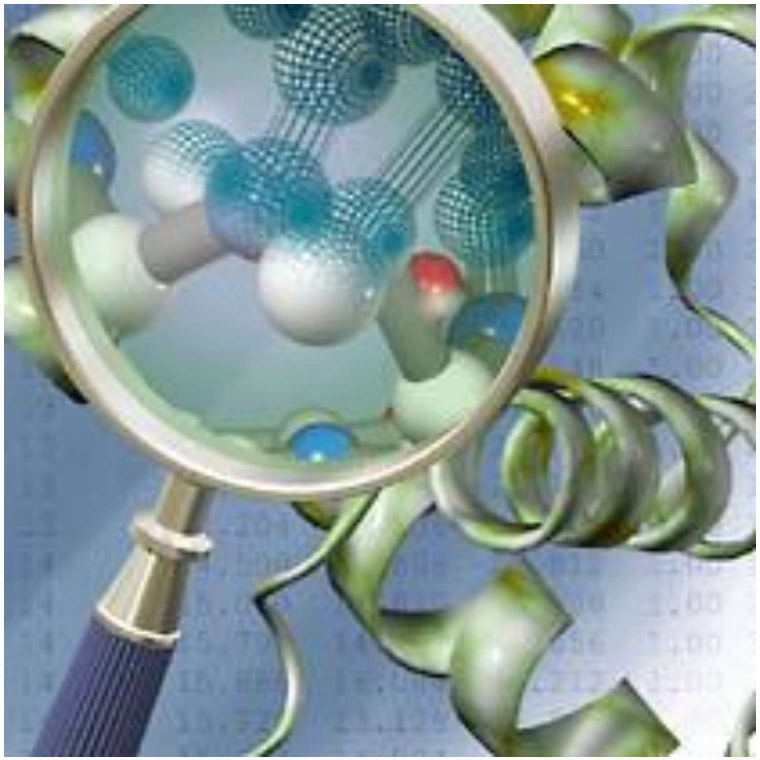
Biochemistry



-the study of molecular basis of life

Biofyzikální ústav,
Akademie věd České republiky, v.v.i.
Královopolská 135
612 65 Brno

Mgr. Marie Brázdová, Ph.D.

brazdovam@vfu.cz, brazdovam@yahoo.com, maruska@ibp.cz

Sylabus

1) **Biochemistry: an introduction**
1.1) Scope of biochemistry
1.2) Living cells
1.3) Water: the medium of life
1.4) Energy
2) **Amino acids and Proteins**
2.1) Amino acids
2.2) Peptides
2.3) Protein structure
3) **Enzymes**
3.1) Properties of Enzymes
3.2) Classification of Enzymes
3.3) Catalysis
3.4) Enzyme regulation
4) **Carbohydrates**
4.1) Monosaccharides
4.2) Disaccharides
4.3) Oligosaccharides
4.4) Polysaccharides
5) **Carbohydrate metabolism**
5.1) Glycogen metabolism
5.2) Glycolysis
5.3) Glyconeogenesis
6) **Aerobic metabolism**
6.1) Citric Acid Cycle
6.2) Electron transport
6.3) Oxidative phosphorylation
6.4) Oxidative stress
7) **Lipids and membranes**
7.1) Lipids classes
7.2) Membranes
8) **Lipid metabolism**
8.1) Fatty acids and triacylglycerols
8.2) Membrane lipid metabolism
8.3) Isoprenoid metabolism
9) Nitrogen metabolism I: synthesis
10) Nitrogen metabolism II: degradation
11) Integration of metabolism
12) Nucleic acids
13) Nucleic acids metabolism
14) Protein synthesis
15) Biotransformation

Literature

- MURRAY,R.K.; GRANNER,D.K.;RODWELL,V.W. *Harper´s Illustrated Biochemistry*. Appleton & Lange, 2012.
- T.McKee, J.S.McKEe. *Biochemistry*. USA, 1996. ISBN 0-697-21159-2.
- MURRAY,R.K.; GRANNER,D.K.;RODWELL,V.W. *Harper´s Illustrated Biochemistry*. Appleton & Lange, 2006. ISBN 07-147885-X.
- A. L. Lehninger, D. L. Nelson, M. M. Cox. *Principles of biochemistry*. USA, 2005. ISBN 0716743396.
- Color Atlas of Biochemistry, Second edition, revised and enlarged, J. Koolman, KH Roehm; ISBN-13: 978-1-58890-247-4, ISBN-10: 1-58890-247-1
- J. Tomandl Biochemistry I Seminars, 2012

The exam from Biochemistry:

<u>conditions for exam</u>

1. credit from practical course
(100% presence, credit test 80%)
2. preparation of „Seminars from Biochemistry“ (download to Moodle)
3. 60% of presence on lectures, 60% of week tests

<u>Exam: 2 parts</u>

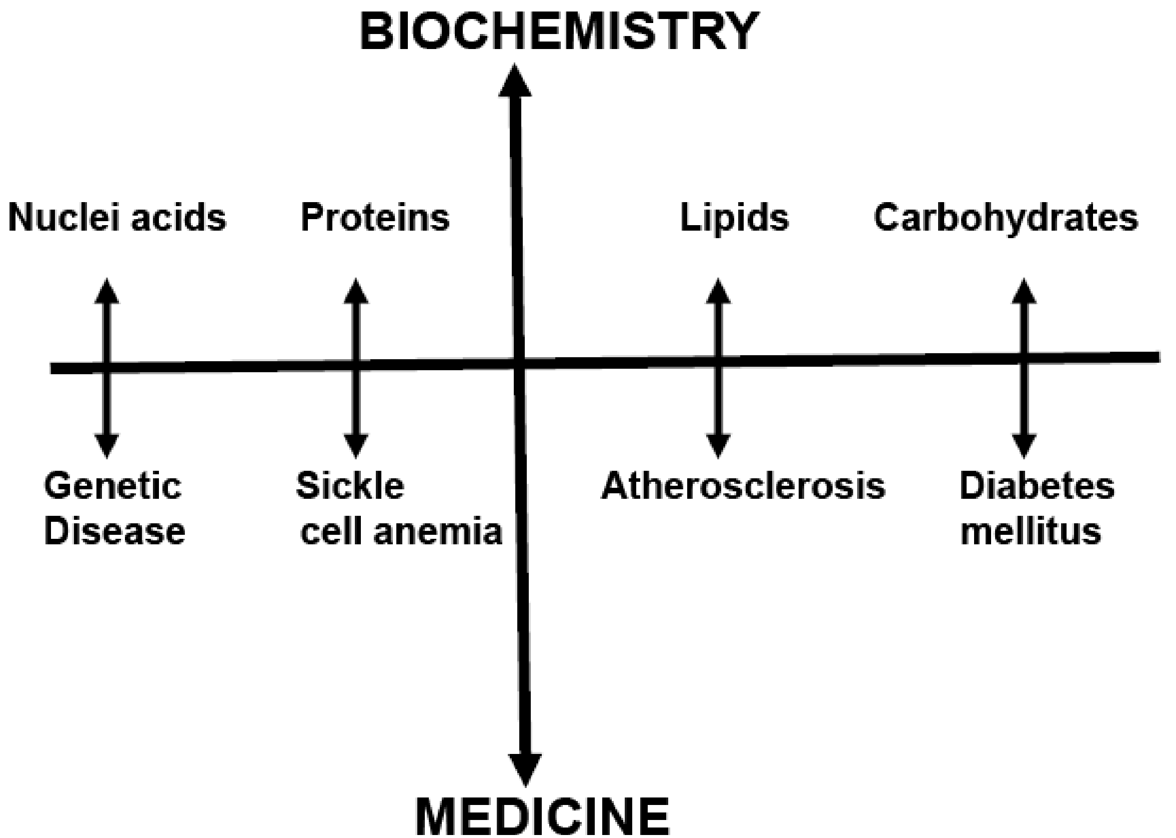
- test (60% limit), majority question from „Seminars from Biochemistry, formulas of AA, carbohydrates, vitamins, hormones, lipids, base of NA…..
- oral examination

from A (90-95% of test)
    B (90-80%), C(90-80%), D (80-70%, E (70-60%)

Biochemistry

- Biochemistry is the study of the molecular basis of life.
- Lying at the interface between chemistry and biology, biochemistry
- is concerned with the structure and interaction of proteins, nucleic acids, and other biomolecules as related to their function in biological systems.
- As one of the most dynamic areas of science,
- biochemistry has led to improved medicines and diagnostic agents, new ways of controlling disease, and greater understanding of the chemical factors that control our general health and well-being.

Biochemistry and Medicine



- Examples of two way street connectiong biochemistry and medicine,
- Knowledge of the biochemsitry – understending of diseases

Central principes:

1. **<u>Cellular foundation:</u>** Cells – highly organized structural basic of all living organism
2. **<u>Chemical foundation:</u>**

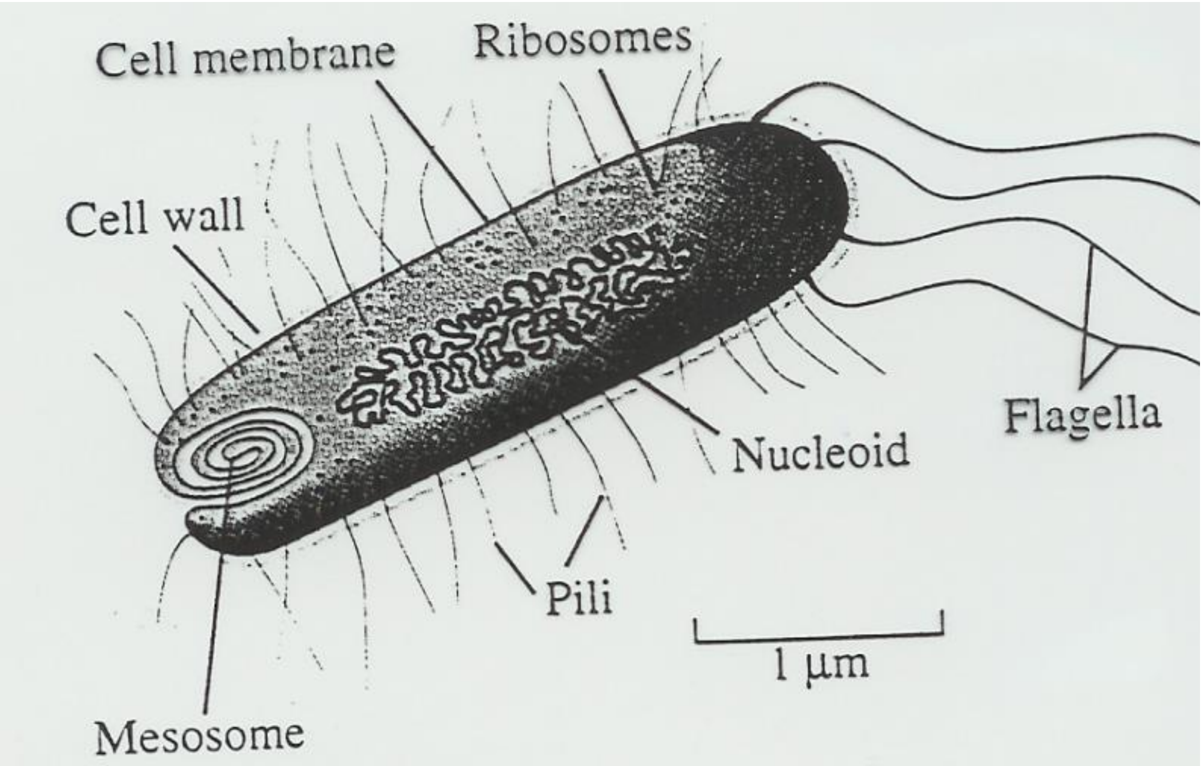
- Living processes – thousand chemical reaction, regulation and integration – maintenance of live

- Reaction pathways (glycolysis) –all organism

3. **<u>Physical foundation:</u>** All organism utilize the same types of molecules (carbohydrates, lipids, proteins, nucleic acids)

4. **<u>Genetic foundation:</u>** The instruction for growth, development, reproduction – nucleic acids

Prokaryotic cells



-Bacteria, mostly unicellular

- cell size 1–10 μm

-Cytomplasmatic membrane, cell wall

-No membrane organene (subcellular comartmentation)

-No separated nucleus

-Circular DNA (mainly)

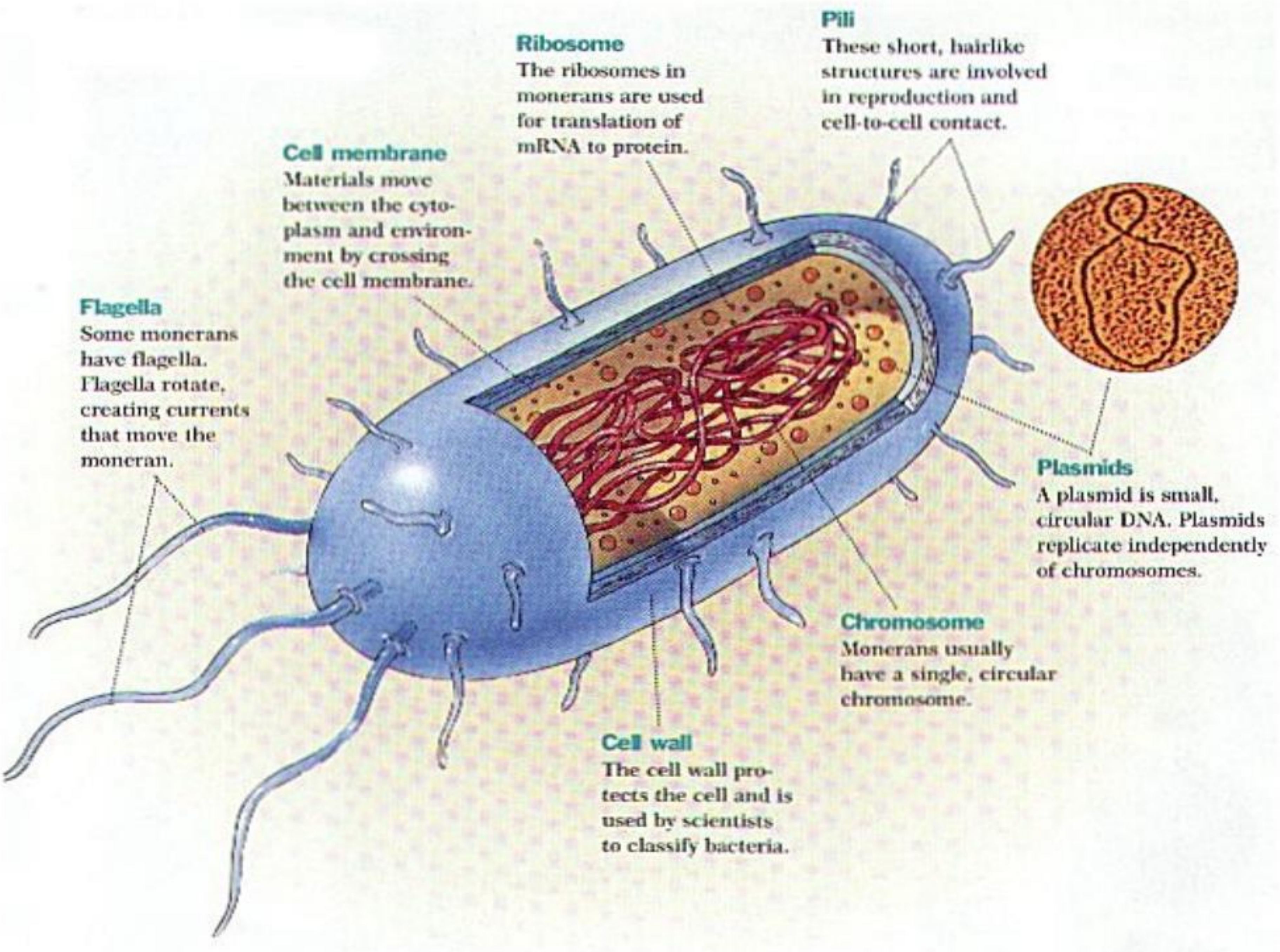
-Ribosome size 70S

-Cell division

-DNA without histones

-Protein synthesis events – cytomplasm

-Respiration enzymes – in plasmatic membrane


Pili
These short, hairlike structures are involved in reproduction and cell-to-cell contact.
Ribosome
The ribosomes in monerans are used for translation of mRNA to protein.
Cell membrane
Materials move between the cytoplasm and environment by crossing the cell membrane.
Flagella
Some monerans have flagella. Flagella rotate, creating currents that move the moneran.
Plasmids
A plasmid is small, circular DNA. Plasmids replicate independently of chromosomes.
Chromosome
Monerans usually have a single, circular chromosome.
Cell wall
The cell wall protects the cell and is used by scientists to classify bacteria.

