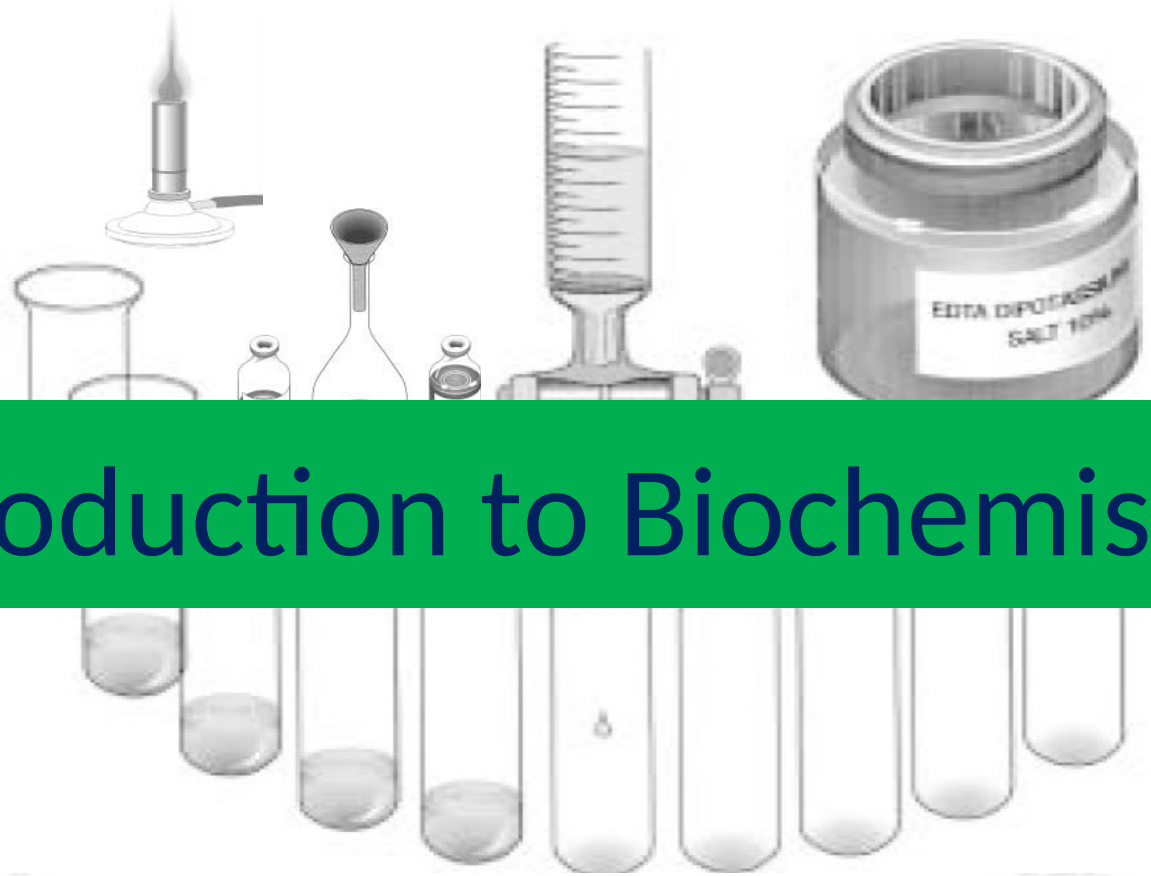


Introduction to Biochemistry

By: Alemayehu Z. Golla, M.Sc. in Medical Biochemistry

Outline

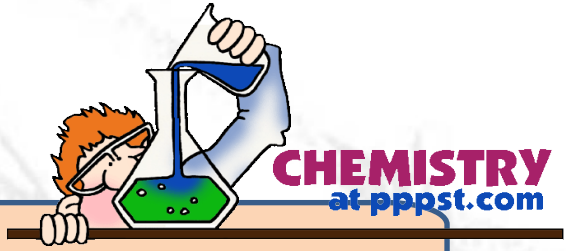
- Definition and scope
- Relevance of biochemistry to health
- Organization of life
- Biomolecules and functional groups
- Weak non-covalent interactions
- Cells

