energy to ADP to produce ATP. Succinate dehydrogenase then converts succinate into fumarate, forming a molecule of FADH2. Fumarase then converts fumarate into malate, which malate dehydrogenase then converts back into oxaloacetate while reducing NAD+ to NADH. Oxaloacetate is then ready to combine with the next acetyl CoA to start the Krebs cycle again (see Figure 1). For each turn of the cycle, three NADH, one ATP (through GTP), and one FADH2 are created. Each carbon of pyruvate is converted into CO_2, which is released as a by product of oxidative (aerobic) respiration.

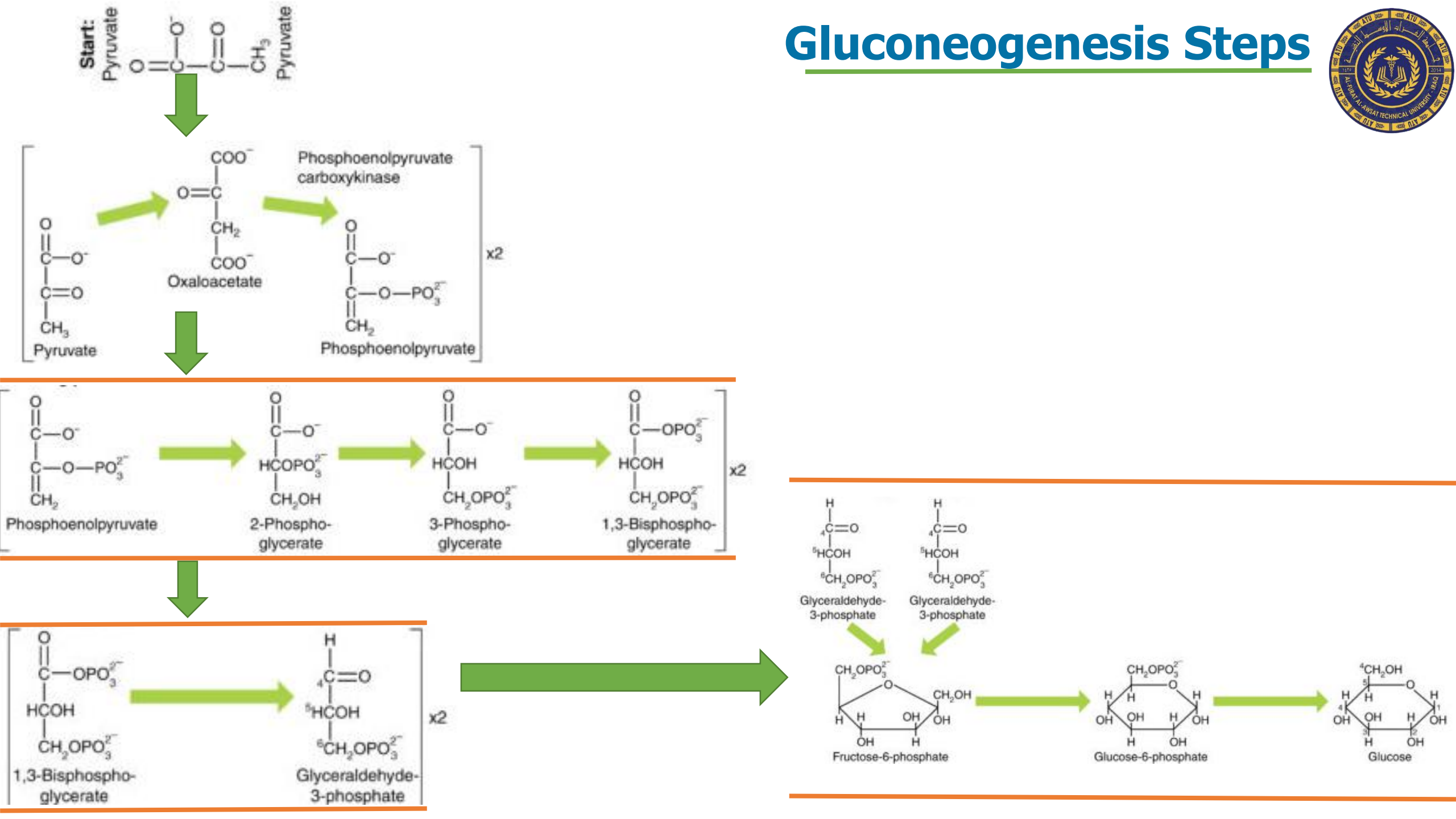
Gluconeogenesis

Gluconeogenesis is the synthesis of new glucose molecules from pyruvate, lactate, glycerol, or the amino acids alanine or glutamine. This process takes place primarily in the liver during periods of low glucose, that is, under conditions of fasting, starvation, and low carbohydrate diets. So, the question can be raised as to why the body would create something it has just spent a fair amount of effort to break down? Certain key organs, including the brain, can use only glucose as an energy source; therefore, it is essential that the body maintain a minimum blood glucose concentration. When the blood glucose concentration falls below that certain point, new glucose is synthesized by the liver to raise the blood concentration to normal.

Gluconeogenesis is not simply the reverse of glycolysis. There are some important differences . Pyruvate is a common starting material for gluconeogenesis. First, the pyruvate is converted into oxaloacetate. Oxaloacetate then serves as a substrate for the enzyme phosphoenolpyruvate carboxykinase (PEPCK), which transforms oxaloacetate into phosphoenolpyruvate (PEP). From this step, gluconeogenesis is nearly the reverse of glycolysis. PEP is converted back into 2-phosphoglycerate, which is converted into 3-phosphoglycerate. Then, 3-phosphoglycerate is converted into 1,3 bisphosphoglycerate and then into glyceraldehyde-3-phosphate. Two molecules of glyceraldehyde-3-phosphate then combine to form fructose-1-6-bisphosphate, which is converted into fructose 6-phosphate and then into glucose-6-phosphate.

Finally, a series of reactions generates glucose itself. In gluconeogenesis (as compared to glycolysis), the enzyme hexokinase is replaced by glucose-6-phosphatase, and the enzyme phosphofructokinase-1 is replaced by fructose-1,6-bisphosphatase. This helps the cell to regulate glycolysis and gluconeogenesis independently of each other.
As will be discussed as part of lipolysis, fats can be broken down into glycerol, which can be phosphorylated to form dihydroxyacetone phosphate or DHAP. DHAP can either enter the glycolytic pathway or be used by the liver as a substrate for gluconeogenesis.

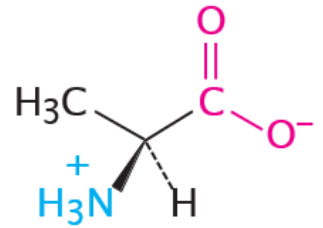
Gluconeogenesis Steps



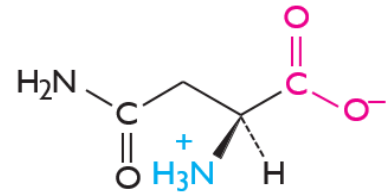
Classification of Amino Acid

In addition to the amino and carboxyl groups, amino acids have a side chain or R group attached to the α-carbon. Each amino acid has unique characteristics arising from the size, shape, solubility, and ionization properties of its R group. As a result, the side chains of amino acids exert a profound effect on the structure and biological activity of proteins. Although amino acids can be classified in various ways, one common approach is to classify them according to whether the functional group on the side chain at neutral pH is nonpolar, polar but uncharged, negatively charged, or positively charged.