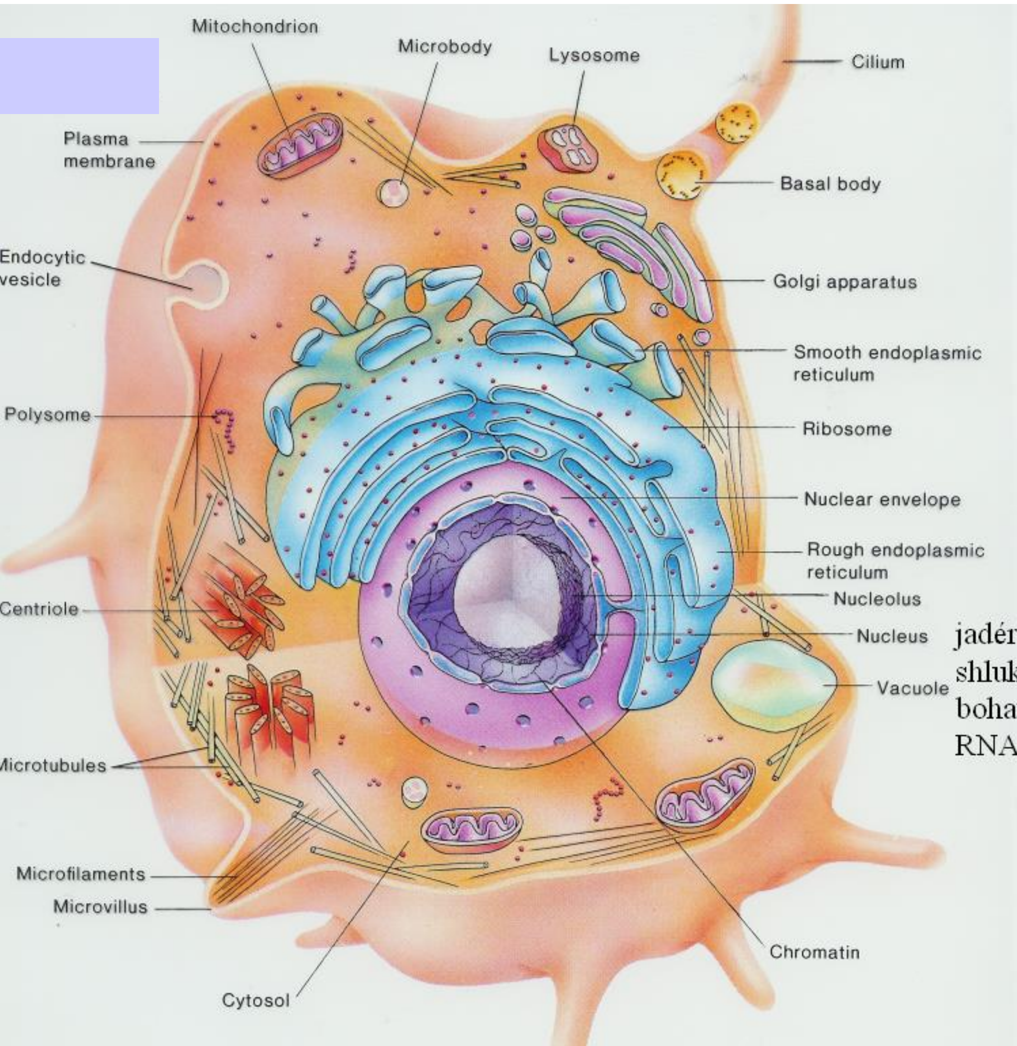
Eukaryotic cells – variety of membrane organelles

-Unicellular organism, Multicellular organism

10-20 μm, but upto 150μm

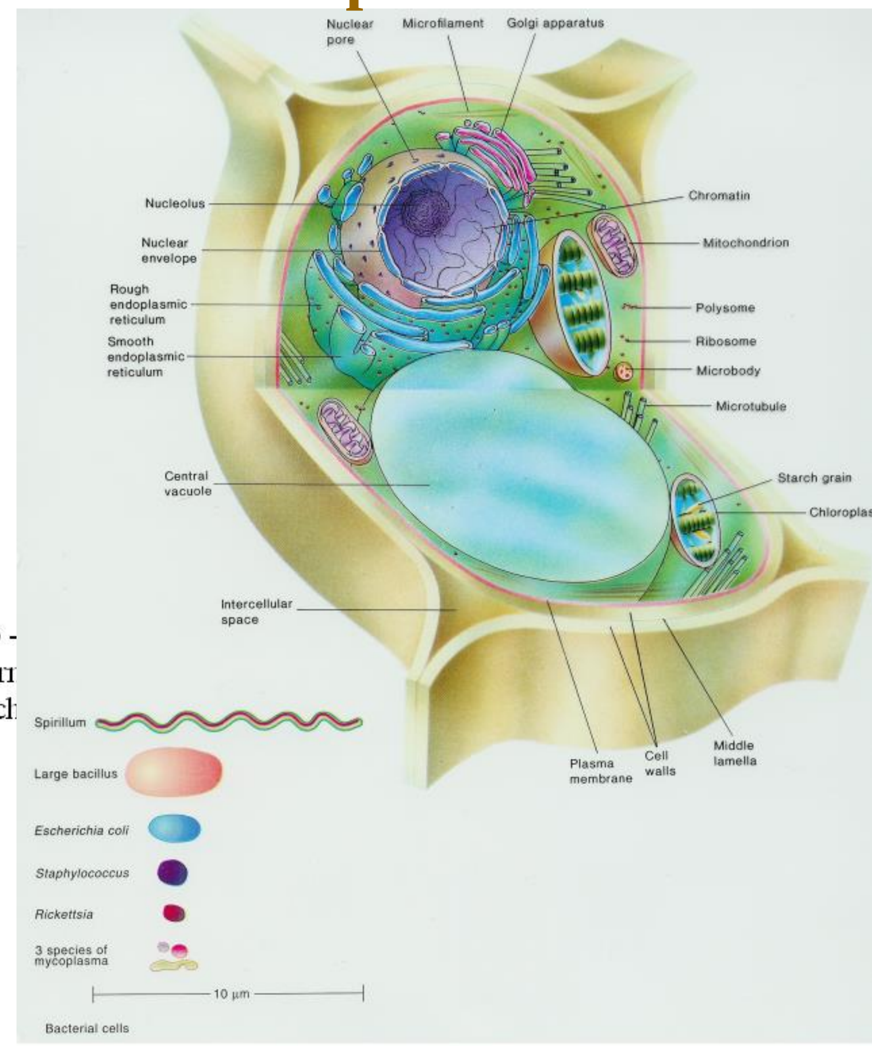
- Cells in tissues, organs –specialized functions

animal

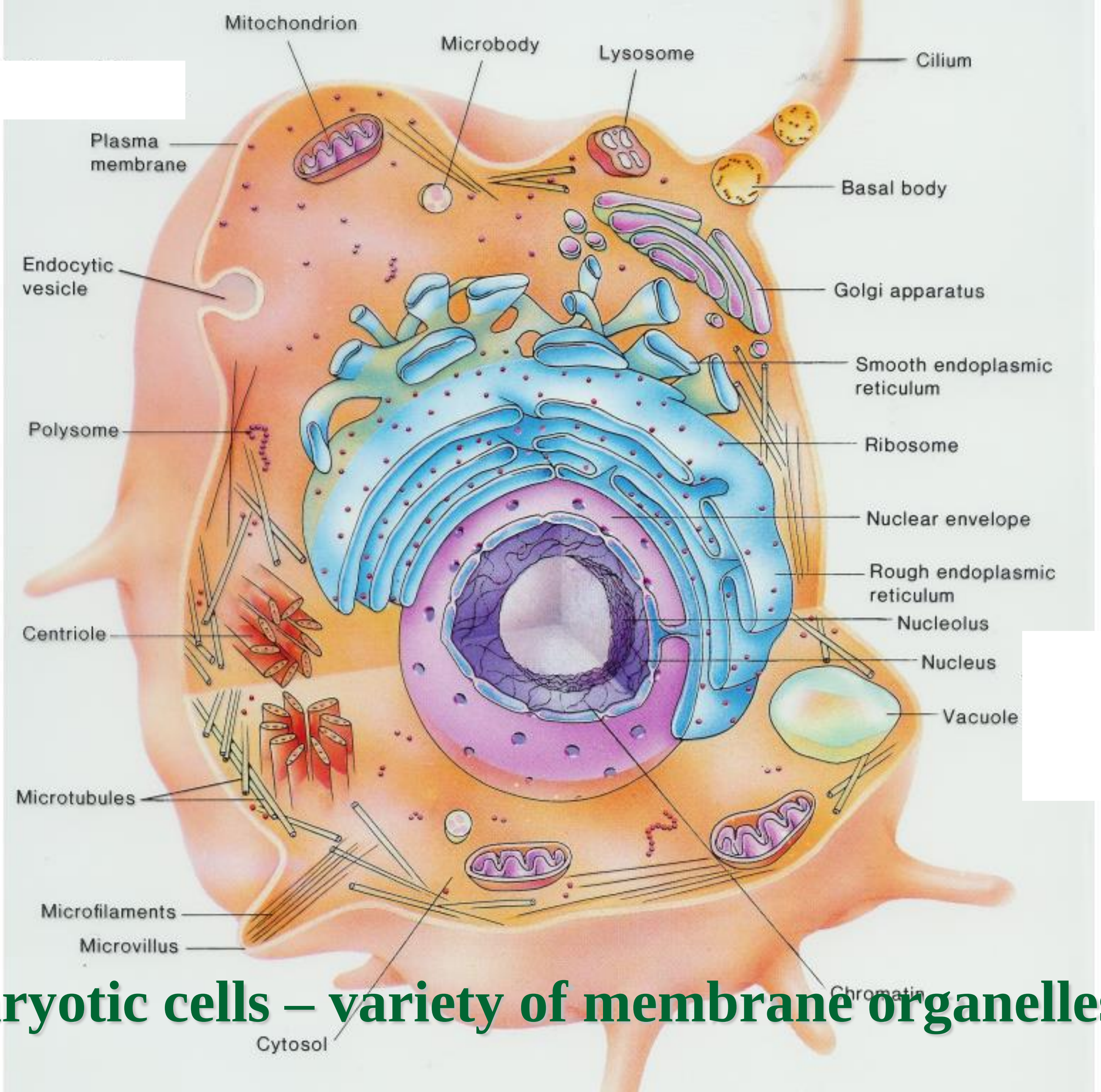


jadérko -
shluk zr
bohatýc
RNA

plant



Animal cell



Eukaryotic cells – variety of membrane organelles

The differences between the eukaryotic and prokaryotic cells

- Prokaryotic organisms are simpler than eukaryotic organisms - that is probably the main difference that must be taken into account.

- Among **prokaryotic organisms** belong unicellular organisms such as bacteria and cyanobacteria. Size of the cell is mostly in the range 1 to 10 microns.
- Around a cell can be found at the cytoplasmic membrane and the cell wall stronger. Since the cell is bounded by a cell wall contains cytoskeleton. The internal contents of the cell is further divided in any way, because in prokaryotes are not talking about compartmentalization.

- **Genetic information** is stored in prokaryotes the circular DNA. Transcription and translation take place in the cytoplasm, translation, specifically on ribosomes, **having a size 70S**.
  Enzymes cellular respiration are stored at the cytoplasmic membrane.
  Among the **eukaryotic organisms** are those which are composed of eukaryotic cells - these are multicellular organisms, such as fungi, plants and animals.
  Eukaryotic cells are larger than prokaryotic - average size is 10 to 20 micron, although some may reach the size of 150 microns.
- On the surface of a cell is the cell membrane, cytoskeleton maintains cell shape. Similar membranes such as those on the surface, can also be found in cell organelles, which are thus separated from the internal environment of the cell forming the cytosol.
- Genetic information is stored in the core of the fiber in the form of DNA molecules (together with proteins named histones produces bodies - chromosomes). **DNA synthesis** occurs in the nucleus, as well as transcription. T
- ranslation takes place in the cytosol or in the smooth endoplasmic reticulum membrane, but in both cases the size **80S ribosomes**.
  Enzymes cellular respiration are deposited on the inner membrane of mitochondria.
  The above summarized in the following table:

Differences between prokaryotic and eukaryotic cells

Feature	Prokyryotic cells	Eukaryotic cell
Organisms	Bacterie, cyanobacteria, unicellular	Protozoa, fungi, plants, animals, multicellular
Cell size (uM)	1 – 10 µm	10 – 20 µm
Separated nucleus	No	Yes
Subcellular organels	No	Yes
Character of Chromosomes	Circular DNA	Linear DNA
Ribosome size	70S	80S
Presence of cytoskeleton	No	Yes
Cell division	Lateral/binary fission	Mitosis
DNA	Free	Connected with protiens (histones)
Protein synthesis events	In cytoplasm	Cytoplasm, ER
Location of respiratory enzymes	In plasmatic membrane	In mitochondrial membrate (inner)

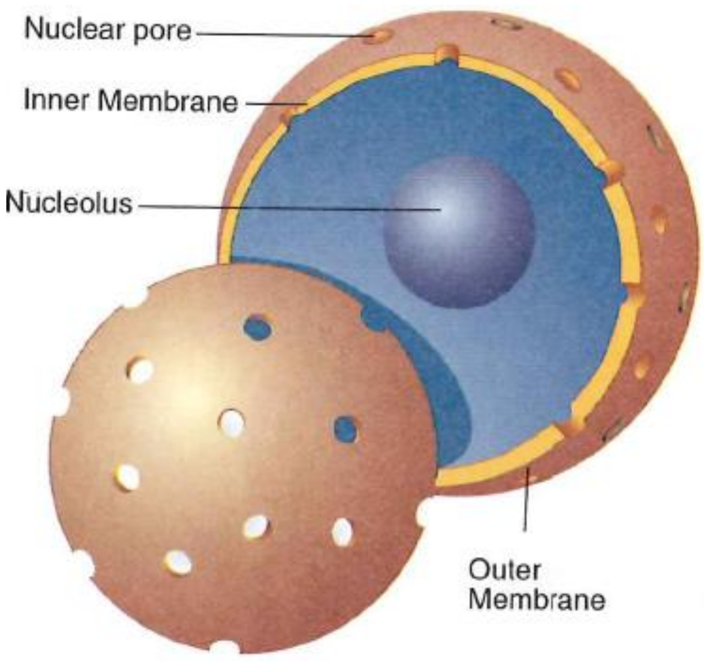
Eukaryotic NUCLEUS

- is a membrane-enclosed organelle found in eukaryotic cells.
- It contains most of the cell's genetic material, organized as multiple long linear DNA molecules in complex with a large variety of proteins, such as histones, to form chromosomes.
- The genes within these chromosomes are the cell's nuclear genome. The function of the nucleus is to maintain the integrity of these genes and to control the activities of the cell by regulating gene expression—the nucleus is, therefore, the control center of the cell.
- The main structures making up the nucleus are the nuclear envelope, a double membrane that encloses the entire organelle and isolates its contents from the cellular cytoplasm, and the nucleoskeleton (which includes nuclear lamina), a network within the nucleus that adds mechanical support, much like the cytoskeleton, which supports the cell as a whole. Because the nuclear membrane is impermeable to large molecules, nuclear pores are required that regulate nuclear transport of molecules across the envelope.
- The pores cross both nuclear membranes, providing a channel through which larger molecules must be actively transported by carrier proteins while allowing free movement of small molecules and ions.
- Movement of large molecules such as proteins and RNA through the pores is required for both gene expression and the maintenance of chromosomes.
- The interior of the nucleus does not contain any membrane-bound sub compartments, its contents are not uniform, and a number of *sub-nuclear bodies* exist, made up of unique proteins, RNA molecules, and particular parts of the chromosomes.
- The best-known of these is the nucleolus, which is mainly involved in the assembly of ribosomes. After being produced in the nucleolus, ribosomes are exported to the cytoplasm where they translate mRNA.

Eukaryotic NUCLEUS

- Genetic information
- DNA with histones
- Metabolism:

- replication of DNA,
- synthesis of RNA,
- RNA processing
- protein biosynthesis
- RNA transport



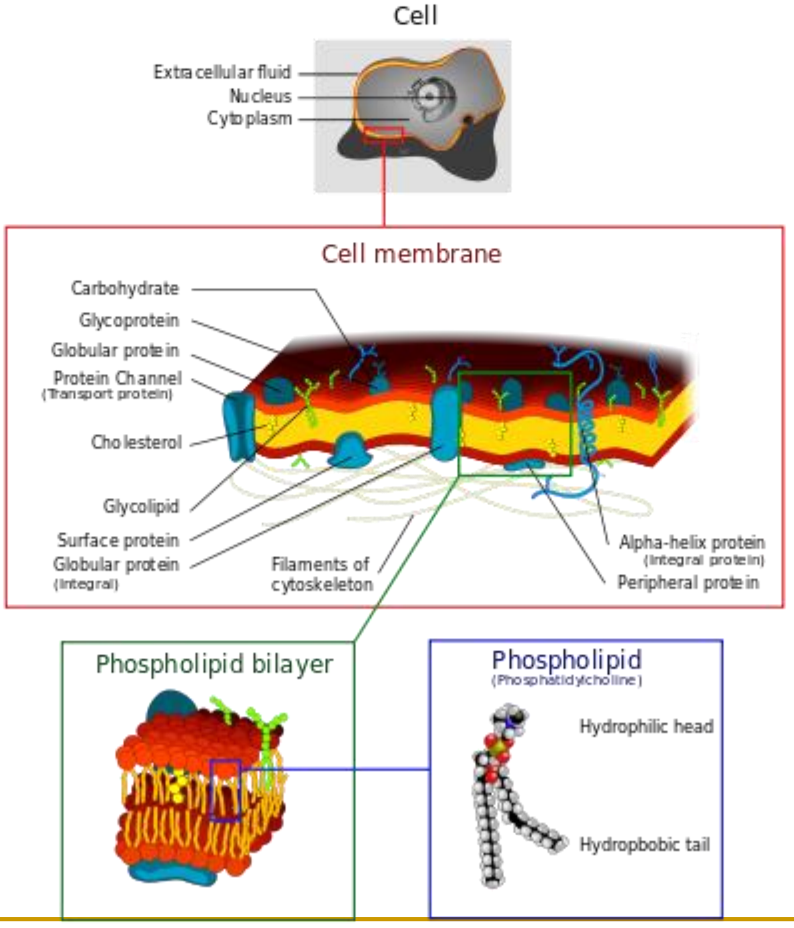
Cell membranes:

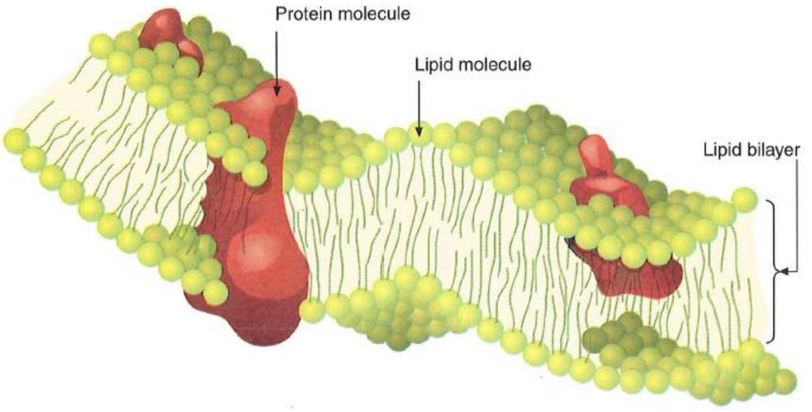
- plasmatic membrane

- The **cell membrane** (also known as the **plasma membrane** or **cytoplasmic membrane**) is a biological membrane that separates the interior of all cells from the outside environment.
- The cell membrane is selectively permeable to ions and organic molecules and controls the movement of substances in and out of cells.[3]
- The basic function of the cell membrane is to protect the cell from its surroundings. **It consists of the phospholipid bilayer with embedded proteins.**
- Cell membranes are involved in a variety of cellular processes such as cell adhesion, ion conductivity and cell signalling and serve as the attachment surface for several extracellular structures, including the **cell wall, glycocalyx**, and intracellular cytoskeleton. Cell membranes can be artificially reassembled

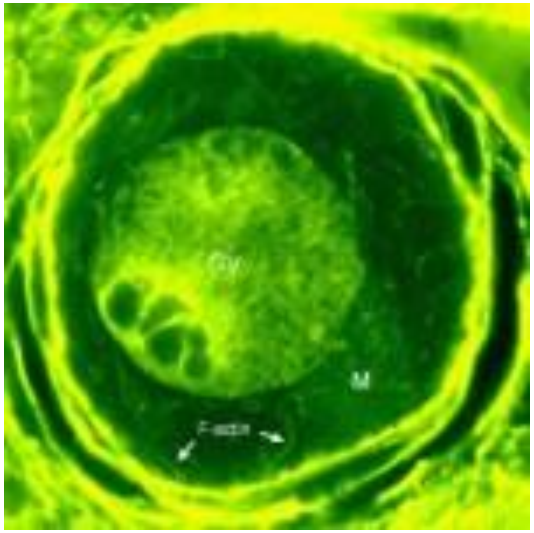
Cell membranes:

- plasmatic membrane





Cytoplasm



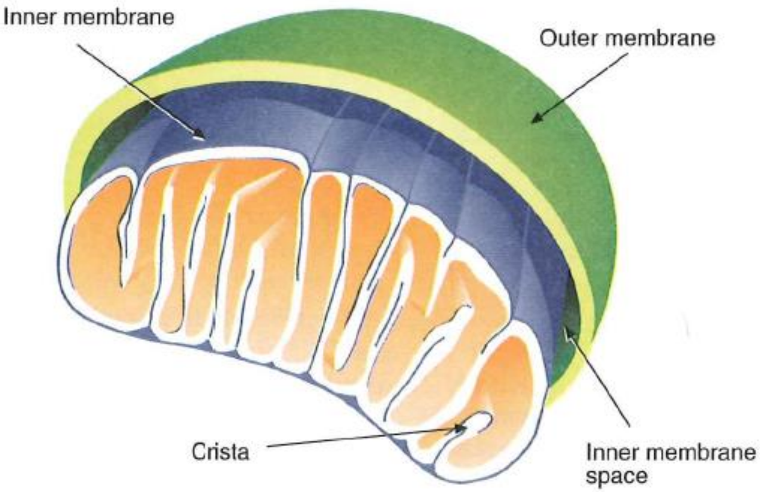
- Cytoplasm form a uniform environment in which the other cellular organelles, located between them and the cell wall.