Definition and scope

STUDY OF THE STRUCTURE, COMPOSITION, PROPERTIES, FUNCTIONS AND CHEMICAL REACTIONS OF SUBSTANCES IN LIVING SYSTEMS

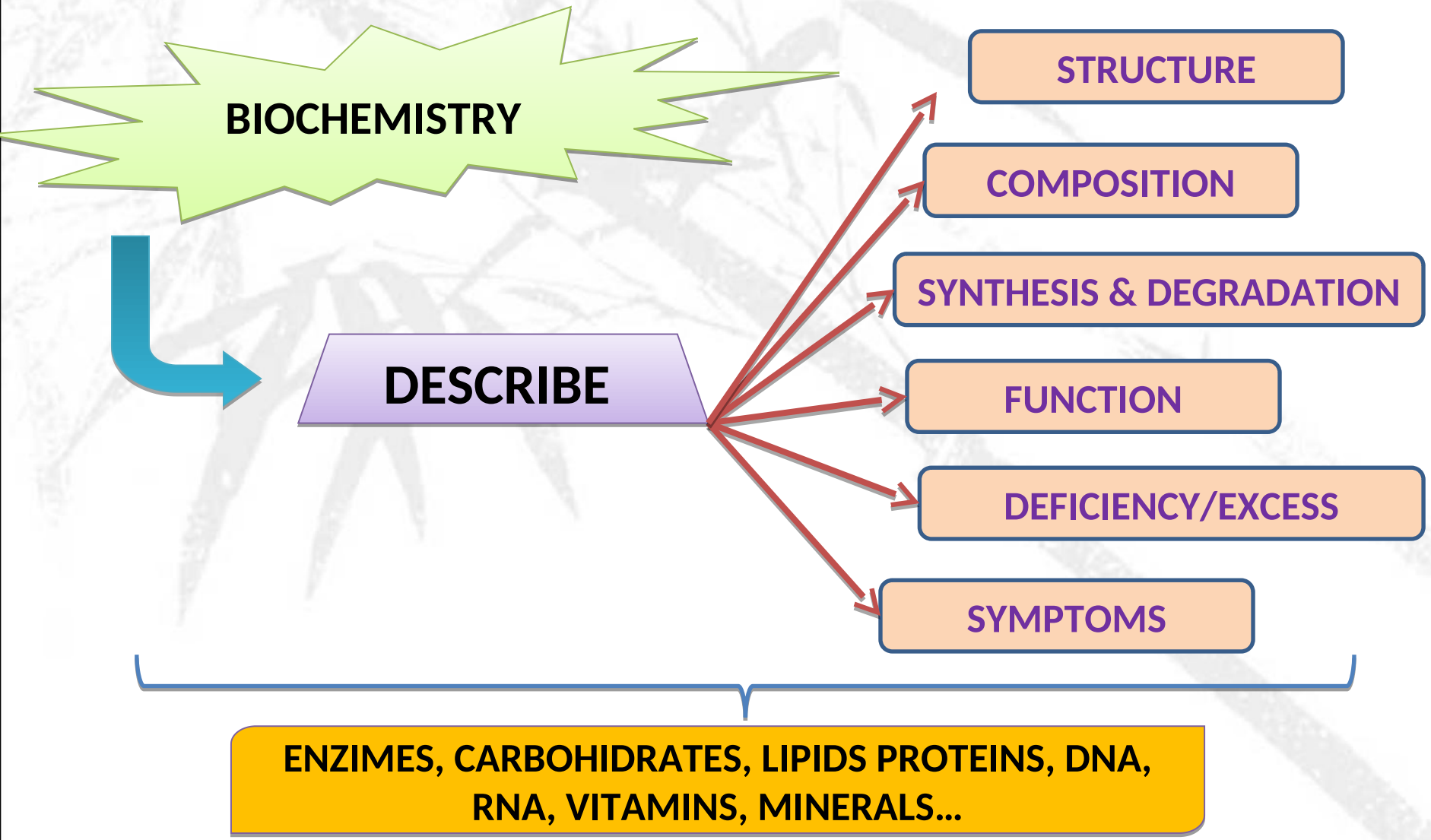


BIOLOGY + **CHEMISTRY**

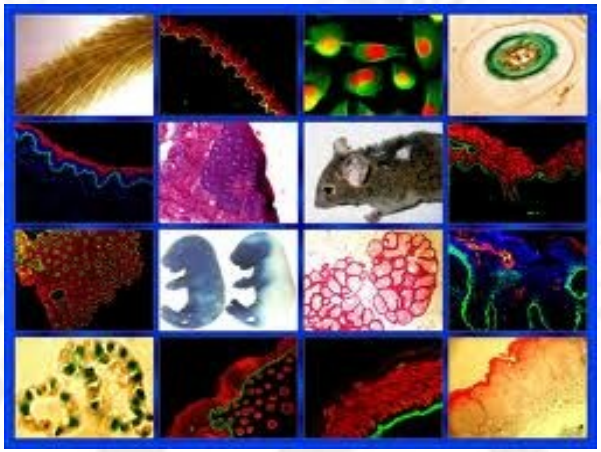


BIOCHEMISTRY

Biochemistry is concerned with the chemical basis of life.