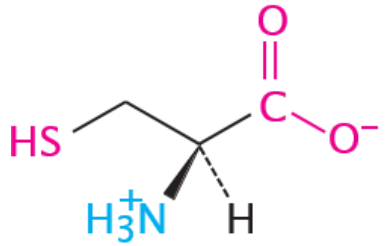
Alanine
Ala



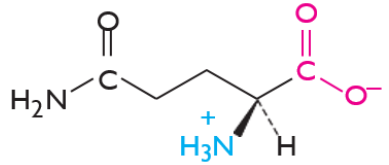
Asparagie
Asn



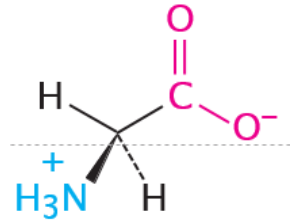
Cysteine
Cys



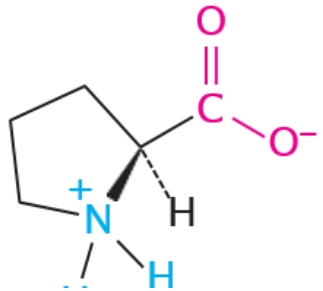
Glutamine
Gln



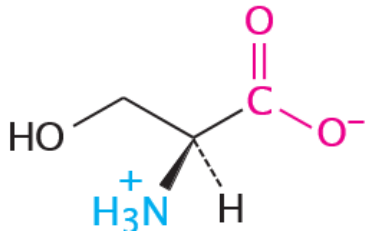
Glycine
Gly



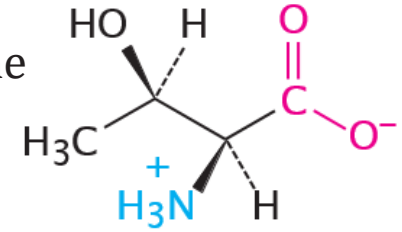
Proline
Pro



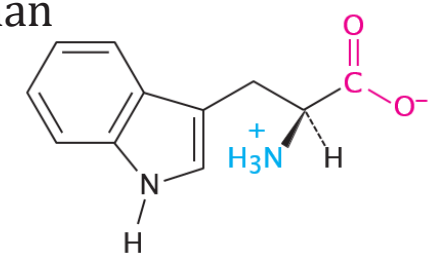
Serine
Ser



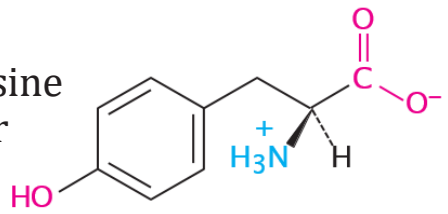
Threonine
Thr



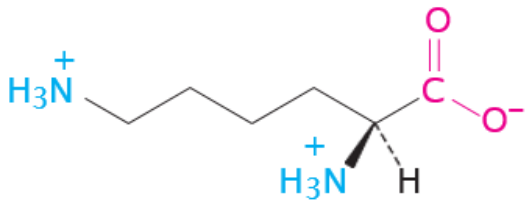
Tryptophan
Trp



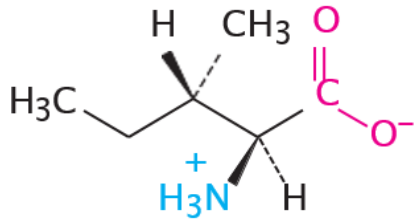
Tyrosine
Tyr



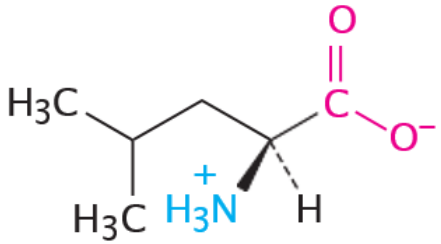
Lysine
Lys



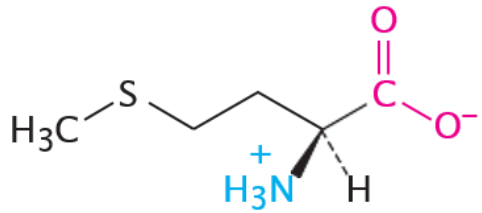
Isoleucine
Ile



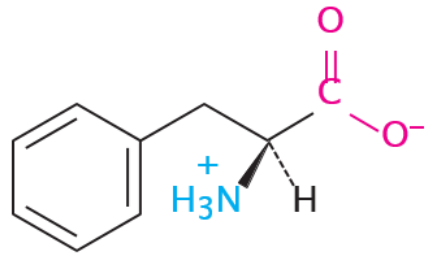
Leucine
Leu



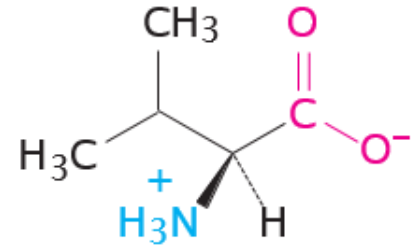
Methionine
Met



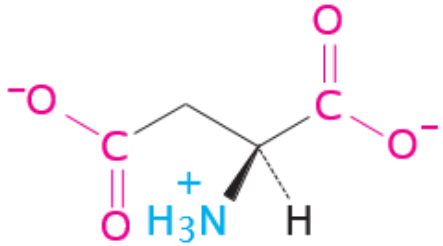
Phenylalanine
Phe



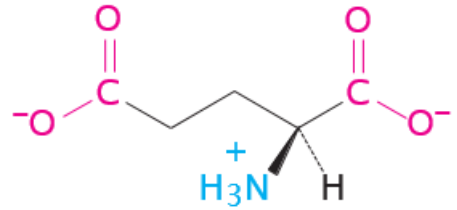
Valine
Val



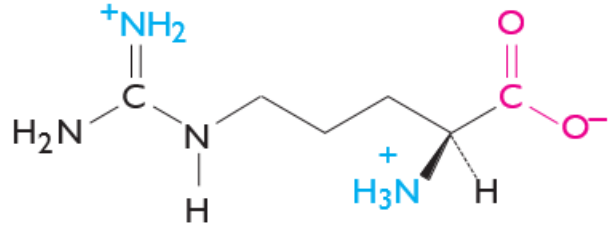
Aspartic acid
Asp



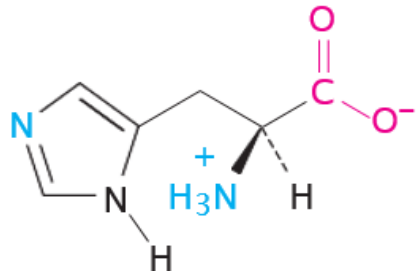
Glutamic acid
Glu



Arginine
Arg

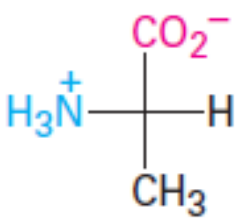


Histidine
His

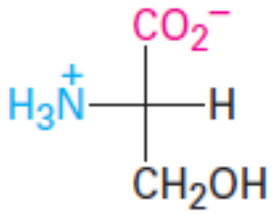


Configuration of Amino Acid

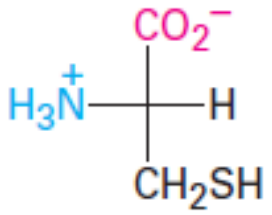
Prevoius slide (6-5) showed that glycine is the only amino acid whose α-carbon is not chiral. Therefore, with the exception of glycine, the amino acids could theoretically exist in either the D- or the L-enantiomeric form and rotate plane-polarized light. As with sugars, chemists used L-glyceraldehyde as the reference compound for the assignment of absolute configuration to amino acids. Its structure closely resembles an amino acid structure except that in the latter, an amino group takes the place of the OH group on the chiral carbon of the L-glyceraldehyde and a carboxylic acid replaces the aldehyde. Modern stereochemistry assignments using the Cahn-Ingold-Prelog priority rules used ubiquitously in chemistry show that all of the naturally occurring chiral amino acids are S except Cys which is R.



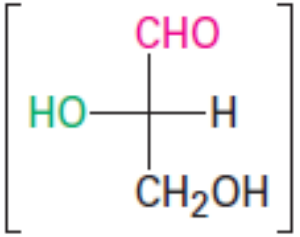
L-Alanine
(*S*)-Alanine



L-Serine
(*S*)-Serine



L-Cysteine
(*R*)-Cysteine



L-Glyceraldehyde

Biochemistry

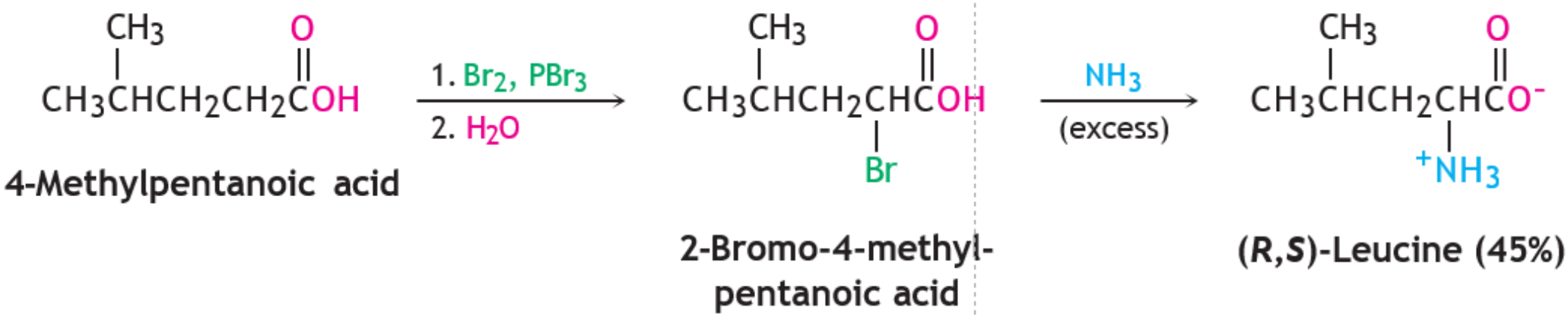
Najaf Polytechnic Collage

Amino Acid
2st Lecture

Assistant lecturer. Hayder Abed

Synthesis of Amino Acids

a-Amino acids can be synthesized in the laboratory using some of the reactions discussed in previous chapters. One of the oldest methods of *a*-amino acid syn- thesis begins with *a* bromination of a carboxylic acid by treatment with Br_2 and PBr_3 (the Hell–Volhard–Zelinskii reaction). substitution of the *a*-bromo acid with ammonia then yields an *a*-amino acid.



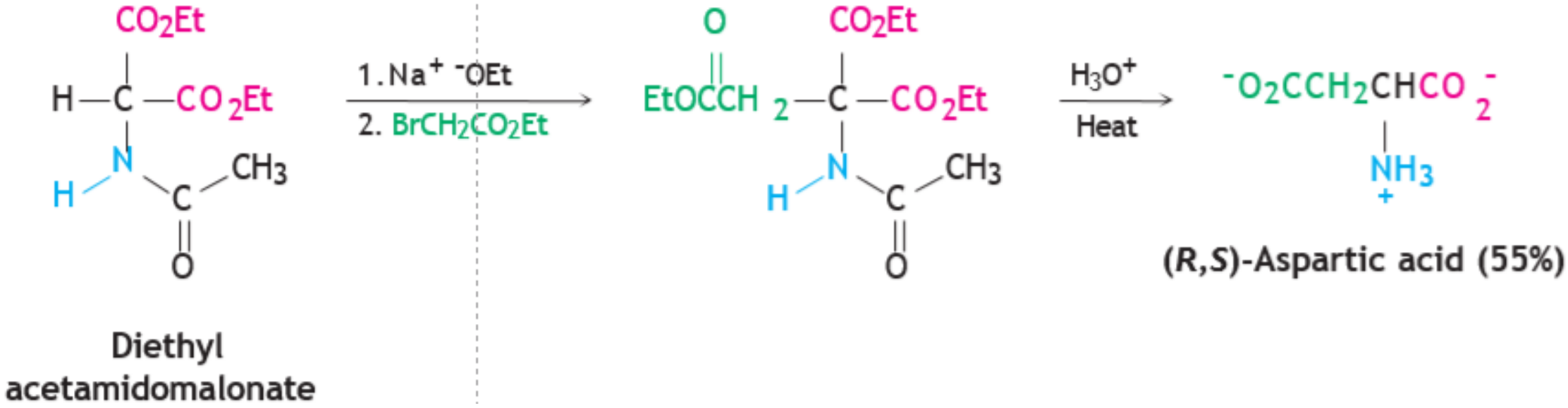
4-Methylpentanoic acid

2-Bromo-4-methyl-pentanoic acid

(*R*,*S*)-Leucine (45%)

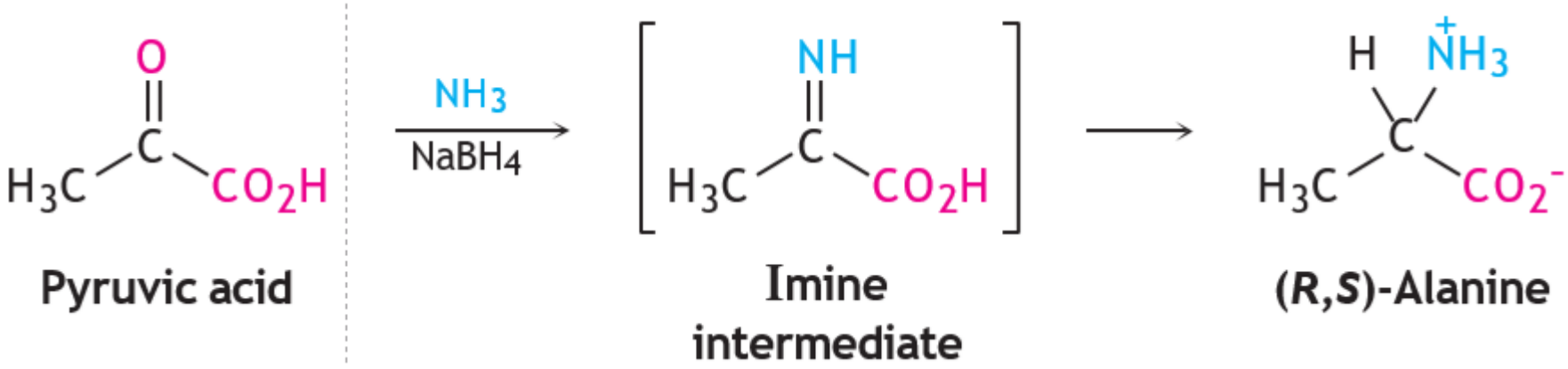
The Amidomalonate Synthesis

A more general method for preparation of *a*-amino acids is the *amidomalonate synthesis*, a straightforward extension of the malonic ester synthesis. The reaction begins with conversion of diethyl acetamidomalonate into an enolate ion by treatment with base, followed by alkylation with a primary alkyl halide. Hydrolysis of both the amide protecting group and the esters occurs when the alkylated product is warmed with aqueous acid, and decarboxylation then takes place to yield an *a*-amino acid. For example, aspartic acid can be prepared from ethyl bromoacetate, $BrCH_2CO_2Et$:



Reductive Amination of a-Keto Acids

Yet another method for the synthesis of *a*-amino acids is by reductive amination of an *a*-keto acid with ammonia and a reducing agent. Alanine, for instance, is prepared by treatment of pyruvic acid with ammonia in the presence of $NaBH_4$. The reaction proceeds through formation of an intermediate imine that is then reduced.