- Its main component is water in which is located a number of other substances (from simple inorganic substances to complex enzyme complexes).

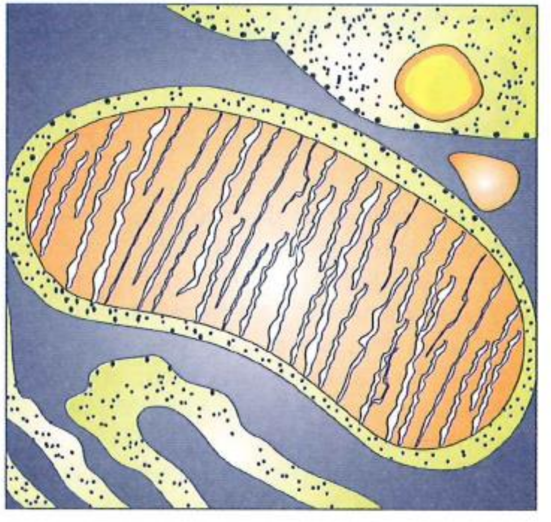
- Important role in cell metabolism and **distribution of the ions**.
- In the cytoplasm are the **cations K +, Mg2 +, Na +, anions then phosphates, sulfates, anionic proteins (proteins) and bicarbonates**.

Mitochondria

- Mitochondria are semi-autonomous organelles that contain their **own DNA, own proteosynthetic apparatus** and are wrapped in a **double membrane**.
- The outer membrane is relatively **high penetrability**, the inner membrane is almost impermeable and therefore contains a number of protein carriers, which allow transfer of the necessary substances.
- Besides the **transporters** are located **inner mitochondrial membrane** as well as **enzymes of the respiratory chain and ATP-synthase enzyme, which occurs aerobic ATP formation phosphorylation**.
- The material filling the content of mitochondria is called the **mitochondrial matrix**. It takes place in the series of important events, such as the **Krebs cycle, urea synthesis, heme synthesis, synthesis of ketones, β oxidation of fatty acids ...**



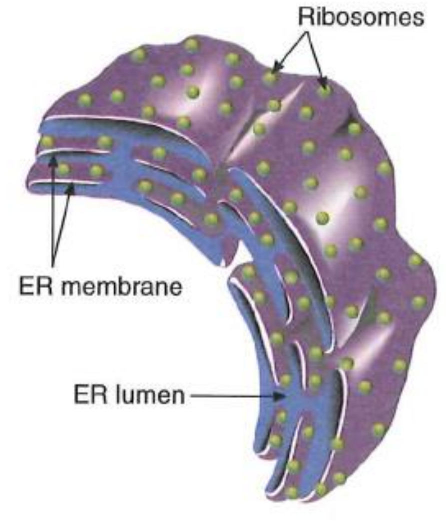
(a)

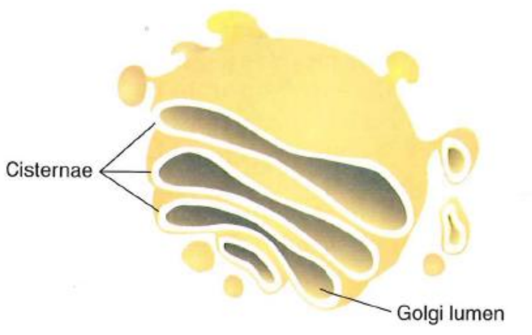


(b)

The endoplasmic reticulum

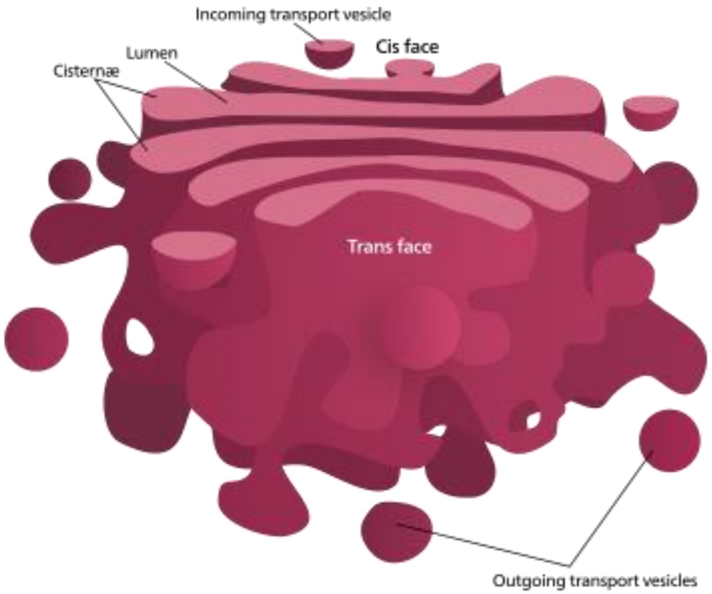
- The endoplasmic reticulum is composed of a system of cisterns and vesicles.
- We distinguish between **smooth ER** (mainly consisting of vesicles on the surface is not bound **ribosomes**) and **rough** ER (composed mainly tanks, are located on the surface of ribosomes).
- In muscle cells, the ER is called **sarcoplasmic reticulum**, and contains in its vesicles large amount of **calcium ions**.
  The **rough** ER occurs **desaturation of fatty acids or hydroxylation various** other substances (eg. Xenobiotics). Both types of reactions are involved in cytochrome P-450 (CYP).
- **smooth ER** (mainly consisting of vesicles on the surface is not bound **ribosomes-proteosynthesis**)





Golgi apparatus

- Golgi apparatus consisting of tanks and transport vesicles.
- This is a polarized organelle - we can distinguish the trans-side (which are received by agents - especially proteins - for editing and roztřízení) and cis-side on which these substances are also released.
- Part of the cellular endomembrane system, the Golgi apparatus packages proteins inside the cell before they are sent to their destination; it is particularly important in the processing of proteins for secretion.



Peroxisomes

Peroxisomes are coated membrane vesicles, which are intended primarily for the disposal of **hydrogen peroxide**.

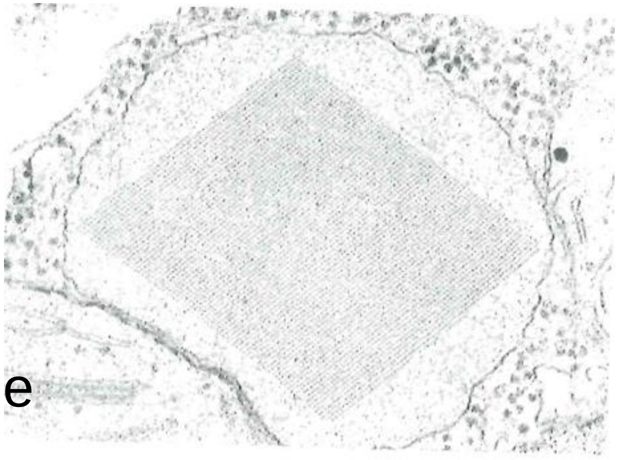
They contain the enzyme **catalase**, which is responsible for the two types of reactions:

a) the decomposition of hydrogen peroxide

$2\ H_2O_2 \rightarrow 2\ H_2O + O_2$

b) the use of hydrogen peroxide to oxidize the substrate

$RH_2 + H_2O_2 \rightarrow 2\ H_2O + R$



Reactions of type b) is for example used for the **degradation of ethanol** in the event that it is too much in the organism and enzyme **alcohol dehydrogenase** has not worked:

Ethanol + $H_2O_2 \rightarrow 2\ H_2O$ + acetaldehyde

Lysosomes

- Lysosomes are organelles of the **cell digestion**.
- In its membrane comprises a **hydrogen pump**, which is involved in maintaining an **acidic pH** within them.

- Distinguish between primary and secondary lysosomes.

- Primary are those that have not participated in the digestion process, and do not contain remnants of organelles, proteins etc.., And their enzymes have not yet been used.

- Secondary lysosomes are those that are already involved in digestion. Most enzymes found in lysosomes, belongs to the group of **hydrolases**, and the cleavage of various bonds on different molecules.

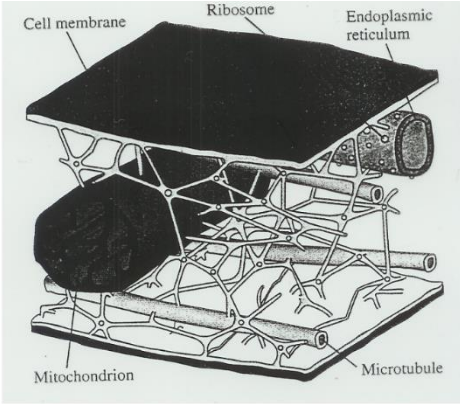
- They are structurally and chemically spherical vesicles containing hydrolitic enzymes, which are capable of breaking down virtually all kinds of biomolecules, including proteins, nucleic acids, carbohydrates, lipids, and cellular debris. They are known to contain more than fifty different enzymes which are all active at an acidic environment of about pH 5.

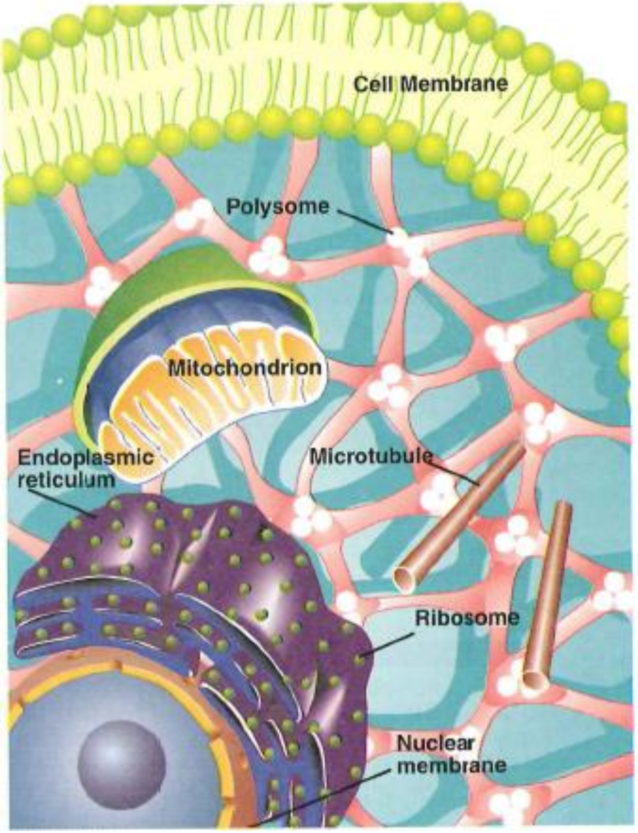
The enzyme - type bonds

- α-glucosidase cleaves α-glycosidic linkage between the glucosamine
- β-galactosidase cleaves the β-glycosidic linkage between galactose
- Hyaluronidase cleaves a bond between molecules of hyaluronic acid
- arylsulphatase cleaves the bond sulfoesterovou
- Lysozyme cleaves the glycosidic bond
- cathepsin cleave a peptide bond (the protease)
- collagenase cleaves the triple helix collagen chain
- elastase cleaves a peptide bond (the protease)
- ribonuclease cleaves ribonucleotides diester linkage between
- lipase cleaves the ester bond between glycerol and fatty acids
- phosphatase cleaves the ester linkage (cleaves phosphate)
- ceramidasa cleave the ester bond between the ceramide, and fatty acid

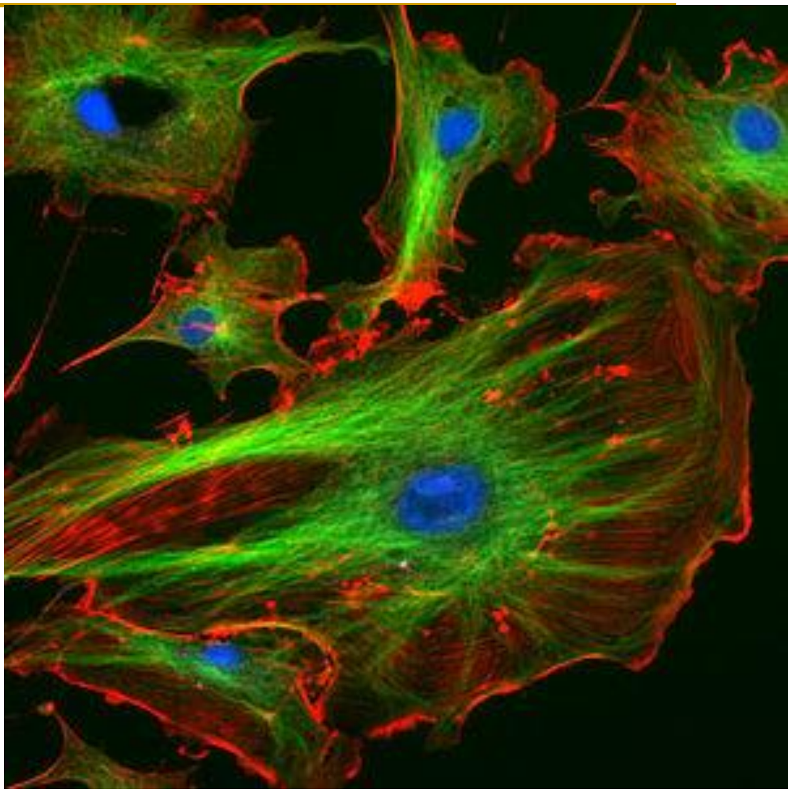
The cytoskeleton

- The cytoskeleton is a structure that contributes to the maintenance of **cell shape, cell division and movement within the cell.**
- It consists of three main types of fiber:
  a) microfibrils
  b) microfilaments
  c) intermediate filaments
- The microfibrils are used **dynein and kinesin** proteins that serve as cell engines and can move along the fiber (thus allowing intracellular movement).





The cytoskeleton



- The cytoskeleton of eukaryotes (including human and all animals cells) has three major components:
- microfilaments composed of the protein actin and
- microtubules composed of the protein tubulin are present in all eukaryotic cells.[2]
- By contrast intermediate filaments, which have more that 60 different building block proteins have so far only been found in animal cells (apart from one non-eukaryotic bacterial intermediate filament crescentin).[4]
- The complexity of the eukaryotic cytoskeleton emerges from the interaction with hundreds of associated proteins like molecular motors, crosslinkers, capping proteins and nucleation promoting factors.[2][3]
- There is a multitude of functions the cytoskeleton can perform: It gives the cell shape and mechanical resistance to deformation;[1] through association with extracellular connective tissue and other cells it stabilizes entire tissues;[1][4] it can actively contract, thereby deforming the cell and the cell's environment and allowing cells to migrate;[3] it is involved in many cell signaling pathways; it is involved in the uptake of extracellular material (endocytosis);[5] it segregates chromosomes during cellular division;[1] it is involved in cytokinesis - the division of a mother cell into two daughter cells;[2] it provides a scaffold to organize the contents of the cell in space [3] and for intracellular transport (for example, the movement of vesicles and organelles within the cell);[1] it can be a template for the construction of a cell wall.[1] Furthermore, it forms specialized structures such as flagella, cilia, lamellipodia and podosomes.

Cytoplasm is organized by the cytoskeleton is highly dynamic

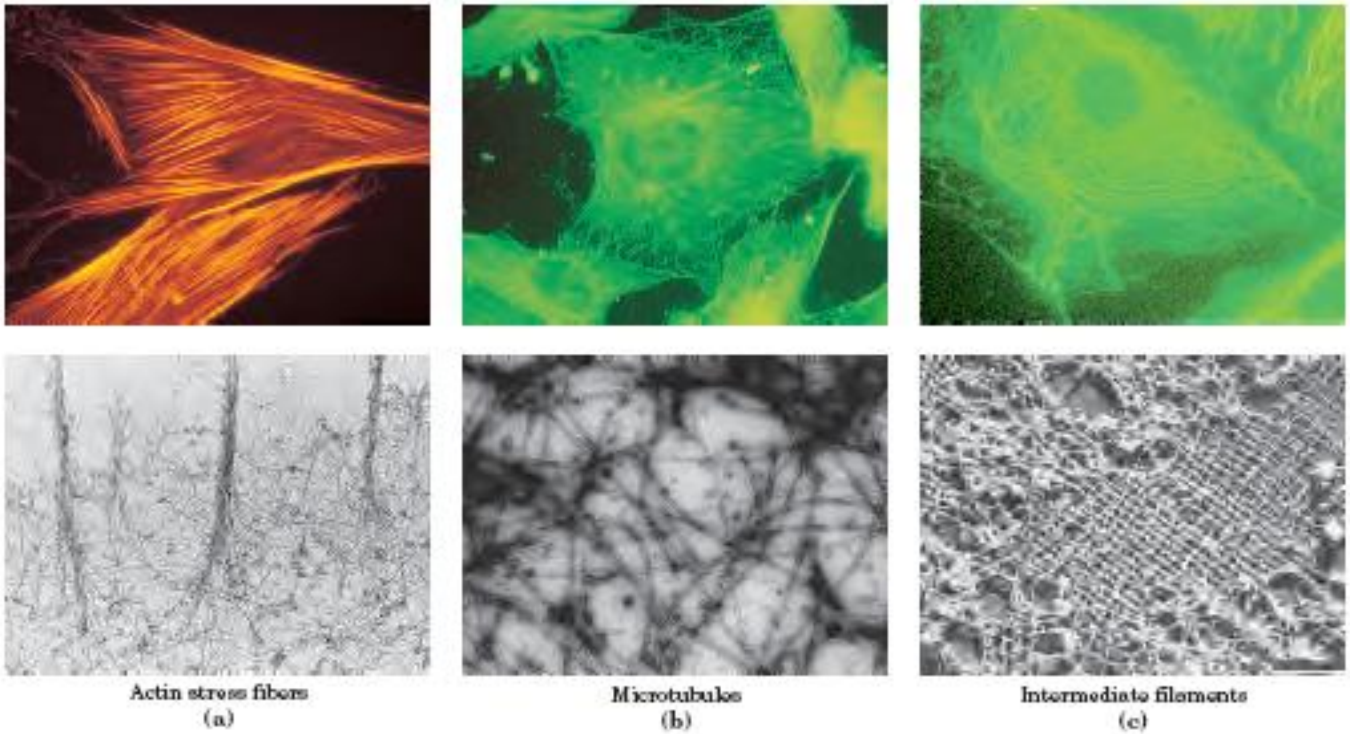


FIGURE 1-9 The three types of cytoskeletal filaments. The upper panels show epithelial cells photographed after treatment with antibodies that bind to and specifically stain (a) actin filaments bundled together to form "stress fibers," (b) microtubules radiating from the cell center, and (c) intermediate filaments extending throughout the cytoplasm. For these experiments, antibodies that specifically recognize actin, tubulin, or intermediate filament proteins are covalently attached to a fluorescent compound. When the cell is viewed with a fluorescence microscope, only the stained structures are visible. The lower panels show each type of filament as visualized by (a, b) transmission or (c) scanning electron microscopy.

