Cell

- Compartment
- Cell membrane
- Chemical Reactions
- Biomolecules

Central Dogma

AIDS virus

DNA

RNA

Proteins

Transcription

Translation
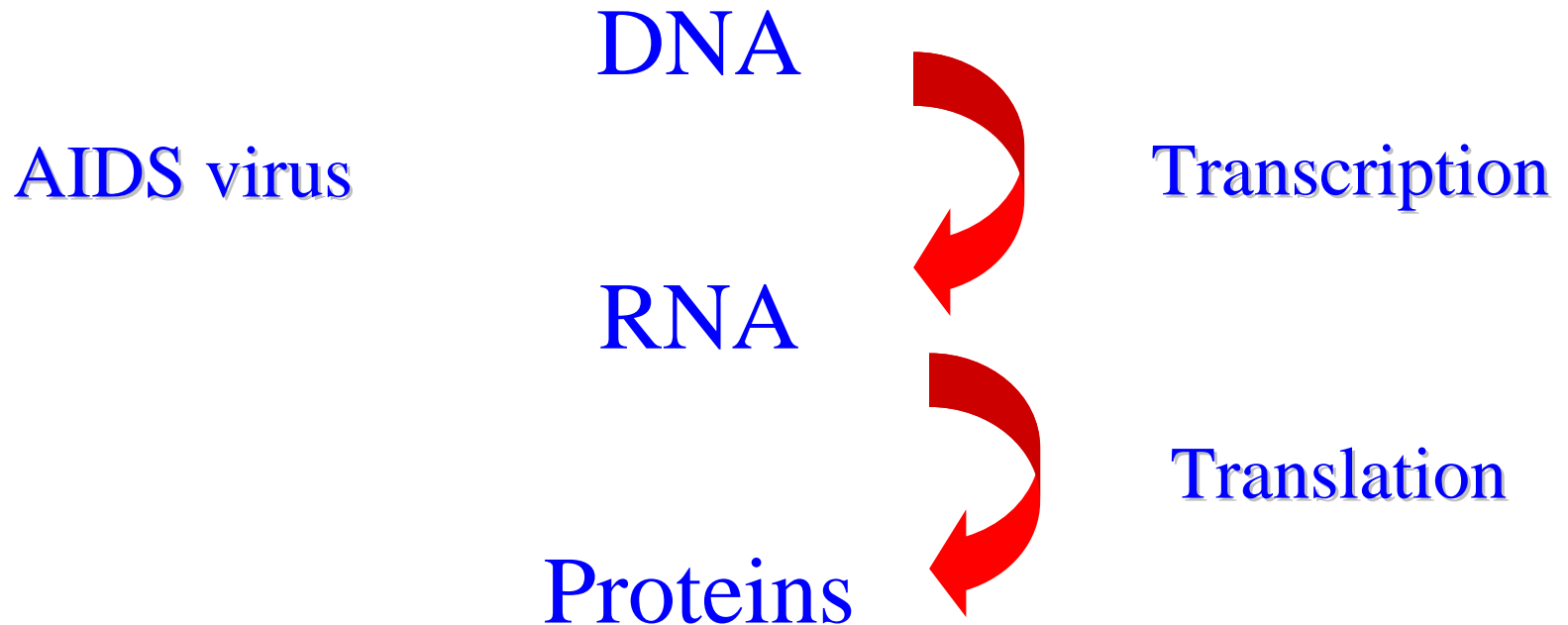
Life

Replication: reproduction

Function: catalytic functions

RNA world:

Virus is not alive

18.1 An Introduction to Biochemistry

Biochemistry - chemical basis of life. Biochemical reactions are involved in such areas as breaking down food molecules, generate and store energy, buildup new biomolecules, and eliminate waste. Some biomolecules are small and have only a few functional groups others are huge and contains a large number of functional groups. The principal classes of biomolecules are: *Proteins, lipids, and nucleic acids.*

**TABLE 18.1 Functional Groups of Importance in Biochemical Molecules**

Functional Group	Structure	Type of Biomolecule
Amino group	$-NH_3^+$, $-NH_2$	Amino acids and proteins (Sections 18.3, 18.7)
Hydroxyl group	$-OH$	Monosaccharides (carbohydrates) and glycerol: a component of triacylglycerols (lipids) (Sections 22.4, 24.2)
Carbonyl group	$$-\overset{\displaystyle O}{\overset{\|}{C}}-$$	Monosaccharides (carbohydrates); in acetyl group (CH_3CO) used to transfer carbon atoms during catabolism (Sections 22.4, 21.4, 21.8)
Carboxyl group	$$-\overset{\displaystyle O}{\overset{\|}{C}}-OH,\ -\overset{\displaystyle O}{\overset{\|}{C}}-O^-$$	Amino acids, proteins, and fatty acids (lipids) (Sections 18.3, 18.7, 24.2)
Amide group	$$-\overset{\displaystyle O}{\overset{\|}{C}}-\overset{\displaystyle }{\underset{\|}{N}}-$$	Links amino acids in proteins; formed by reaction of amino group and carboxyl group (Section 18.7)
Carboxylic acid ester	$$-\overset{\displaystyle O}{\overset{\|}{C}}-O-R$$	Triacylglycerols (and other lipids); formed by reaction of carboxyl group and hydroxyl group (Section 24.2)
Phosphates, mono-, di-, tri-	$$-\overset{\|}{\underset{\|}{C}}-O-\overset{\displaystyle O}{\underset{\underset{\displaystyle O^-}{\|}}{\overset{\|}{P}}}-O^-$$ $$-\overset{\|}{\underset{\|}{C}}-O-\overset{\displaystyle }{\underset{\underset{\displaystyle O^-}{\|}}{\overset{\|}{P}}}-O-\overset{\displaystyle O}{\underset{\underset{\displaystyle O^-}{\|}}{\overset{\|}{P}}}-O^-$$ $$-\overset{\|}{\underset{\|}{C}}-O-\overset{\displaystyle O}{\underset{\underset{\displaystyle O^-}{\|}}{\overset{\|}{P}}}-O-\overset{\displaystyle O}{\underset{\underset{\displaystyle O^-}{\|}}{\overset{\|}{P}}}-O-\overset{\displaystyle O}{\underset{\underset{\displaystyle O^-}{\|}}{\overset{\|}{P}}}-O^-$$	ATP and many metabolism intermediates (Sections 17.8, 21.5, and throughout metabolism sections)
Hemiacetal group	$$-\overset{\|}{\underset{\underset{\displaystyle OR}{\|}}{C}}-OH$$	Cyclic forms of monosaccharides; formed by a reaction of carbonyl group with hydroxyl group (Sections 16.7, 22.4)
Acetal group	$$-\overset{\|}{\underset{\underset{\displaystyle OR}{\|}}{C}}-OR$$	Connects monosaccharides in disaccharides and larger carbohydrates; formed by reaction of carbonyl group with hydroxyl group (Sections 16.7, 22.7, 22.9)

18.2 Protein Structure and Function: An Overview

◆ Proteins are polymers of amino acids.

◆ Each amino acids in a protein contains a amino group, $-NH_2$, a carboxyl group, -COOH, and an R group, all bonded to the central carbon atom. The R group may be a hydrocarbon or they may contain functional group.

- All amino acids present in a proteins are *α-amino acids* in which the amino group is bonded to the carbon next to the carboxyl group.

- Two or more amino acids can join together by forming amide bond, which is known as a *peptide bond* when they occur in proteins.

- A dipeptide results when two amino acids combine together by forming a peptide bond using amino group of one amino acid and carboxyl group of another amino acid.

Valine   Cysteine   A dipeptide
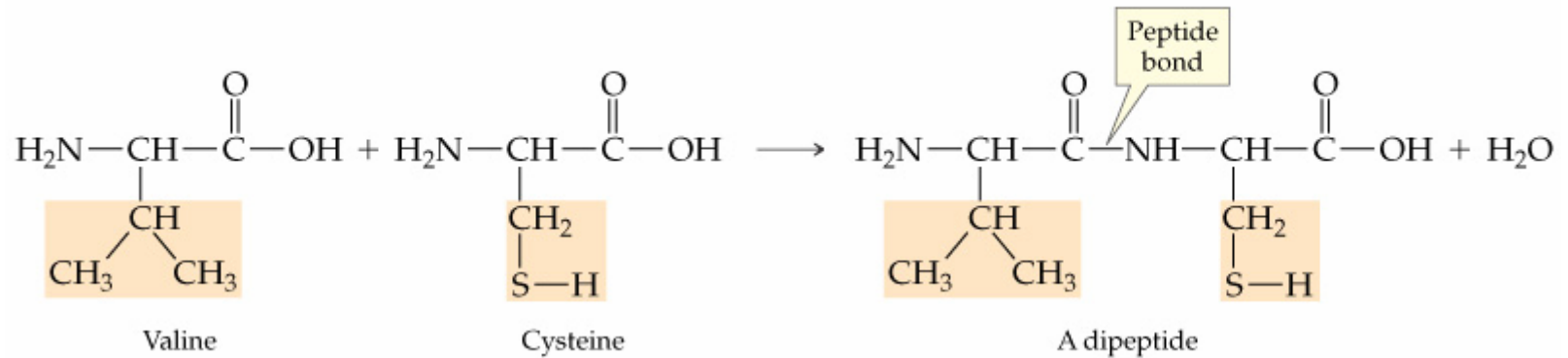
- A *tripeptide* results when three amino acids combine together by forming two peptide bonds, and so on. Any number of amino acids can link together and form a linear chain like polymer – *polypeptide*.
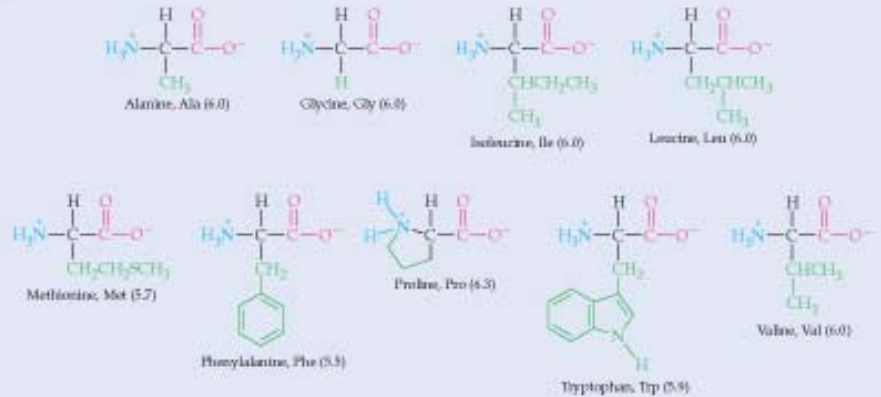
NH2-C-R-COOH

TABLE 18.3 The 20 Protein Amino Acids with their Abbreviations and Isoelectric Points. The structures are written here in their fully ionized forms. These ions and the isoelectric points given in parantheses are explained in Section 18.4.

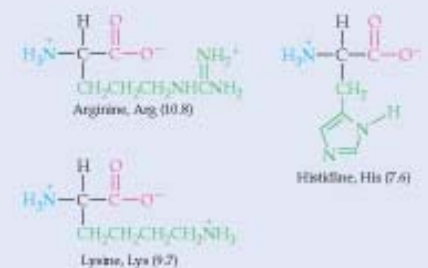- All but one natural amino acids differ only in the identity of the R group or side chain.

- The remaining amino acid (proline) is a five membered secondary amine.

- Each amino acid has a three letter shorthand code- for example, Ala (alanine), Gly (glycine), Pro (proline).

- 20 amino acids present in proteins are classified as neutral, acidic, or basic depending on the nature of the side chain.

- 15 neutral amino acids are divided into two groups – polar and nonpolar on the basis of the nature of their side chain.

18.4 Acid-Base Properties of Amino Acids

◆ Amino acids contain both an acidic group, -COOH, and a basic group, $-NH_2$.

◆ As a result of intermolecular acid base reaction, a proton is transferred from the $-COOH$ group to the $-NH_2$ group producing a dipolar ion or zwitterions that has a positive and also a negative charge and is thus electrically neutral.
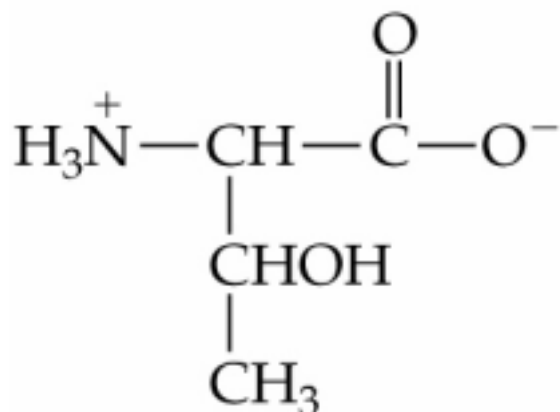
Threonine—zwitterion

Because they are zweitterion, amino acids have many properties that are common for salts. Such as

➢ amino acids crystalline
➢ amino acids have high melting points
➢ amino acids are water soluble.

- In acidic media (low pH), amino acid zweitterion accept a proton on their basic –COO^- group to leave only the positively charged –NH_3^+ group.

- In basic media (high pH), amino acid zweitterion loses a proton from their acidic –NH_3^+ group to leave only the negatively charged –COO^- group.

- The charge of an amino acid molecule at any given moment depends on the identity of the amino acid and pH of the medium.

- The pH at which the net positive and negative charges are evenly balanced is the amino acid's *isoelectric point*- the overall charges is zero.

18.5 Handedness
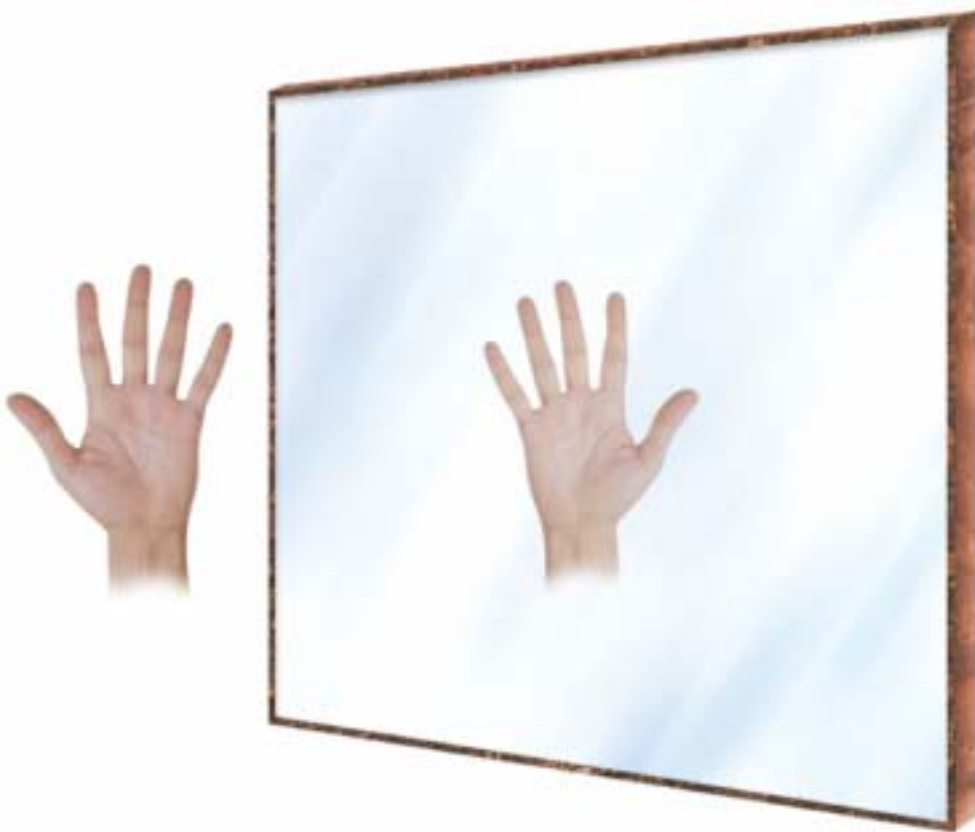
Mirror images of hand do not superimposes on each other. Image of left hand on the mirror looks like the right hand – objects that have handedness in this manner are said to be *chiral.*

18.6 Molecular Handedness and Amino Acids

◆ Like objects, organic molecules can also have handedness, that is they can be chiral.

Alanine, a chiral molecule

Mirror

"Left-handed"
L-alanine

"Right-handed"
D-alanine
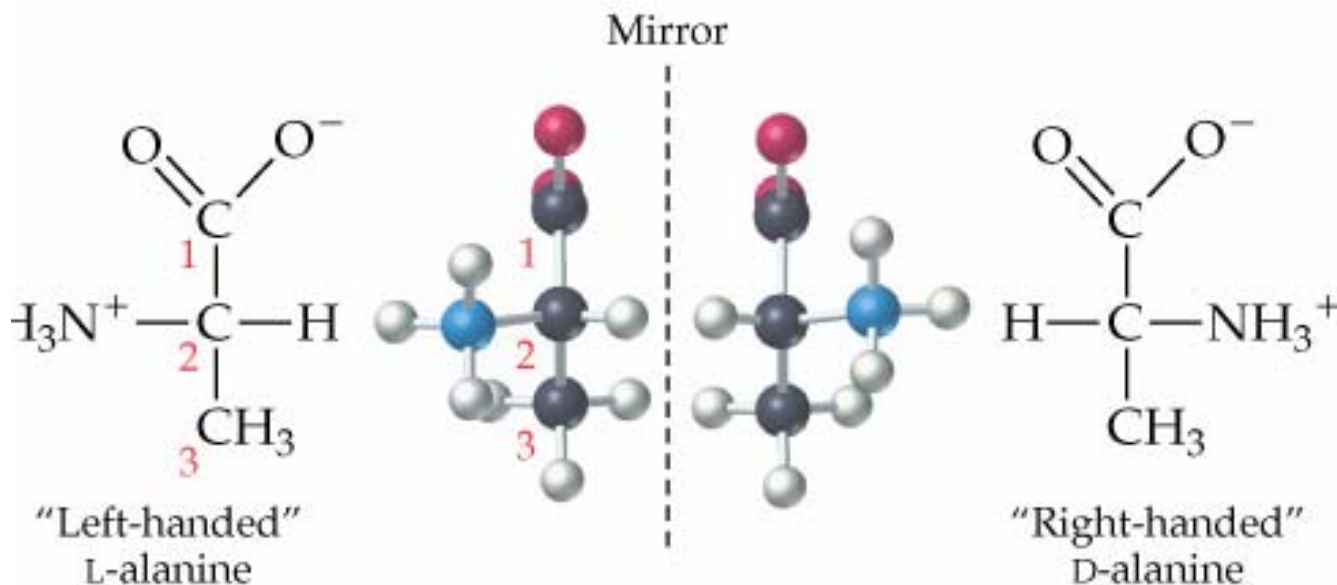
◆ A molecule is a chiral molecule if four different atoms or groups are attached to a carbon. The carbon carrying four different groups called a chiral carbon. Chiral molecules has no plane of symmetry.

◆ The two mirror image forms of a chiral molecule like alanine are called *enantiomers or optical isomers*.

◆ Enantiomers have the same formula but different arrangements of their atoms.

◆ 19 out of 20 natural amino acids are chiral – they have four different groups on the α-carbon. Only glycine is achiral.

◆ Nature uses only one isomer out of a pair of enantiomers for each amino acid to build the proteins.

◆ The naturally occurring amino acids are classified as left-handed or L-amino acids.

18.7 Primary Protein Structure

◆ Primary structure of a proteins is the sequence of amino acids connected by peptide bonds. Along the backbone of the proteins is a chain of alternating peptide bonds and α-carbons and the amino acid side chains are connected to these α-carbons.