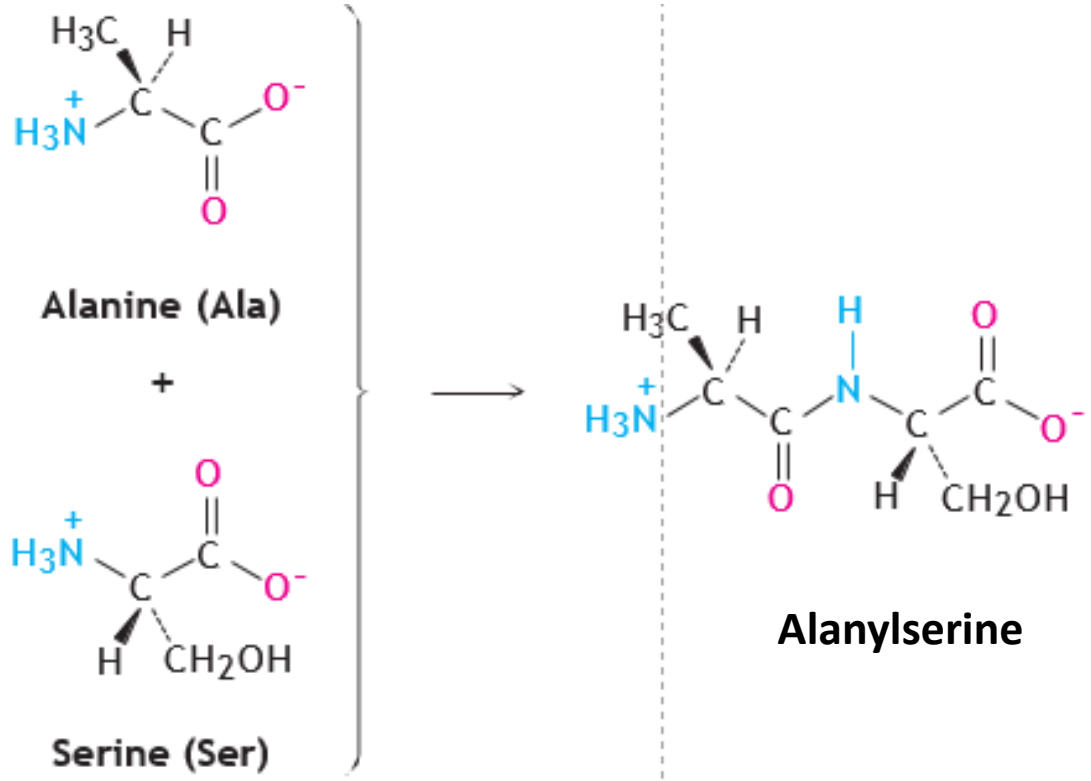
Pyruvic acid

Imine intermediate

(*R*,*S*)-Alanine

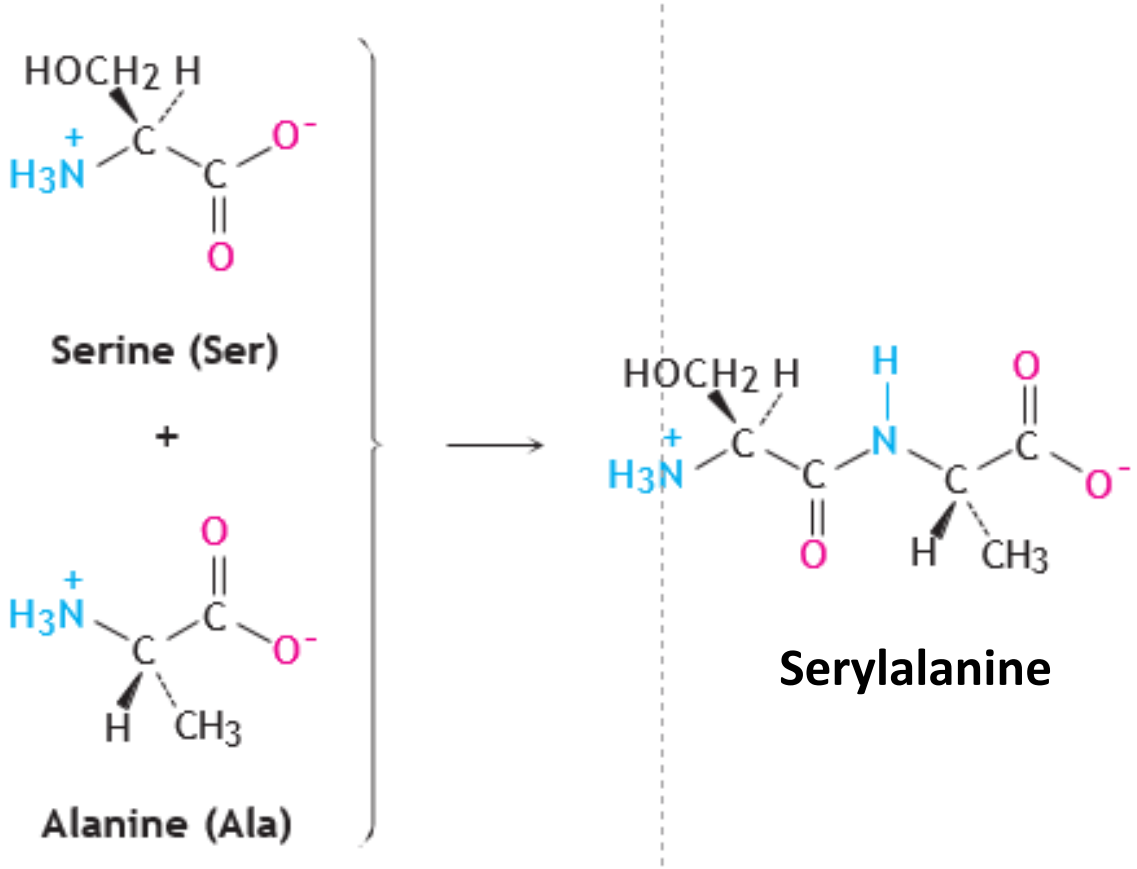
Peptides

Proteins and peptides are amino acid polymers in which the individual amino acids, called **residues**, are linked together by amide bonds, or *peptide bonds*. An amino group from one residue forms an amide bond with the carboxyl of a second residue, the amino group of the second forms an amide bond with the carboxyl of a third, and so on. For example, alanylserine is the dipeptide that results when an amide bond forms between the alanine carboxyl and the serine amino group.



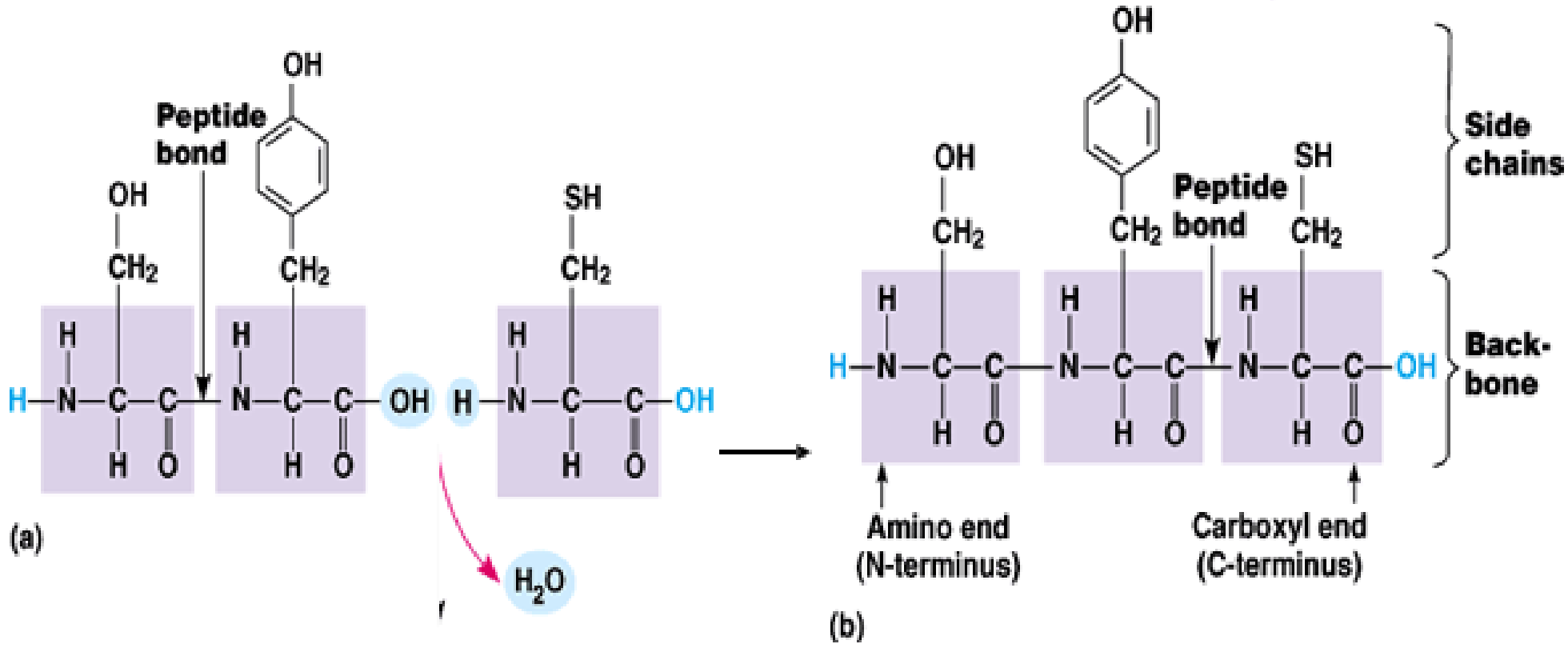
Peptides

Note that two dipeptides can result from reaction between alanine and serine, depending on which carboxyl group reacts with which amino group. If the alanine amino group reacts with the serine carboxyl, serylalanine results.



Peptides

A chain consisting of only two amino acid units is called a dipeptide; a chain consisting of three is a tripeptide. By convention, peptide and protein structures are depicted with the amino acid whose amino group is free (the N-terminal end) on the left and the amino acid with a free carboxyl group (the C-terminal end) to the right.



Biochemistry

Najaf Polytechnic Collage

Protein & Enzym
3st Lecture

Assistant lecturer. Hayder Abed

Structure of protein

A protein's primary structure is the unique sequence of amino acids in each polypeptide chain that makes up the protein. Really, this is just a list of which amino acids appear in which order in a polypeptide chain, not really a structure. But, because the final protein structure ultimately depends on this sequence, this was called the primary structure of the polypeptide chain. For example, the pancreatic hormone insulin has two polypeptide chains, A and B.
The primary structure of a protein is its unique sequence of amino acids.