Comparison -Cytoskeleton types

Cytoskeleton type[8]	Diameter (nm)[9]	Structure	Subunit examples[8]
Microfilaments	6	double helix	actin
Intermediate filaments	10	two anti-parallel helices/dimers, forming tetramers	•vimentin (mesenchyme) •glial fibrillary acidic protein (glial cells) •neurofilament proteins (neuronal processes) •keratins (epithelial cells) •nuclear lamins
Microtubules	23	protofilaments, in turn consisting of tubulin subunits in complex with stathmin[10]	α- and β-tubulin

Localization of metabolic processes

- We continue to focus on eukaryotic cell. They occur in the organism **in many types** - each type is designed to perform different functions, there are other active enzymes like.
- Cells produce a single type of **tissue**, which are also specialized to perform certain functions. The following table lists some of the metabolic process, and cells which take place:

The Process	Where to find
glycogen synthesis	hepatocytes, muscle cells
oxygenation of hemoglobin	lung cells
synthesis of adrenaline	cells of adrenal medulla
urea synthesis	hepatocytes
lipid deposition	adipocyte
actin and myosin synthesis	muscle cells
Synthesis of the insulin	β-cells of the islets of Langerhans
conjugation of toxic substances	hepatocytes

Many Important Biomolecules are Polymers

- **Biopolymers** - macromolecules created by joining many smaller organic molecules (**monomers**)
- **Condensation reactions** join monomers (H_2O is removed in the process)
- **Residue** - each monomer in a chain

30

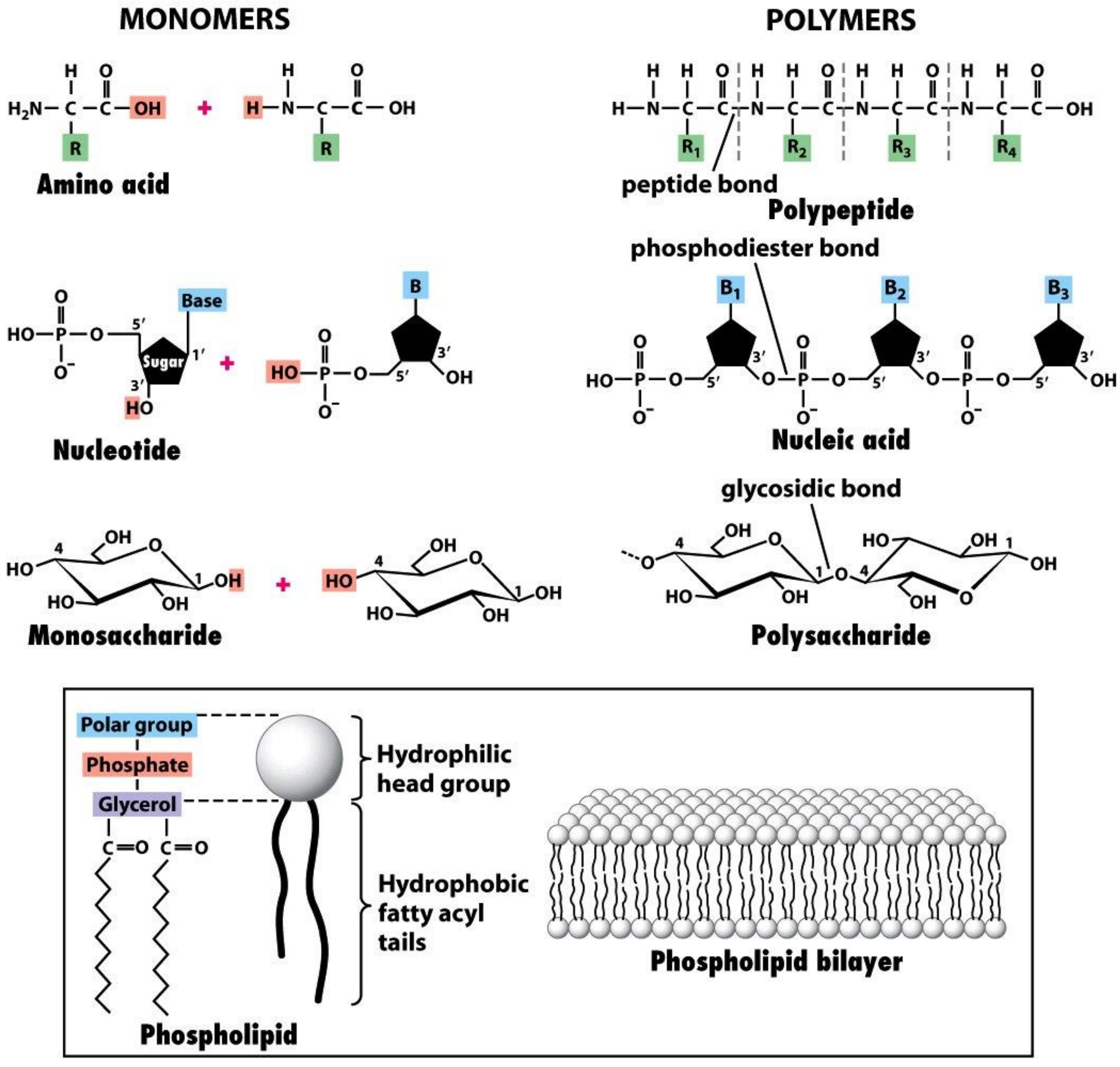
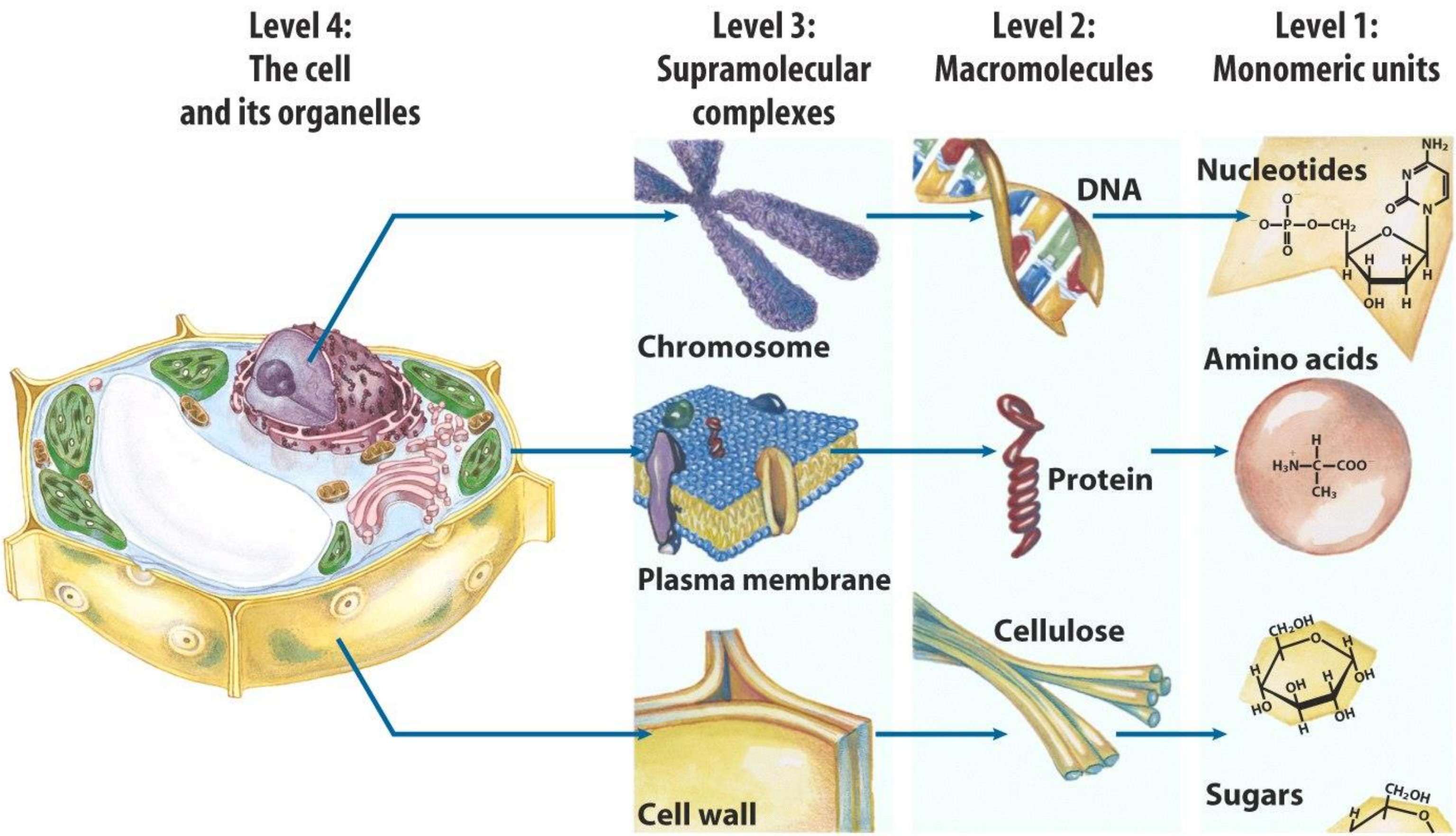


Figure 2-13
Molecular Cell Biology, Sixth Edition

Molecular Organisation of a cell



32

2. Chemical Foundations

- Biochemistry aims to explain biological form and function in chemical terms.
- Composition of living matter – C, O, N, P (99%)

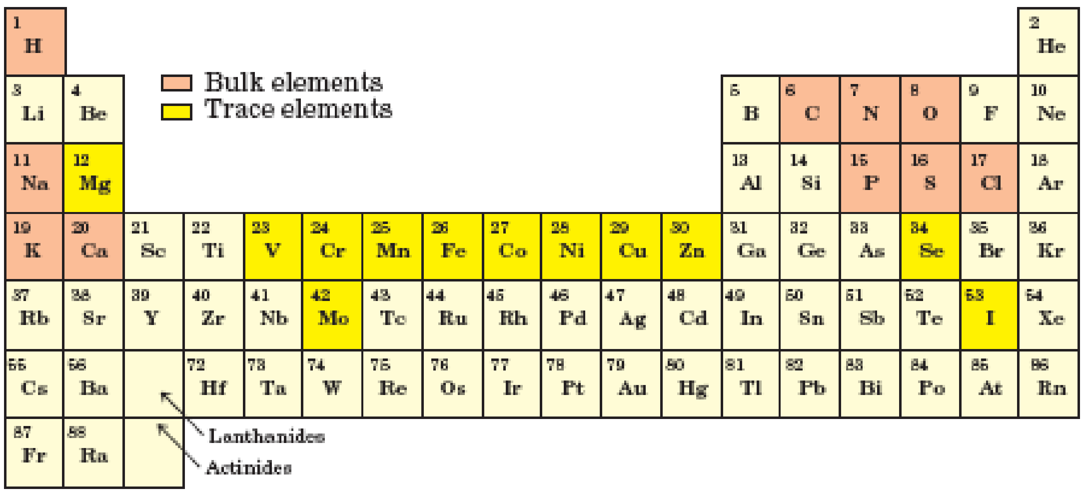


FIGURE 1-12 Elements essential to animal life and health. Bulk elements (shaded orange) are structural components of cells and tissues and are required in the diet in gram quantities daily. For trace elements (shaded bright yellow), the requirements are much smaller: for humans, a few milligrams per day of Fe, Cu, and Zn, even less of the others. The elemental requirements for plants and microorganisms are similar to those shown here; the ways in which they acquire these elements vary.

- 30 elements are essential

- trace elements – Fe hemoglobin (0.3%)

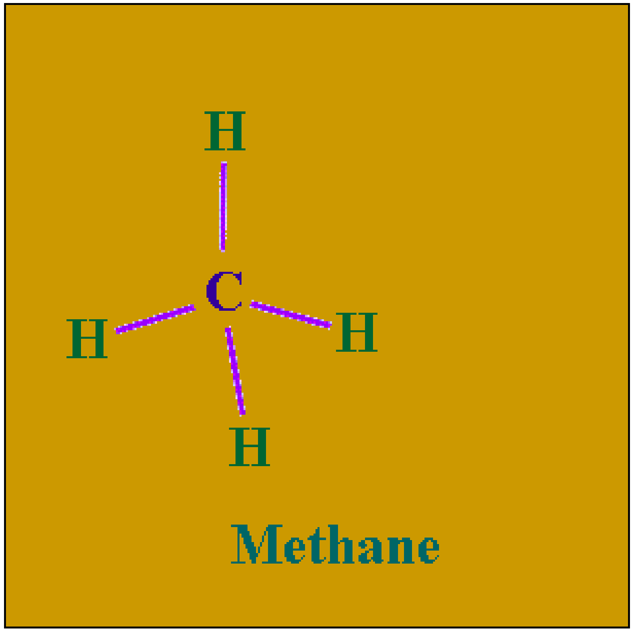
Biomolecules

- **Are Compounds of <u>Carbon</u> with a Variety of Functional Groups**

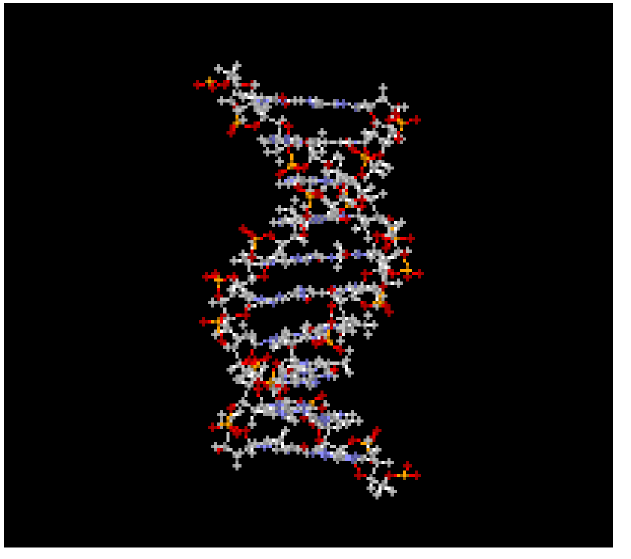
Organic Chemistry

- Organic chemistry is the study of Carbon compounds.
- Organic compounds are compounds composed primarily of a Carbon skeleton.
- All living things are composed of organic compounds.

Carbon can form immensely diverse compounds, from simple to complex.



Methane with 1 Carbon atom



DNA with tens of Billions of Carbon atoms

Tetrahedral structure

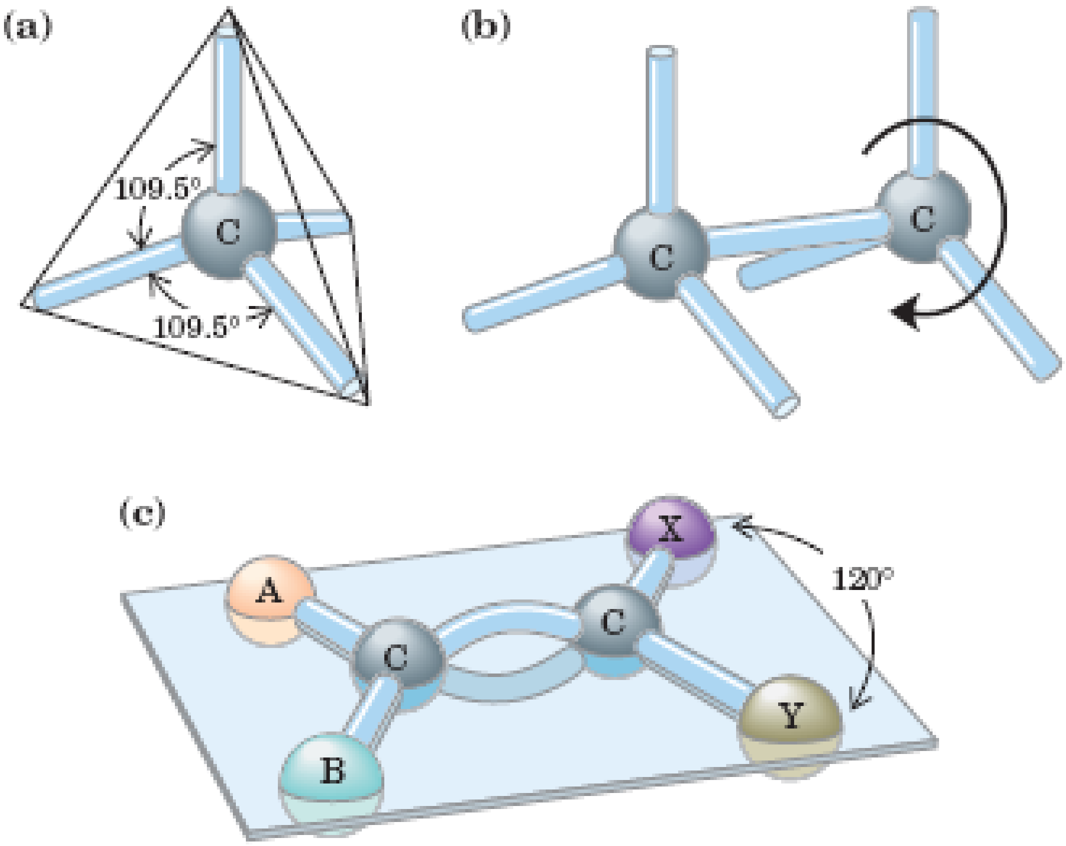


FIGURE 1–14 **Geometry of carbon bonding.** (a) Carbon atoms have a characteristic tetrahedral arrangement of their four single bonds. (b) Carbon–carbon single bonds have freedom of rotation, as shown for the compound ethane (CH_3—CH_3). (c) Double bonds are shorter and do not allow free rotation. The two doubly bonded carbons and the atoms designated A, B, X, and Y all lie in the same rigid plane.