Planar units along a protein chain

One planar unit
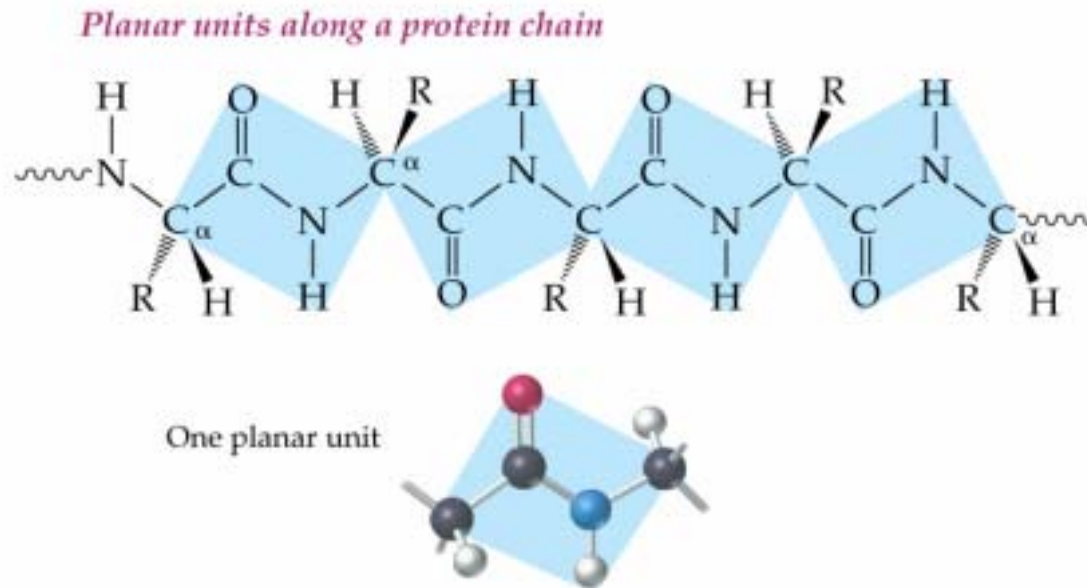
◆ By convention, peptides and proteins are always written with the amino terminal amino acid (N-terminal) on the left and carboxyl-terminal amino acid (C-terminal) on the right.

N ➡ C

18.8 Shape-Determining Interactions in Proteins

The essential structure-function relationship for each protein depends on the polypeptide chain being held in its necessary shape by the interactions of atoms in the side chains.

The kinds of interaction that determine the shape protein molecules are shown in Fig 18.4.
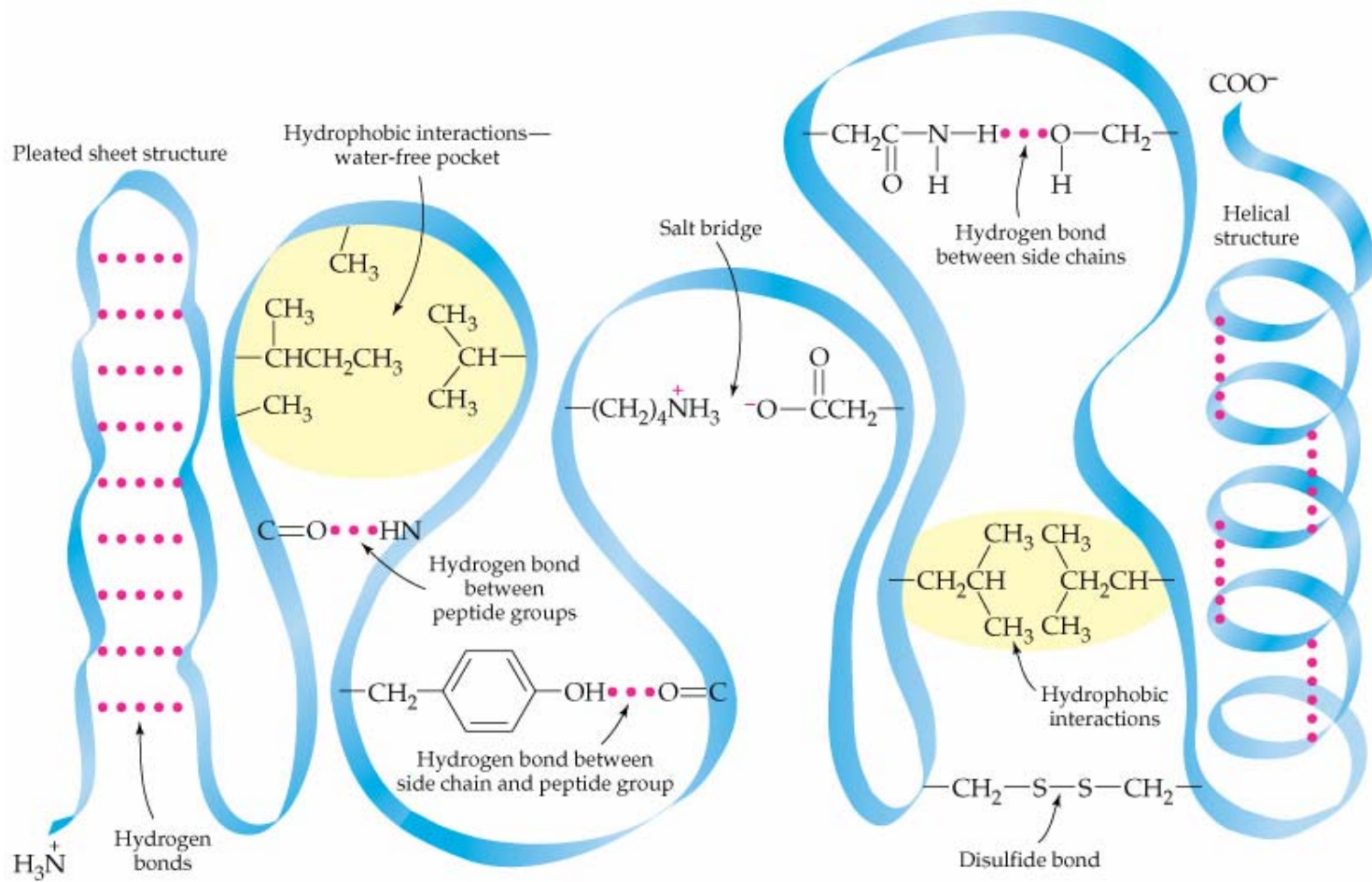
Fig 18.4 Interactions that determine protein shape

Protein shape determining interactions are summarized below:

◆ Hydrogen bond between neighboring backbone segments.

◆ Hydrogen bonds of side chains with each other or with backbone atoms.

◆ Ionic attractions between side chain groups or salt bridge.

◆ Hydrophobic interactions between side chain groups.

◆ Covalent sulfur-sulfur bonds.

18.9 Secondary Protein Structure

◆ Secondary structure of a protein is the arrangement of polypeptide backbone of the protein in space. The secondary structure includes two kinds of repeating pattern known as the *α-helix* and *β-sheet*.

Hydrogen bonding between backbone atoms are responsible for both of these secondary structures.

C-terminal end

3.6 amino acid
residues per turn

••••• H bonds
⬤ α-Carbon
⬤ Carbonyl carbon
○ Hydrogen
⬤ Nitrogen
⬤ Oxygen
⬤ Side chain

N-terminal end
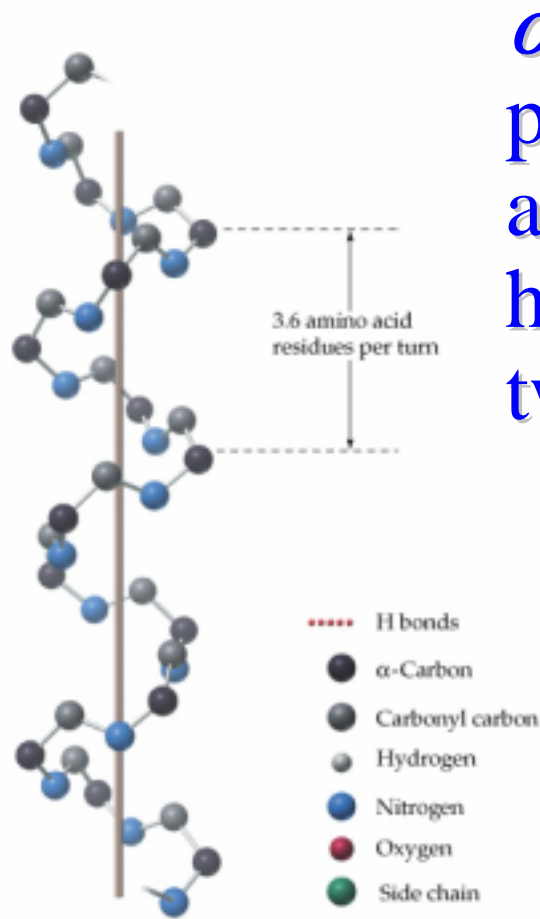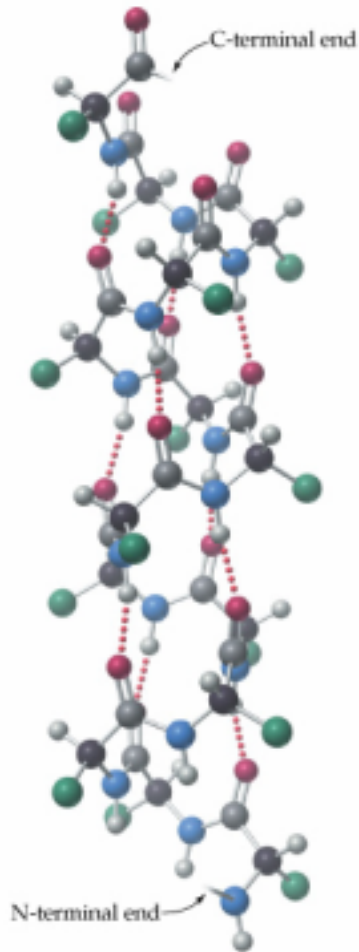
α-Helix: A single protein chain coiled in a spiral with a right-handed (clockwise) twist.

β-Sheet: The polypeptide chain is held in place by hydrogen bonds between pairs of peptide units along neighboring backbone segments.
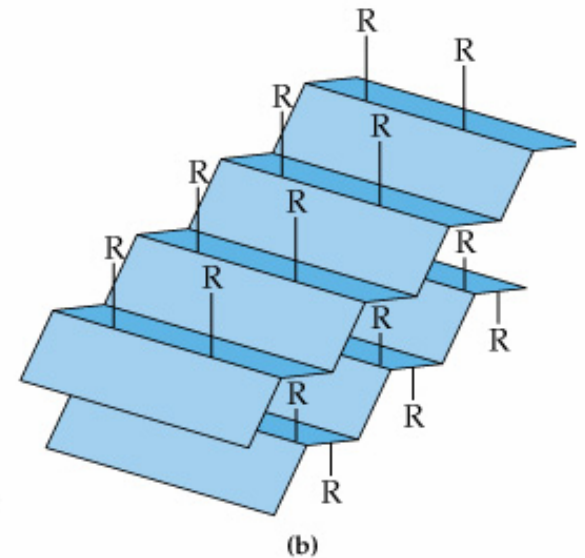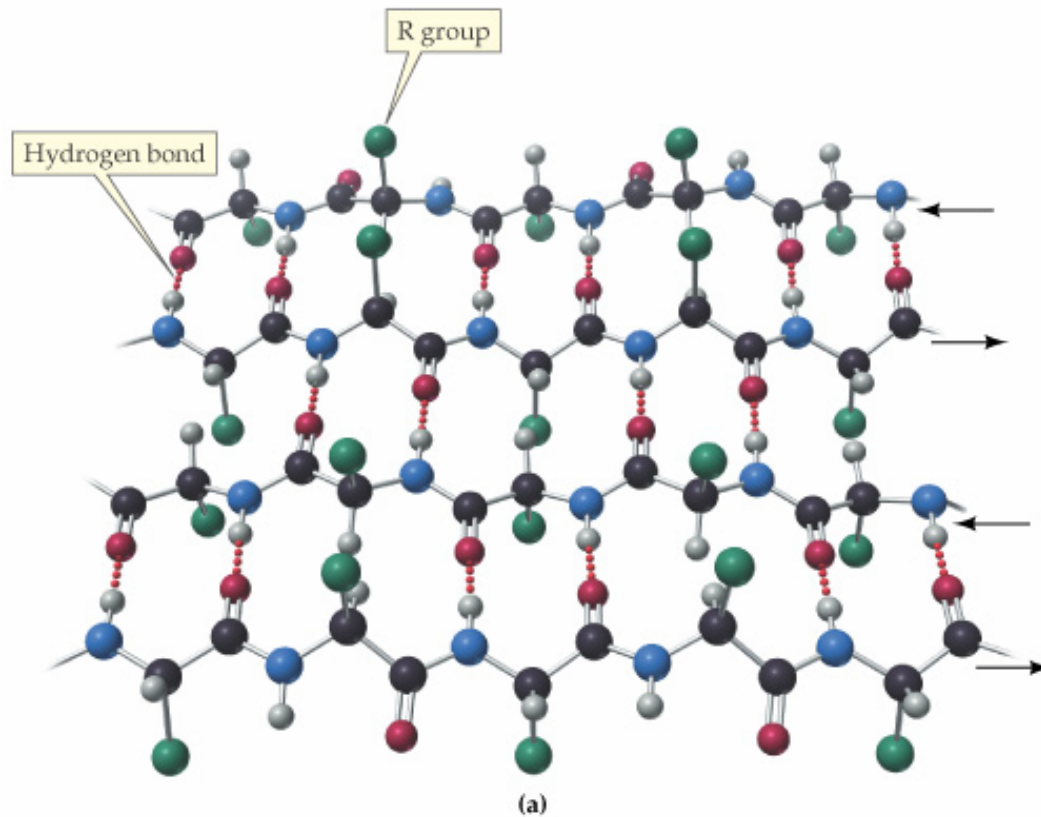
Fibrous and Globular proteins: one of the several classifications of proteins.

Fibrous protein: Tough and insoluble protein in which the chain form long fibers or sheet. Secondary structure is responsible for the shape of fibrous proteins. Wool, hair, and finger nails are made of fibrous proteins.

Globular protein: water soluble proteins whose chains are folded into compact, globular shape with hydrophilic groups on the outside.

18.10 Tertiary Protein Structure

Tertiary Structure of a proteins The overall three dimensional shape that results from the folding of a protein chain. Tertiary structure depends mainly on attractions of amino acid side chains that are far apart along the same backbone. Non-covalent interactions and disulfide covalent bonds govern tertiary structure.

A protein with the shape in which it exist naturally in living organisms is known as a *native protein.*

Simple protein: A protein composed of only amino acid residues.

Conjugated protein: A protein that incorporates one or more non-amino acid units in its structure.

18.11 Quaternary Protein Structure

Quaternary protein structure: The way in which two or more polypeptide sub-units associate to form a single three-dimensional protein unit. Non-covalent forces are responsible for quaternary structure essential to the function of proteins.
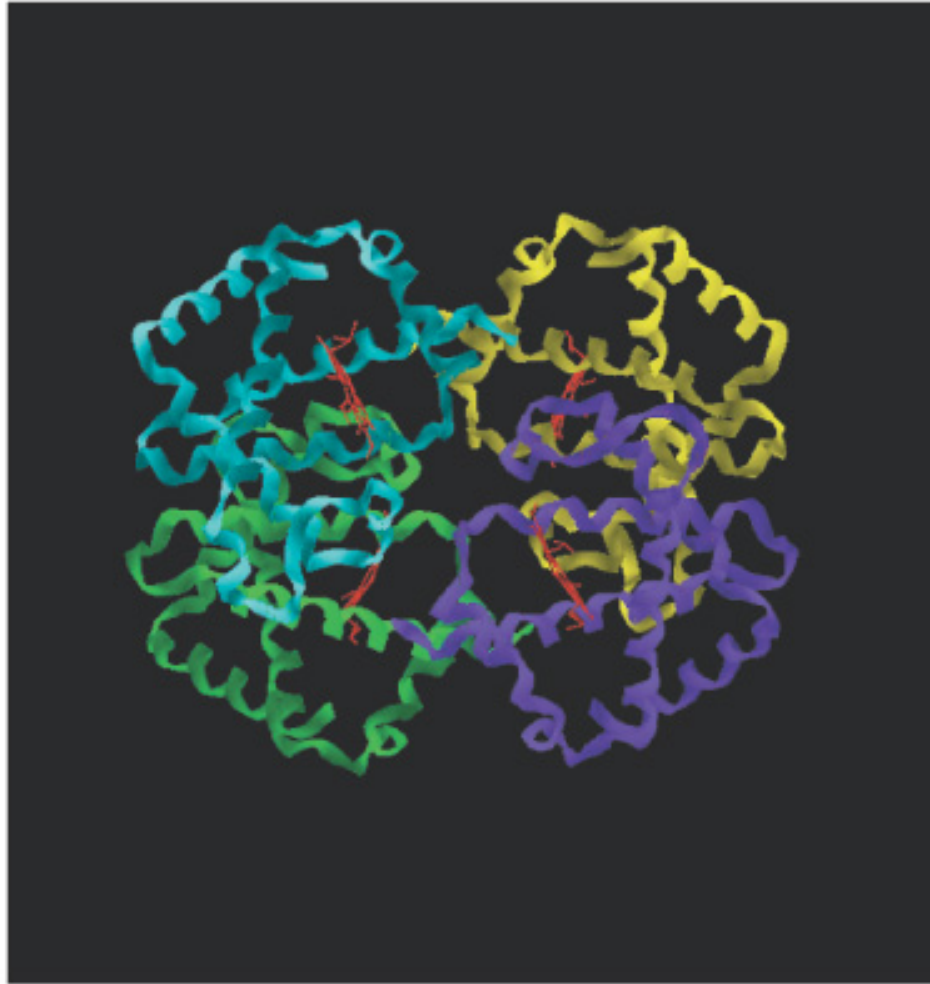
Fig 18.8(b) Hemoglobin, a protein with quaternary structure

18.12 Chemical Properties of Proteins

◆ *Protein hydrolysis:* In protein hydrolysis, peptide bonds are hydrolyzed to yield amino acids. This is reverse of protein formation.

◆ *Protein denaturation*: The loss of secondary, tertiary, or quaternary protein structure due to disruption of non-covalent interactions and or disulfide bonds that leaves peptide bonds and primary structure intact.

Heat denatures protein
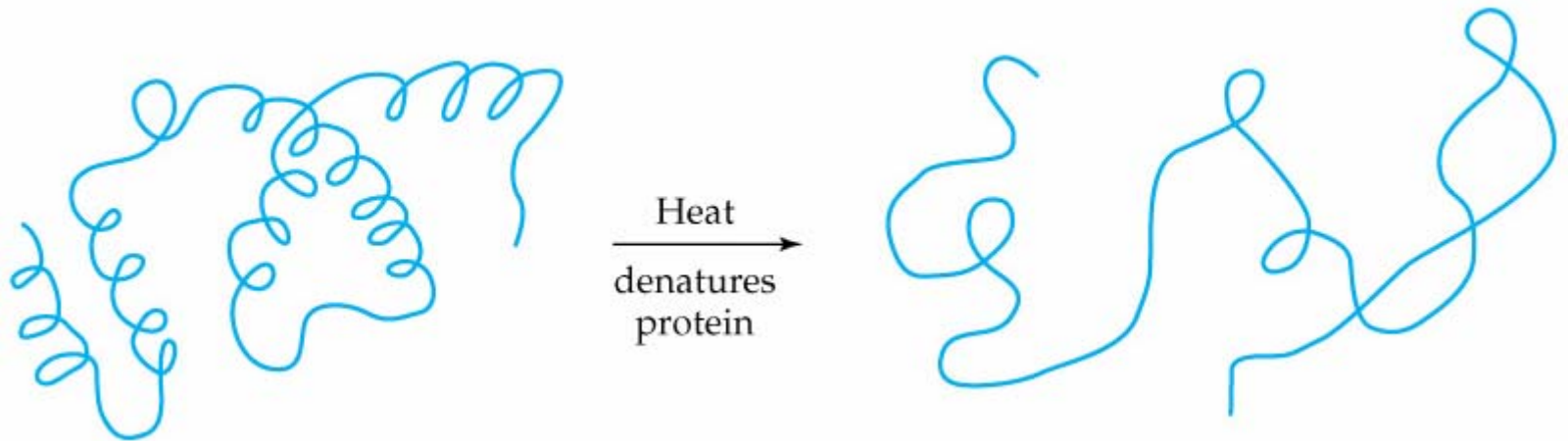
Agents that causes denaturation includes:

◆ *Heat* The weak side-chain attractions in globular proteins are easily broken by heating. Cooking meat converst some of the insoluble collagens into soluble gelatin.