1- Primary Structure

A protein's primary structure is the unique sequence of amino acids in each polypeptide chain that makes up the protein. Really, this is just a list of which amino acids appear in which order in a polypeptide chain, not really a structure. But, because the final protein structure ultimately depends on this sequence, this was called the primary structure of the polypeptide chain. For example, the pancreatic hormone insulin has two polypeptide chains, A and B.

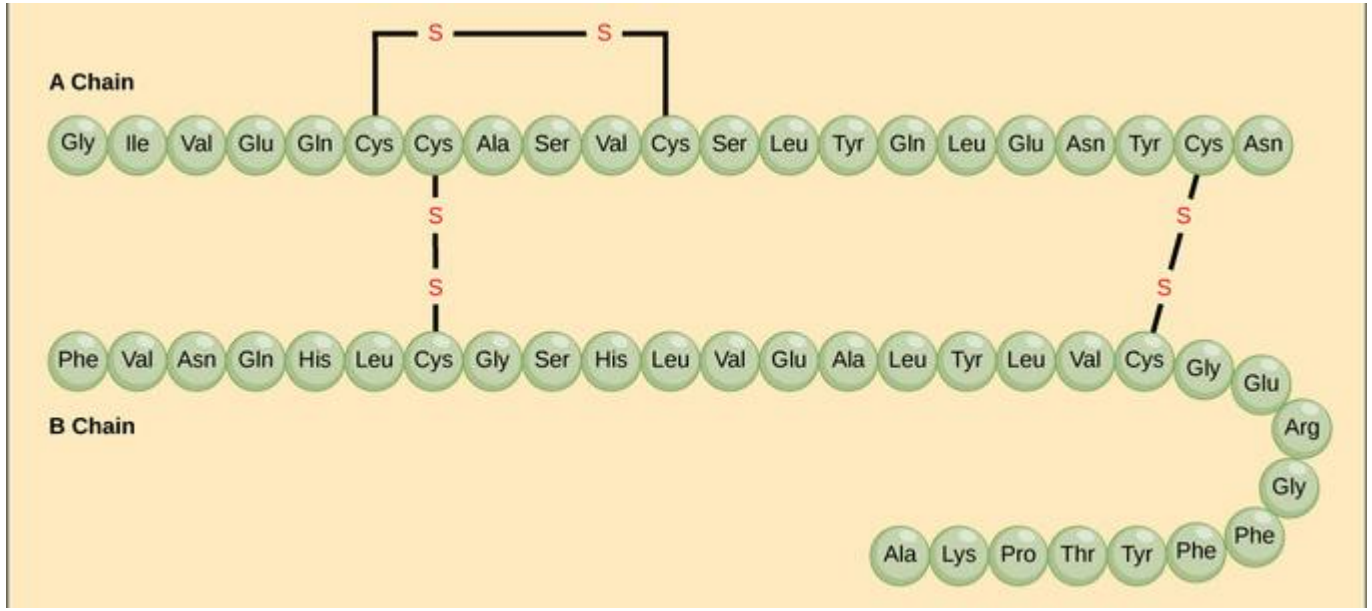


Figure 1 Primary structure: The A chain of insulin is 21 amino acids long and the B chain is 30 amino acids long, and each sequence is unique to the insulin protein.

Structure of protein

2- Secondary Structure

A protein's secondary structure is whatever regular structures arise from interactions between neighboring or near-by amino acids as the polypeptide starts to fold into its functional three-dimensional form. Secondary structures arise as H bonds form between local groups of amino acids in a region of the polypeptide chain. Rarely does a single secondary structure extend throughout the polypeptide chain. It is usually just in a section of the chain. The most common forms of secondary structure are the α-helix and β-pleated sheet structures and they play an important structural role in most globular and fibrous proteins.

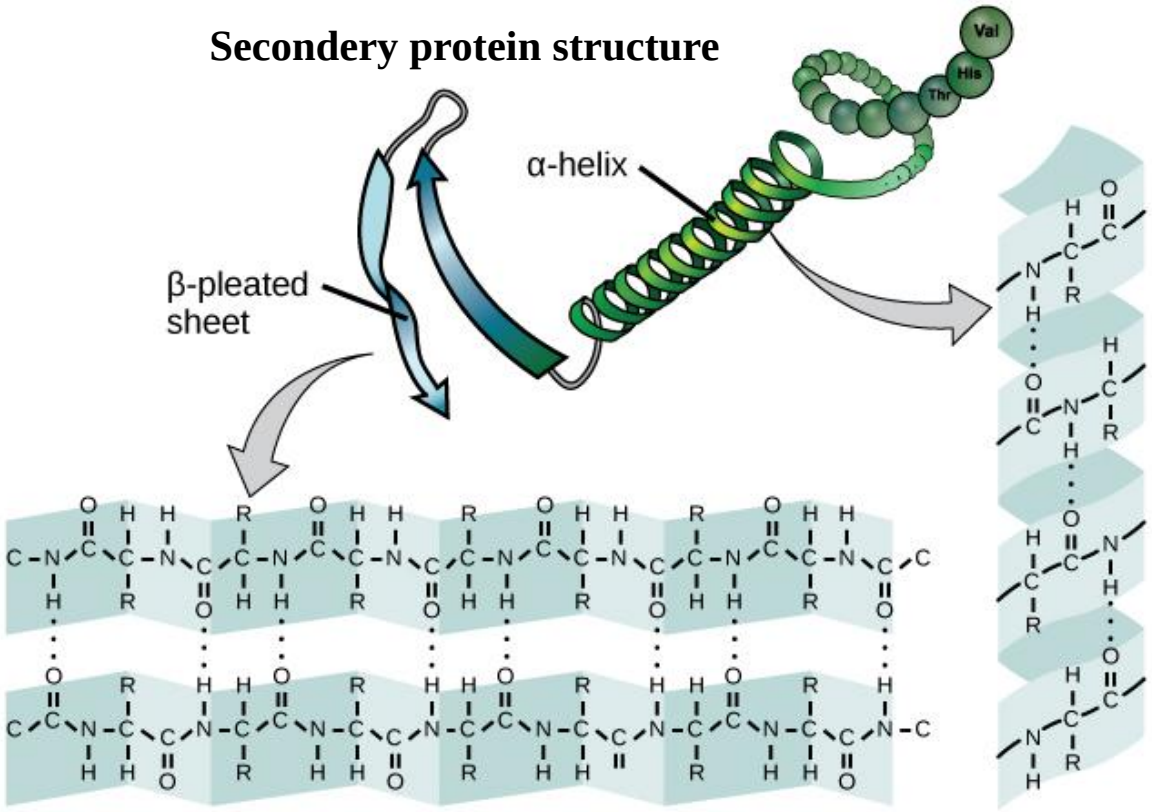


Figure 2: Secondary structure: The α-helix and β-pleated sheet form because of hydrogen bonding between carbonyl and amino groups in the peptide backbone. Certain amino acids have a propensity to form an α-helix, while others have a propensity to form a β-pleated sheet.

Structure of protein

In the α-helix chain, the hydrogen bond forms between the oxygen atom in the polypeptide backbone carbonyl group in one amino acid and the hydrogen atom in the polypeptide backbone amino group of another amino acid that is four amino acids farther along the chain.

This holds the stretch of amino acids in a right-handed coil. Every helical turn in an alpha helix has 3.6 amino acid residues. The R groups (the side chains) of the polypeptide protrude out from the α-helix chain and are not involved in the H bonds that maintain the α-helix structure.

In β-pleated sheets, stretches of amino acids are held in an almost fully-extended conformation that “pleats” or zig-zags due to the non-linear nature of single C-C and C-N covalent bonds. β-pleated sheets never occur alone. They have to held in place by other β-pleated sheets.

The stretches of amino acids in β-pleated sheets are held in their pleated sheet structure because hydrogen bonds form between the oxygen atom in a polypeptide backbone carbonyl group of one β-pleated sheet and the hydrogen atom in a polypeptide backbone amino group of another β-pleated sheet.

The β-pleated sheets which hold each other together align parallel or antiparallel to each other. The R groups of the amino acids in a β-pleated sheet point out perpendicular to the hydrogen bonds holding the β-pleated sheets together, and are not involved in maintaining the β-pleated sheet structure.

Structure of protein

3- Tertiary Structure

The tertiary structure of a polypeptide chain is its overall three-dimensional shape, once all the secondary structure elements have folded together among each other. Interactions between polar, nonpolar, acidic, and basic R group within the polypeptide chain create the complex three-dimensional tertiary structure of a protein. When protein folding takes place in the aqueous environment of the body, the hydrophobic R groups of nonpolar amino acids mostly lie in the interior of the protein, while the hydrophilic R groups lie mostly on the outside. Cysteine side chains form disulphide linkages in the presence of oxygen, the only covalent bond forming during protein folding. All of these interactions, weak and strong, determine the final three-dimensional shape of the protein. When a protein loses its three-dimensional shape, it will no longer be functional.

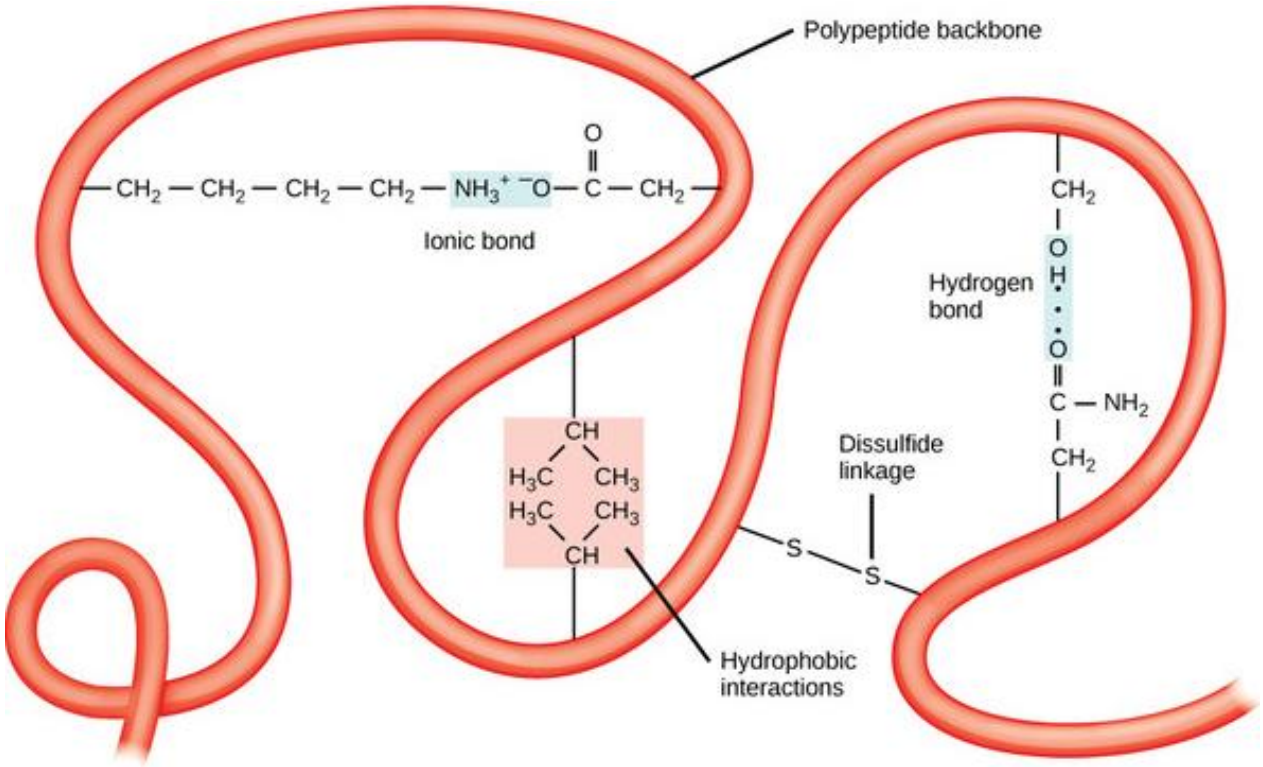


Figure 3: Tertiary structure: The tertiary structure of proteins is determined by hydrophobic interactions, ionic bonding, hydrogen bonding, and disulfide linkages.