Hydrocarbons in biochemistry

- Most biomolecules are derivated from hydrocarbons
- Nonpolar (bonding electrones are shared equally between atoms), in water-insoluble, hydrophobic

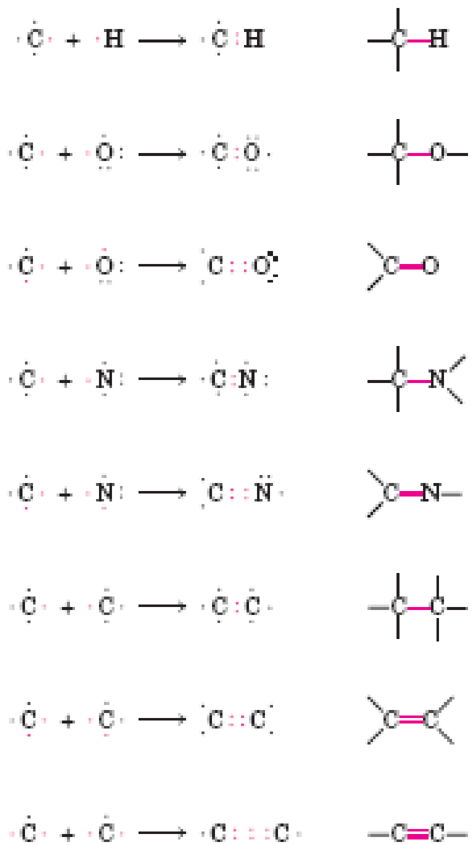
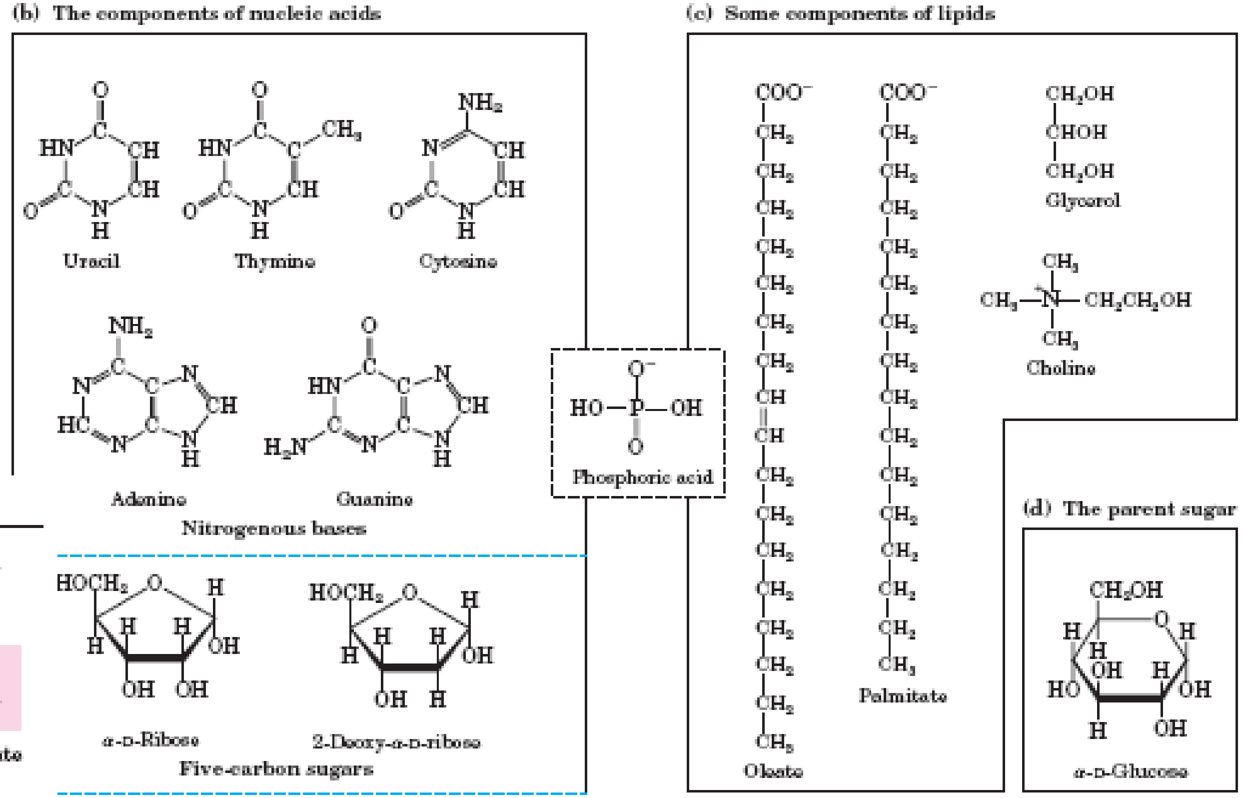
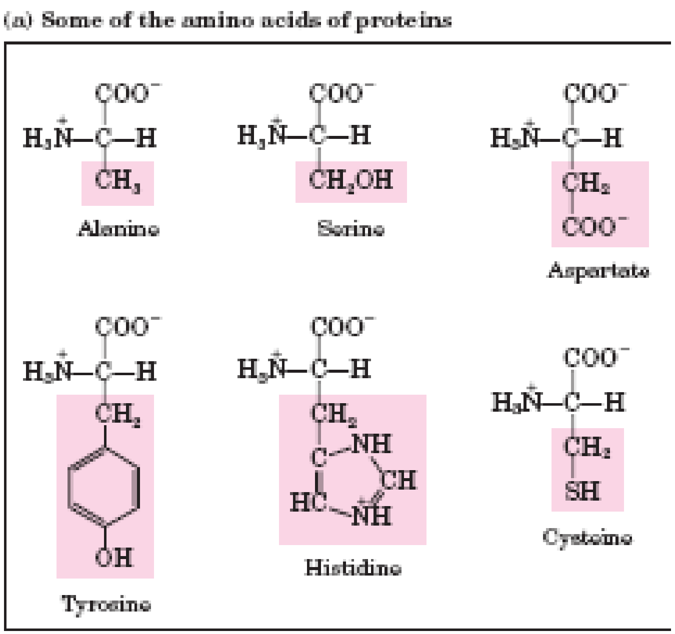


FIGURE 1-13 Versatility of carbon bonding. Carbon can form covalent single, double, and triple bonds (in red), particularly with other carbon atoms. Triple bonds are rare in biomolecules.

Major classes of small biomolecules

- Amino acids
- Sugars
- Fatty acids
- Nucleotides

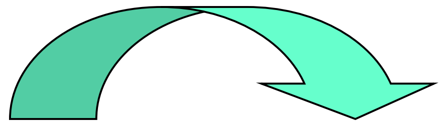




Bio-molecules

- Just like cells are building blocks of tissues likewise molecules are building blocks of cells.
- Animal and plant cells contain approximately 10, 000 kinds of molecules (bio-molecules)
- Water constitutes 50-95% of cells content by weight.
- Ions like Na^{+}, K^{+} and Ca^{+} may account for another 1%
- Almost all other kinds of bio-molecules are organic (C, H, N, O, P, S)
- Infinite variety of molecules contain C.
- Most bio-molecules considered to be derived from hydrocarbons.
- The chemical properties of organic bio-molecules are determined by their functional groups. Most bio-molecules have more than one.

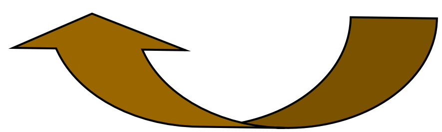
Biomolecules - Structure



Anabolic

<u>Building block</u>	<u>Macromolecule</u>
Simple sugar	Polysaccharide
Amino acid	Protein (peptide)
Nucleotide	RNA or DNA
Fatty acid	Lipid

Catabolic



40

Important reaction types in biochemical processes

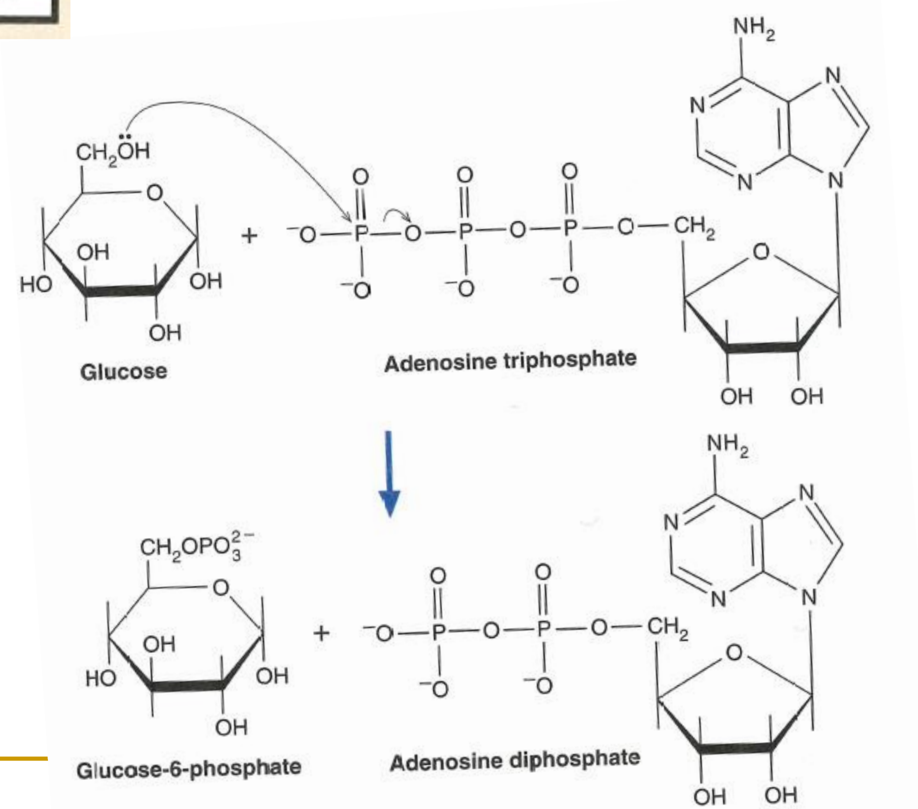
- Nucleophilic substitution reaction
- Elimination reaction
- Isomerization reaction
- Oxidation-reduction reaction
- Hydrolysis reaction

Nucleophilic substitution reaction

Nucleophilic Substitution Reactions

In nucleophilic substitution reactions, as the name suggests, one atom or group is substituted for another:

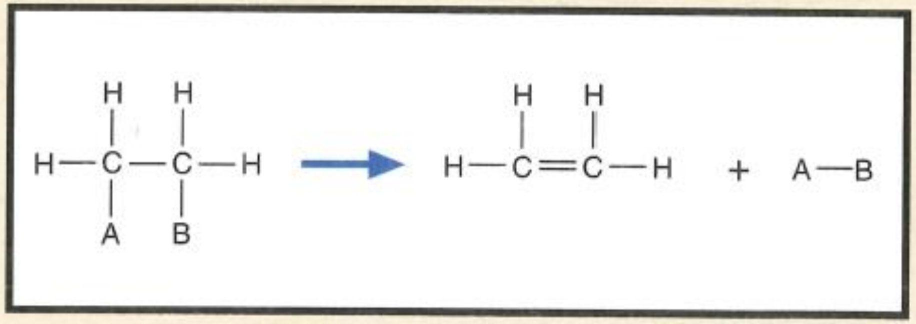
$$A\!: \; + \; B{-}X \longrightarrow A{-}B \; + \; X\!:$$



Elimination

Elimination Reactions

In elimination reactions a double bond is formed when atoms in a molecule are removed:



The removal of H_2O from biomolecules containing alcohol functional groups is a commonly encountered elimination reaction. A prominent example of this type of reaction is provided by the dehydration of 2-phosphoglycerate, an important step in carbohydrate metabolism (Figure 1.10). Other products of elimination reactions include ammon amines (RNH_2), and alcohols (ROH).

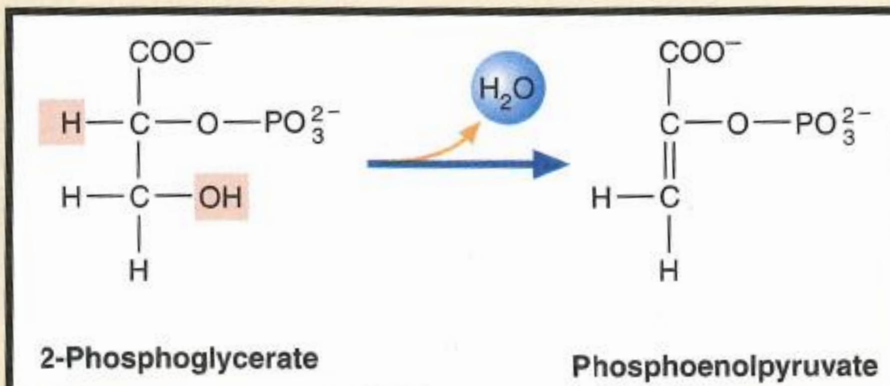


FIGURE 1.10
Dehydration of 2-Phosphoglycerate.

Izomerization

Isomerization Reactions

Isomerization reactions involve the intramolecular shift of atoms or groups. One of the most common biochemical isomerizations is the interconversion between aldose and ketose sugars (Figure 1.11).

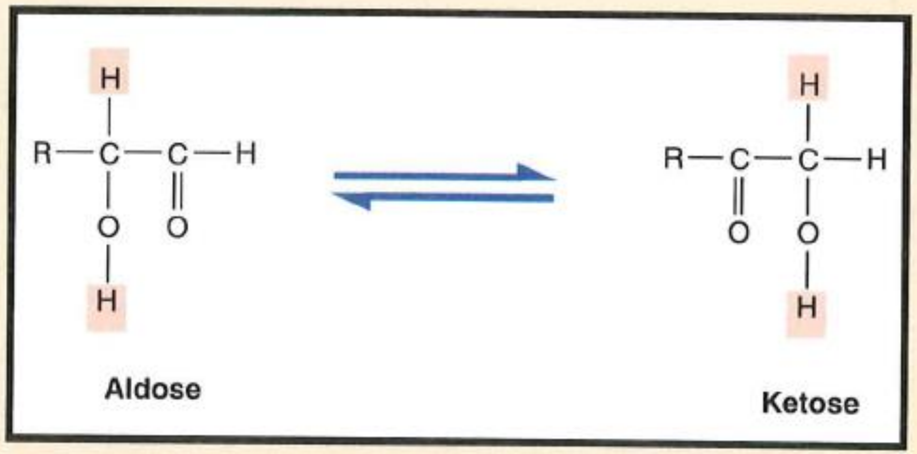


FIGURE 1.11
Isomerization of Sugar Molecules.

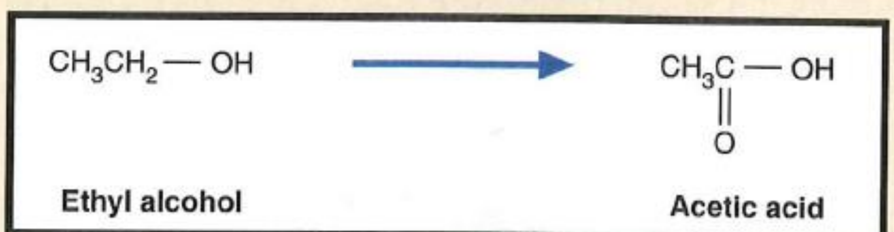
Oxido-reduction reaction

Oxidation-Reduction Reactions

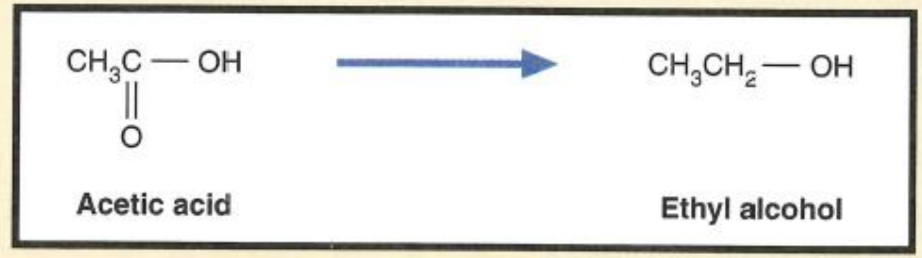
Oxidation-reduction reactions (also called **redox** reactions) occur when there is a transfer of electrons from a donor (called the **reducing agent**) to an electron acceptor (called the **oxidizing agent**). When reducing agents donate their electrons, they become **oxidized**. As oxidizing agents accept electrons, they become **reduced**. The two processes always occur simultaneously.

It is not always easy to determine whether biomolecules have gained or lost electrons. However, there are two simple rules that may be used to ascertain whether a molecule has been oxidized or reduced:

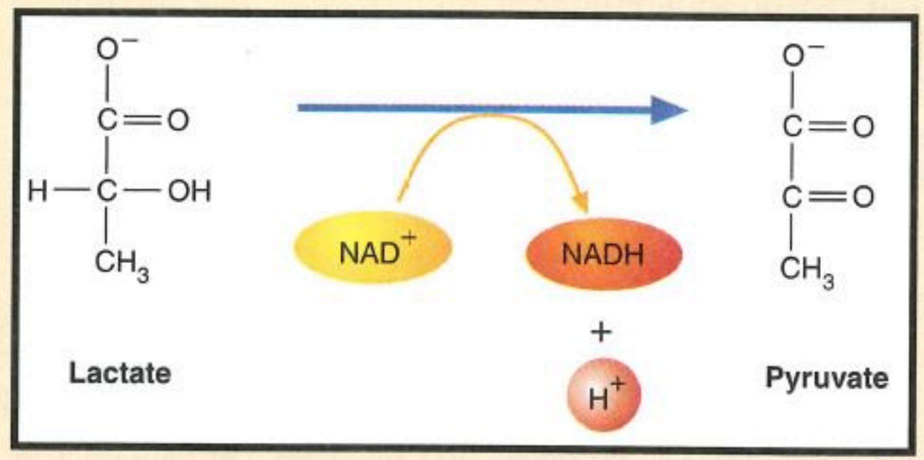
1. Oxidation has occurred if a molecule gains oxygen or loses hydrogen:



2. Reduction has occurred if a molecule loses oxygen or gains hydrogen:



In biological redox reactions, electrons are transferred to electron acceptors such as the nucleotide NAD^+ (nicotinamide adenine dinucleotide) (Figure 1.12).



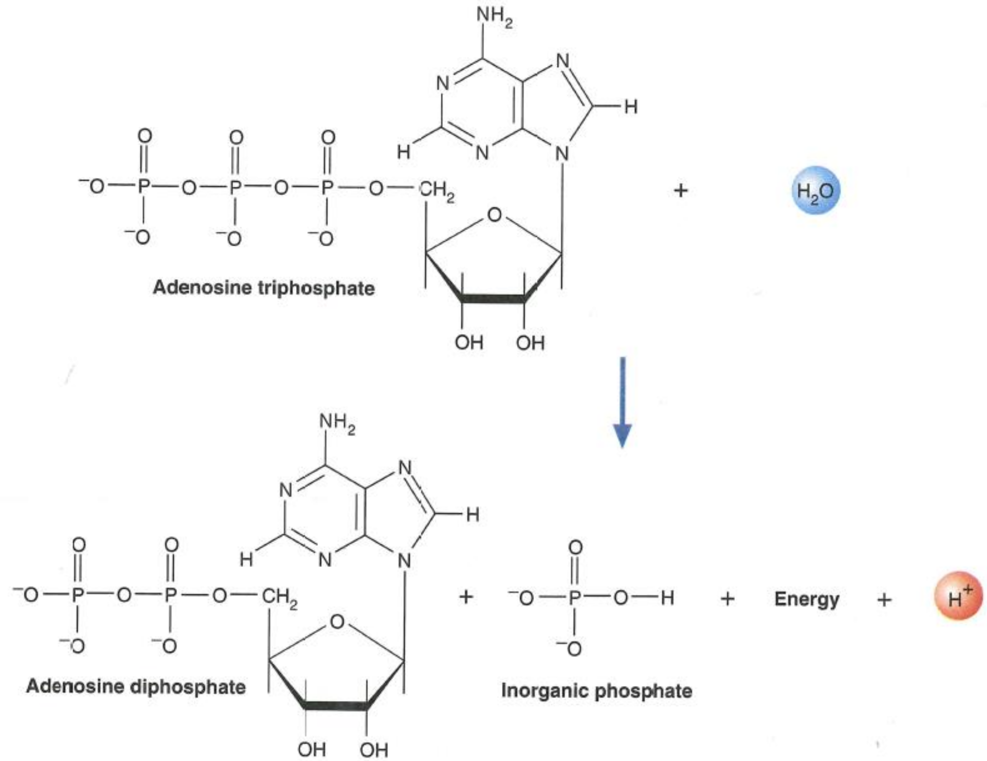
Hydrolysis reactions

Hydrolysis Reactions

Hydrolysis is the cleavage of a covalent bond by water:

$$R{-}C({=}O){-}O{-}R' + H_2O \rightarrow R{-}C({=}O){-}OH + R'OH$$

Hydrolytic reactions may be catalyzed by acid or base. The digestion of many food molecules involves hydrolysis. For example, proteins are degraded in the stomach in an acid-catalyzed reaction. Another important example is provided by the breaking of the phosphate bonds of ATP (Figure 1.13). The energy obtained during this reaction is used to drive many cellular processes.