◆ *Mechanical agitation* Most familiar example of denaturation of protein by mechanical agitation is the foaming that occurs during beating of egg whites.

◆ *Detergents* very low concentration of detergents can cause denaturation by disrupting the association of hydrophobic side chains.

- ***Organic compounds*** Polar solvents such as acetone or ethanol can interfere with hydrogen bonding by competing for bonding sites.

- ***pH change*** Excess H^+ or OH^- ions reacts with the basic or acidic side chains in amino acid residues and disrupt salt bridges.

- ***Inorganic salts*** Sufficiently high concentrations of ions can disrupt salt bridges.

19.1 Catalysis by Enzymes

◆ ***Enzyme*** A protein that acts as a catalyst for a biochemical reaction.

◆ ***Active site*** A pocket in an enzyme with the specific shape and chemical makeup necessary to bind a substrate and where the reaction takes place.

◆ ***Substrate*** A reactant in an enzyme catalyzed reaction.

- Enzymes activity is limited to a certain substrate and a certain type of reaction, is referred as the *specificity* of the enzyme.

- Enzymes differs greatly in their specificity. Catalase, for example, is almost completely specific for one reaction – decomposition of hydrogen peroxide, a necessary reaction that destroys hydrogen peroxide before it damages biomolecules by oxidizing them.

◆ Enzymes are specific with respect to stereochemistry – catalyze reaction of only one of the pair of enantiomers. For example, the enzyme lactate dehydrogenase catalyzes the removal of hydrogen from L-lactate but not from D-lactate.

The specificity of an enzyme for one of two enantiomers is a matter of fit. One enantiomer fits better into the active site of the enzyme than the other enantiomer. Enzyme catalyzes reaction of the enantiomer that fits better into the active site of the enzyme.

Mismatch
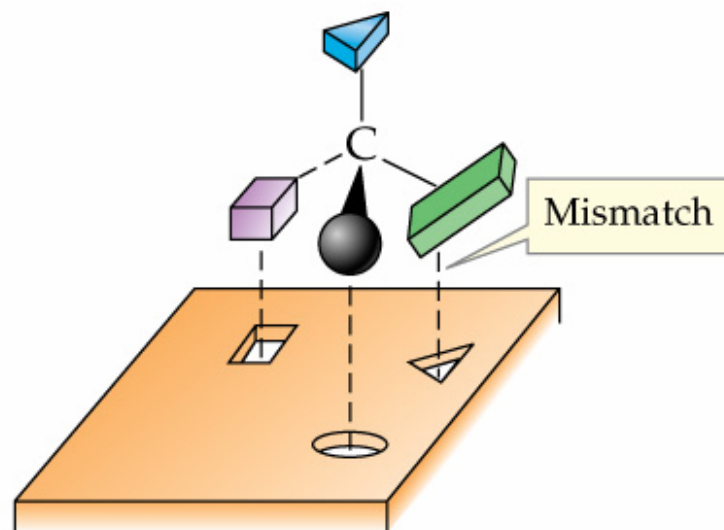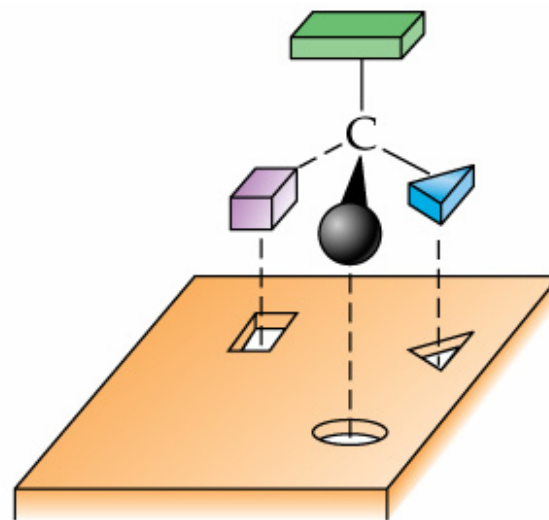
19.2 Enzyme Cofactors

◆ Many enzymes are conjugated proteins that require nonprotein portions known as *cofactors*.

◆ Some cofactors are metal ions, others are nonprotein organic molecules called *coenzymes*.

◆ An enzyme may require a metal-ion, a coenzyme, or both to function.

Chapter Eighteen

◆ Cofactors provide additional chemically active functional groups which are not present in the side chains of amino acids that made up the enzyme.

◆ Metal ions may anchor a substrate in the active site or may participate in the catalyzed reaction.

19.3 Enzyme Classification

Enzymes are divided into six main classes according to the general kind of reaction they catalyze, and each class is further subdivided.

◆ *Oxidoreductases:* Catalyze oxidation-reduction reactions, most commonly addition or removal of oxygen or hydrogen.

◆ *Transferases:* Catalyze transfer of a group from one molecule to another.

- *Hydrolases*: Catalyze the hydrolysis of substrate – the breaking of bond with addition of water.

- *Isomerases*: Catalyze the isomerization (rearrangement of atoms) of a substrate in reactions that have one substrate and one product.

- *Lyases*: Catalyze the addition of a molecule such as H_2O, CO_2, or NH_3 to a double bond or reverse reaction in which a molecule is eliminated to create a double bond.

- *Lygases* Catalyze the bonding of two substrate molecules.

19.4 How Enzyme Work

Two modes are invoked to represent the interaction between substrate and enzymes. These are:

◆ *Lock-and-key model*: The substrate is described as fitting into the active site as a key fit into a lock.

Induced-fit-model: The enzyme has a flexible active site that changes shape to accommodate the substrate and facilitate the reaction.
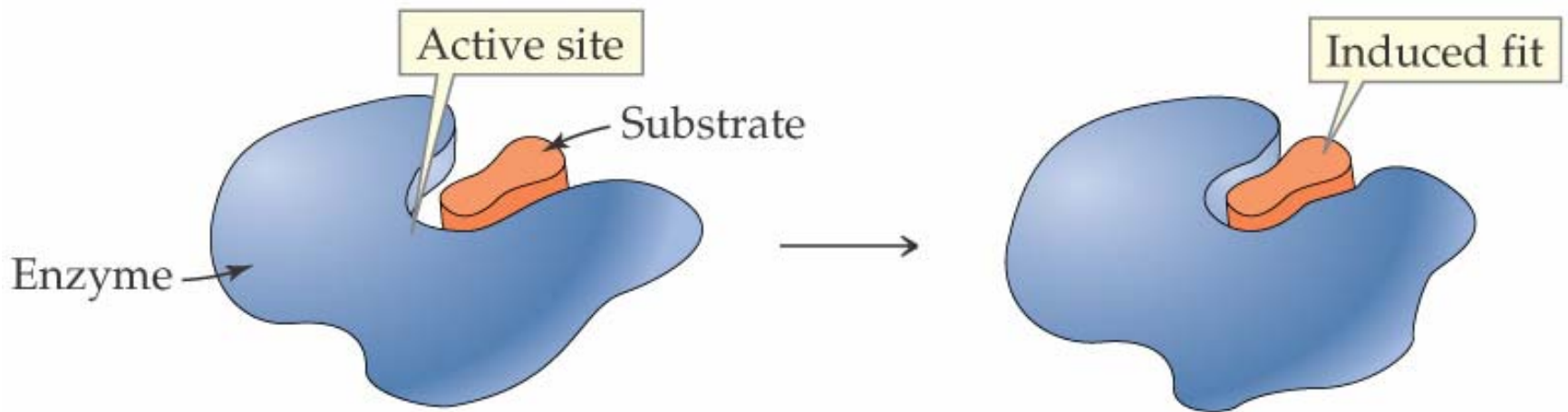
- In enzyme catalyzed reactions, substrates are drawn into the active site to form enzyme-substrate complex. Within the enzyme-substrate complex, the enzyme promoted reactions takes place.

- Once the chemical reaction is over, enzyme separates from the substrate and restores its original conditions, becomes available for another reaction.

19.5 Effect of Concentration on Enzyme Activity

Variation in concentration of enzyme or substrate alters the rate of enzyme catalyzed reactions.

◆ *Substrate concentration*: At low substrate concentration, the reaction rate is directly proportional to the substrate concentration. With increasing substrate concentration, the rate drops off as more of the active sites are occupied.
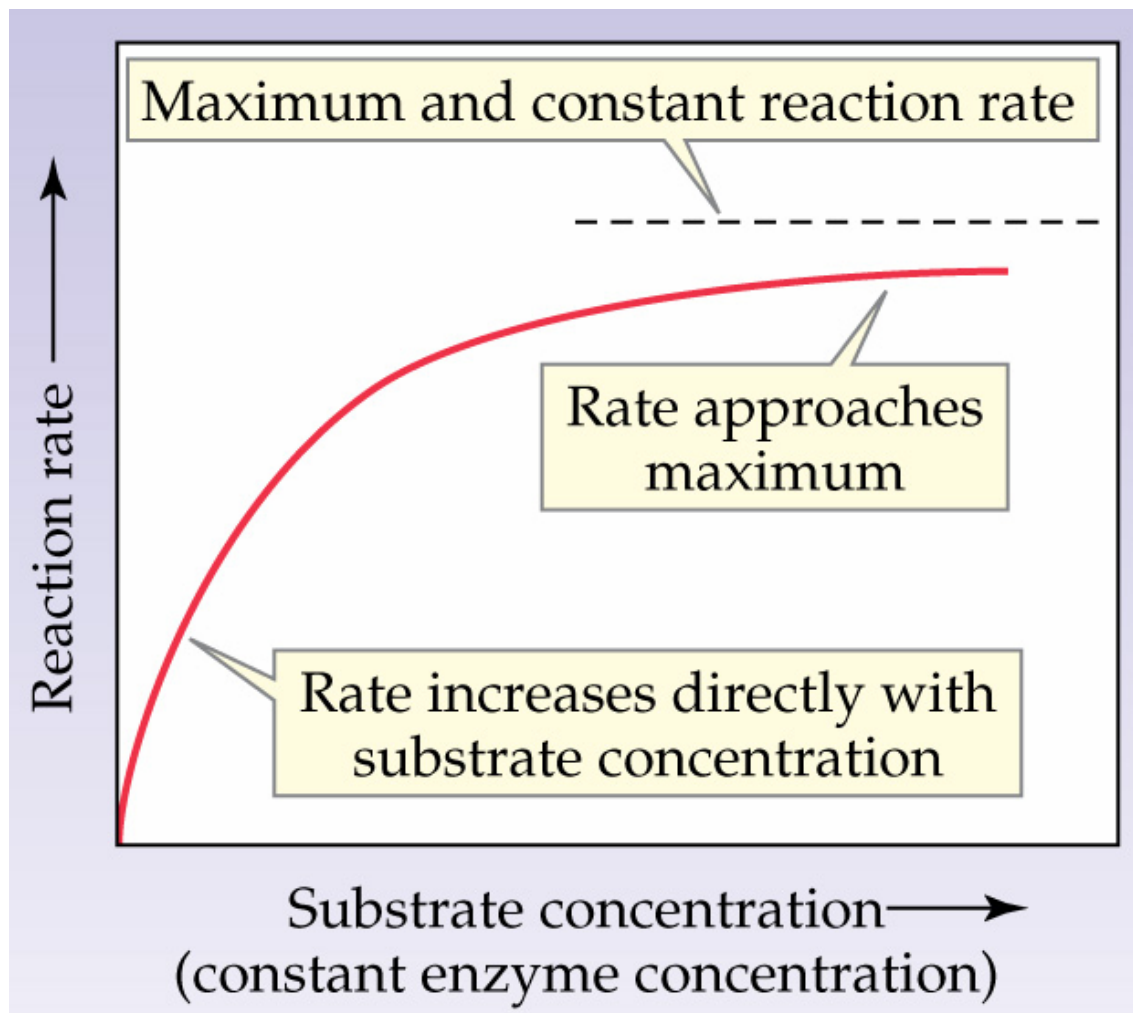
Fig 19.5   Change of   reaction   rate   with   substrate concentration when enzyme concentration is constant.

◆ *Enzyme concentration*: The reaction rate varies directly with the enzyme concentration as long as the substrate concentration does not become a limitation, Fig 19.6 below.
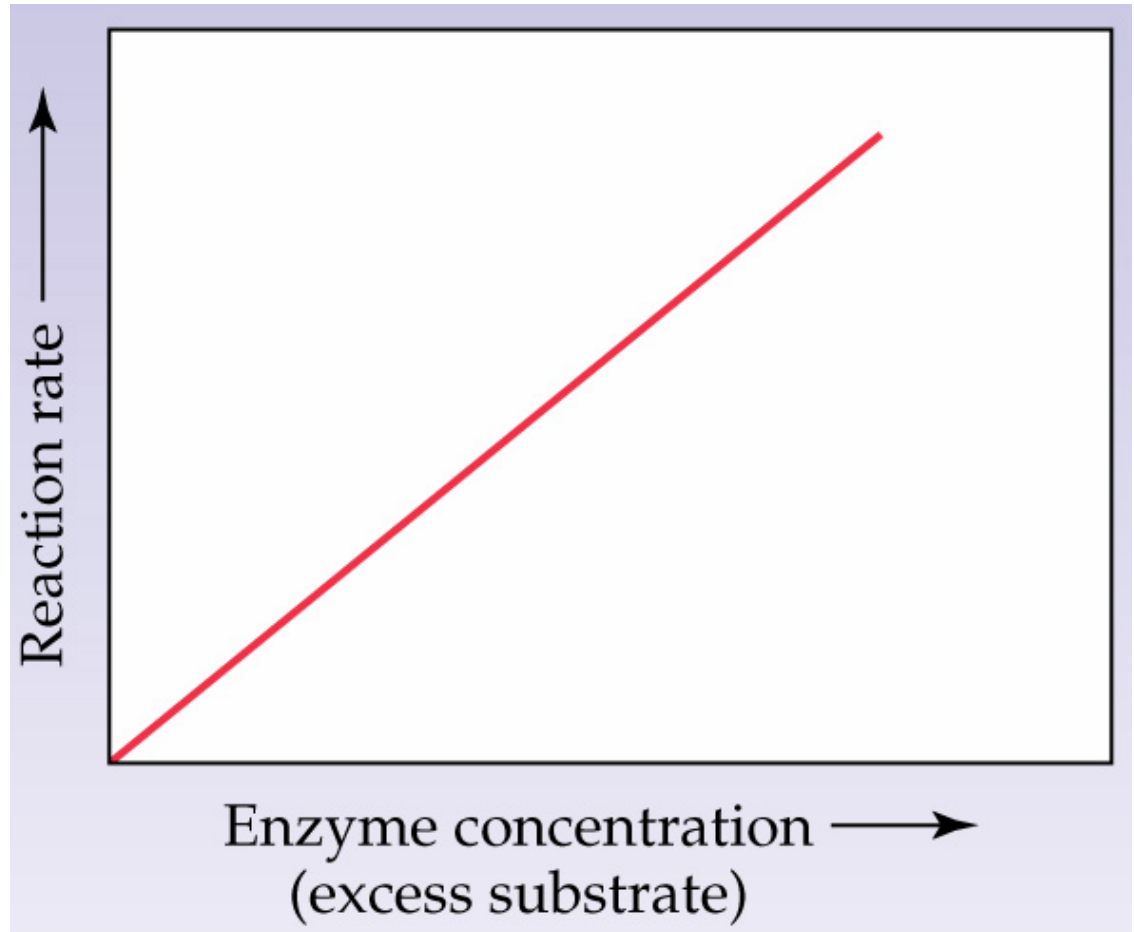
19.6 Effect of Temperature and pH on Enzyme Activity

Enzymes maximum catalytic activity is highly dependent on temperature and pH.

◆ Increase in temperature increases the rate of enzyme catalyzed reactions. The rates reach a maximum and then begins to decrease. The decrease in rate at higher temperature is due to denaturation of enzymes.
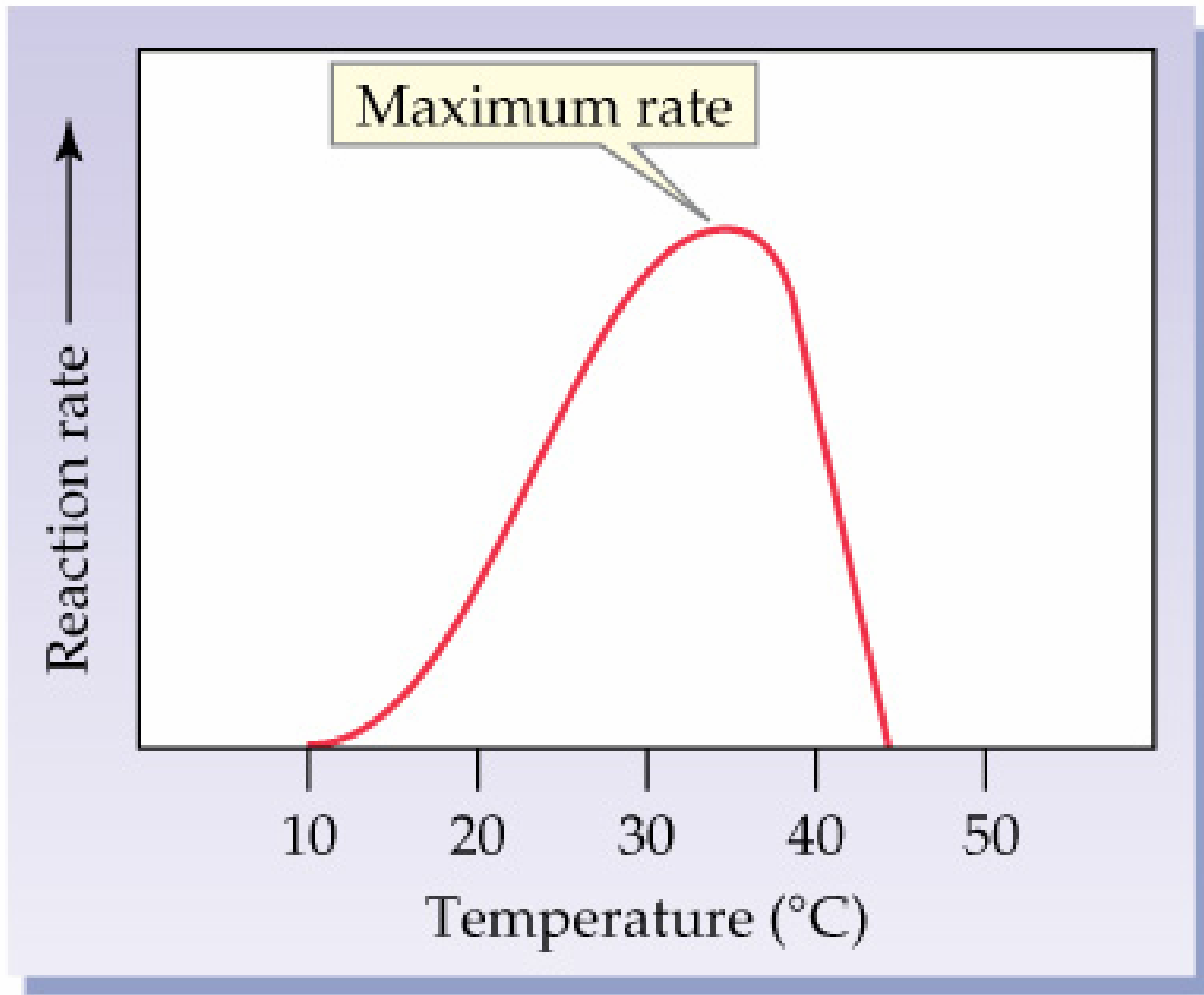
Fig 19.7 (a) Effect of temperature on reaction rate

◆ Effect of pH on Enzyme activity: The catalytic activity of enzymes depends on pH and usually has a well defined optimum point for maximum catalytic activity Fig 19.7 (b) below.
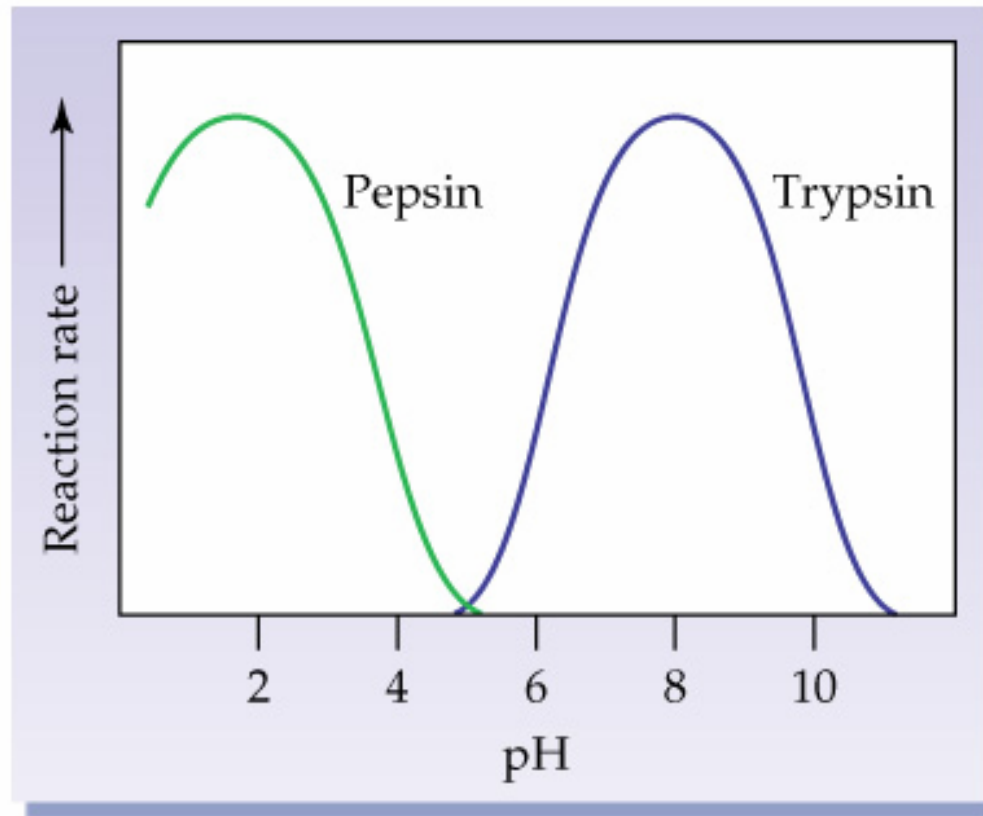
19.7 Enzyme Regulation: Feedback and Allosteric Control

Concentration of thousands of different chemicals vary continuously in living organisms which requires regulation of enzyme activity.