IT TRIES TO EXPLAIN LIFE IN TERMS OF BIOCHEMICAL REACTIONS







Life depends on biochemical reactions and processes

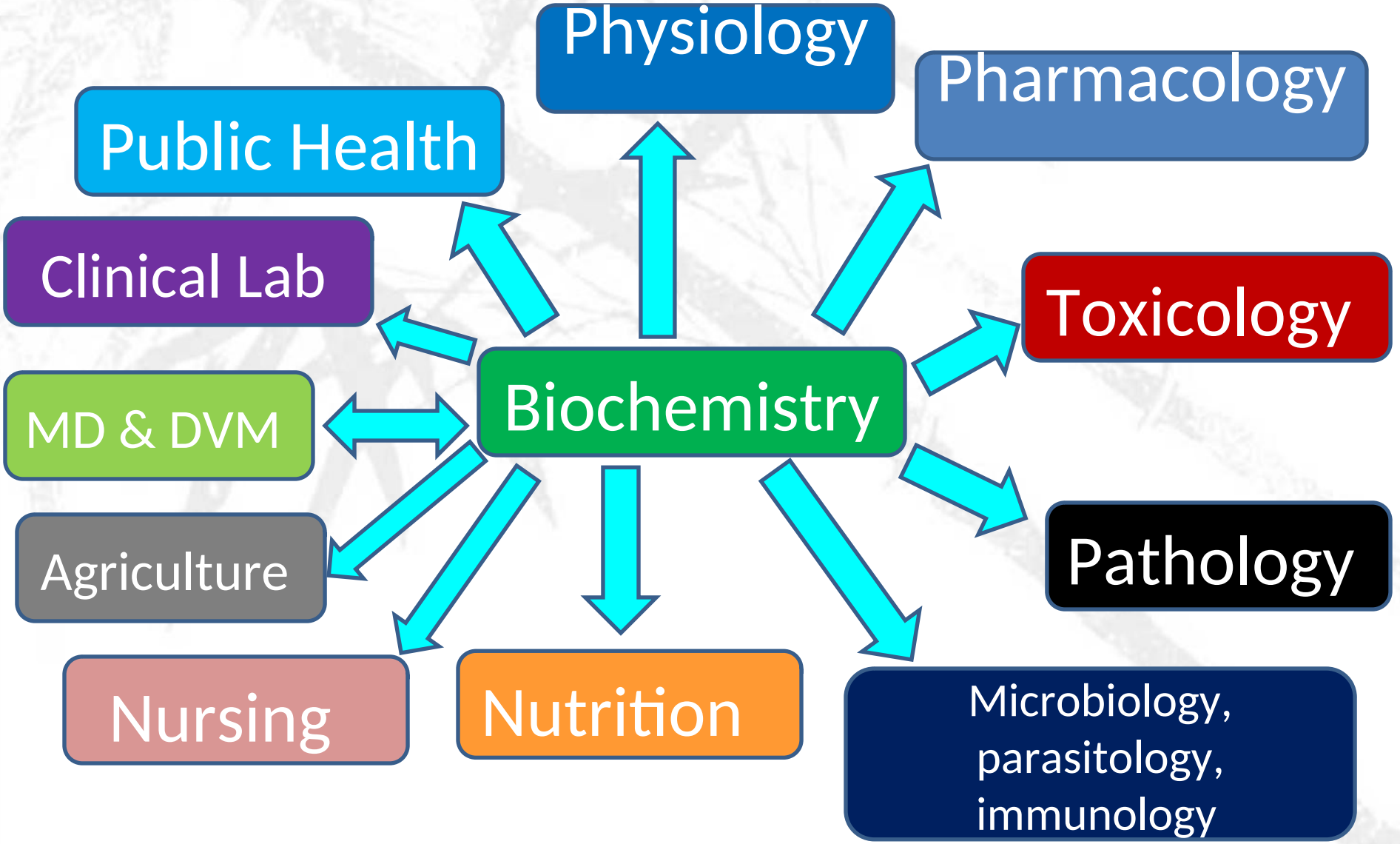
Related to other sciences as physiology, anatomy, pharmacy, nutrition, agriculture, etc