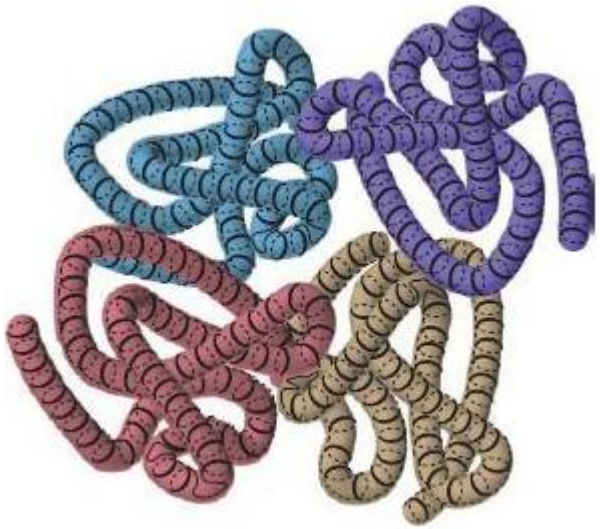
Structure of protein

4- Quaternary Structure

The quaternary structure of a protein is how its subunits are oriented and arranged with respect to one another. As a result, quaternary structure only applies to multi-subunit proteins; that is, proteins made from more than one polypeptide chain. Proteins made from a single polypeptide will not have a quaternary structure.

In proteins with more than one subunit, weak interactions between the subunits help to stabilize the overall structure. Enzymes often play key roles in bonding subunits to form the final, functioning protein.

For example, insulin is a ball-shaped, globular protein that contains both hydrogen bonds and disulphide bonds that hold its two polypeptide chains together. Silk is a fibrous protein that results from hydrogen bonding between different β-pleated chains.



Quatenary Structure

Figure 4: Quatenary structure

Key Points

1. Protein structure depends on its amino acid sequence and local, low-energy chemical bonds between atoms in both the polypeptide backbone and in amino acid side chains.
2. Protein structure plays a key role in its function; if a protein loses its shape at any structural level, it may no longer be functional.
3. Primary structure is the amino acid sequence.
4. Secondary structure is local interactions between stretches of a polypeptide chain and includes α-helix and β-pleated sheet structures.
5. Tertiary structure is the overall the three-dimension folding driven largely by interactions between R groups.
6. Quarternary structures is the orientation and arrangement of subunits in a multi-subunit protein.

Enzyme (catalyst)

Enzymes are catalysts that drive reaction rates forward. Most catalysts, but not all, are made up of amino acid chains called proteins that accelerate the rate of reactions in chemical systems. The functionality of a catalyst depends on how the proteins are folded, what they bind to, and what they react with. For protein-based catalysts, amino acid polarization lies at the core of catalytic activity.

Activation Energy

In chemistry, a catalyst is a chemical that drives a reaction forward. Catalysts lower the activation energy, which is the amount of energy required for reactants to form products (Figure 5). Catalysts also lower the kinetic barrier, which is needed to drive a reaction forward and backward. A certain amount of energy contained in the molecules is required when the two molecules react together to form a product. If the two molecules do not have enough energy to react, then no product is produced. By lowering the activation energy, a catalyst allows the molecules to gain sufficient energy to overcome the barrier and form products.

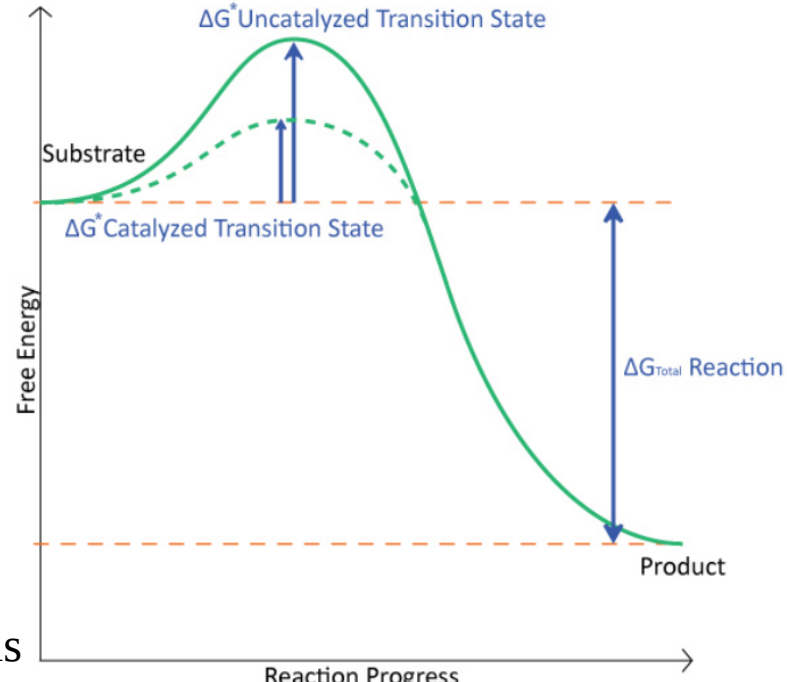


Figure 5: Energetic considerations of catalysis

Enzyme Action

Enzyme-catalyzed reactions occur in at least two steps. In the first step, an enzyme molecule (E) and the substrate molecule or molecules (S) collide and react to form an intermediate compound called the *enzyme-substrate* (E–S) *complex*. (This step is reversible because the complex can break apart into the original substrate or substrates and the free enzyme.) Once the E–S complex forms, the enzyme is able to catalyze the formation of product (P), which is then released from the enzyme surface:

$$E + S \rightarrow E - S$$
$$E - S \rightarrow P + E$$

Hydrogen bonding and other electrostatic interactions hold the enzyme and substrate together in the complex. The structural features or functional groups on the enzyme that participate in these interactions are located in a cleft or pocket on the enzyme surface. This pocket, where the enzyme combines with the substrate and transforms the substrate to product is called the active site of the enzyme (Figure 6).

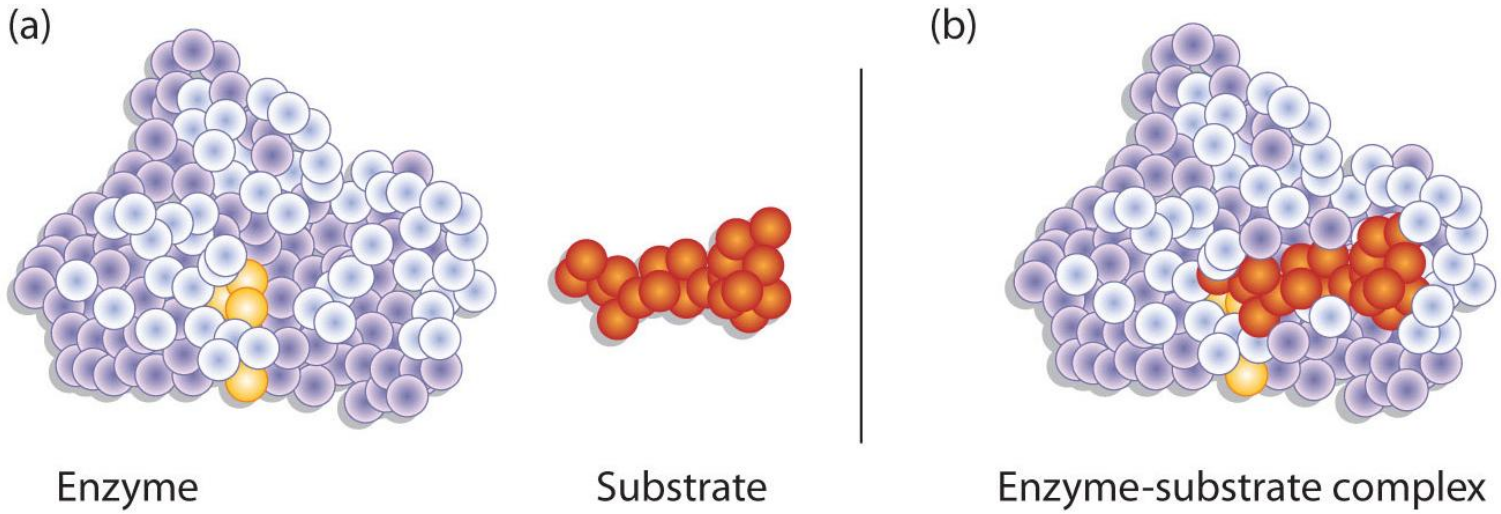


Figure 6 : Substrate Binding to the Active Site of an Enzyme. The enzyme dihydrofolate reductase is shown with one of its substrates: NADP (a) unbound and (b) bound. The NADP (shown in red) binds to a pocket that is complementary to it in shape and ionic properties.

Models of Enzyme-Substrate Interaction

1- lock-and-key model

The active site of an enzyme possesses a unique conformation (including correctly positioned bonding groups) that is complementary to the structure of the substrate, so that the enzyme and substrate molecules fit together in much the same manner as a key fits into a tumbler lock. In fact, an early model describing the formation of the enzyme-substrate complex was called the **lock-and-key model** (Figure). This model portrayed the enzyme as conformational rigid and able to bond only to substrates that exactly fit the active site. Working out the precise three-dimensional structures of numerous enzymes has enabled chemists to refine the original lock-and key model of enzyme actions. They discovered that the binding of a substrate often leads to a large conformational change in the enzyme, as well as to changes in the structure of the substrate or substrates.