Any process that starts or increase the activity of an enzyme is *activation.*

Any process that stops or slows the activity of an enzyme is *inhibition.*

Two of the mechanism that control the enzymes activity are:

◆ *Feedback control*: Regulation of an enzyme's activity by the product of a reaction later in a pathway.

◆ *Allosteric control*: Activity of an enzyme is controlled by the binding of an activator or inhibitor at a location other than the active site. Allosteric controls are further classified as positive or negative.

- A positive regulator changes the activity site so that the enzyme becomes a better catalyst and rate accelerates.

- A negative regulator changes the activity site so that the enzyme becomes less effective catalyst and rate slows down.

Positive allosteric control
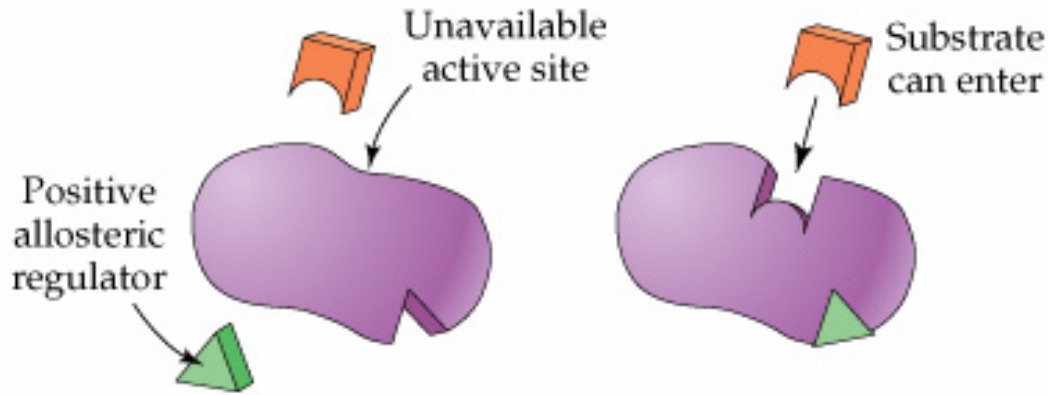
Positive allosteric regulator

Unavailable active site

Substrate can enter

A positive regulator changes the activity site so that the enzyme becomes a better catalyst and rate accelerates.

Negative allosteric control
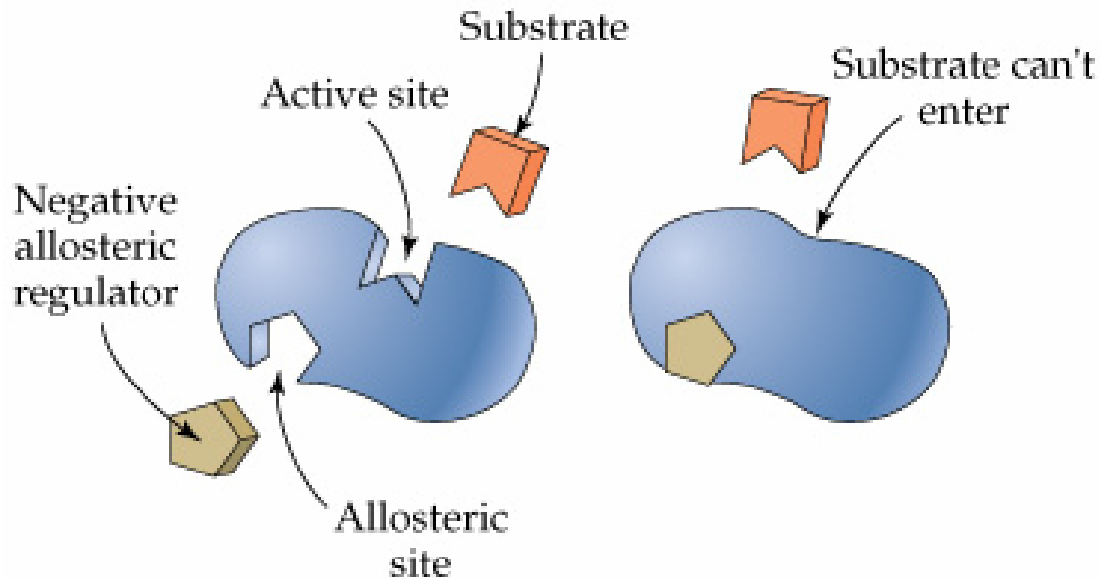
Substrate

Active site

Substrate can't enter

Negative allosteric regulator

Allosteric site

A negative regulator changes the activity site so that the enzyme becomes less effective catalyst and rate slows down.

19.8 Enzyme Regulation: Inhibition

◆ The inhibition of an enzyme can be *reversible* or *irreversible*.

◆ In *reversible inhibition*, the inhibitor can leave, restoring the enzyme to its uninhibited level of activity.

◆ In *irreversible inhibition*, the inhibitor remains permanently bound to the enzyme and the enzyme is permanently inhibited.

Inhibitions are further classified as:

◆ *Competitive inhibition if* the inhibitor binds to the active site.

Competitive inhibition

Competitive inhibitor

Substrate can't enter
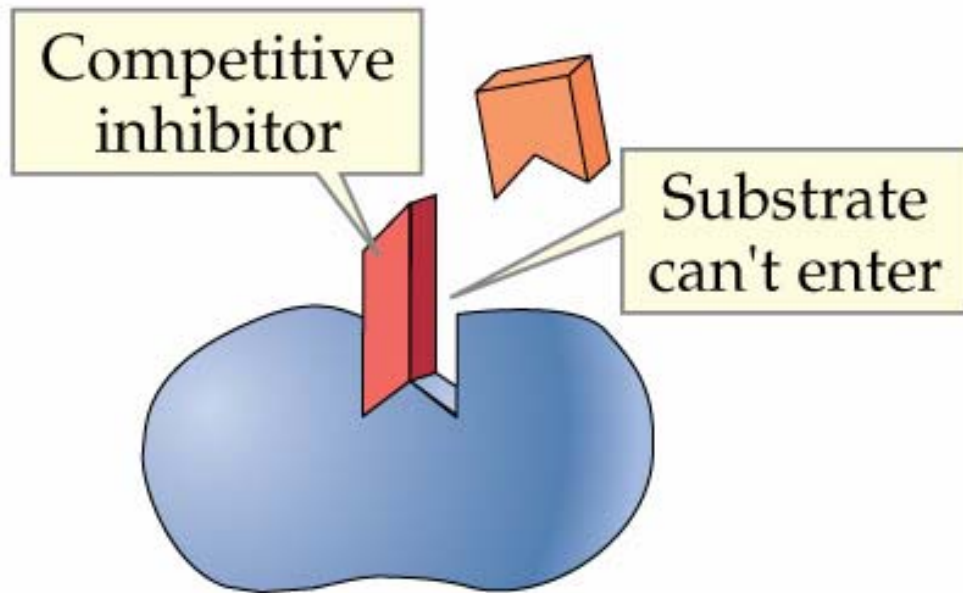
◆ *Noncompetitive inhibition,* if the inhibitor binds elsewhere and not to the active site.

Noncompetitive inhibition

Substrate can't enter

Noncompetitive inhibitor
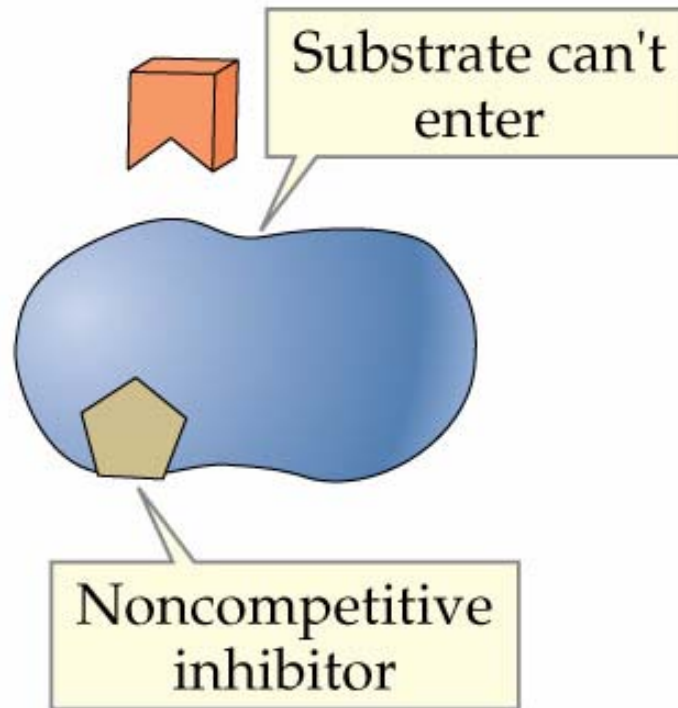
The rates of enzyme catalyzed reactions with or without a competitive inhibitor are shown in the Fig 19.9 below.
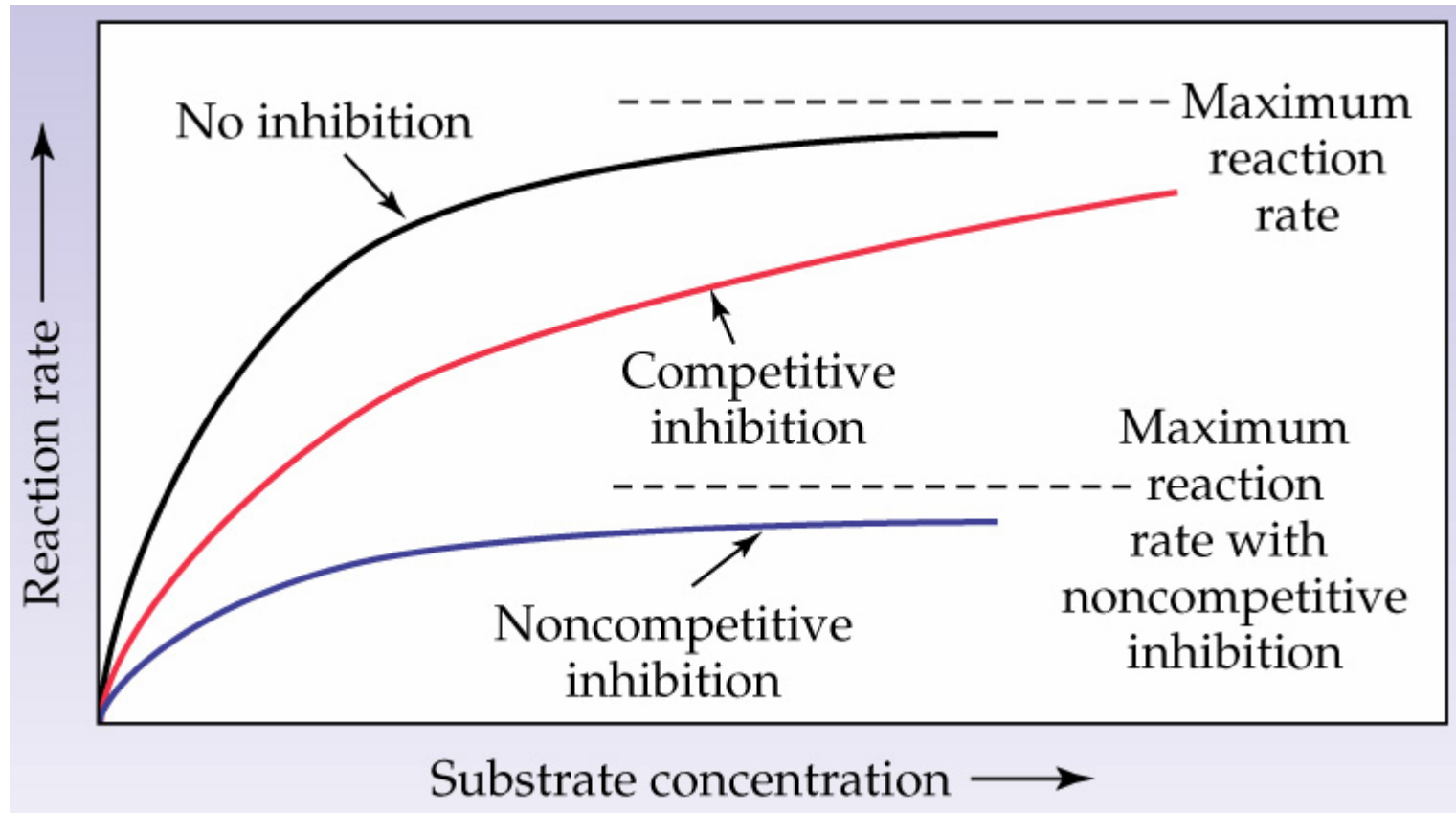
19.9 Enzyme Regulation: Covalent Modification and Genetic Control

◆ *Covalent modification*: Two general modes of enzyme regulation by covalent modification – removal of a covalently bonded portion of an enzyme, or addition of a group. Zymogens or pro-enzymes becomes active only when a chemical reaction splits off part of the molecule.

◆ *Genetic control:* The synthesis of enzymes is regulated by genes. Mechanisms controlled by hormones can accelerates or decelerates enzyme synthesis.

19.10 Vitamins

Vitamins: An organic molecule, essential in trace amounts that must be obtained in the diet because it is not synthesized in the body. Vitamins are classified as *water-soluble* and *fat-soluble*.

21-1 Energy and Life

◆ All living organisms need energy to carry out various functions.

◆ In humans, energy released from food allows us to do various kinds of works that need to be done.

◆ Energy used by a very few living organisms comes from the sun.

◆ Plants convert sunlight to potential energy stored mainly in the chemical bonds of carbohydrates.

◆ Plant eating animals utilize the energy stored by the plants, some for immediate needs and the rest to be stored for future needs, mainly in the form of chemical bonds in fats.

◆ Other animals, including humans, are able to eat plants and animals and use the chemical energy these organisms have stored.
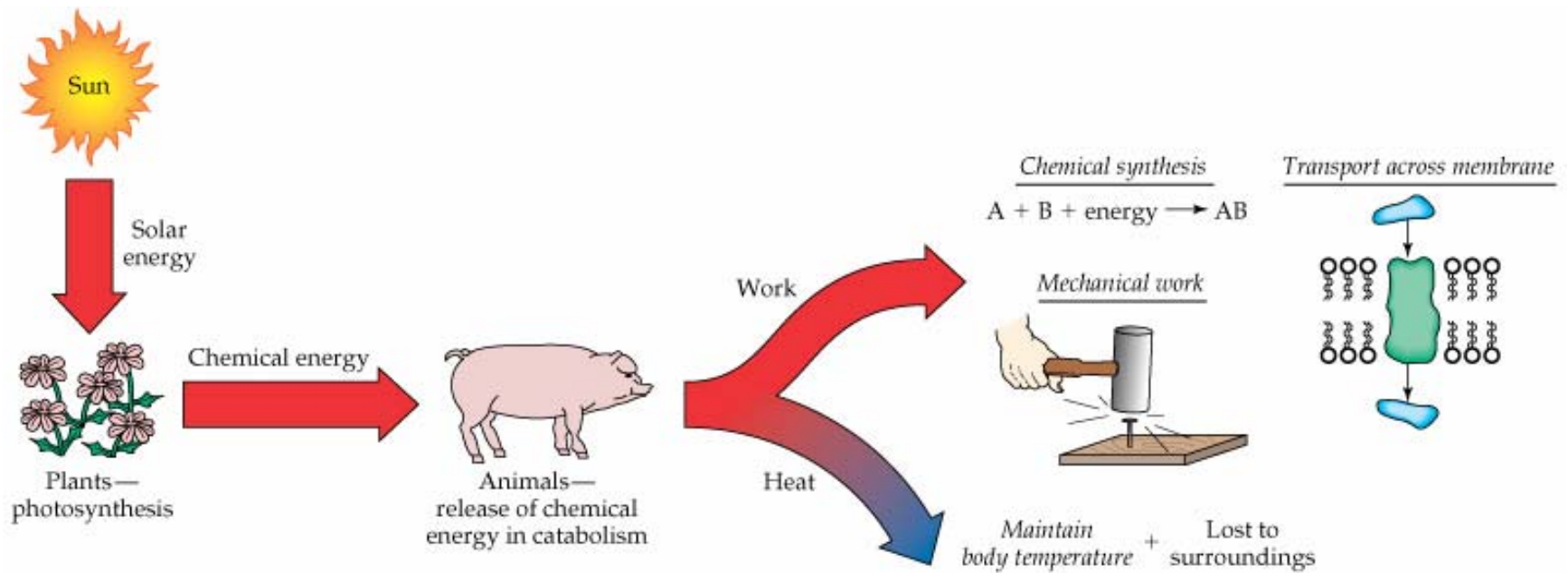
Fig 21.1 The flow of energy through biosphere

Specific requirements for energy to be useful in living organisms:

◆ Energy must be released from food gradually.

◆ Energy must be stored in readily available form. The release of energy from storage must be finely controlled so that it is available when and where it is needed.

◆ Just enough energy must be released as heat to maintain constant body temperature.

◆ Energy must be available to drive chemical reactions that aren't favorable at body temperature.

21.2 Energy and Biochemical Reactions

◆ Reactions in living organisms are similar to reactions in a chemical laboratory.

◆ Spontaneous reactions, those are favorable in the forward direction, release free energy and the energy released is available to do work.

◆ Spontaneous reactions , also known as *exergonic* reactions, are the source of our biochemical energy.