- In biochemistry we
  - Isolate molecules and determine their structure
  - Identify and quantify substances in organisms
  - Study synthesis and degradation of biomolecules in organisms
  - Analyze their role in the operation of the organism
- Scope: Biochemistry encompasses
  - Cell biology, molecular biology (molecular genetics)
  - As vast as life itself
  - Every aspect of life – conception, birth, growth, reproduction, aging & death – involves biochemistry
  - **Biology at molecular level!!**

Relevance of Biochemistry to Health

- Understand basic functions of the body
- Tool for research in biomedical sciences
- The functioning of cells at the molecular level
  - How food is digested, absorbed, and used?
  - How the body transform and utilize energy?
  - How various metabolic pathways are regulated and interrelated?
  - What is the molecular basis for immunological defense against invading organisms
- Laboratory analysis of body fluids for diagnostic purpose
- Production of therapeutic agents by genetic engineering
- Gene therapy – future lookout

Why Biochemistry?

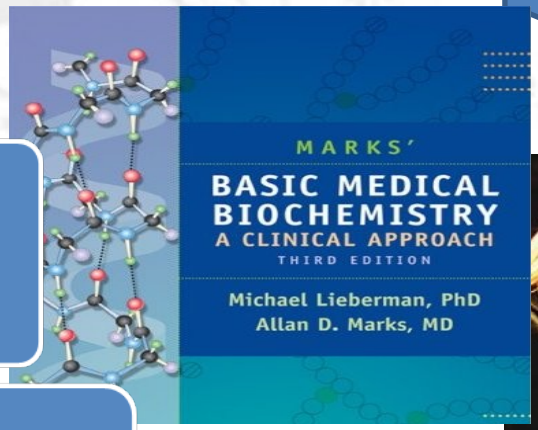


Biochemistry in pharmacology

Biochemistry is a guide to drug discovery and for its application

- Gives an idea of drug constitution
- Change of degradation with varying temperature
- How drugs are metabolized by biochemical reactions in presence of enzymes