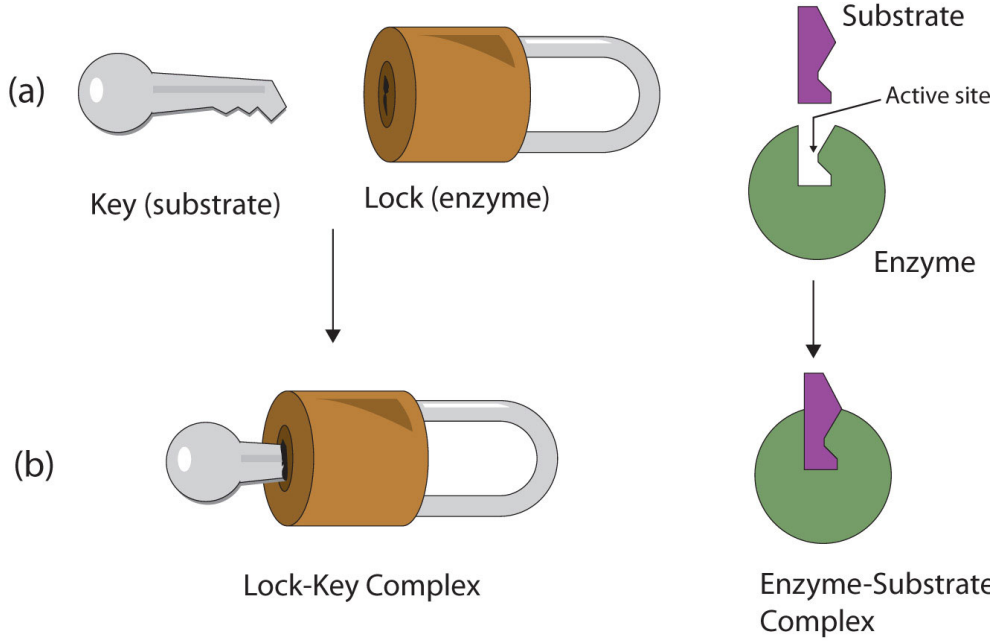


Figure 7 Figure : The Lock-and-Key Model of Enzyme Action. (a) Because the substrate and the active site of the enzyme have complementary structures and bonding groups, they fit together as a key fits a lock. (b) The catalytic reaction occurs while the two are bonded together in the enzyme-substrate complex.

Models of Enzyme-Substrate Interaction

2- induced-fit model

The current theory, known as the **induced-fit model**, says that enzymes can undergo a change in conformation when they bind substrate molecules, and the active site has a shape complementary to that of the substrate only *after* the substrate is bound, as shown for hexokinase in Figure . After catalysis, the enzyme resumes its original structure.

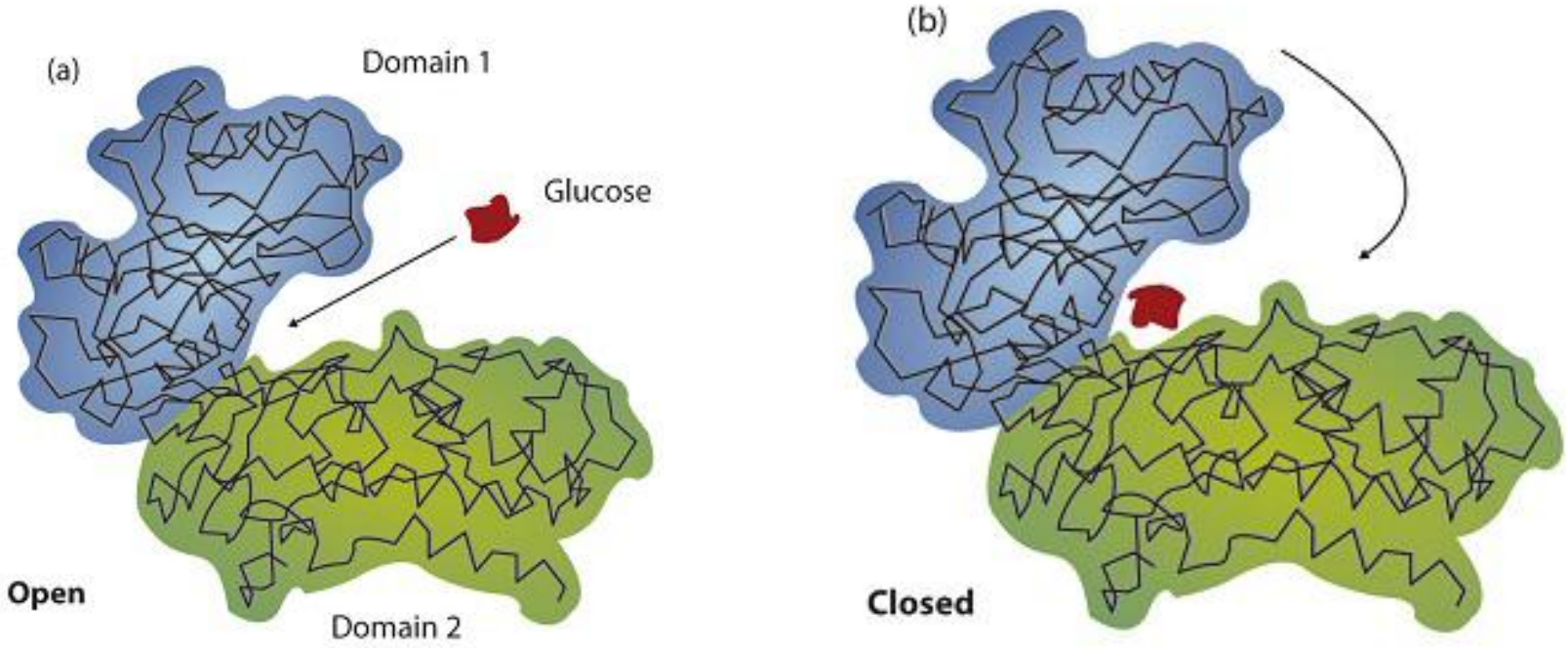
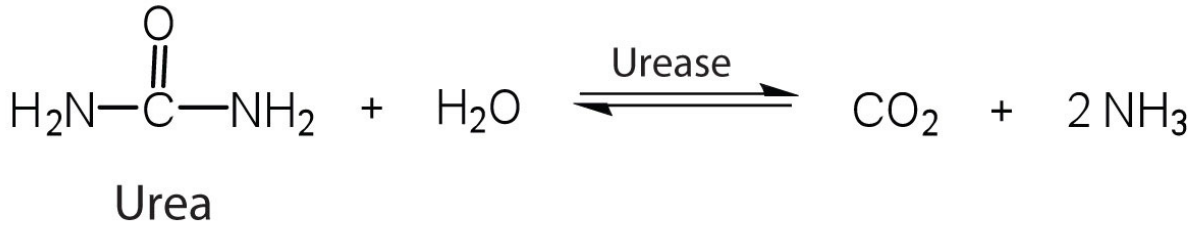


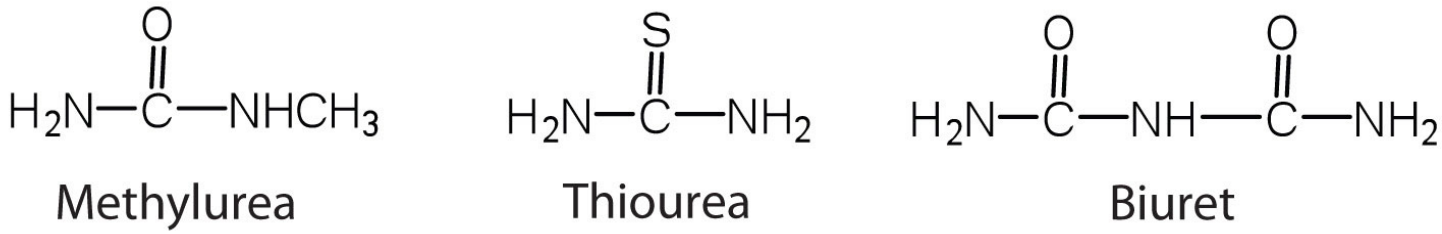
Figure 8: The Induced-Fit Model of Enzyme Action. (a) The enzyme hexokinase without its substrate (glucose, shown in red) is bound to the active site. (b) The enzyme conformation changes dramatically when the substrate binds to it, resulting in additional interactions between hexokinase and glucose.

Models of Enzyme-Substrate Interaction

3- substrate specificity

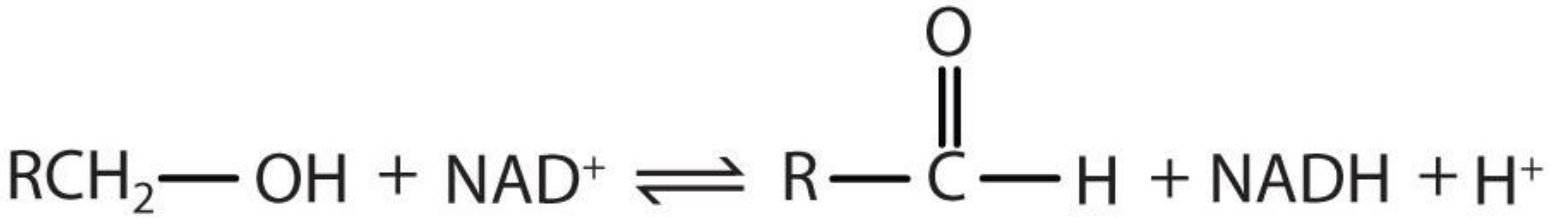
One characteristic that distinguishes an enzyme from all other types of catalysts is its **substrate specificity**. An inorganic acid such as sulfuric acid can be used to increase the reaction rates of many different reactions, such as the hydrolysis of disaccharides, polysaccharides, lipids, and proteins, with complete impartiality. In contrast, enzymes are much more specific. Some enzymes act on a single substrate, while other enzymes act on any of a group of related molecules containing a similar functional group or chemical bond. Some enzymes even distinguish between D- and L-stereoisomers, binding one stereoisomer but not the other. Urease, for example, is an enzyme that catalyzes the hydrolysis of a single substrate—urea—but not the closely related compounds methyl urea, thiourea, or biuret. The enzyme carboxypeptidase, on the other hand, is far less specific. It catalyzes the removal of nearly any amino acid from the carboxyl end of any peptide or protein.





Enzyme Nomenclature

Most enzymes can be recognized because they have the family name ending *–ase*. However, the first enzymes to be discovered were named according to their source or method of discovery. The enzyme *pepsin*, which aids in the hydrolysis of proteins, is found in the digestive juices of the stomach (Greek *pepsis*, meaning “digestion”). *Papain*, another enzyme that hydrolyzes protein (in fact, it is used in meat tenderizers), is isolated from papayas. In addition to the family name, more systematic enzyme names will give two sepcific pieces of information: the first part is the *substrate* upon which the enzyme acts, and the second part is the *type of reaction* it catalyzes. For example, alcohol dehydrogenase catalyzes the *oxidation* of an *alcohol* to an aldehyde.



Enzyme Cofactors

Many enzymes are simple proteins consisting entirely of one or more amino acid chains. Other enzymes contain a non-protein component called a **cofactor** that is necessary for the enzyme's proper functioning. There are two types of cofactors: inorganic ions [e.g., zinc or Cu(I) ions] and organic molecules known as coenzymes. Most **coenzymes** are vitamins or are derived from vitamins. Vitamins are organic compounds that are essential in very small (trace) amounts for the maintenance of normal metabolism. They generally cannot be synthesized at adequate levels by the body and must be obtained from the diet. The absence or shortage of a vitamin may result in a vitamin-deficiency disease. Because organisms differ in their synthetic abilities, a substance that is a vitamin for one species may not be so for another. Over the past 100 years, scientists have identified and isolated 13 vitamins required in the human diet and have divided them into two broad categories: the *fat-soluble vitamins*, which include vitamins A, D, E, and K, and the *water-soluble vitamins*, which are the B complex vitamins and vitamin C. All fat-soluble vitamins contain a high proportion of hydrocarbon structural components. There are one or two oxygen atoms present, but the compounds as a whole are nonpolar. In contrast, water-soluble vitamins contain large numbers of electronegative oxygen and nitrogen atoms, which can engage in hydrogen bonding with water. Most water-soluble vitamins act as coenzymes or are required for the synthesis of coenzymes. The fat-soluble vitamins are important for a variety of physiological functions.