◆ As shown in Fig 21.2a, products of exergonic reactions are more stable than the reactants and the free energy change ΔG has a negative value.

- Reactions in which the products are higher in energy than the reactants are unfavorable or *endergonic* reactions.

- Unfavorable reactions can't occur without the input of energy from an outside source.

- As shown in Fig 21.2b, products of endergonic reactions are less stable than the reactants and the free energy change ΔG has a positive value.

- Oxidation reactions are usually favorable reactions and release energy.

- Oxidation of glucose, the principal source of energy for animals, produces 686 kcal of free energy per mole of glucose.
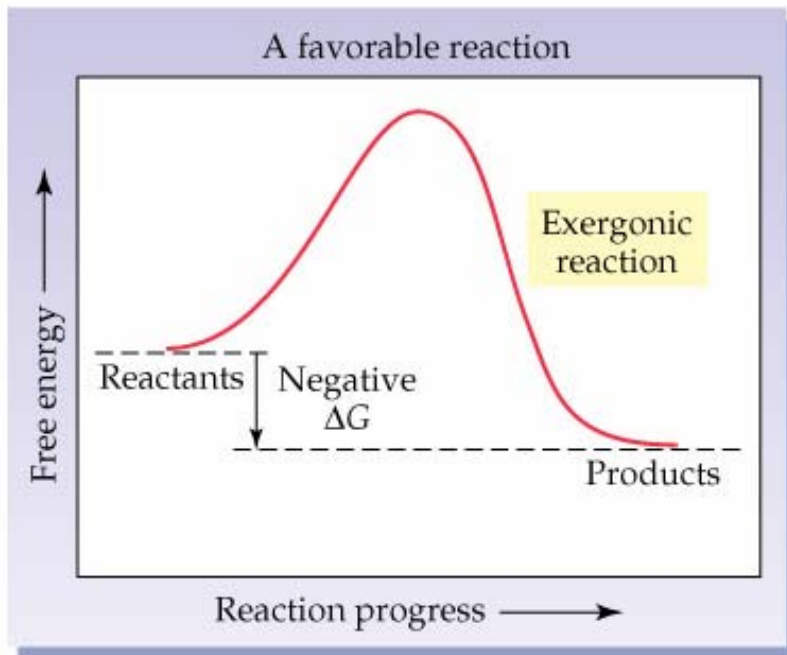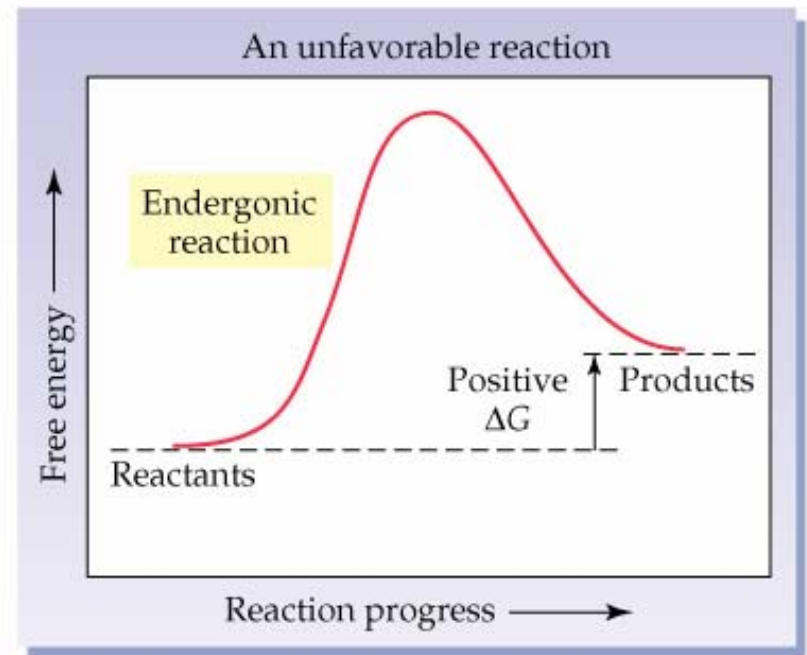
Fig 21.1 (a) Energy diagram of an (a) exergonic and (b) endergonic reaction

◆ *Photosynthesis* in plants, converts CO_2 and H_2O to glucose plus O_2 which is the reverse of oxidation of glucose. The sun provides the necessary external energy for photosynthesis (686 kcal of free energy per mole of glucose formed).

Photosynthesis

$\Delta G = +686$ kcal/mol (endergonic, energy required)

$$6\,CO_2 \;+\; 6\,H_2O \qquad\qquad C_6H_{12}O_6 \;+\; 6\,O_2$$

$\Delta G = -686$ kcal/mol (exergonic, energy released)

Oxidation
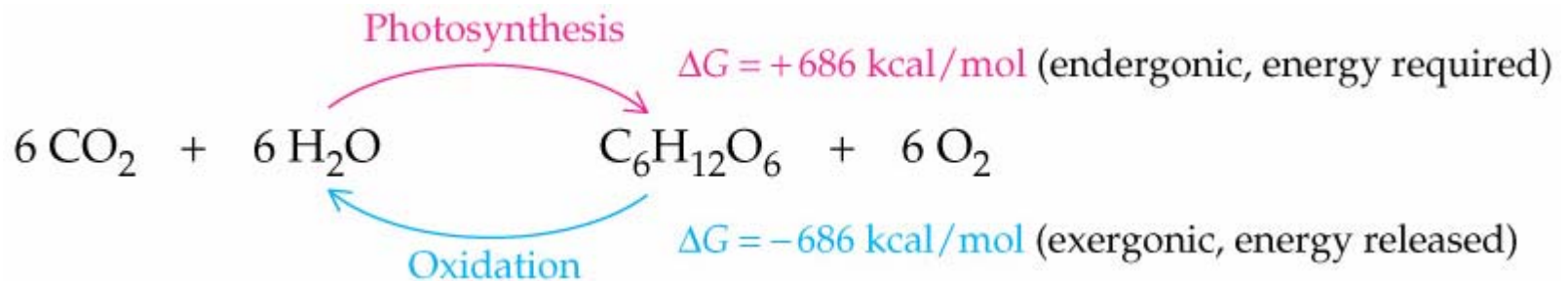
21.3 Cells and Their Structures

◆ Energy generating reactions take place within the cells of living organisms.

◆ There are mainly two kinds of cells:

- *prokaryotic* cells, usually found in single-celled organisms including bacteria and blue-green algae.

- *eukaryotic* cells, found in some single-celled organisms and all plants and animals.

Eukaryotic cells are about 1000 times larger than bacteria cells and also have a membrane enclosed nucleus containing their DNA, and several other internal structures known as organelles.
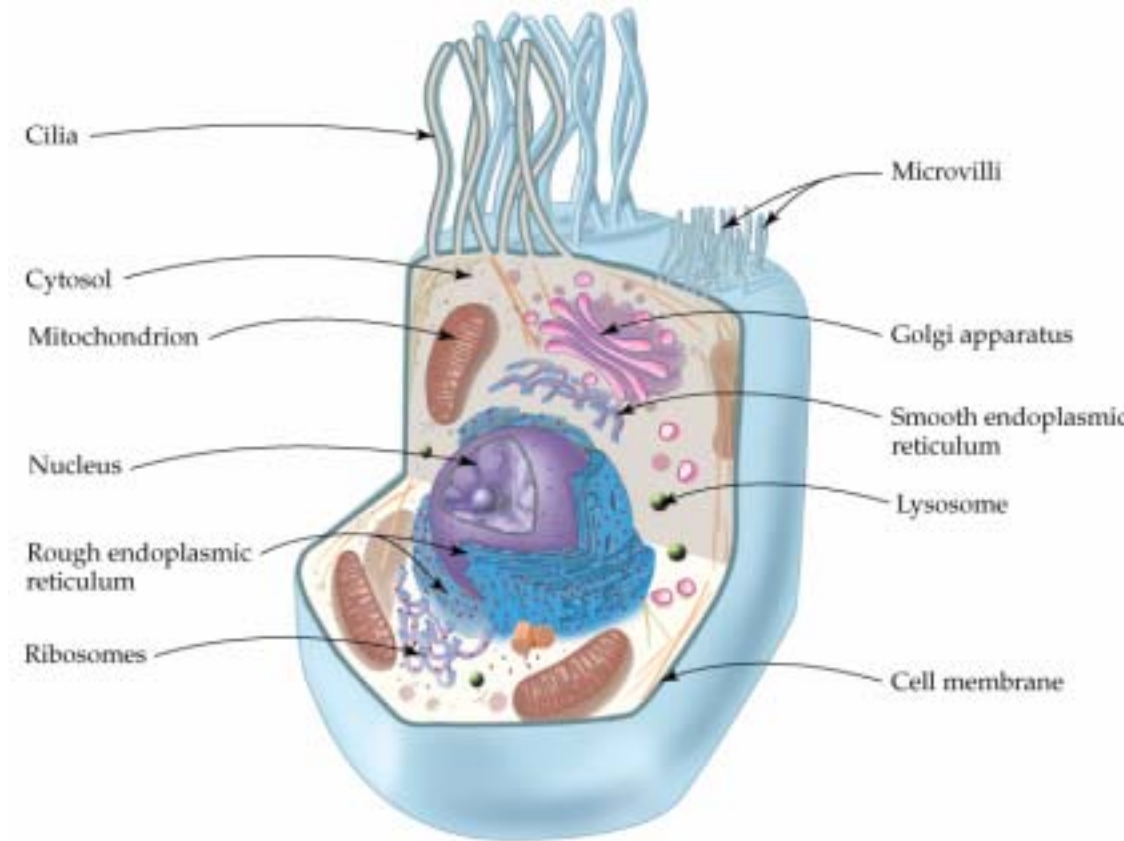
Fig 21.3 A generalized eukaryotic cell.

Cilia

Cytosol

Mitochondrion

Nucleus

Rough endoplasmic reticulum

Ribosomes

Microvilli

Golgi apparatus

Smooth endoplasmic reticulum

Lysosome

Cell membrane

The *mitochondria* is often called the cell's power plants. Within the mitochondria, small molecules are broken down to provide the energy for an organism and also the principle energy carrying molecule adenosine triphosphate (ATP) is produced.
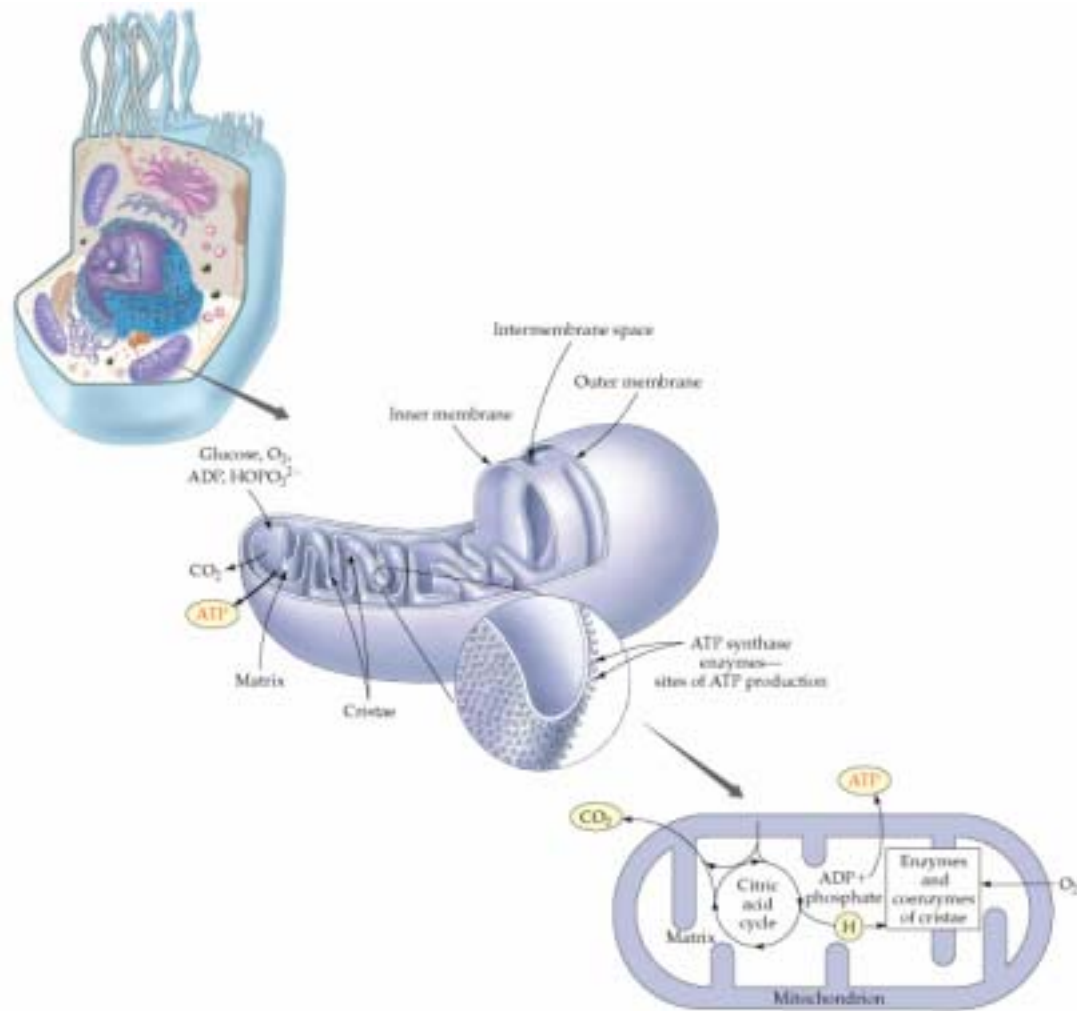
Fig 21.4 The mitochondrion

21.4 An Overview of Metabolism and Energy Production

◆ Metabolism: Together, all chemical reactions that take place in an organism.

◆ Catabolism: Metabolic reaction pathways that break down food molecules and release biochemical energy.

◆ Anabolism: Metabolic reaction pathways that build larger biological molecules including those can store energy from smaller pieces.

CATABOLISM

ANABOLISM

Larger molecules

Smaller molecules + Energy
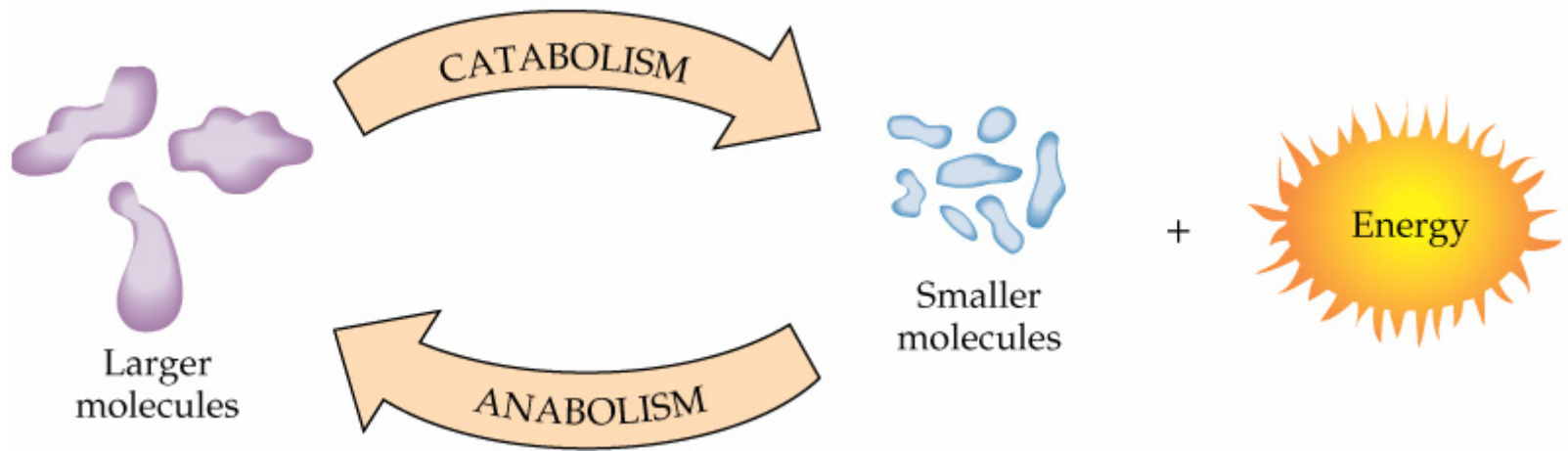
Food molecules undergo catabolism to provide energy in four stages as shown in the following Fig 21.5

Fig 21.5 Pathways for the digestion of food and the production of biochemical energy

FOOD

LIPIDS → **CARBOHYDRATES** → **PROTEINS**

Stage 1. Digestion
Bulk food is digested in the mouth, stomach, and small intestine to yield small molecules.

Fatty acids and glycerol | Glucose and other sugars | Amino acids

Fatty acid oxidation | Glycolysis | Amino acid catabolism

ATP

Pyruvate

Stage 2. Acetyl-SCoA Production
Sugar, fatty acid, and amino acid molecules are degraded in the cytoplasm of cells to yield acetyl-SCoA.

Acetyl-SCoA

Stage 3. Citric Acid Cycle
Acetyl-SCoA is oxidized inside mitochondria by the citric acid cycle to yield CO_2 and reduced coenzymes.

Citric acid cycle

ATP | CO_2

REDUCED COENZYMES

Stage 4. ATP Production
The energy transferred to the reduced coenzymes in stage 3 is used to make ATP by the coupled pathways of electron transport and oxidative phosphorylation.

Electron transport chain | O_2

ATP | H_2O

21.5 Strategies of Metabolism: ATP and Energy Transfer

◆ Adenosine triphosphate (ATP) transport energy in living organisms.

◆ ATP has three $-PO_3^-$ groups.

◆ Removal of one of the $-PO_3^-$ groups from ATP by hydrolysis produces adenosine diphosphate (ADP). Since this reaction is an exergonic process, it releases energy.

◆ The reverse of ATP hydrolysis reaction is known as phosphorylation reaction. Phosphorylation reactions are endergonic.