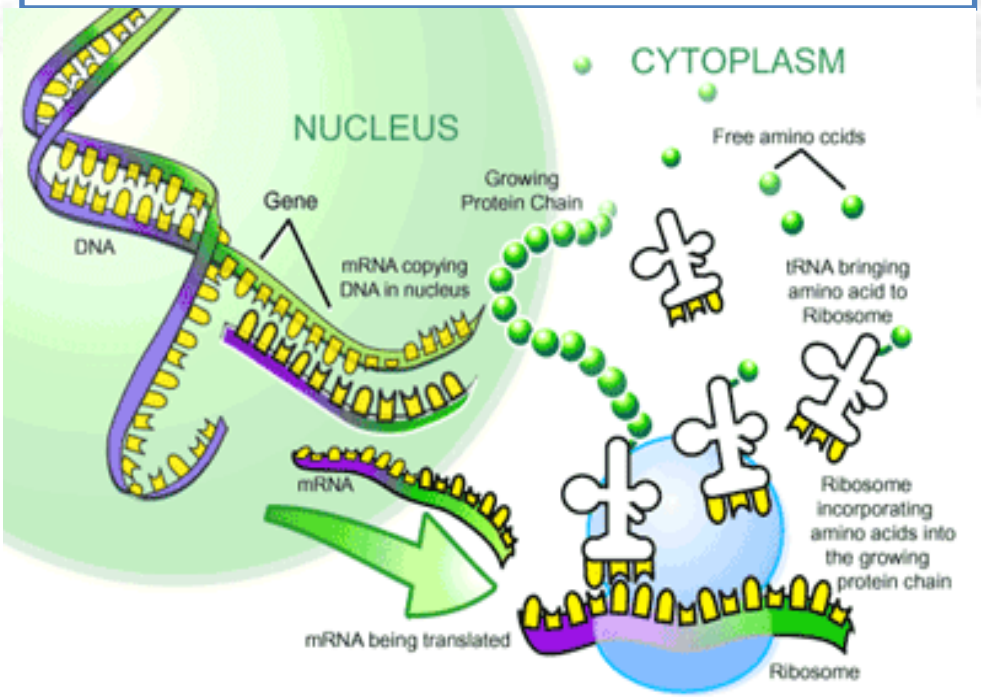


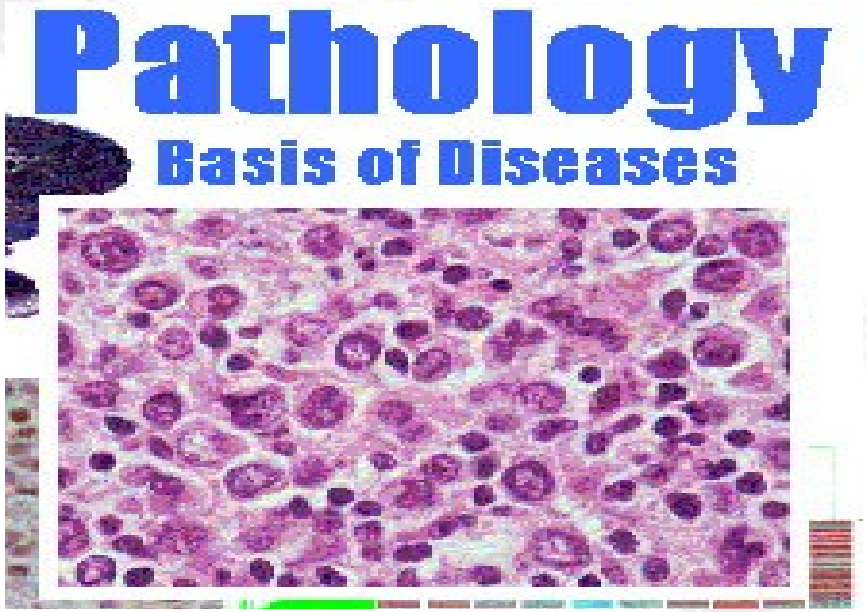
Morphine is a drug that reduce the pain in terminal cáncer

Biochemistry in Pathology

Biochemistry helps us understand the biochemical changes and related physiological alteration in the body

The pathology of any disease is studied through biochemical changes





Biochemistry in Nutrition



- Daily calorie requirement
- Optimum intake of biomolecules, minerals, vitamins, essential fatty acids & amino acids
- Exess intake Vs deficiency
- The function and role of the vitamins is described only by biochemistry