Biochemistry

Najaf Polytechnic Collage

Lipid
1st Lecture

Assistant lecturer. Hayder Abed

Lipid

Fats and oils, found in many of the foods we eat, belong to a class of biomolecules known as **lipids**. Gram for gram, they pack more than twice the caloric content of carbohydrates: the oxidation of fats and oils supplies about 9 kcal of energy for every gram oxidized, whereas the oxidation of carbohydrates supplies only 4 kcal/g. Although the high caloric content of fats may be bad news for the dieter, it says something about the efficiency of nature's designs. Our bodies use carbohydrates, primarily in the form of glucose, for our *immediate* energy needs. Our capacity for storing carbohydrates for later use is limited to tucking away a bit of glycogen in the liver or in muscle tissue. We store our *reserve* energy in lipid form, which requires far less space than the same amount of energy stored in carbohydrate form. Lipids have other biological functions besides energy storage.

They are a major component of the membranes of the 10 trillion cells in our bodies. They serve as protective padding and insulation for vital organs. Furthermore, without lipids in our diets, we would be deficient in the fat-soluble vitamins A, D, E, and K. Lipids are not defined by the presence of specific functional groups, as carbohydrates are, but by a physical property—solubility. Compounds isolated from body tissues are classified as lipids if they are more soluble in organic solvents, such as dichloromethane, than in water. By this criterion, the lipid category includes not only fats and oils, which are esters of the trihydroxy alcohol glycerol and fatty acids, but also compounds that incorporate functional groups derived from phosphoric acid, carbohydrates, or amino alcohols, as well as steroid compounds such as cholesterol (Figure presents one scheme for classifying the various kinds of lipids). We will discuss the various kinds of lipids by considering one subclass at a time and pointing out structural similarities and differences as we go.

Classification of Lipids

Lipids are not defined by the presence of specific functional groups, as carbohydrates are, but by a **physical property—solubility. Compounds isolated** from body tissues are classified as lipids if they are more soluble in organic solvents, such as dichloromethane, than in water. By this criterion, the lipid category includes not only fats and oils, which are esters of the trihydroxy alcohol glycerol and fatty acids, but also compounds that incorporate functional groups derived from phosphoric acid, **carbohydrates**, or **amino alcohols**, as well as **steroid** compounds such as **cholesterol** (Figure 1 presents one scheme for classifying the various kinds of lipids).

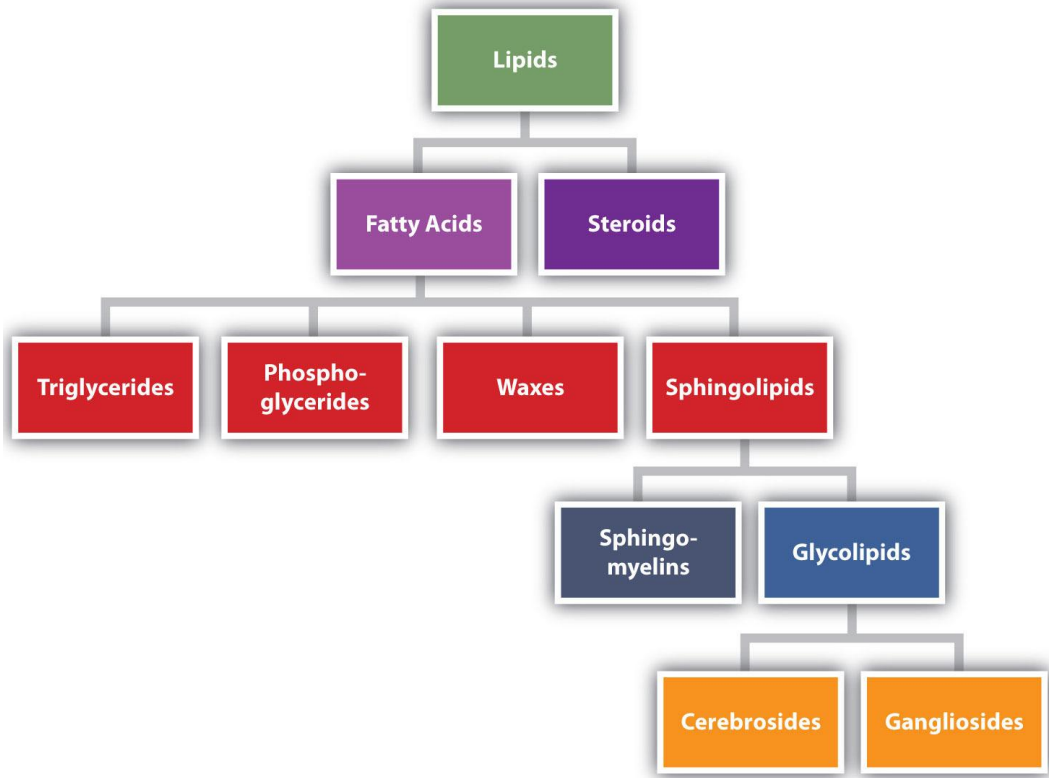
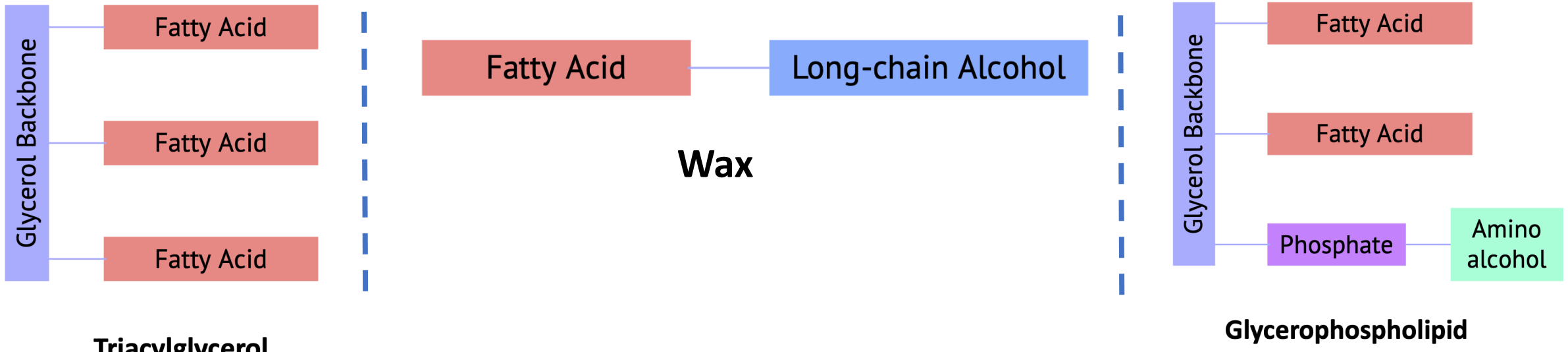


Figure 1 : Lipid Organization Based on Structural Relationships

Lipids Formed from Fatty Acids

Fatty acids are carboxylic acids with 12-22 carbon atoms connected in a long, unbranched chain. As shown in the diagram above, most lipids are classified as *esters* or *amides* of fatty acids.

1. ***Waxes*** are esters formed from long-chain fatty acids and long-chain alcohols. Most natural waxes are mixtures of such esters.
2. ***Triacylglycerol*** (triglycerides) are esters of glycerol, a trialcohol, and three fatty acids. Many organisms store energy in this form.
3. ***Glycerophospholipids*** are esters of glycerol formed from two fatty acid chains and a charged phosphate.
4. ***Sphingolipids*** are fatty acid amides formed from a fatty acid attached to an amino alcohol backbone, called sphingosine, along with either a phosphate (*sphingomyelin*) or a carbohydrate (*glycolipid*). These along with glycerophospholipids are important for the structure and function of cellular membranes.



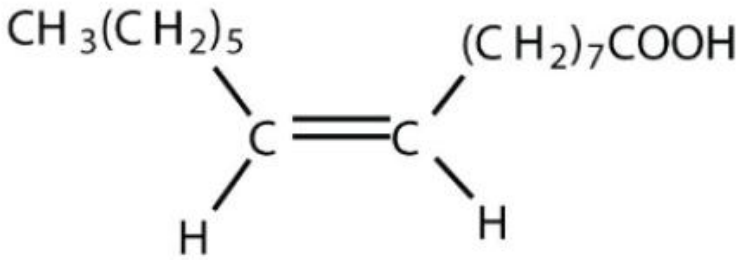
Fatty Acids

A fatty acid is a carboxylic acid with a long aliphatic chain, which is either saturated or unsaturated. Fatty acids that have carbon–carbon double bonds are known as unsaturated, while fatty acids without double bonds are known as saturated. Most naturally occurring fatty acids have an unbranched chain of an even number of carbon atoms, from 4 to 28. Fatty acids are usually derived from triglycerides or phospholipids. Fatty acids are important dietary sources of fuel for animals because, when metabolized, they yield large quantities of ATP. Many cell types can use either glucose or fatty acids for this purpose.

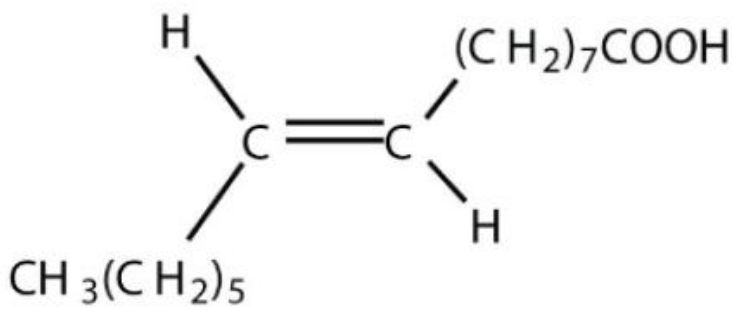
$$CH_3(CH)_nCOOH$$

Saturated and unsaturated fatty acids

Fatty acids are carboxylic acids that are structural components of fats, oils, and all other categories of lipids, except steroids. More than 70 have been identified in nature. They usually contain an even number of carbon atoms (typically 12–20), are generally unbranched, and can be classified by the presence and number of carbon-to-carbon double bonds. Thus, Fatty acids may be **saturated**, containing all carbon-carbon *single* bonds, or **unsaturated**, containing at least one or more carbon-carbon *double* bonds. Saturated fatty acids are *saturated with hydrogens*; in other words, the number of hydrogen atoms attached to the carbon skeleton is maximized. Stearic acid is an example of a saturated fatty acid (Figure 3). When the hydrocarbon chain contains a double bond, there are less hydrogens attached to the carbon skeleton and the fatty acid is said to be unsaturated. Oleic acid is an example of a *monounsaturated* fatty acid (Figure 3), because it contains one double bond. A fatty acid with two or more double bonds is a *polyunsaturated* fat. The atoms or groups around the double bonds in unsaturated fatty acids can be arranged in either the *cis* or *trans* isomeric form, compare *cis* vs. *trans* oleic acid in (Figure 3).Naturally occurring fatty acids are generally in the *cis* configuration.



cis fatty acid



trans fatty acid

Nomenclature of fatty acids

The position of the carbon atoms in a fatty acid can be indicated from the -COOH (or carboxy) end. Therefore, the C-1, C-2, C-3, (etc.) notation is used, where C-1 is the –COOH carbon. The positions of the double bonds in a fatty acid chain can, therefore, be indicated by the symbol (Δ). Thus, in an 18 carbon fatty acid, a double bond between C-12 and C-13 is reported as Δ^{12} (counted from the –COOH end), indicating only the beginning of the double bond, and the fatty acid is refer to as $18\Delta^{12}$. The "Δ" is the Greek letter "delta", which translates into "D" (for Double bond) in the Roman alphabet. Also, it can be refer to the fatty acid by numbering as follow (18:1:12). Fatty acids with an odd number of carbon atoms are called odd-chain fatty acids, whereas the rest are even-chain fatty acids.