Biochemical energy production, transport, and use all depends on the ATP $\rightleftarrows$ ADP interconversions.
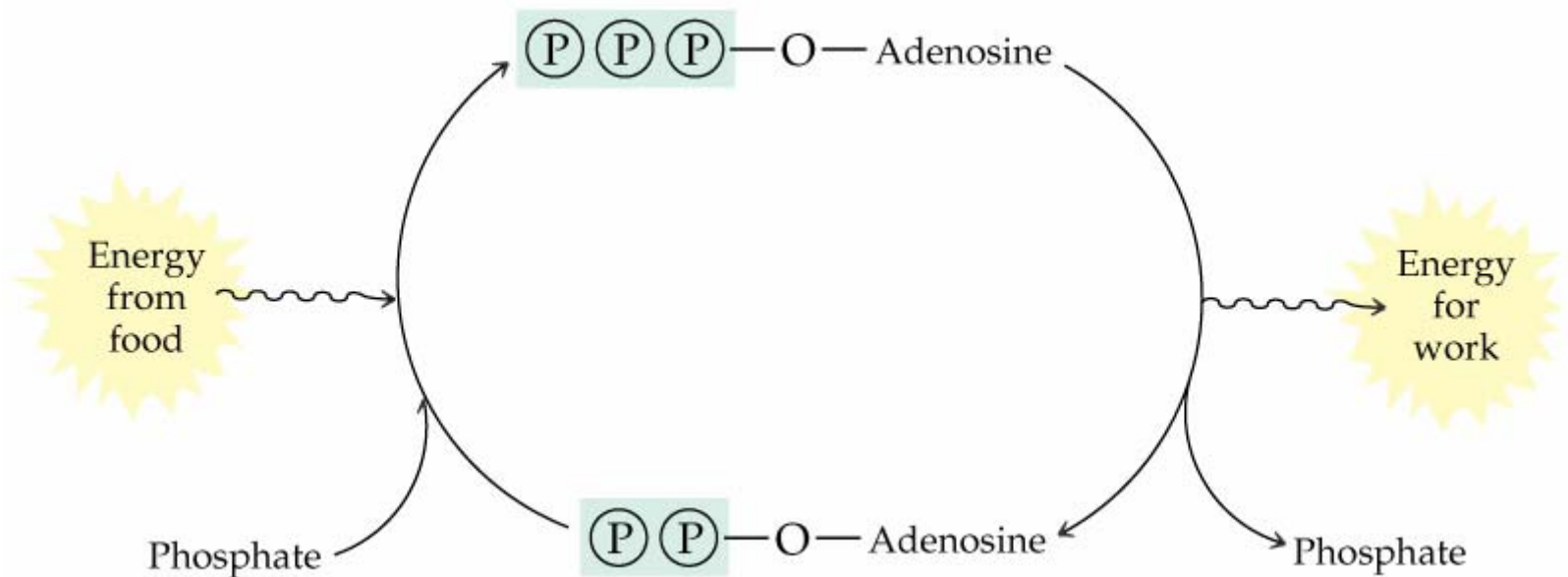
TABLE 21.1 Free Energies of Hydrolysis of Some Phosphates

$$R-O-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O^-}{|}}{P}}-O^- \ + \ H_2O \ \rightleftharpoons \ ROH \ + \ HO-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O^-}{|}}{P}}-O^-$$
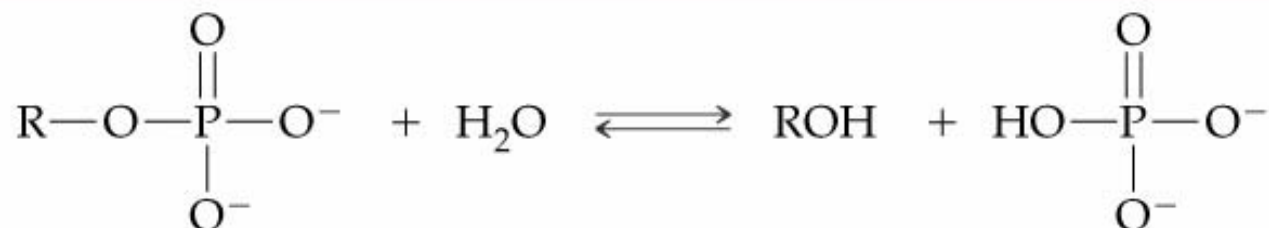
Compound Name	Function	ΔG (kcal/mol)
Phosphoenol pyruvate	Final intermediate in conversion of glucose to pyruvate (glycolysis)—stage 2, Figure 21.5	−14.8
1, 3-Bisphosphoglycerate	Another intermediate in glycolysis	−11.8
Creatine phosphate	Energy storage in muscle cells	−10.3
ATP ($\longrightarrow$ADP)	Principal energy carrier	−7.3
Glucose 1-phosphate	First intermediate in breakdown of carbohydrates stored as starch or glycogen	−5.0
Glucose 6-phosphate	First intermediate in glycolysis	−3.3
Fructose 6-phosphate	Second intermediate in glycolysis	−3.3

21.6 Strategies of Metabolism: Metabolic Pathways and Coupled Reactions

◆ Metabolic pathways of catabolism release energy bit by bit in a series of reactions.

◆ The overall reaction and the overall free-energy change for any series of reactions can be found by summing up the equations and the free-energy changes for the individual steps.

◆ The reactions of all metabolic pathways add up to favorable processes with negative free-energy changes.

◆ Not every individual step in every metabolic pathway is a favorable reaction.

◆ Metabolic strategy is to couple an energetically unfavorable step (endergonic) with an energetically favorable (exergonic) step so that the overall energy change for the two reactions is favorable.

21.7 Strategies of Metabolism: Oxidized and Reduced Coenzymes

◆ The net result of catabolism is the oxidation of food molecules to release energy.

◆ Many metabolic reactions are therefore oxidation-reduction reactions.

◆ A steady supply of oxidizing and reducing agents must be available to accomplish the oxidation-reduction reactions.

◆ **A few enzymes continuously cycle between their oxidized and reduced forms.**

AH_2 ⟶ Coenzyme (oxidized) ⟵ BH_2

A ⟵ Coenzyme-H_2 (reduced) ⟶ B

Coenzyme	As Oxidizing Agent	As Reducing Agent
Nicotinamide adenine dinucleotide	NAD^+	$NADH/H^+$
Nicotinamide adenine dinucleotide phosphate	$NADP^+$	$NADPH/H^+$
Flavin adenine dinucleotide	FAD	$FADH_2$
Flavin mononucleotide	FMN	$FMNH_2$

◆ Nicotinamide adenine dinucleotide (NAD) and its phosphate (NADP) are widespread coenzyme required for redox reactions.

◆ As oxidizing agents (NAD^+ and $NADP^+$) they remove hydrogen from a substrate and as reducing agents (NADH and NADP) they provide hydrogen that adds to a substrate.

21.8 The Citric Acid Cycle

◆ Citric acid cycle also known as Krebs cycle: The series of biochemical reactions that breaks down acetyl groups to produce energy carried by reduced coenzymes and carbon dioxide.

◆ The eight steps of the cycle produce two molecules of carbon dioxide, four molecules of reduced coenzymes, and one energy rich phosphate. The final step regenerates the reactant for step 1 of the next turn of the cycle.

transferred from acetyl-SCoA
to oxaloacetate produced in step 8.

$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-SCoA$

Oxaloacetate

COO^-
$|$
$C=O$
$|$
CH_2
$|$
COO^-

H—SCoA

H_2O

Citrate

COO^-
$|$
CH_2
$|$
$HO-C-COO^-$
$|$
CH_2
$|$
COO^-

1

Step 2. Citrate is
isomerized by transfer of
the OH group to yield
isocitrate.

Step 8. The cycle of
reactions is completed
by oxidation of malate
to regenerate
oxaloacetate.

8

→ NADH + H⁺

— NAD⁺

2

COO^-
$|$
CH_2
$|$
$HC-COO^-$
$|$
$HO-CH$
$|$
COO^-

Isocitrate

Malate

COO^-
$|$
$HO-CH$
$|$
CH_2
$|$
COO^-

Citric acid
cycle

NAD⁺

3

Step 3. Isocitrate loses
CO_2 and is oxidized to
yield α-ketoglutarate.

Step 7. Addition of water
to the double bond of
fumarate yields malate.

7

H_2O

NADH + H⁺
+ CO_2

COO^-
$|$
CH
$\|$
HC
$|$
COO^-

Fumarate

H—SCoA + NAD⁺

NADH + H⁺
+ CO_2

4

COO^-
$|$
CH_2
$|$
CH_2
$|$
COO^-

α-Ketoglutarate

Step 4. α-Ketoglutarate
reacts with coenzyme A
and loses CO_2 to yield
succinyl-SCoA.

FADH₂

FAD

6

COO^-
$|$
CH_2
$|$
CH_2
$|$
COO^-

H—SCoA

5

COO^-
$|$
CH_2
$|$
CH_2
$|$
$C=O$
$|$
SCoA

Step 6. Two hydrogens are
removed from succinate

ccinate

GTP   GDP

Step 5. Succinyl-SCoA is set free
to give succinate plus CoA in
a reaction coupled with
ATP formation.

Succinyl-SCoA.

Enzymes of the Citric Acid Cycle		
Step no.	Enzyme Name	Reaction Product
1	Citrate synthase	Citrate
2	Aconitase	Isocitrate
3	Isocitrate dehydrogenase complex	α-Ketoglutarate
4	α-Ketoglutarate dehydrogenase complex	Succinyl-SCoA
5	Succinyl CoA synthetase	Succinate
6	Succinate dehydrogenase	Fumarate
7	Fumarase	Malate
8	Malate dehydrogenase	Oxaloacetate

Fig 21.9 The citric acid cycle

21.9 The Electron-Transport Chain and ATP Production

◆ Electron transport chain: The series of biochemical reactions that passes electrons from reduced coenzymes to oxygen and is coupled to ATP formation. The electrons combine with the oxygen we breathe and with hydrogen ions from their surrounding to produce water.

◆ Electron transport involves four enzyme complexes held in fixed positions within the inner membrane of mitochondria and two electron carriers move from one complex to another.

◆ The four enzymes involved in electron transport chain complexes are polypeptides and electron acceptors.
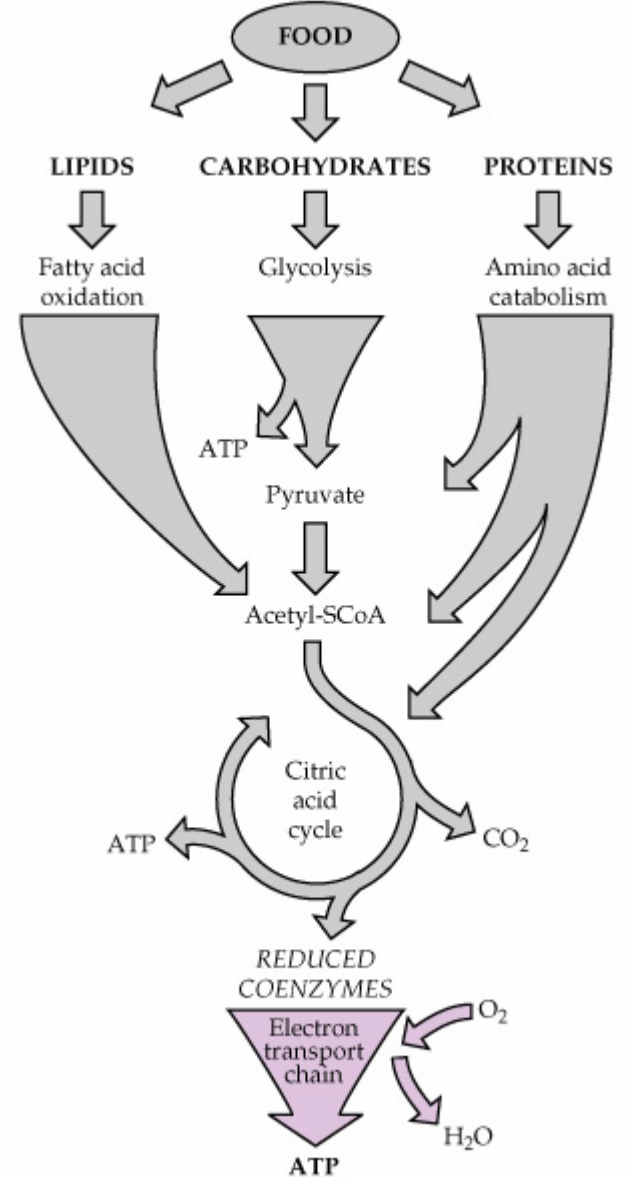
Electron transport chain

The most important electron acceptors are:

◆ Various cyctochromes that contain heme groups in which the iron cycles between Fe^{2+} and Fe^{3+}.

◆ Proteins with iron-sulfur groups in which the iron also cycles between Fe^{2+} and Fe^{3+}, and

◆ The coenzyme Q, often known as ubiquinone because of its widespread occurrence and the presence of a quinone group in its structure.
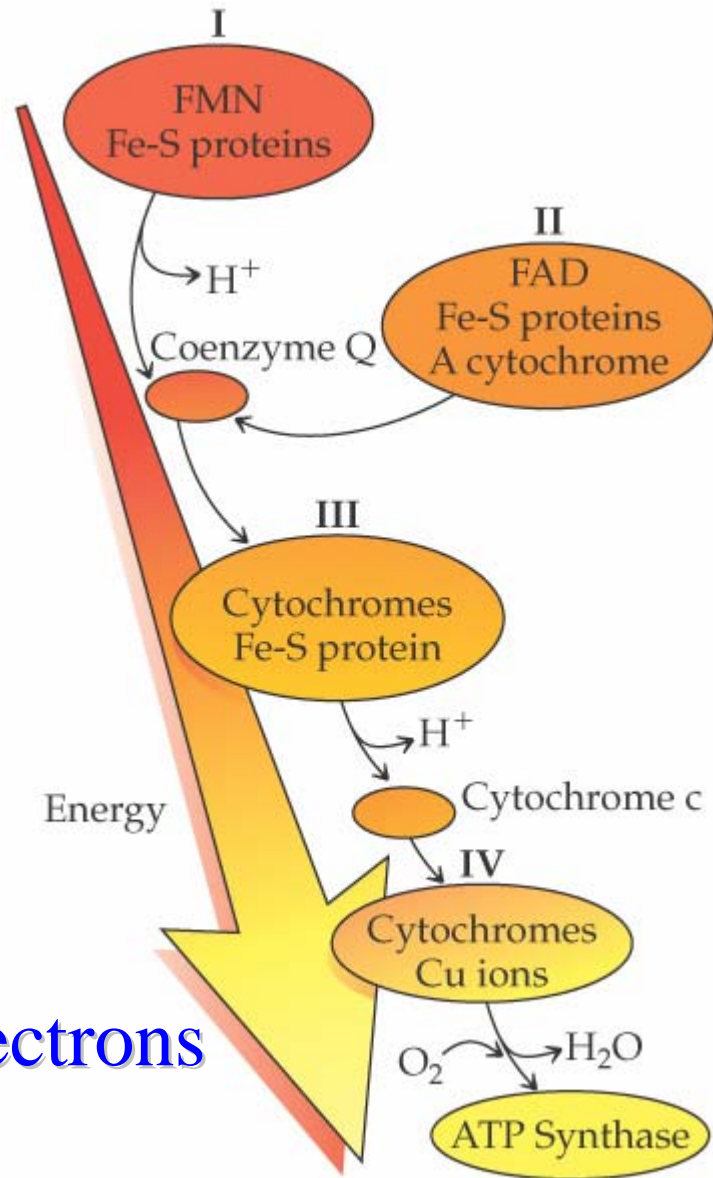
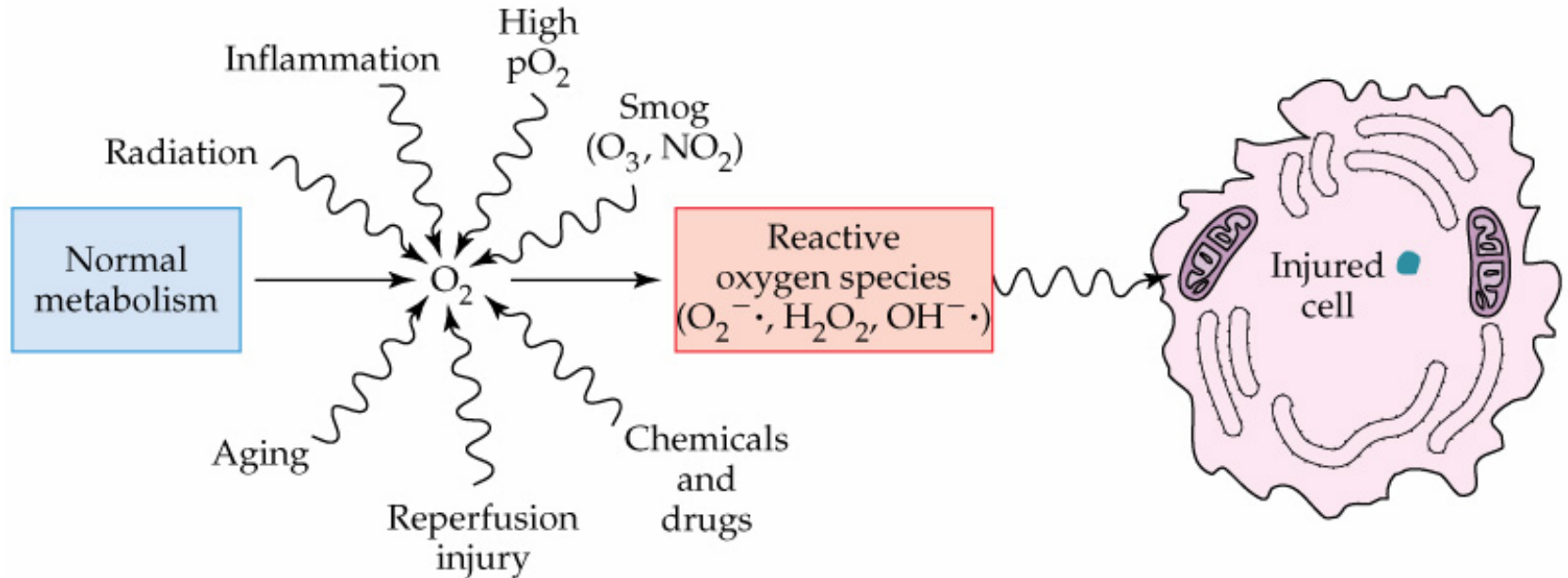Fig 21.12 Pathway of electrons in electron transport

ATP Synthesis

ADP is converted to ATP by a reaction between ADP and hydrogen phosphate ion. This is both an oxidation and phosphorylation reaction. Energy released in the electron transport chain drives this reaction forward.

21.10 Harmful Oxygen By-Products and Antioxidant Vitamins

About 90% of the oxygen we breathe are utilized in the electron transport-ATP synthesis reactions. These and other oxygen consuming reactions produces some harmful oxygen containing highly reactive products such as hydroxyl free radical, $HO\cdot$, superoxide ion, $O_2^{-\cdot}$, and hydrogen peroxide, H_2O_2. These reactive species can cause damage by breaking covalent bonds in enzymes and other proteins, DNA, and the lipids in the cell membranes.

The outcomes of such damages are cancer, liver damage, heart disease, immune system damage etc.

Inflammation High pO$_2$

Radiation Smog (O$_3$, NO$_2$)

Normal metabolism → O$_2$ → Reactive oxygen species (O$_2^-\cdot$, H$_2$O$_2$, OH$^-\cdot$) → Injured cell

Aging

Reperfusion injury Chemicals and drugs

Superoxide dismutase and catalase, some very fast acting enzymes in our body, provides protection against these harmful free radicals and hydrogen peroxide by destroying them as they are produced. Protection is also provided by the vitamins E, C, and A. These vitamins make the free radicals harmless by bonding with them.

22.1 An Introduction to Carbohydrates

◆ *Carbohydrates* are a large class of naturally occurring polyhydroxy aldehydes and ketones.

◆ Monosaccharides also known as simple sugars, are the simplest carbohydrates containing 3-7 carbon atoms.

◆ sugar containing an aldehydes is known as an aldose.

◆ sugar containing a ketones is known as a ketose.

- *Carbohydrates* are a large class of naturally occurring polyhydroxy aldehydes and ketones.

- Monosaccharides also known as simple sugars, are the simplest carbohydrates containing 3-7 carbon atoms.

- sugar containing an aldehydes is known as an aldose.

- sugar containing a ketones is known as a ketose.

- The family name ending -ose indicates a carbohydrate.

- Simple sugars are known by common names such as glucose, ribose, fructose, etc.

- The number of carbon atoms in an aldose or ketose may be specified as by tri, tetr, pent, hex, or hept. For example, glucose is aldohexose and fructose is ketohexose.

- Monosaccharides react with each other to form disaccharides and polysaccharides.

- Monosaccharides are chiral molecules and exist mainly in cyclic forms rather than the straight chain.

22.2 Handedness in Carbohydrates

◆ Carbohydrates are chiral molecules since they have carbon atoms carrying four different groups.