- Many people rely in taking multivitamin and minerals for better health



Biochemistry Laboratory

The nutrients value of food material

can also



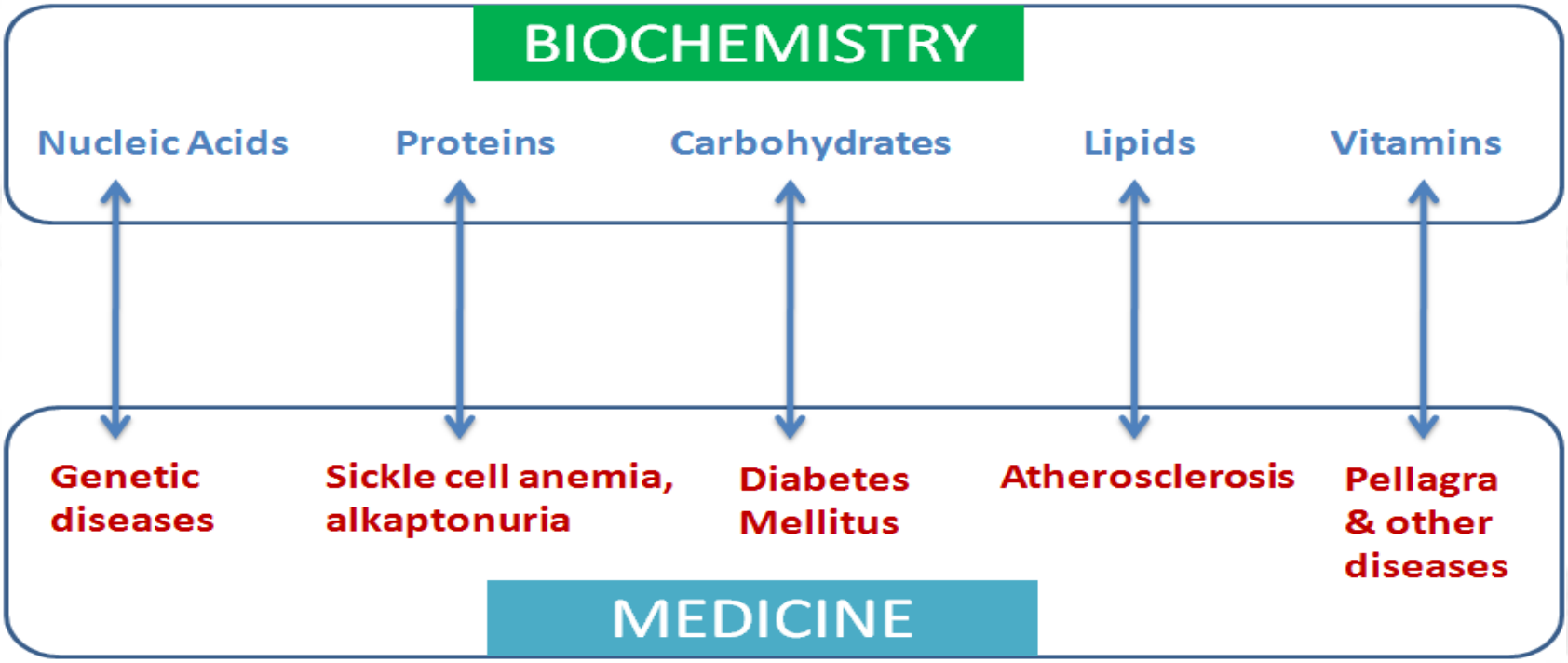
Be determined by biochemical tests



Estimation of different analytes in biological samples (blood, urine, CSF, etc) is based on application of biochemistry

- Glucose
- Cholesterol
- BUN
- Creatinine
- Enzymes
- Many others

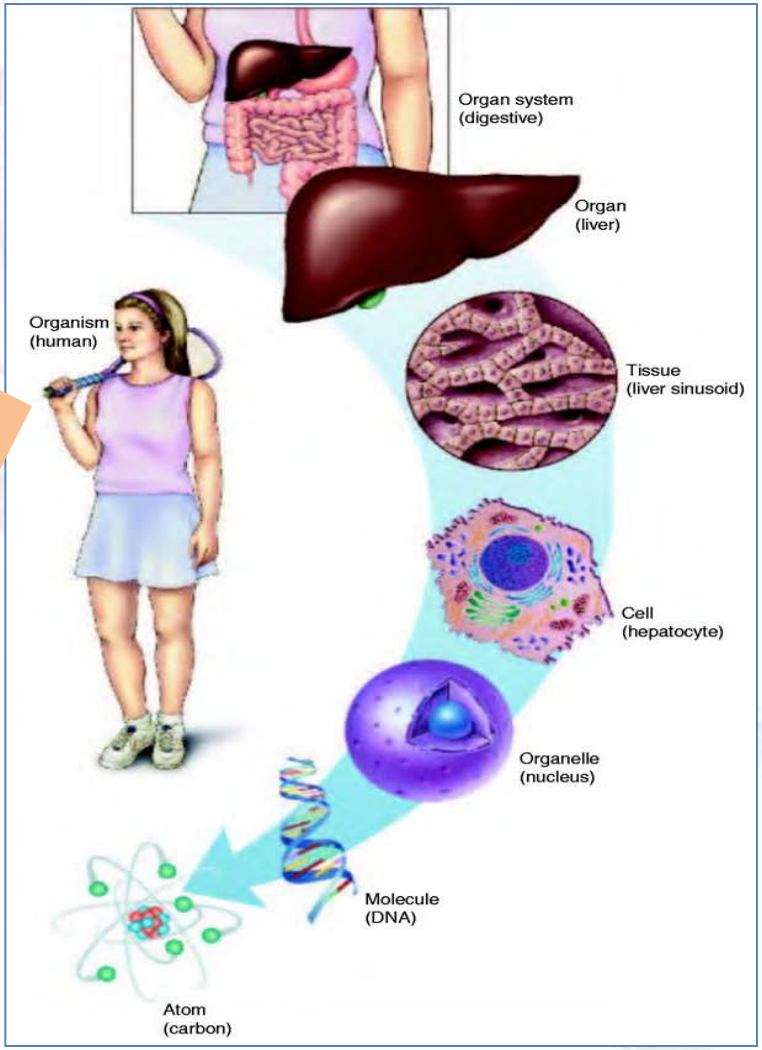
- Two-way street relationship between biochemistry and medicine
  - Knowledge of biomolecules for clear understanding of diseases
  - Analysis of the diseases have cast light on many areas of biochemistry



Organization of Life

- Elements
- Simple inorganic compounds
- Simple organic compounds (monomers)
- Macromolecules (polymers)
- Supramolecular structures
- Organelles
- Cells
- Tissues (organs)
- Organ system
- Organisms