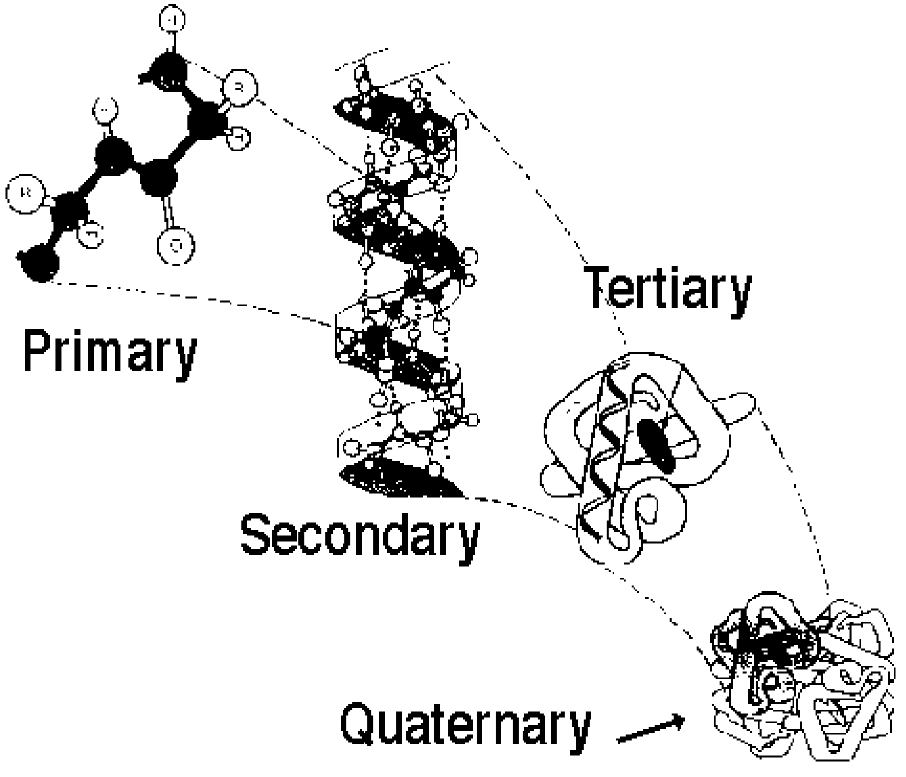
Non covalent interactions

- Coherence of cells and their interaction with each other between molecules (eg. interaction between molecules and receptor molecules and enzymes, etc.)
- And similar interactions are based on non covalent interactions The most important non covalent interactions are:
   - hydrogen bonds
   - electrostatic interactions
   - hydrophobic interactions

  Their main use in various situations described by the following table:

Structure / system	prevailing type of non-covalent interactions :
Proteins: Structure secondary	hydrogen bonding
Proteins: the tertiary structure	hydrophobic and electrostatic interactions
Proteins: Structure quaternary	electrostatic interactions
DNA	hydrogen bonds
Phospholipid bilayer	hydrophobic interactions
Binding of the enzyme-substrate	electrostatic interactions
Binding of antibody-antigen	electrostatic interactions

Protein structure



<u>Description</u>

The amino acid sequence

Helices and Sheets

Disulfide bridges

Multiple polypeptides connect

Biomolecules - Structure

Anabolic

- <u>Building block</u>
- Simple sugar
- Amino acid
- Nucleotide
- Fatty acid

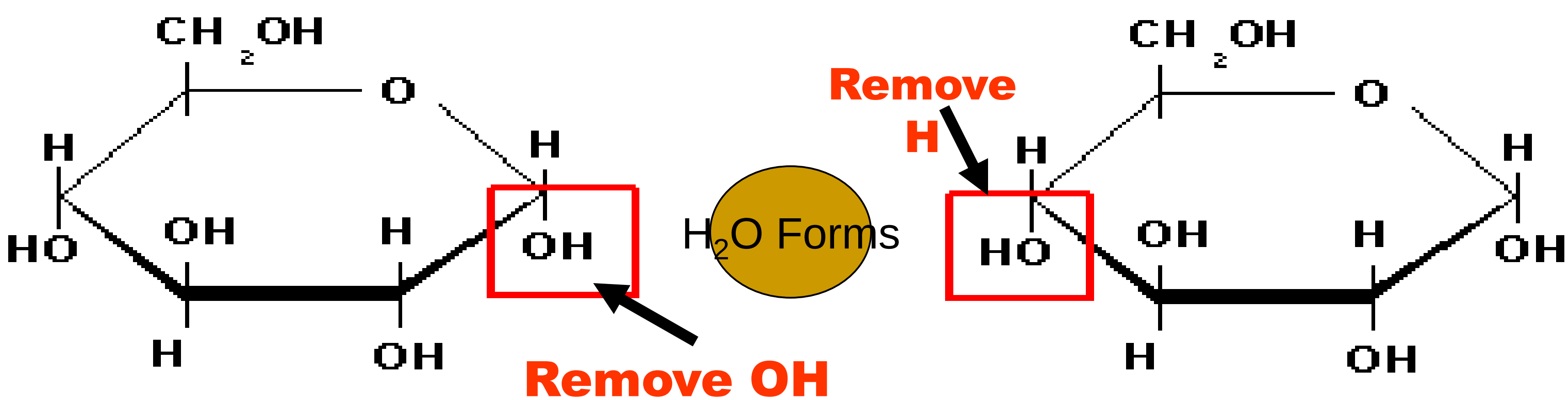
- <u>Macromolecule</u>
- Polysaccharide
- Protein (peptide)
- RNA or DNA
- Lipid

Catabolic

50

Linking Monomers

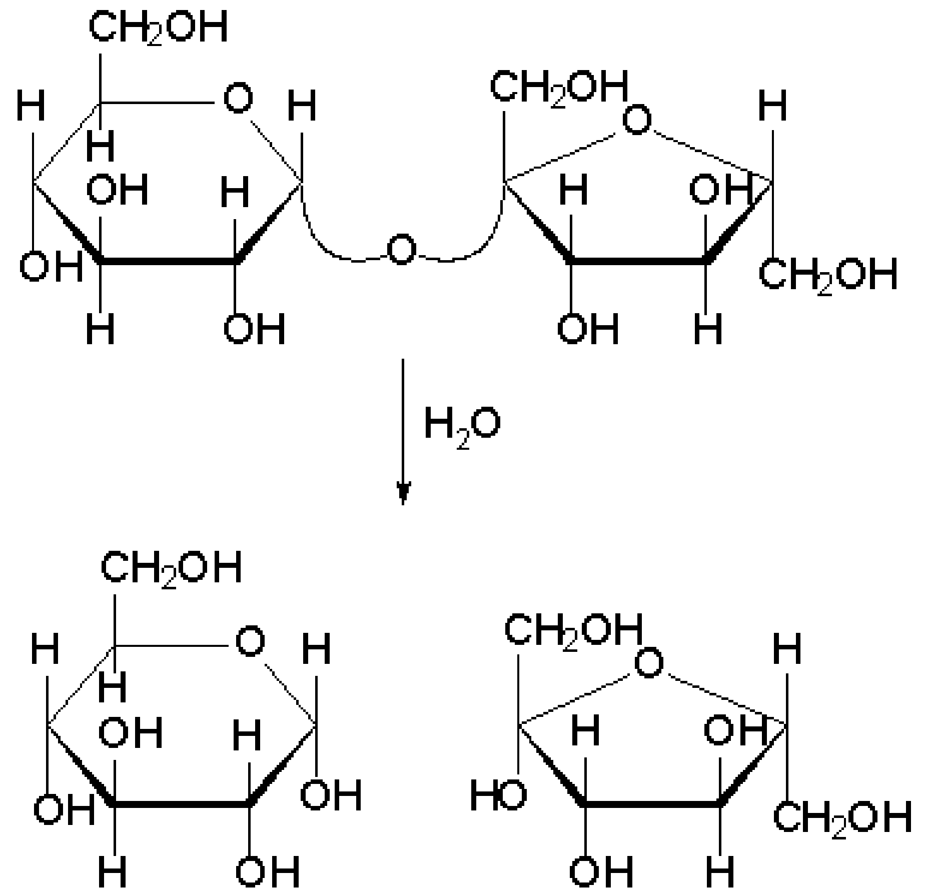
Cells link monomers by a process called dehydration synthesis (removing a molecule of water)



This process joins two sugar monomers to make a double sugar

Breaking Down Polymers

- Cells break down macromolecules by a process called hydrolysis (adding a molecule of water)



Water added to split a double sugar

Sugars

- Carbohydrates most abundant organic molecule found in nature.
- Initially synthesized in plants from a complex series of reactions involving photosynthesis.
- Basic unit is monosaccharides.
- Monosaccharides can form larger molecules e.g. glycogen, plant starch or cellulose.

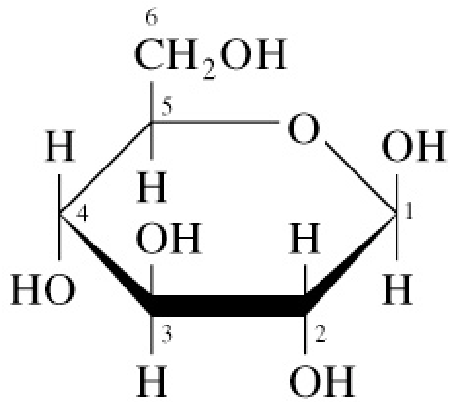
Functions

- Store energy in the form of starch (photosynthesis in plants) or glycogen (in animals and humans).
- Provide energy through metabolism pathways and cycles.
- Supply carbon for synthesis of other compounds.
- Form structural components in cells and tissues.
- Intercellular communications

53

Monosaccharides -Polysaccharides

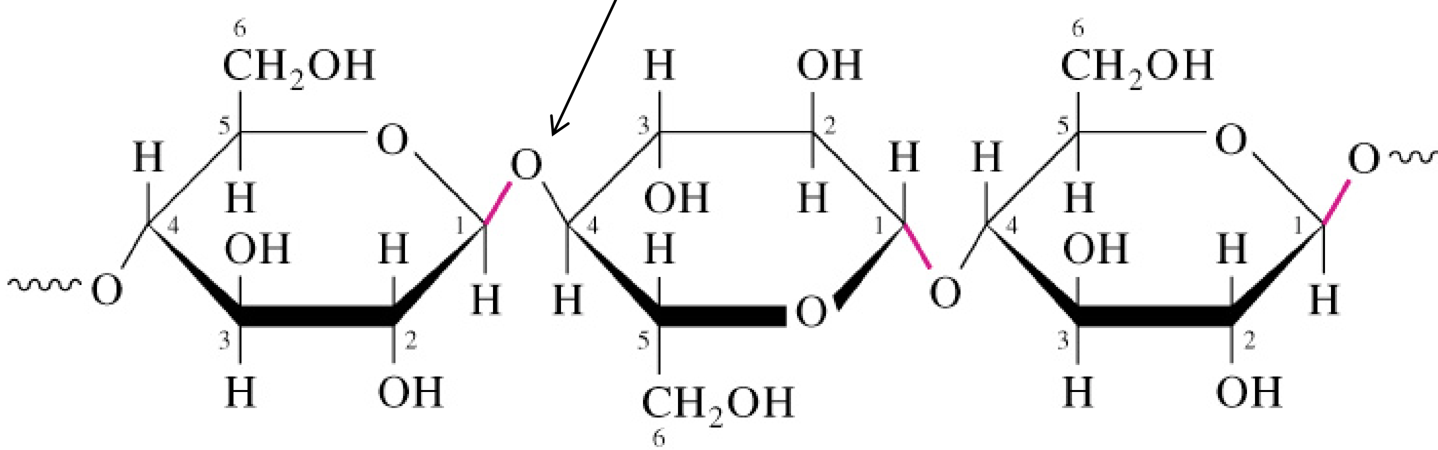
(a)



Glucose - Cellulose

Glycosidic bonds connecting glucose residues are in red

(b)



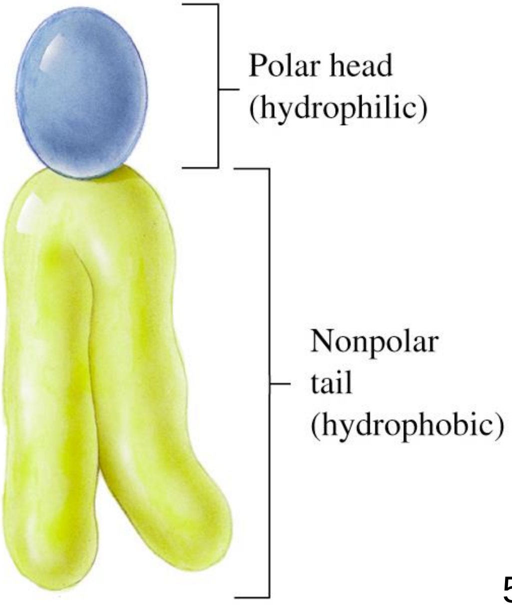
54

Fatty acids - Lipids

- Are monocarboxylic acid contains even number C atoms
- Two types: saturated (C-C sb) and unsaturated (C-C db)
- Fatty acids are components of several lipid molecules.
- E,g. of lipids are triacylglycerol, steriods (cholestrol, sex hormones), fat soluble vitamins.

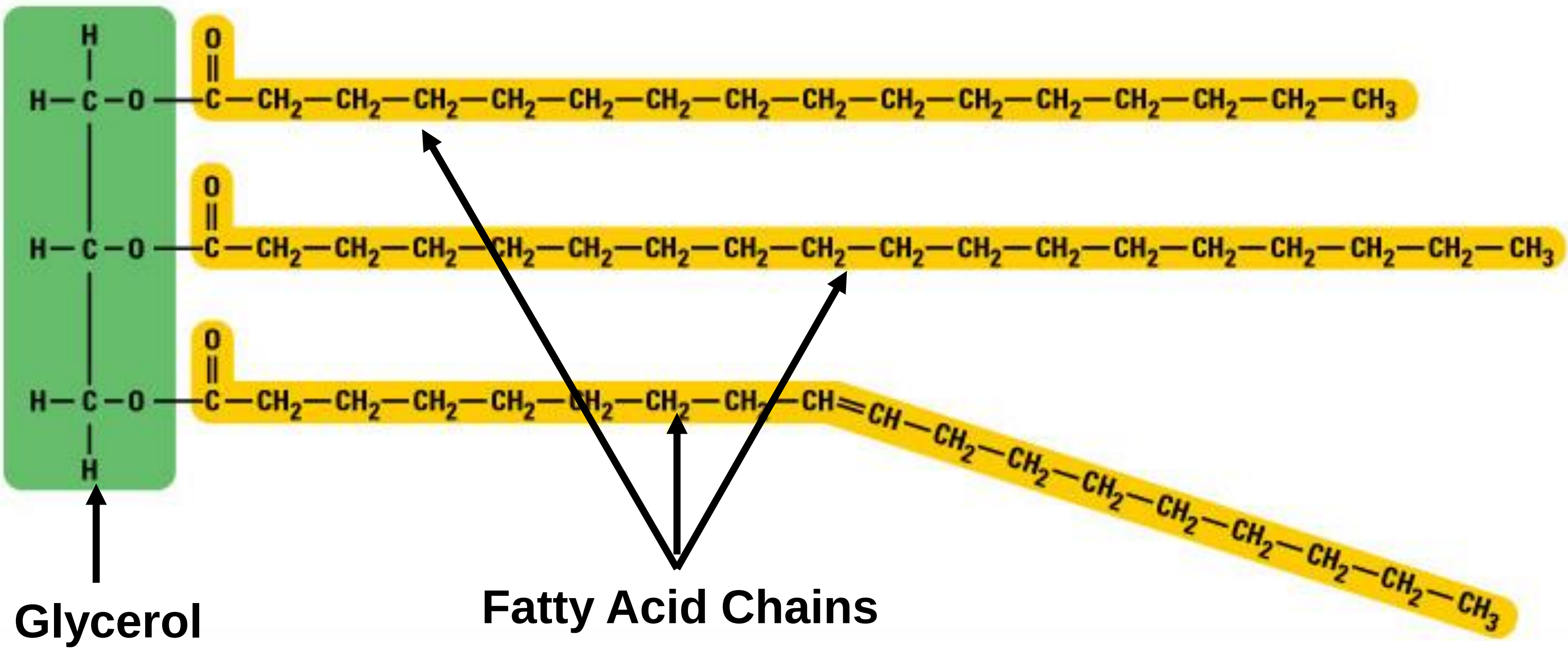
Functions

- Storage of energy in the form of fat
- Membrane structures
- Insulation (thermal blanket)
- Synthesis of hormones



55

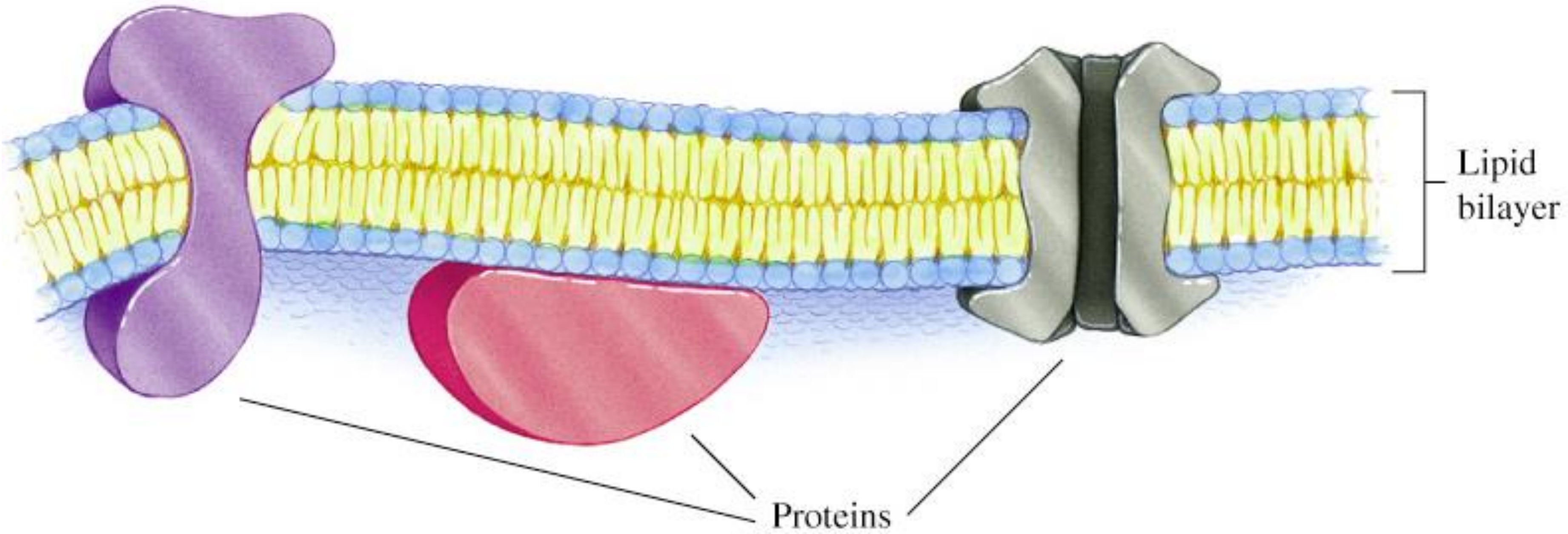
Triglyceride



56

Structure of a biological membrane

- A lipid bilayer with associated proteins



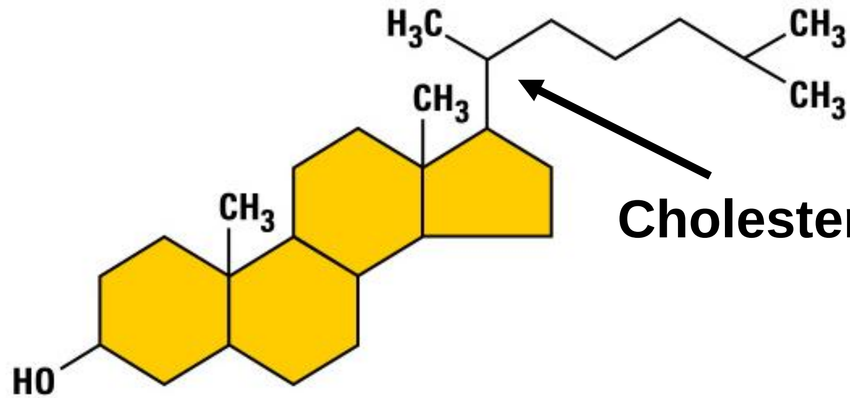
57

Steroids

- The carbon skeleton of steroids is bent to form 4 fused rings

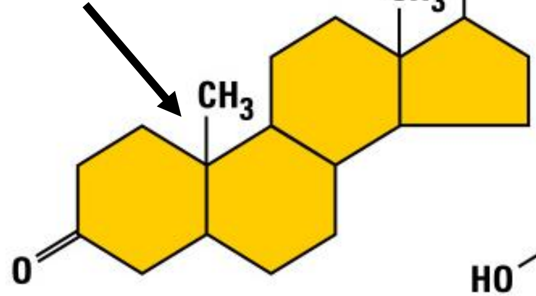
Cholesterol is the "base steroid" from which your body produces other steroids