In fact, there are two systems of nomenclature in use for fatty acids. Systematic names (or IUPAC names) derive from the standard IUPAC Rules for the Nomenclature of Organic Chemistry and Trivial names (or common names, non-systematic historical names) which are the most frequent naming system used in literature. The table below shows the name and structure of some fatty acids.

Nomenclature of fatty acids

Carbon skeleton	Structure*	Systematic name†	Common name (derivation)
12:0	$CH_3(CH_2)_{10}COOH$	*n*-Dodecanoic acid	Lauric acid (Latin *laurus*, "laurel plant")
14:0	$CH_3(CH_2)_{12}COOH$	*n*-Tetradecanoic acid	Myristic acid (Latin *Myristica*, nutmeg genus)
16:0	$CH_3(CH_2)_{14}COOH$	*n*-Hexadecanoic acid	Palmitic acid (Latin *palma*, "palm tree")
18:0	$CH_3(CH_2)_{16}COOH$	*n*-Octadecanoic acid	Stearic acid (Greek *stear*, "hard fat")
20:0	$CH_3(CH_2)_{18}COOH$	*n*-Eicosanoic acid	Arachidic acid (Latin *Arachis*, legume genus)
24:0	$CH_3(CH_2)_{22}COOH$	*n*-Tetracosanoic acid	Lignoceric acid (Latin *lignum*, "wood" + *cera*, "wax")
16:1(Δ^9)	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	*cis*-9-Hexadecenoic acid	Palmitoleic acid
18:1(Δ^9)	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	*cis*-9-Octadecenoic acid	Oleic acid (Latin *oleum*, "oil")
18:2($\Delta^{9,12}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-9,12-Octadecadienoic acid	Linoleic acid (Greek *linon*, "flax")
18:3($\Delta^{9,12,15}$)	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-,*cis*-9,12,15-Octadecatrienoic acid	α-Linolenic acid
20:4($\Delta^{5,8,11,14}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$	*cis*-,*cis*-,*cis*-,*cis*-5,8,11,14-Icosatetraenoic acid	Arachidonic acid

Physical properties of fatty acids:

The properties of lipids (fats and oils) are due to the two component units: fatty acids and alcohols. The physical properties of the fatty acids, and of compounds that contain them, are largely determined by the length and degree of unsaturation of the hydrocarbon chain. Fats containing saturated fatty acids are solid at ordinary room temperature. The animal fats belong to this category. Most plant fats, on the contrary, possess unsaturated fatty acids and are liquid at room temperature.

The melting point of fats depends on the chain length of the constituent fatty acid and the degree of unsaturation. Fats containing saturated fatty acids from C4 to C8 are liquid at room temperature but those containing C10 or higher saturated fatty acids are solid and their melting points increase with increasing chain length. With the introduction of double bond in the fat molecule, the melting point lowers considerably. It may be stated, in general, that greater the degree of unsaturation (or higher the number of double bonds) of the constituent fatty acid, the lower is the melting point of the fat. Short chain length and unsaturation enhance the fluidity of fatty acids and of their derivatives. The presence of double bond (s) in the unsaturated fatty acid part of the fat molecule produces geometric (or cis-trans) isomerism.

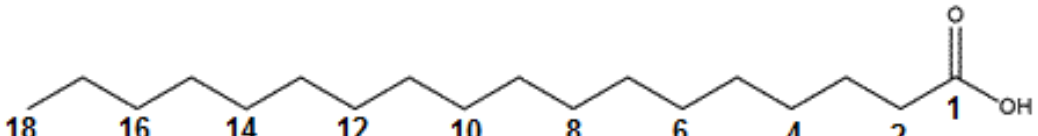
In fact, this difference in melting points is due to different degrees of packing of the fatty acid molecules. In the fully saturated compounds, free rotation around each carbon–carbon bond gives the hydrocarbon chain great flexibility; the most stable conformation is the fully extended form, in which the steric hindrance of neighboring atoms is minimized. These molecules can pack together tightly in nearly crystalline arrays, with atoms all along their lengths in van der Waals contact with the atoms of neighboring molecules. In unsaturated fatty acids, a cis-double bond forces a kink in the hydrocarbon chain. Fatty acids with one or several such kinks cannot pack together as tightly as fully saturated fatty acids, and their interactions with each other are therefore weaker. Because it takes less thermal energy to disorder these poorly ordered arrays of unsaturated fatty acids, they have markedly lower melting points than saturated fatty acids of the same chain length.

Physical properties of fatty acids:

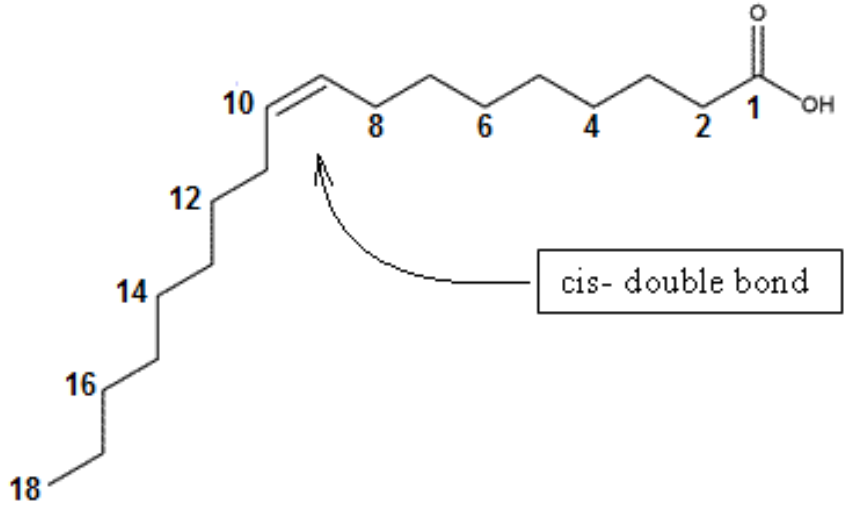
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Name	no. of C-atoms	no. of double bonds	Formula	Melting point
Stearic acid	18	none	$CH_3(CH_2)_{16}COOH$	70
Oleic acid	18	1	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	13
Linoleic acid	18	2	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COOH$	-5
Linolenic acid	18	3	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COOH$	-11
Arachidic acid	20	none	$CH_3(CH_2)_{18}COOH$	76
Arachidonic acid	20	4	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COOH$	-50

Physical properties of fatty acids:

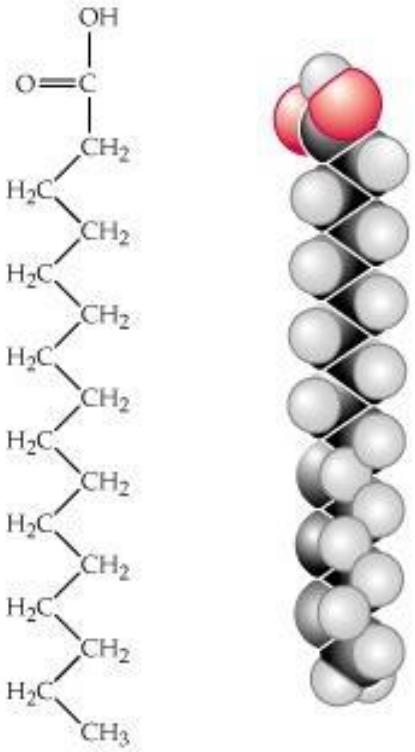


Stearic acid



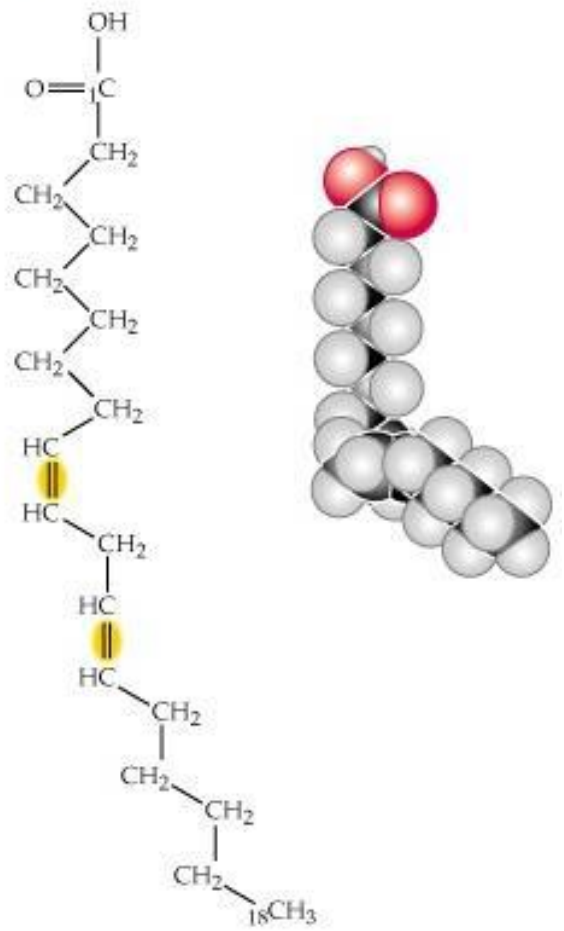
Oleic acid

(a) Saturated fatty acid



Palmitic acid

(b) Unsaturated fatty acid



Linoleic acid

Micelles

Micelles are lipid molecules that arrange themselves in a spherical form in aqueous solutions. The formation of a micelle is a response to the amphipathic nature of fatty acids, meaning that they contain both hydrophilic regions (polar head groups, acidic carboxyl groups) as well as hydrophobic regions (the long hydrophobic chain). Micelles contain polar head groups that usually form the outside as the surface of micelles. They face to the water because they are polar. The hydrophobic tails are inside and away from the water since they are nonpolar. Fatty acids from micelles usually have a single hydrocarbon chain as opposed to two hydrocarbon tails. This allows them to conform into a spherical shape for lesser steric hindrance within a fatty acid. Fatty acids from Glycolipids and phospholipids, on the other hand, have two hydrophobic chains that are too bulky to fit into the spherical shape as micelles do. Thus, they preferred to form glycolipids and phospholipids as lipid bilayers. Micelles form spontaneously in water, as stated above this spontaneous arrangement is due to the amphipatic nature of the molecule.