Hierarchical organization of multicellular organism: The human being



Elements of Life

IA	IIA	IIIB	IVB	VB	VIB	VIIB	VIIIB			IB	IIB	IIIA	IVA	VA	VIA	VIIA	0
1 H 1.008																	2 He 4.003
3 Li 6.941	4 Be 9.012											5 B 10.81	6 C 12.01	7 N 14.01	8 O 16.00	9 F 19.00	10 Ne 20.18
11 Na 22.99	12 Mg 24.31											13 Al 26.98	14 Si 28.09	15 P 30.97	16 S 32.07	17 Cl 35.45	18 Ar 39.95
19 K 39.10	20 Ca 40.08	21 Sc 44.96	22 Ti 47.87	23 V 50.94	24 Cr 52.00	25 Mn 54.94	26 Fe 55.85	27 Co 58.93	28 Ni 58.69	29 Cu 63.55	30 Zn 65.39	31 Ga 69.72	32 Ge 72.61	33 As 74.92	34 Se 78.96	35 Br 79.90	36 Kr 83.80
37 Rb 85.47	38 Sr 87.62	39 Y 88.91	40 Zr 91.22	41 Nb 92.91	42 Mo 95.94	43 Tc (98)	44 Ru 101.1	45 Rh 102.9	46 Pd 106.4	47 Ag 107.9	48 Cd 112.4	49 In 114.8	50 Sn 118.7	51 Sb 121.8	52 Te 127.6	53 I 126.9	54 Xe 131.3
55 Cs 132.9	56 Ba 137.3	57 * La 138.9	72 Hf 178.5	73 Ta 180.9	74 W 183.8	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.1	79 Au 197.0	80 Hg 200.6	81 Tl 204.4	82 Pb 207.2	83 Bi 209.0	84 Po (209)	85 At (210)	86 Rn (222)
87 Fr (223)	88 Ra (226)	89** Ac (227)	104 Rf (261)	105 Db (262)	106 Sg (263)	107 Bh (264)	108 Hs (265)	109 Mt (268)	110 (269)	111 (272)	112 (277)	113	114 (285)	115	116 (289)	117	118 (293)

58* Ce 140.1	59 Pr 140.9	60 Nd 144.2	61 Pm (145)	62 Sm 150.4	63 Eu 152.0	64 Gd 157.3	65 Tb 158.9	66 Dy 162.5	67 Ho 164.9	68 Er 167.3	69 Tm 168.9	70 Yb 173.0	71 Lu 175.0
90** Th 232.0	91 Pa 231	92 U 238.0	93 Np (237)	94 Pu (244)	95 Am (243)	96 Cm (247)	97 Bk (247)	98 Cf (251)	99 Es (252)	100 Fm (257)	101 Md (258)	102 No (259)	103 Lr (262)

- **Most abundant, essential for all organisms**
- **Less abundant, essential for all organisms**
- **Trace levels, essential for all organism**
- **Trace levels, essential for some organisms**

- Four elements
  - C, H, O, and N (account for more than 99% of total mass)
  - Major constituents of biomolecules, together with P & S
  - Most of the H and O occur as H_2O (60-70% of cell mass)

Essential mineral elements:

- Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, S and P
- Account for about 0.7% of the body mass
- Dissolved in the ECF and ICF and form electrolytes
- Most of the body's calcium and phosphorus is in bone
- Phosphate and sulfate

Human Body†	
Element	%
H	63
O	25.5
C	9.5
N	1.4
Ca	0.31
P	0.22
Cl	0.08
K	0.06
S	0.05
Na	0.03
Mg	0.01

Trace elements:

- Small quantities (mg, µg)
- Trace elements are essential to life, because they are essential to the function of specific proteins, including enzymes
  - Fe for oxygen-transporting capacity of the hemoglobin
  - Iodine for synthesis of thyroid hormones (T3 and T4)
  - Zn, Cu, Se, etc, cofactors for enzymes

Electrolytes

- Charged particles (ions) dissolved in body fluids
  - Cations
  - Anions
- Major cations: Na^{+}, K^{+}, Ca^{2+}, and Mg^{2+}
- Major anions: Cl^{-}, HCO_3^{-}, $H_2PO_4^{-}$ & HPO_4^{2-}, SO_4^{2-}, organic acids, and proteins
- Right types and levels of electrolytes in each fluid compartment of the body for proper functioning of neurons, muscle cells, and other cells in the body.