◆ The simplest three carbon naturally occurring carbohydrate glyceraldehyde lack a plane of symmetry and exist as a pair of enantiomers – a right handed D form or a left handed L form.
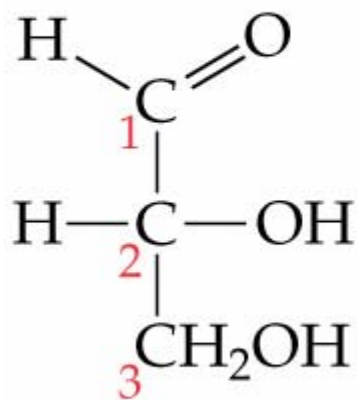
D-Glyceraldehyde
Right-handed
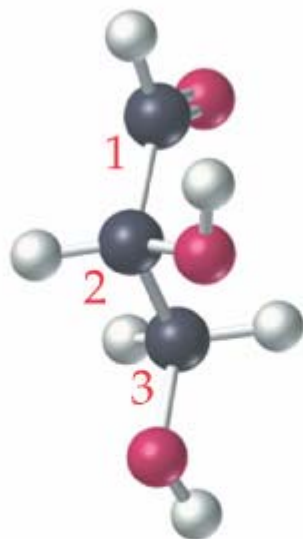
L-Glyceraldehyde
Left-handed

Chapter Eighteen
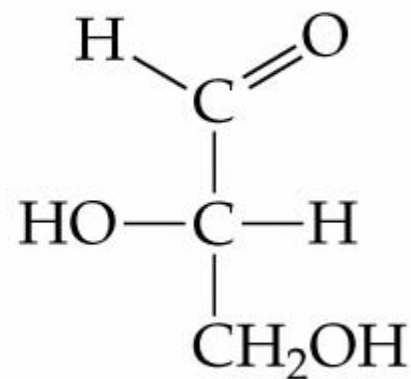
- Two forms of glyceraldehyde (D and L) have the same physical properties except they behave differently in the presence of a polarized light.

- Two forms of glyceraldehyde rotate plane of a polarized light in the opposite direction by the same amount.

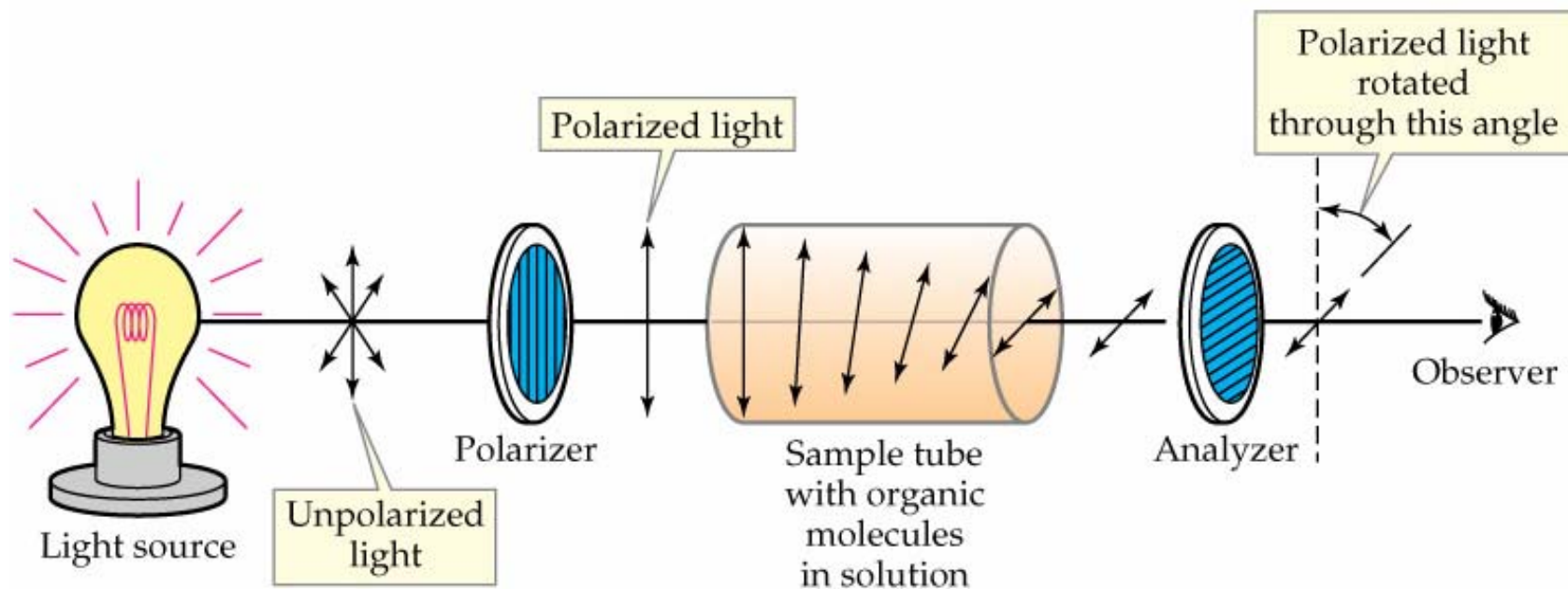- An instrument known as Polarimeter can be used to measure the degree of rotation of the plane of a polarized light.

Fig 22.1 Principles of a polarimeter, used to determine optical activity. A solution of an optically active isomer rotates the plane of the polarized light by a characteristic amount.

- In general, compounds with n chiral carbon atoms has a maximum of 2^n possible steroisomers and half that many pair of enantiomers.

- Glucose, and aldohexose, has four chiral carbon atoms and a total of $2^4 = 16$ possible stereoisomers (8 pairs of enantiomers).
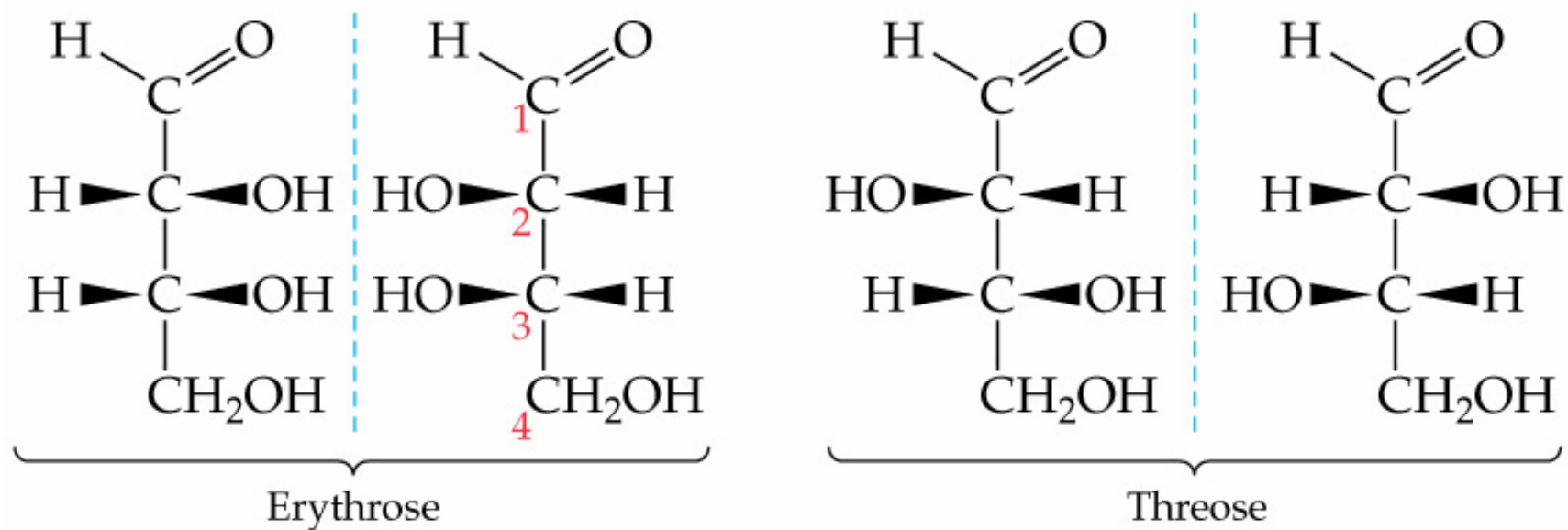
Fig 22.2 Two pairs of enentiomers. The four isomeric aldotetroses, 2,3,4-trihydroxybutanals.

# 22.3 The D and L Families of Sugars: Drawing Sugar Molecules

◆ *Fisher Projection* represent three-dimensional structures of stereoisomers on a flat page.

◆ A chiral carbon atom is represented in the Fisher projection as the intersection of two crossed lines. Bond that points up out of the page are shown as horizontal lines, and bonds that point behind the page are shown as vertical lines, see the following scheme.

Fischer projection
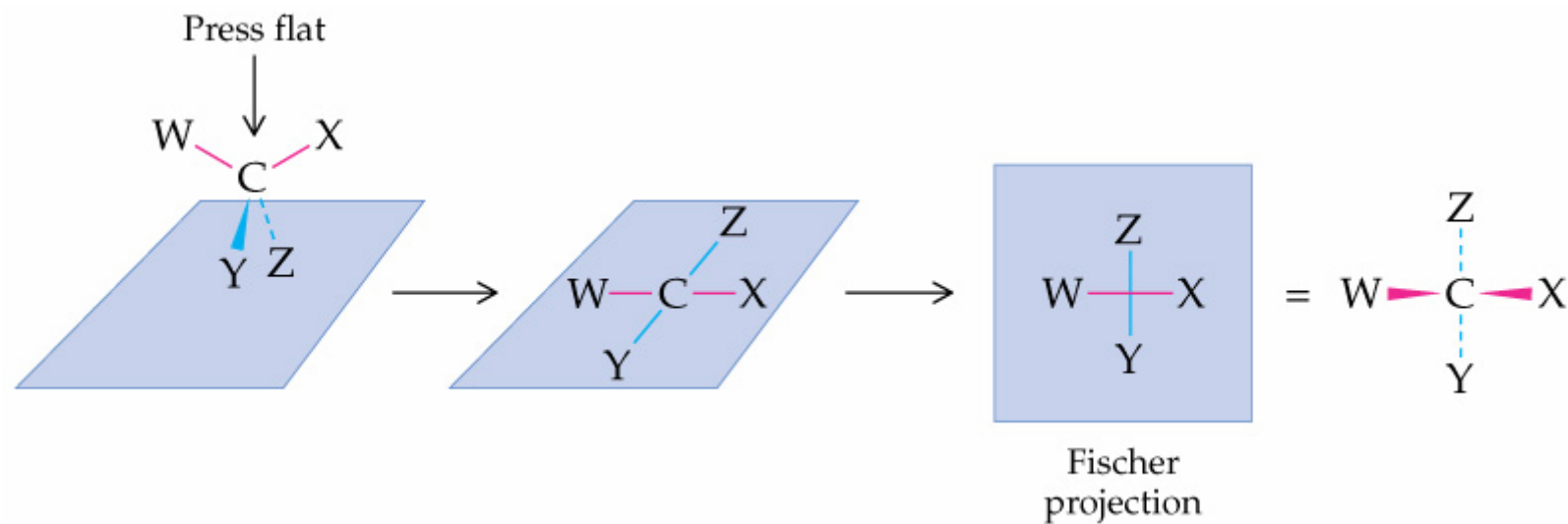
In a Fisher projection, the aldehyde or ketone carbonyl group of a monosaccharide is always placed at the top.

Fischer projection of a glyceraldehyde enantiomer

Bonds out of page

Bonds into page

CHO

HO——H

CH₂OH

Fischer projection

=

CHO

HO——C——H

CH₂OH
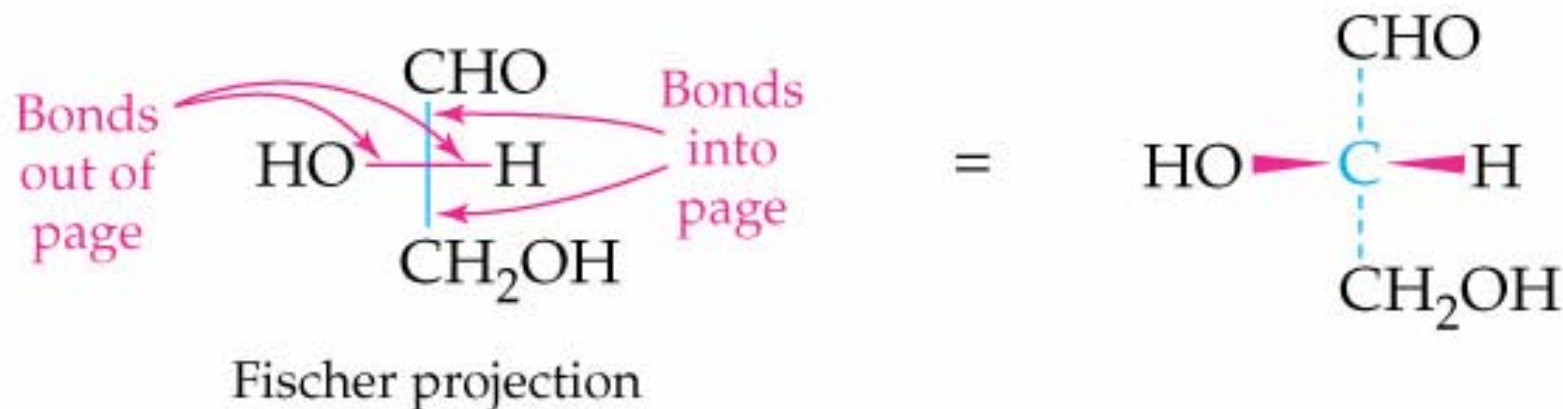
◆ ***Monosaccharides*** are divided into two families –D and L sugars.

- In D form, the –OH group on carbon 2 comes out of the plane of paper and points to the right.

- In L form, the –OH group on carbon 2 comes out of the plane of paper and points to the left.

◆ There is no correlation between the D and L and direction of rotation of a plane of polarized light. The D and L relate directly only to the position of –OH group on the bottom carbon in a Fisher projection.

22.4 Structure of Glucose and Other Monosaccharides

◆ D-Glucose, sometimes called dextrose or blood sugar, is the most widely occurring of all monosaccharides.

◆ In nearly all living organisms, D-glucose serves as a source of energy for all biochemical reactions.

◆ D-glucose is stored in polymeric form as starch in plants and as glycogen in animals.

◆ Monosaccharides with five or six carbon atoms exist mainly in cyclic forms.

Monosaccharides are generally high-melting, white, crystalline solids that are soluble in water and insoluble in nonpolar solvents. Most monosaccharides are sweet tasting, digestible, and nontoxic.

α-D-Galactose

β-D-Galactose

α-D-Fructose

β-D-Fructose
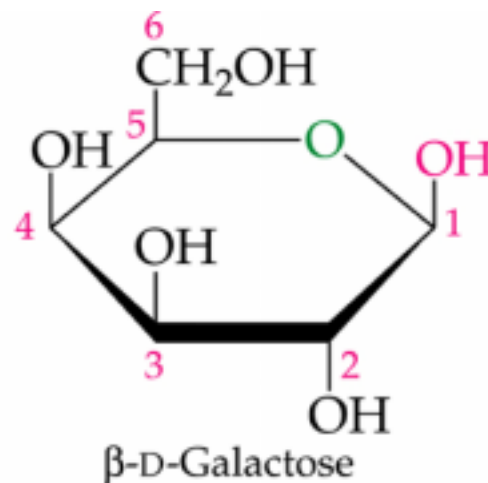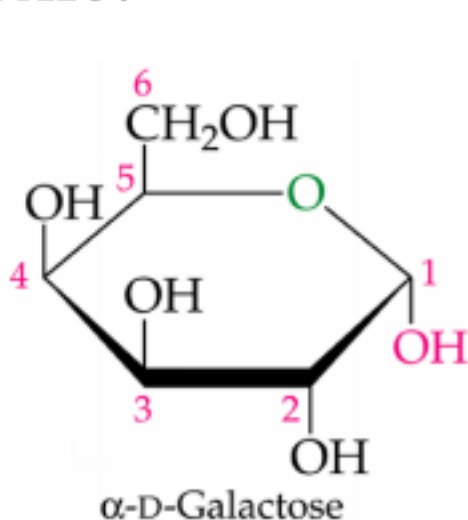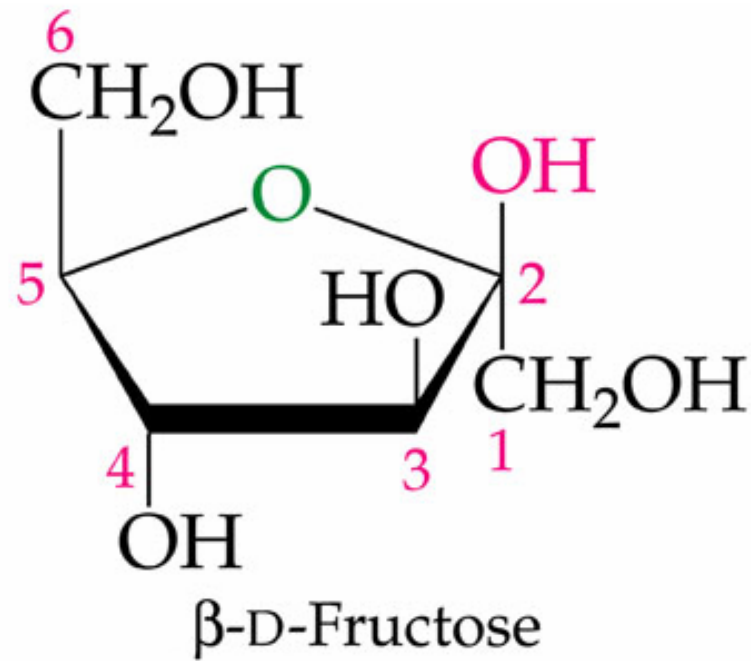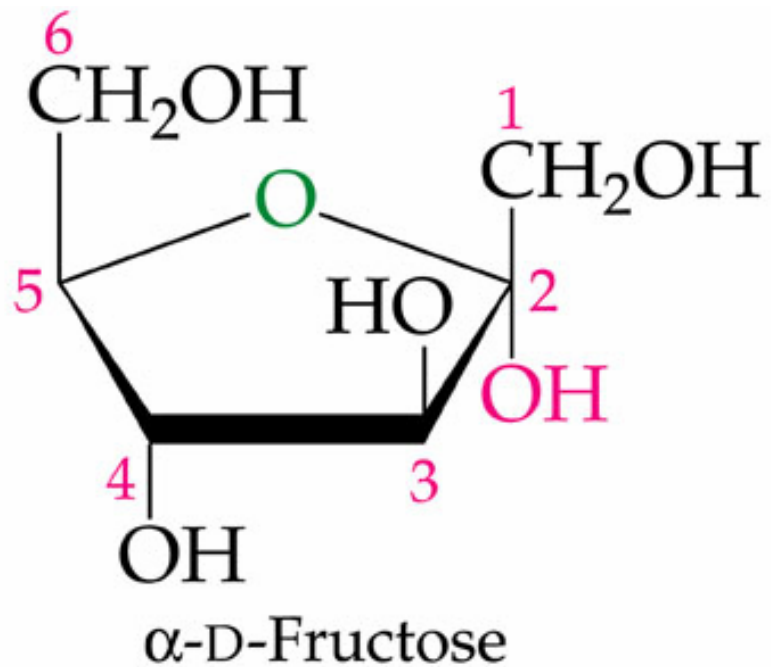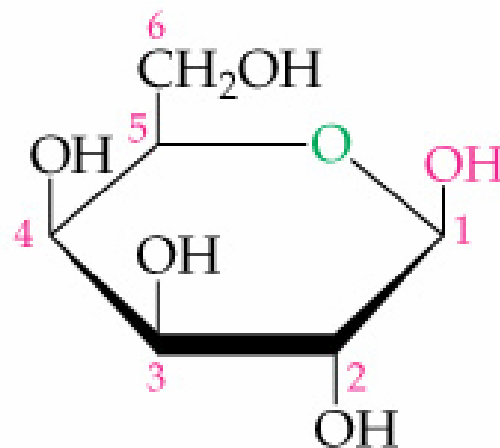
◆ *Anomers:* Cyclic sugars that differs only in positions of substituents at the hemiacetal carbon; the α-form has the –OH group on the opposite side from the –CH$_2$OH; the β-form the –OH group on the same side as the –CH$_2$OH group.
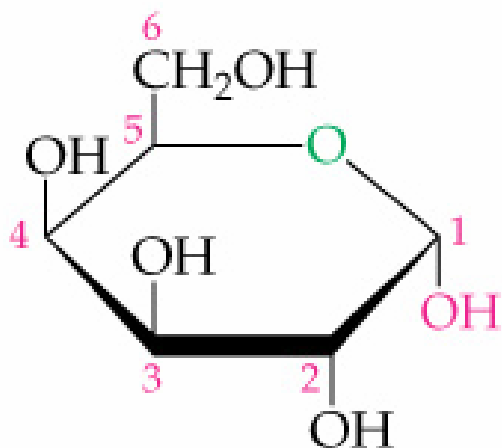
α-D-Galactose

β-D-Galactose

◆ Ordinarily, crystalline glucose is entirely in α-form.