Estrogen & testosterone are also steroids

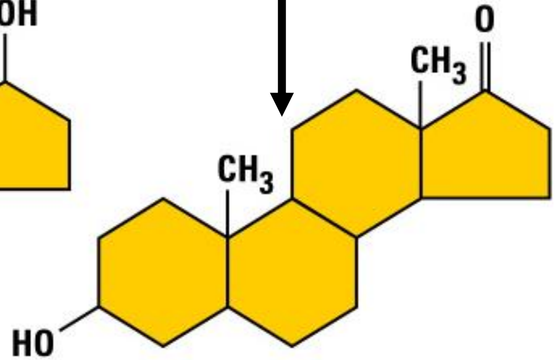


Cholesterol

Testosterone



Estrogen



Synthetic Anabolic Steroids are variants of testosterone

58

Nucleic Acids

- Store hereditary information

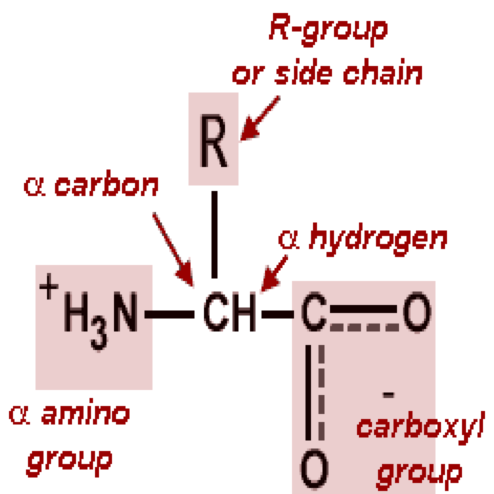
Contain information for making all the body's proteins

Two types exist --- DNA & RNA

59

Amino acids - Proteins:

- Amino acids:



- Building blocks of proteins.
- R Group (side chains) determines the chemical properties of each amino acids.
- Also determines how the protein folds and its biological function.
- Functions as transport proteins, structural proteins, enzymes, antibodies, cell receptors.

Proteins as Enzymes

- Many proteins act as biological catalysts or enzymes

Thousands of different enzymes exist in the body

Enzymes control the rate of chemical reactions by weakening bonds, thus lowering the amount of activation energy needed for the reaction -> Catalysator

-> No not interfere with the equilibrium of reaction

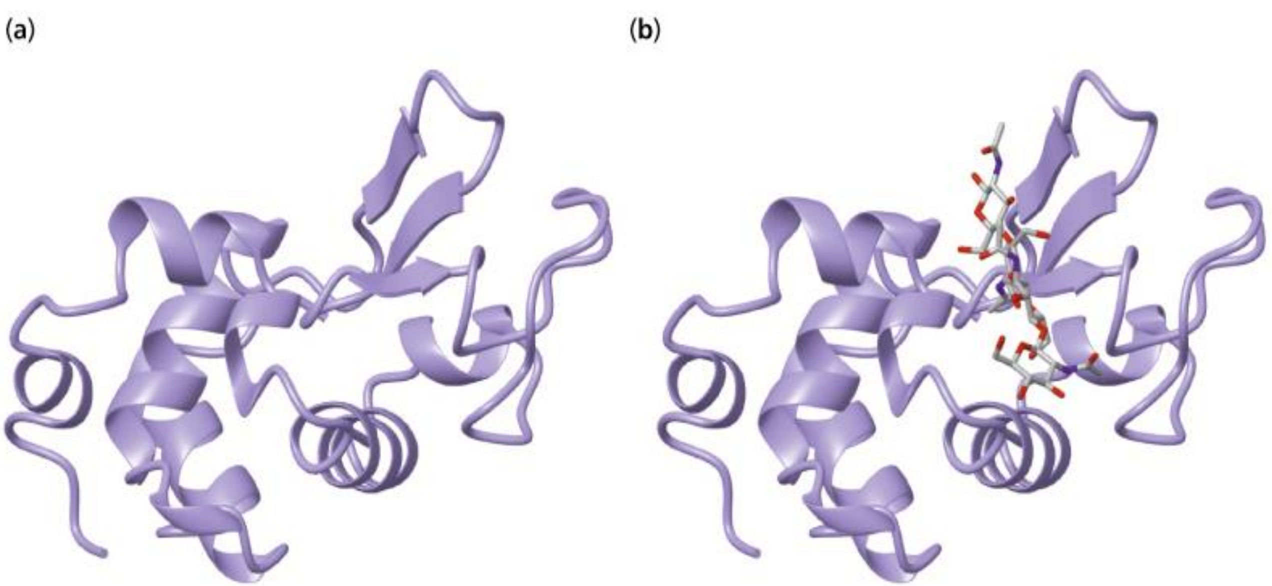
-> Enzymes are reusable !!!!

61

Enzymes:

- **Active site** - a cleft or groove in an enzyme that binds the substrates of a reaction

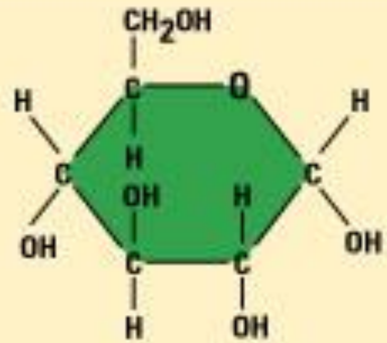
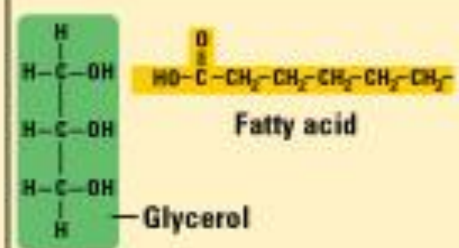
The nature and arrangement of amino acids in the active site make it specific for only one type of substrate. (accepts just one enaniomer)



Egg white lysozyme

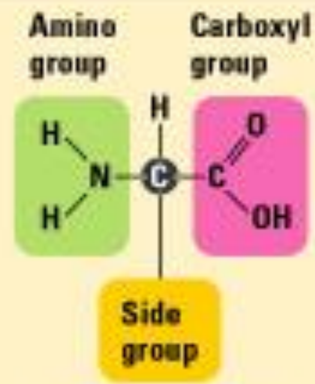
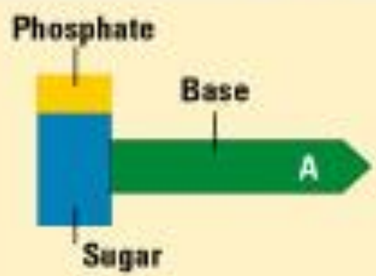
62

Macromolecules

Biological macromolecule	Function	Monomer	Examples
Carbohydrates	Dietary energy; storage; plant structure	 **Monosaccharide**	Monosaccharides: glucose, fructose. dissaccharides: lactose, sucrose. Polysaccharides: starch, cellulose.
Lipids	Long-term energy storage (for fats); hormones (for steroids)	 **Components of a fat molecule**	Fats, oils, steroids

63

Macromolecules

Proteins	Enzymes, structure, storage, contraction, transport, etc.	 Amino acid	Lactase (an enzyme), hemoglobin
Nucleic acids	Information storage	 Nucleotide	DNA, RNA

64

Concepts of Life

Life is characterized by

- Biological diversity: lichen, microbes, jellyfish, sequoias, hummingbirds, manta rays, gila monsters, & you

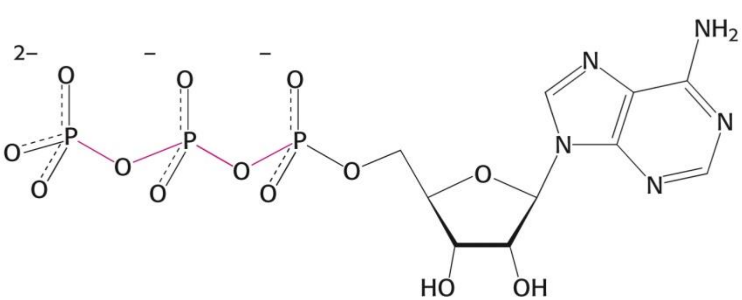
- Chemical unity: living systems (on earth) obey the rules of physical and organic chemistry – there are no *new* principles

65

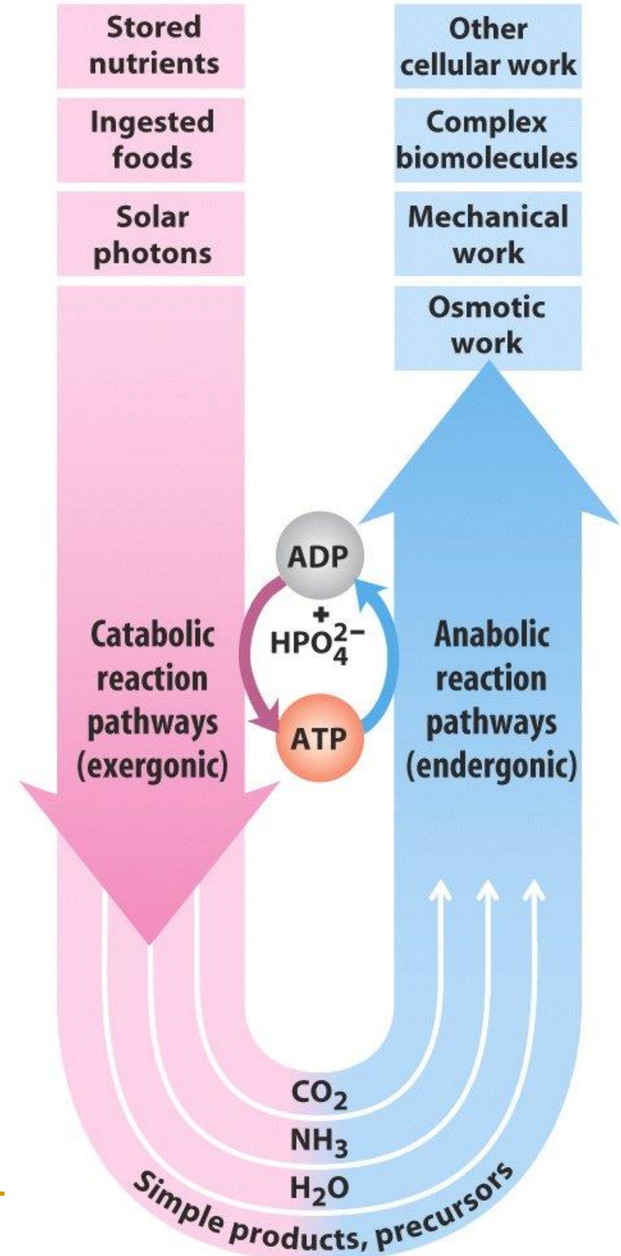
Life needs 3 things:

(1) *ENERGY*, which it must know how to:

- Extract
- Transform
- Utilize

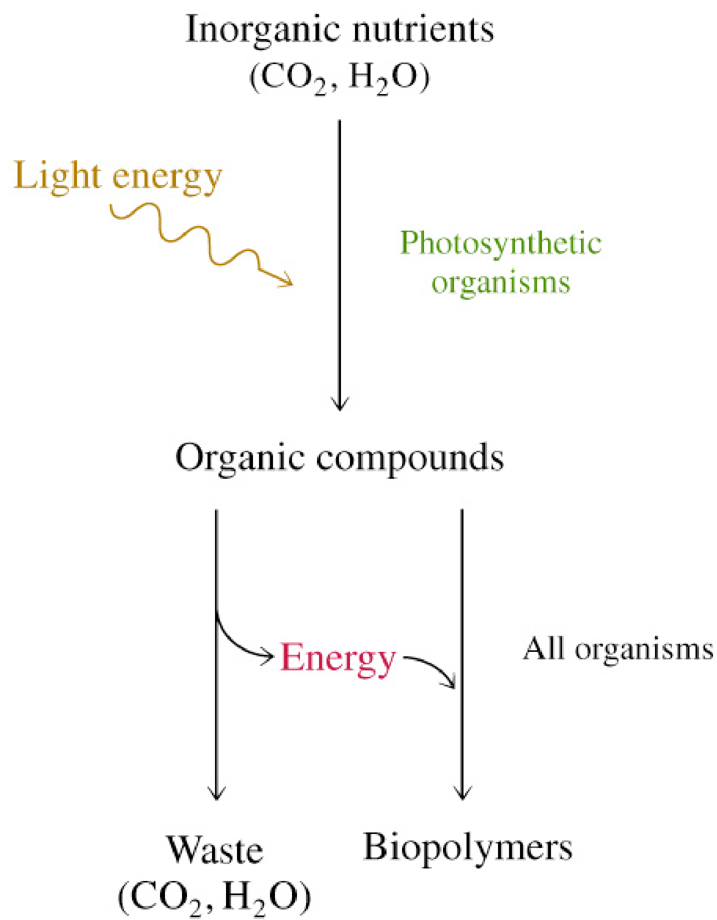


Adenosine triphosphate (ATP)



The Energetics of Life

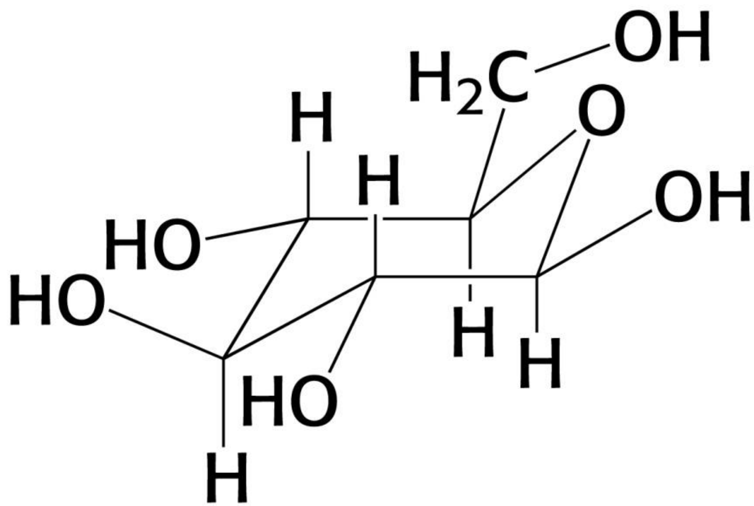
- Photosynthetic organisms capture sunlight energy and use it to synthesize organic compounds
- Organic compounds provide energy for all organisms



67

Using toxic O_2 to generate energy

$2\,H_2O \rightarrow O_2 + 4e^- + 4H^+$ (photosynthesis)

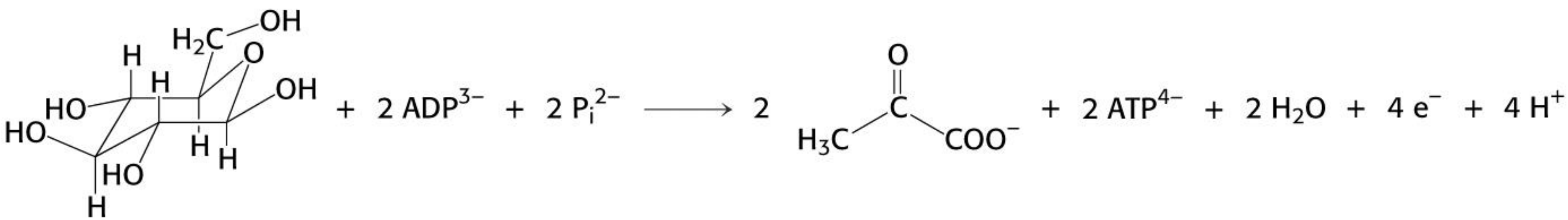


Glucose

$\text{Glucose} + 6O_2 \rightarrow 6CO_2 + 6H_2O + \text{Energy}$

68

Glycolysis: the preferred way for the formation of ATP



Glucose

Pyruvate

69

Life needs (2) *SIMPLE MOLECULES*, which it must know how to:

- Convert
- Polymerize
- Degrade

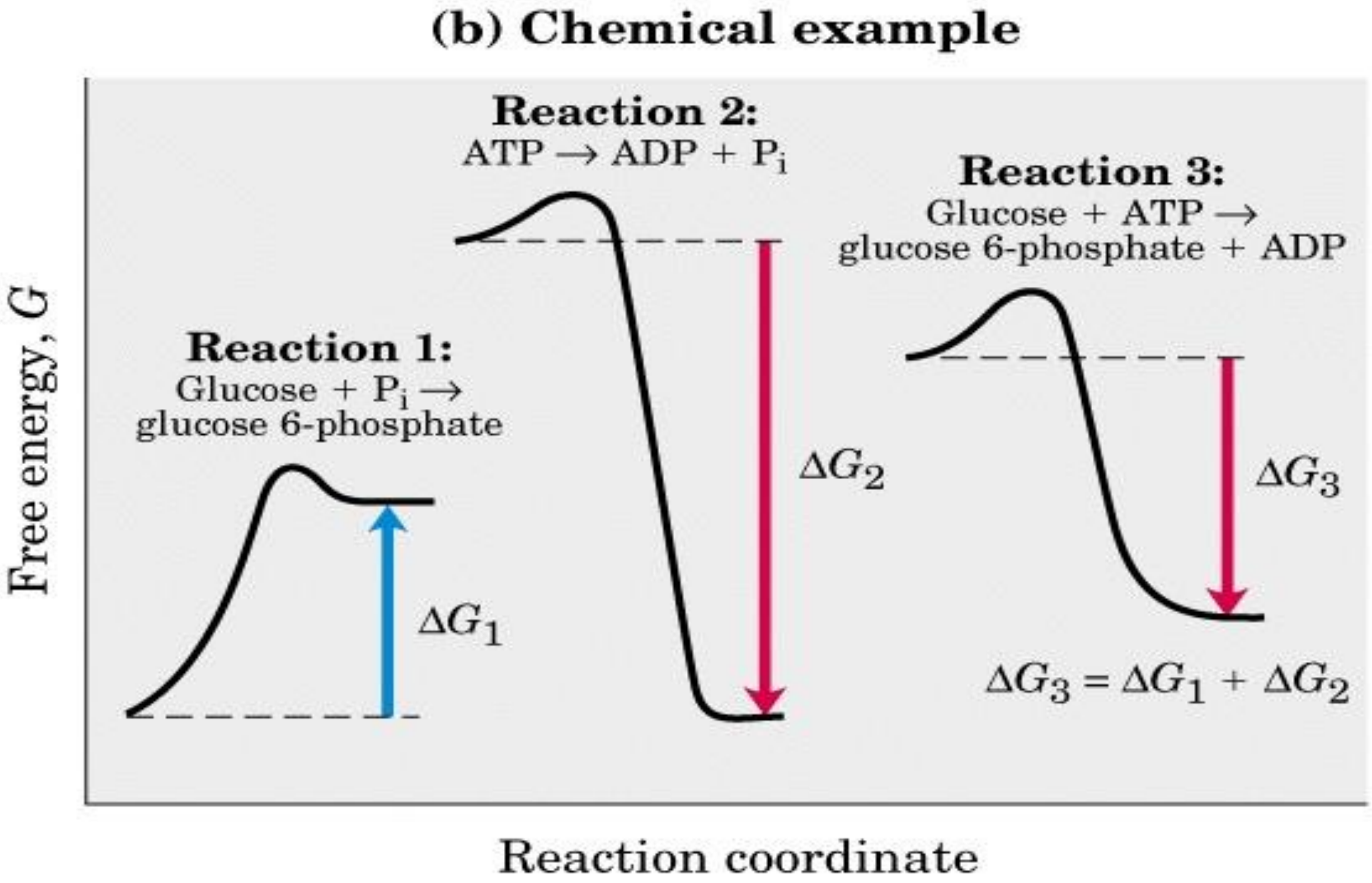
70

Life needs (3) *CHEMICAL MECHANISMS*, to:

- Harness energy
- Drive sequential chemical reactions
- Synthesize & degrade macromolecules
- Maintain a dynamic steady state
- Self-assemble complex structures
- Replicate accurately & efficiently
- Maintain biochemical "order" vs outside

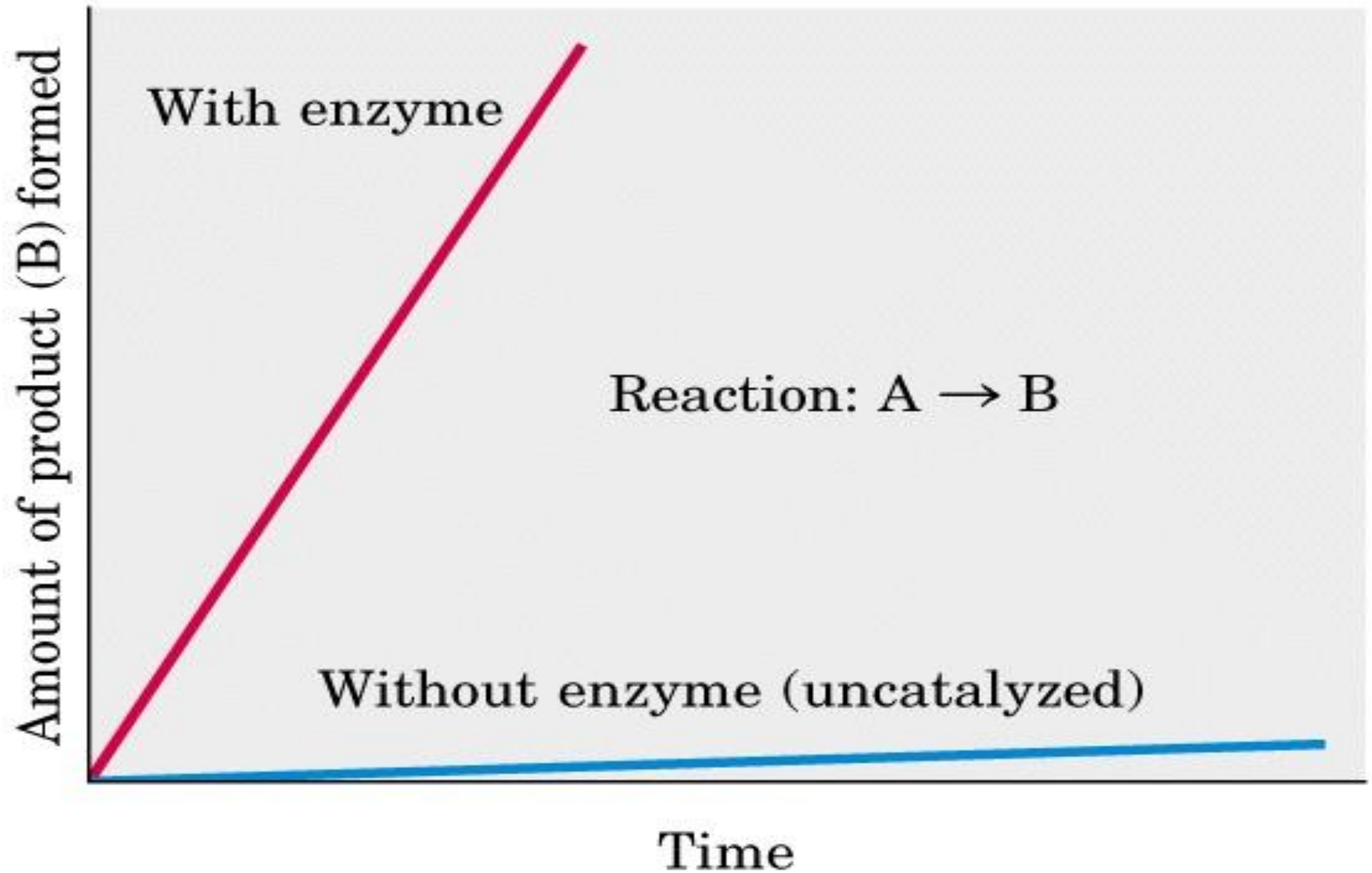
71

Trick #1: Life uses chemical coupling to drive otherwise unfavorable reactions



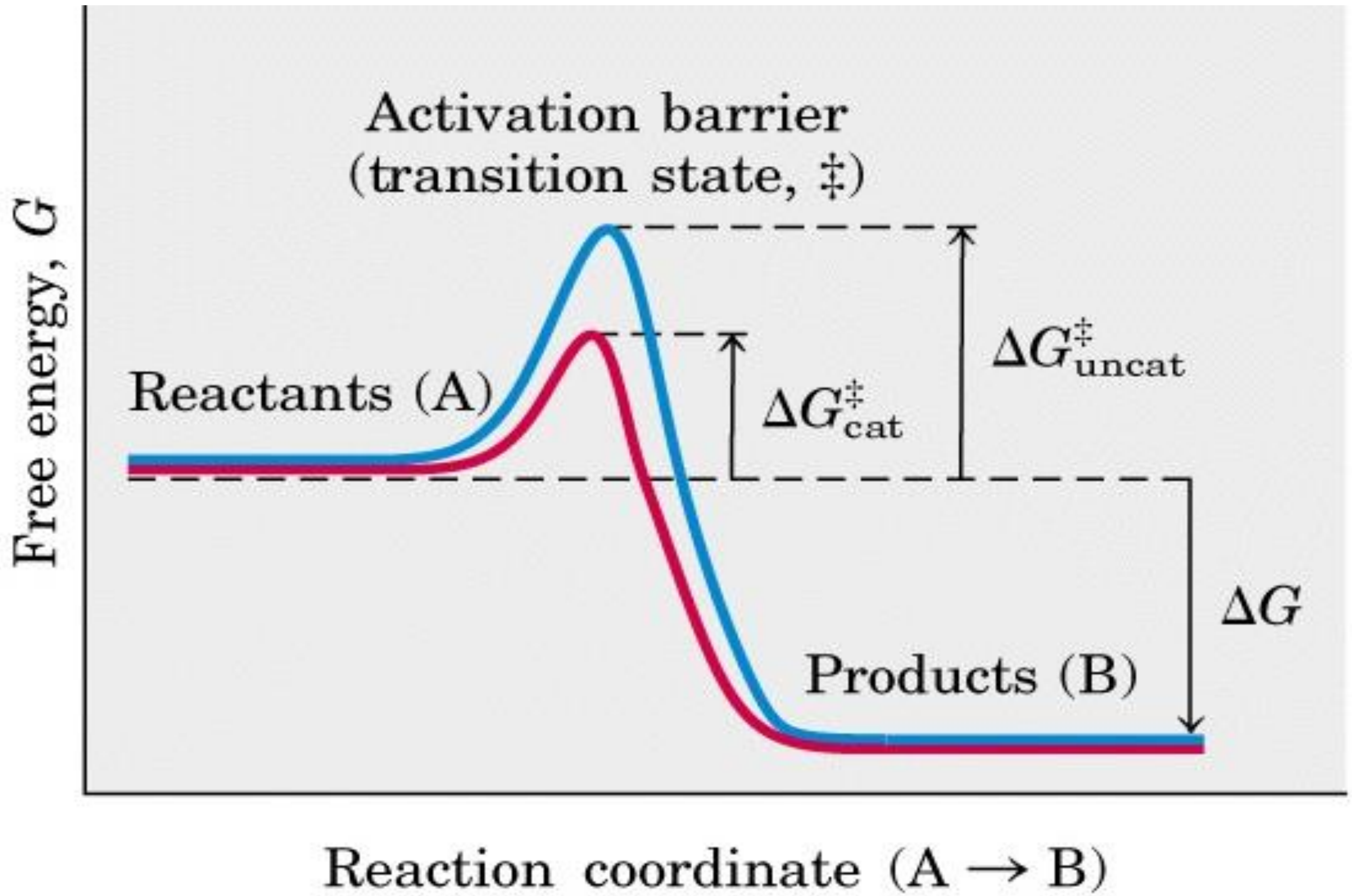
72

Trick #2: Life uses enzymes to speed up otherwise slow reactions



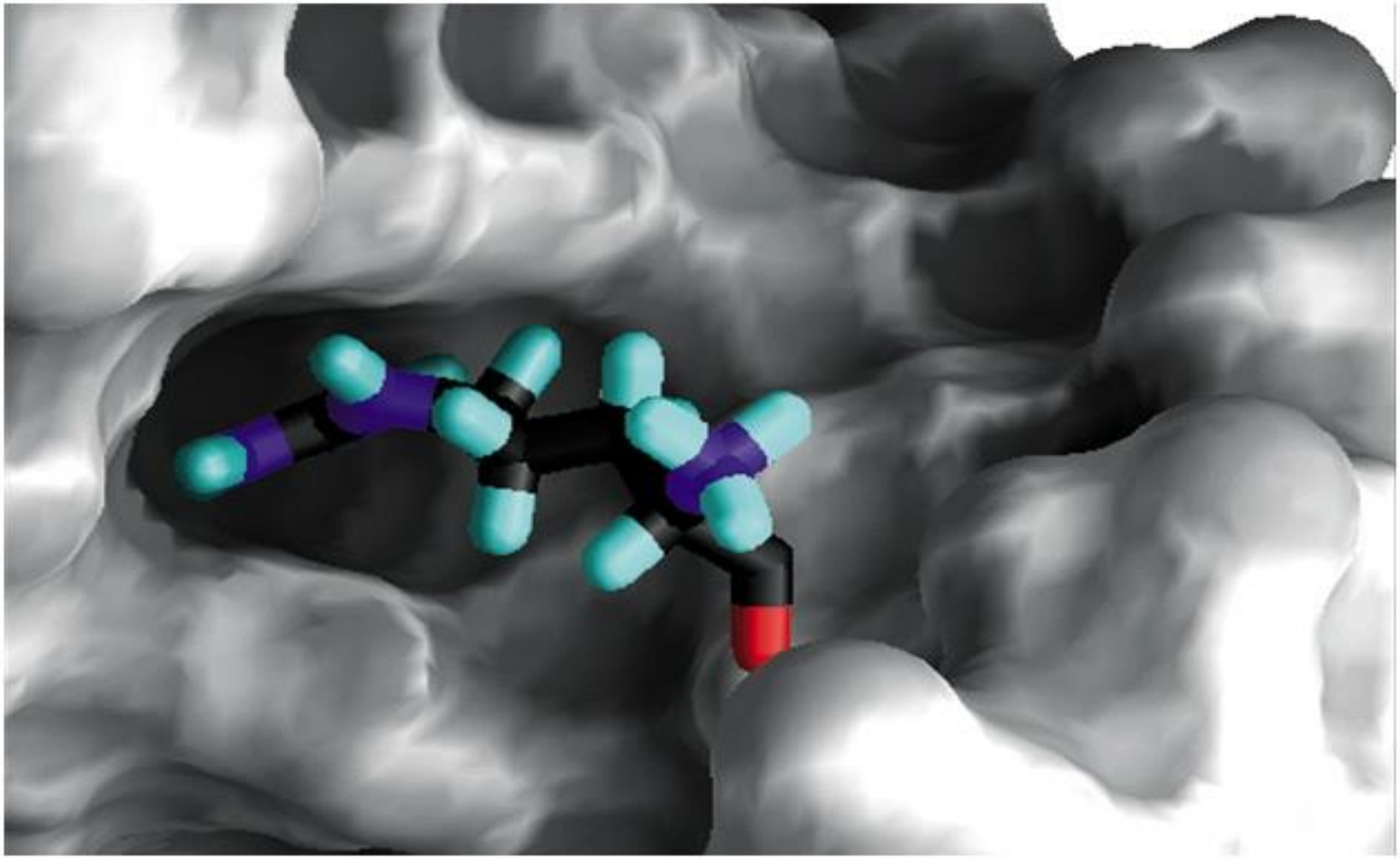
73

How does an enzyme do it, thermodynamically?



74

How does an enzyme do it, mechanistically?



Chemical reaction types encountered in biochemical processes

1. Nucleophilic Substitution

- One atom of group substituted for another

2. Elimination Reactions

- Double bond is formed when atoms in a molecule is removed

3. Addition Reactions:

- Two molecules combine to form a single product.
- A. Hydration Reactions
- Water added to alkene > alcohol (common addition pathway)

4. Isomerization Reactions.

- Involve intramolecular shift of atoms or groups

5. Oxidation-Reduction (redox) Reactions

- Occur when there is a transfer of e- from a donor to an electron acceptor

6. Hydrolysis reactions

- Cleavage of double bond by water.

77

Summary of Key Concepts

Biochemical Reactions

- Metabolism: total sum of the chemical reaction happening in a living organism (highly coordinated and purposeful activity)
  a. Anabolism- energy requiring biosynthetic pathways
  b. Catabolism- degradation of fuel molecules and the production of energy for cellular function

- All reactions are catalyzed by enzymes

- The primary functions of metabolism are:
  a. acquisition & utilization of energy
  b. Synthesis of molecules needed for cell structure and functioning (i.e. proteins, nucleic acids, lipids, & CHO
  c. Removal of waste products

79

Even though thousands of pathways sound very large and complex in a tiny cell:

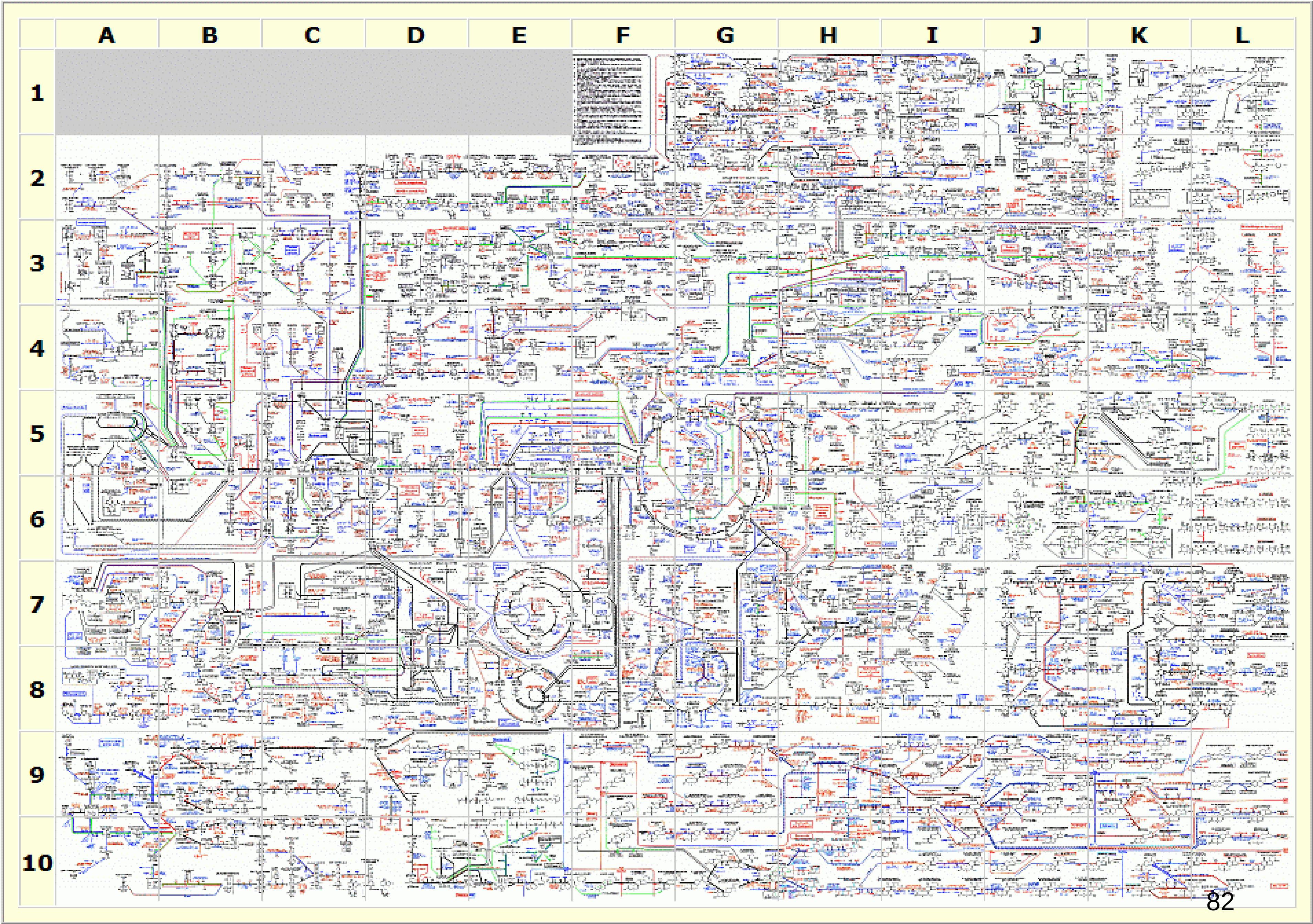
- The types of pathways are small
- Mechanisms of biochemical pathways are simple
- Reactions of central importance (for energy production & synthesis and degradation of major cell components) are relatively few in number

80

Energy for Cells

- Living cells are inherently unstable.
- Constant flow of energy prevents them from becoming disorganized.
- Cells obtains energy mainly by the oxidation of bio-molecules (e- transferred from 1 molecule to another and in doing so they lose energy)
- This energy captured by cells & used to maintain highly organized cellular structure and functions

81


A B C D E F G H I J K L
1
2
3
4
5
6
7
8
9
10