◆ Once dissolved in water, equilibrium is established between the open chain and two anomeric form of the glucose. The optical rotation of a freshly prepared solution of α or β glucose gradually changes from its original value until it reaches a constant value that represents the optical rotation of the equilibrium solution, known as *mutarotation*.

α-D-Galactose   Open-chain galactose   β-D-Galactose
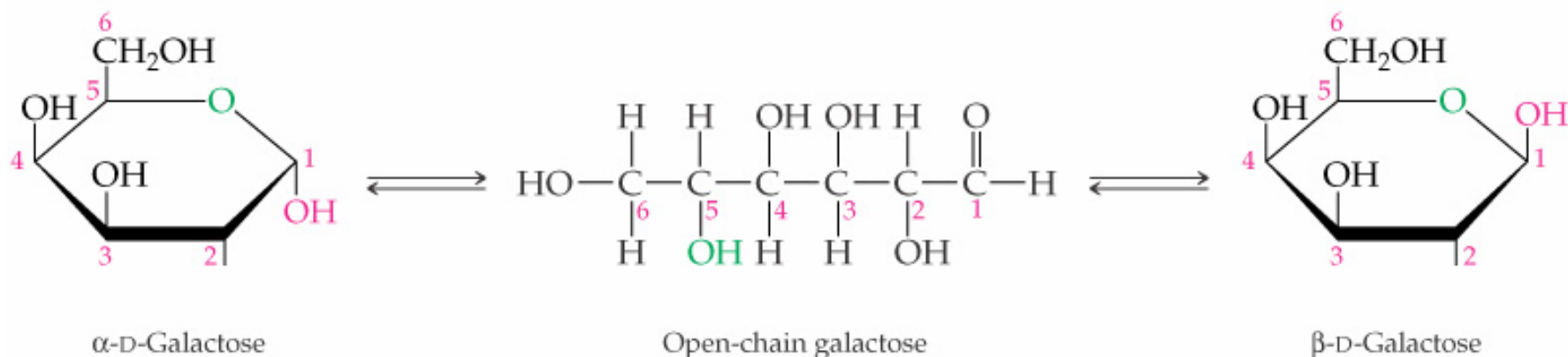
The structure of D-galactose: The molecule can exist as an open chain hydroxy aldehyde or as a pair of cyclic hemiacetals.

◆ The optical rotation of a freshly prepared solution of α or β glucose gradually changes from its original value until it reaches a constant value that represents the optical rotation of the equilibrium solution, known as *mutarotation*.

◆ Monosaccharides are high melting, white crystalline water soluble solids. Most monosaccharides are sweet-tasting, digestible, and non-toxic.

22.6 Reactions of Monosaccharides

Reactions with Oxidizing Agents: Reducing Sugars

◆ When an open chain aldehyde form of an aldose monosaccharide, is oxidized its equilibrium with the cyclic form is displaced. The aldehyde group of the monosaccharide is ultimately oxidized to a carboxylic acid group.

◆ *Reducing sugars*: Carbohydrates that reacts in basic solution with a mild oxidizing agents are classified as reducing sugars. In basic solution, all monosaccharides, whether they aldoses or ketoses, are reducing sugars.

Reactions with Alcohols: Glycoside and disaccharide Formation

◆ *Monosaccharides* react with alcohols to form acetals, which are called *glycosides*.

- The bond between the anomeric carbon atom and the oxygen atom of the –OR group is known as glycosidic bond.

- In disaccharides and polysaccharides, monosaccharides are connected to each other by *glycosidic* bonds.

- ***Hydrolysis***: Reverse of glycosidic reaction that happens during digestion of all carbohydrates.

Formation of Phosphate Esters of Alcohols

◆ The –OH group of sugar can add –PO_3^{2-} group to form *phosphate esters*.

◆ Phosphate esters of monosaccharides appear as reactants and products throughout the metabolism of carbohydrates.

◆ *Disaccharides* are made up of two monosaccharides. For example, sucrose, table sugar, is a disaccharide made up of one glucose and one fructose.

◆ Most fruits and fresh vegetable contain mono and disaccharides.

◆ Disaccharides contain a glycosidic link between the hemiacetal hydroxyl group at C1 of one sugar and the hydroxyl group at C4 of another sugar.

The three naturally occurring common disaccharides are:

Maltose: Two α-glucose are joined by an α-1,4-link.

Lactose, also known as milk sugar: The major carbohydrate found in mammalian milk. Two β-monosaccharides are joined by an β-1,4-link.

Sucrose, table sugar: Sugar beets and sugarcane are the most common sources of sucrose. One molecule of D-fructose and one molecule of D-glucose joined together by a 1,2-link between the anomeric carbons.

22.8 Variations on the Carbohydrate Theme

◆ Monosaccharides with modified functional groups are components of a wide variety of biomolecules.

◆ Short chains of monosaccharides, known as *oligosaccharides*, enhance the function of proteins and lipids to which they are bonded.

◆ A few of these carbohydrate variations are,

- *chitin*: the shells of lobster, beetles, and spiders are made of chitin.

- *heparin*: an agent that prevents or retards the clotting of blood.

- *glycoproteins*: performs iomportant function at the cell suface. They can function as receptor for molecular messengers or drugs. They are also responsible for the familiar A, B, O system of typing blood.

22.9 Some Important Polysaccharides

Polysaccharides are polymers of many monosaccharides linked together through glycosidic bonds. Three of the most important polysaccharidies are cellulose, starch, and glycogen.

Cellulose is a fibrous substance that provides structure in plants. They consist entirely of several thousand β-units joined together in a long straight chain by β-1,4-links.
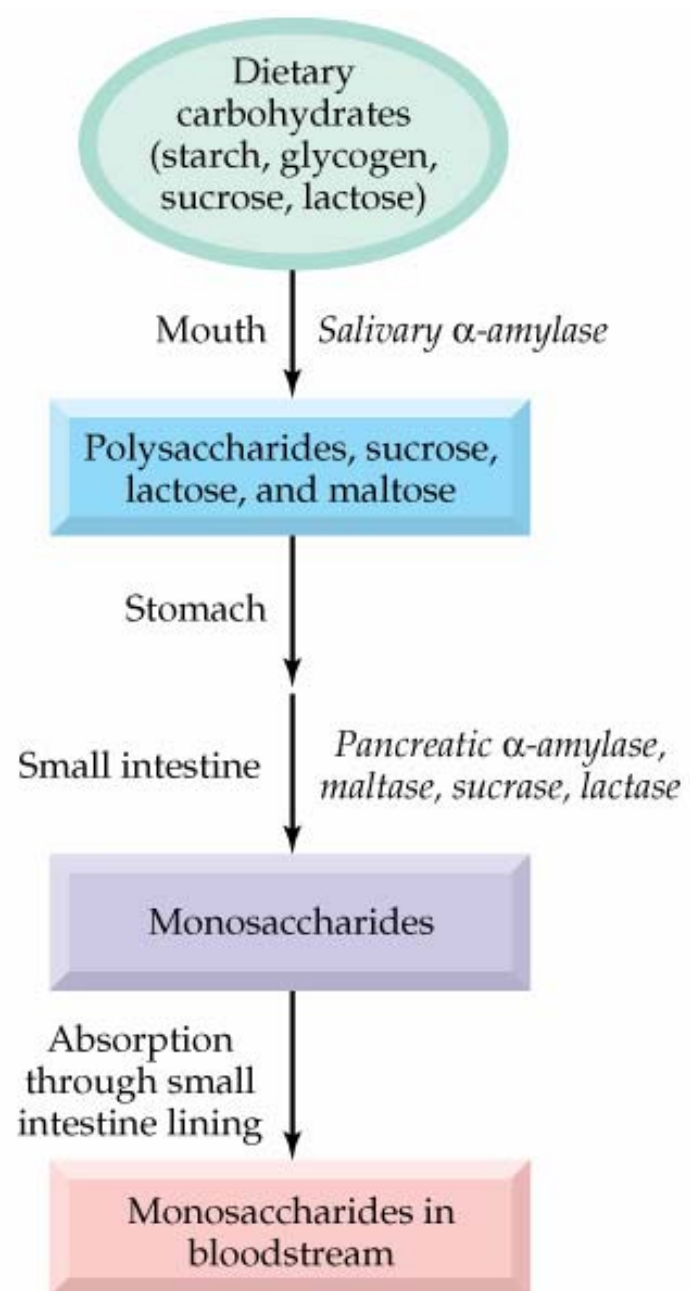
Starch, like cellulose, is a polymer of glucose. Starch is fully digestible and is an essential part of human diet. In starch, glucose units are joined by α-1,4-links.

Glycogen, also called animal starch, serves as the energy storage role as starch serves in plants. Some of the glucose from starches in our diet used immediately as fuel, and some are stored as glycogen for later use.

23.1 Digestion of Carbohydrates

Digestion entails physical grinding, softening, mixing of food, and enzyme-catalyzed hydrolysis of carbohydrates, proteins, and fats. The products of digestion are mostly small molecules that are absorbed from the intestine tract. The digestion of carbohydrates is summarized in Fig 23.1.

Fig 23.1 The digestion of carbohydrates

Dietary carbohydrates (starch, glycogen, sucrose, lactose)

Mouth | Salivary α-amylase

Polysaccharides, sucrose, lactose, and maltose

Stomach

Small intestine | Pancreatic α-amylase, maltase, sucrase, lactase

Monosaccharides

Absorption through small intestine lining

Monosaccharides in bloodstream

23.4 Entry of Other Sugars into Glycolysis

◆ Major monosaccharides from digestion other than glucose also enters into glycolysis pathway.

◆ Fructose from fruits or hydrolysis of the disaccharides sucrose is converted to glycolysis intermediates in two pathways:

- In muscle, it is phosphorylated to fructose 6-phosphate.

- In the liver, it is converted to glyceraldehyde 3-phosphate.

◆ Galactose from hydrolysis of the disaccharides lactose is converted to glucose 6-phosphate by a five-step pathway.

◆ Mannose, a product of hydrolysis of plant polysaccharides other than starch, is converted by hexokinase to a 6-phosphate which is then undergoes a multistep, enzyme catalyzed rearrangement and enters glycolysis as fructose 6-phosphate.

23.5 The Fate of Pyruvate

The conversion of glucose to pyruvate is a central metabolic pathway in most living organisms. The further reactions of pyruvate depend on metabolic conditions and on the nature of organism.

◆ Under normal oxygen rich (aerobic) conditions, pyruvate is converted to acetyl-S-coenzyme A.

$$\text{Ethyl alcohol} \longleftarrow \text{Pyruvate} \longrightarrow \text{Lactate}$$
$$\downarrow$$
$$\text{Acetyl-SCoA}$$
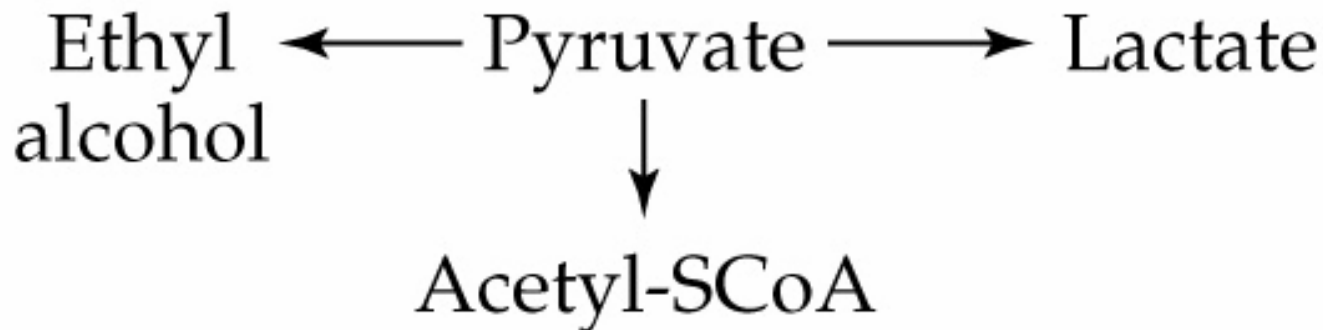
- Under anaerobic (not enough oxygen) conditions, pyruvate is reduced to lactate. When sufficient oxygen becomes available, lactate is recycled to pyruvate.

- When body is starved for glucose, pyruvate is converted back to glucose by gluconeogenesis.

- Yeast is an organism that converts pyruvate to ethanol under anaerobic conditions.

23.7 Regulation of Glucose Metabolism and Energy Production

Normal blood glucose concentration a few hours after a meal ranges roughly between 65 and 110 mg/dL. Departure from normal has serious effects on our body, Fig 23.5.

◆ Low blood glucose (***Hypoglycemia***) causes weakness, sweating, and rapid heartbeat, and in severe cases it can cause coma, and eventually to death.

◆ High blood glucose (***Hyperglycemia***) causes increased urine flow. Prolonged hyperglycemia can cause low blood pressure, coma, and death.
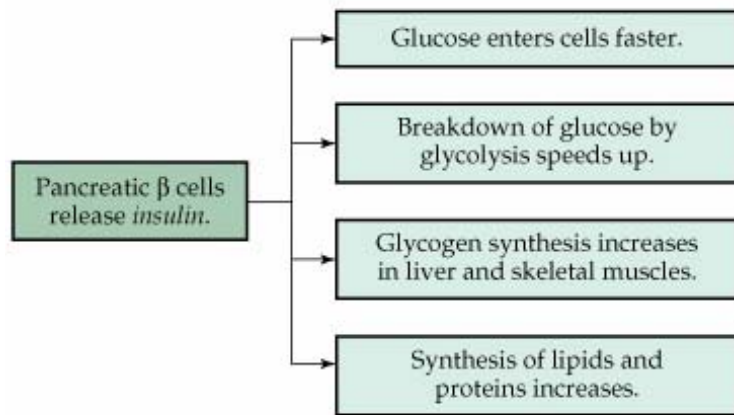
Fig 23.5 Blood glucose

The following two hormones from pancreas have the major responsibility for blood glucose regulation.

   - *Insulin* is released when blood glucose level rises. Its role is to decrease blood glucose concentration by accelerating the passage of glucose into cells where it is used for energy production, and stimulating synthesis of glycogen, proteins, and lipids.

- *Glucagon* is released when blood glucose concentration drops. Glucagon stimulates the break down of glycogen in the liver and release glucose. Amino acids from proteins and glycerol from lipids are also converted to glucose in the liver by gluconeogenesis.

Rising blood glucose concentration

	Glucose enters cells faster.
	Breakdown of glucose by glycolysis speeds up.
Pancreatic β cells release *insulin*.	Glycogen synthesis increases in liver and skeletal muscles.
	Synthesis of lipids and proteins increases.

Falling blood glucose concentration

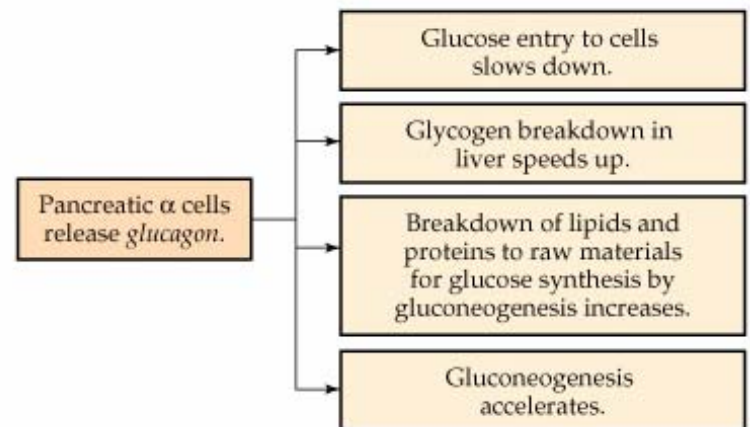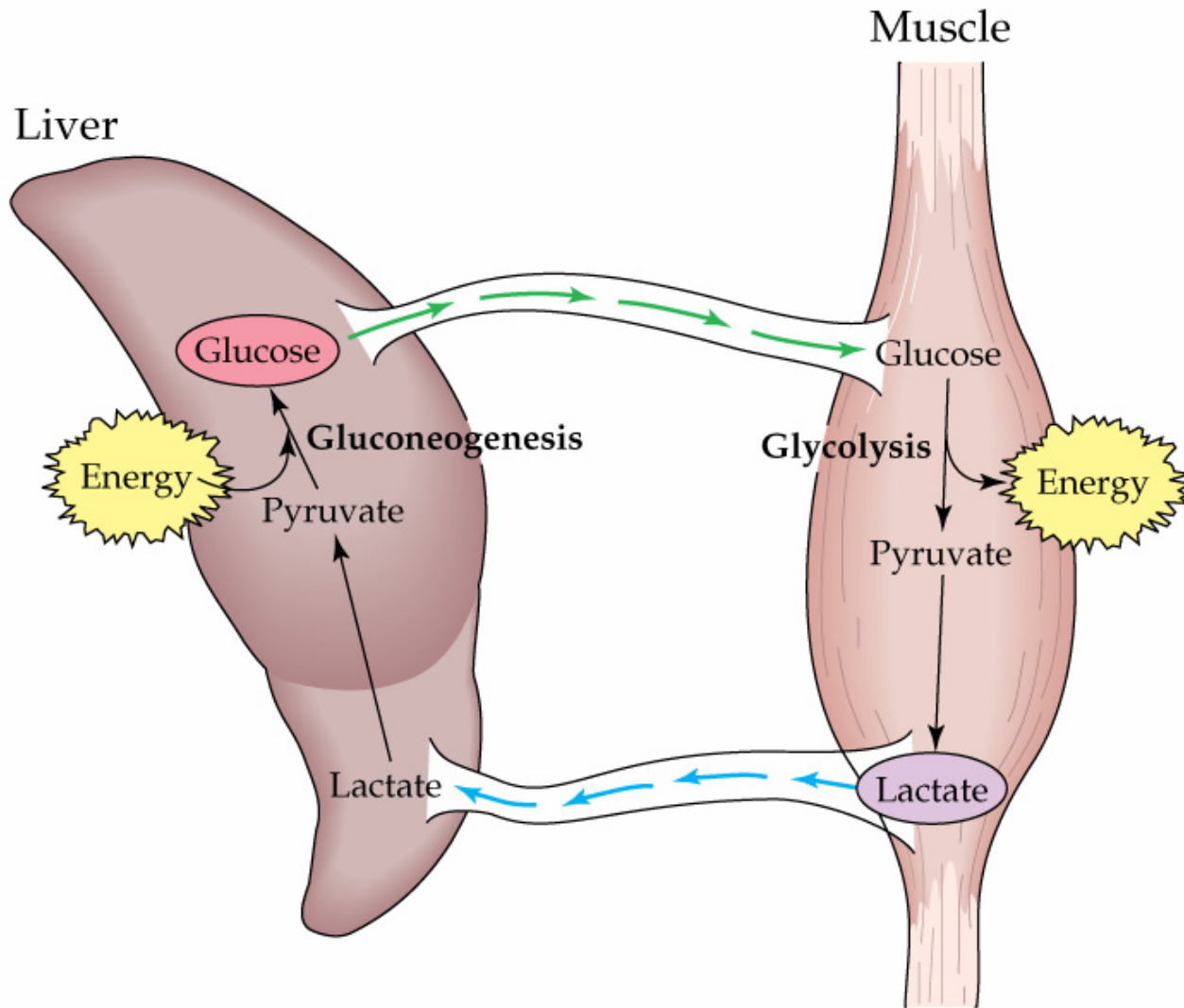|	
	Glucose entry to cells slows down.
	Glycogen breakdown in liver speeds up.
Pancreatic α cells release *glucagon*.	Breakdown of lipids and proteins to raw materials for glucose synthesis by gluconeogenesis increases.
	Gluconeogenesis accelerates.

Fig 23.6 Regulation of glucose concentration by insulin and glucagon from pancreas.

Fig 23.10 Glucose production during exercise.