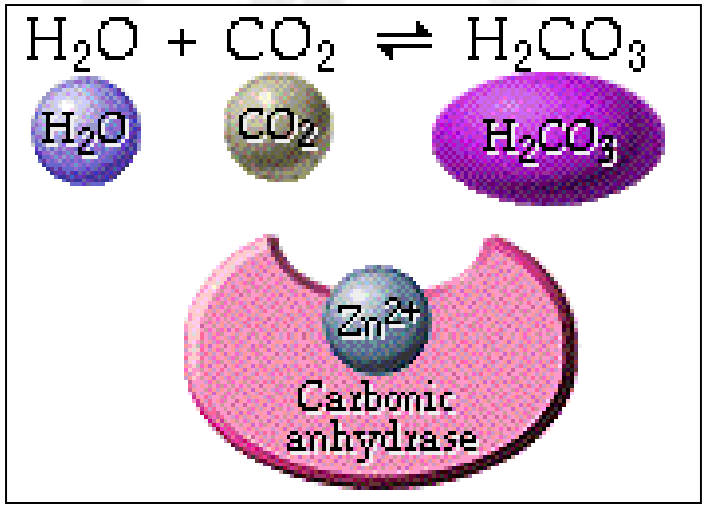
- The electrolyte composition of ECF & ICF has significant differences.
  - ✓ The major cation of the ECF
  - ✓ Other cations of ECF
  - ✓ The major cation in the ICF
  - ✓ Other positive ions
  - ✓ The major extracellular anion
  - ✓ Other anion found in the ECF
  - ✓ Major intracellular anions
  - ✓ Other anions in the ICF
  - ✓ Proteins in ICF vs IF

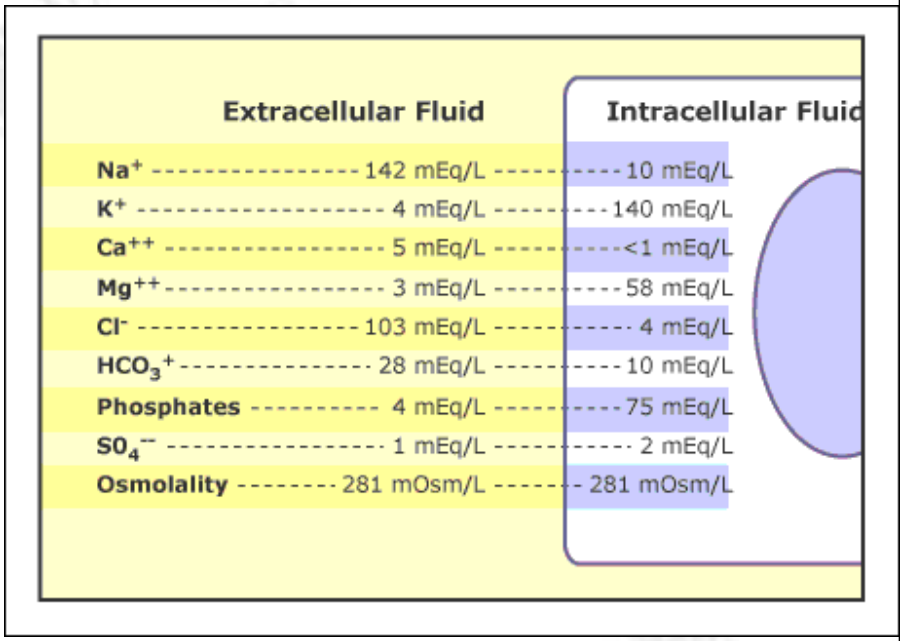
Composition of Extracellular and Intracellular Fluids

	Extracellular Concentration, mM	Intracellular Concentration,* mM
Na^+	145	15
K^+	4	150
Ca^{2+}	1	1.5
Mg^{2+}	1.5	12
Cl^-	110	10
HCO_3^-	24	10
P_i	2	40
Amino acids	2	8
Glucose	5.6	1
ATP	0	4
Protein	0.2	4

*The intracellular concentrations differ slightly from one tissue to another, but the concentrations shown above are typical of most cells. The intracellular concentrations listed above may not reflect the *free* concentration of the substance in the cytosol since some may be bound to proteins or confined within cell organelles. For example, the free cytosolic concentration of calcium is only about 0.0001 mM.

- Functions of electrolytes in the body
  - Maintain fluid balance
  - Action potential in neurons and muscle cells
  - Secretion and action of hormones and neurotransmitters
  - Muscle contraction
  - Cofactors for enzymes

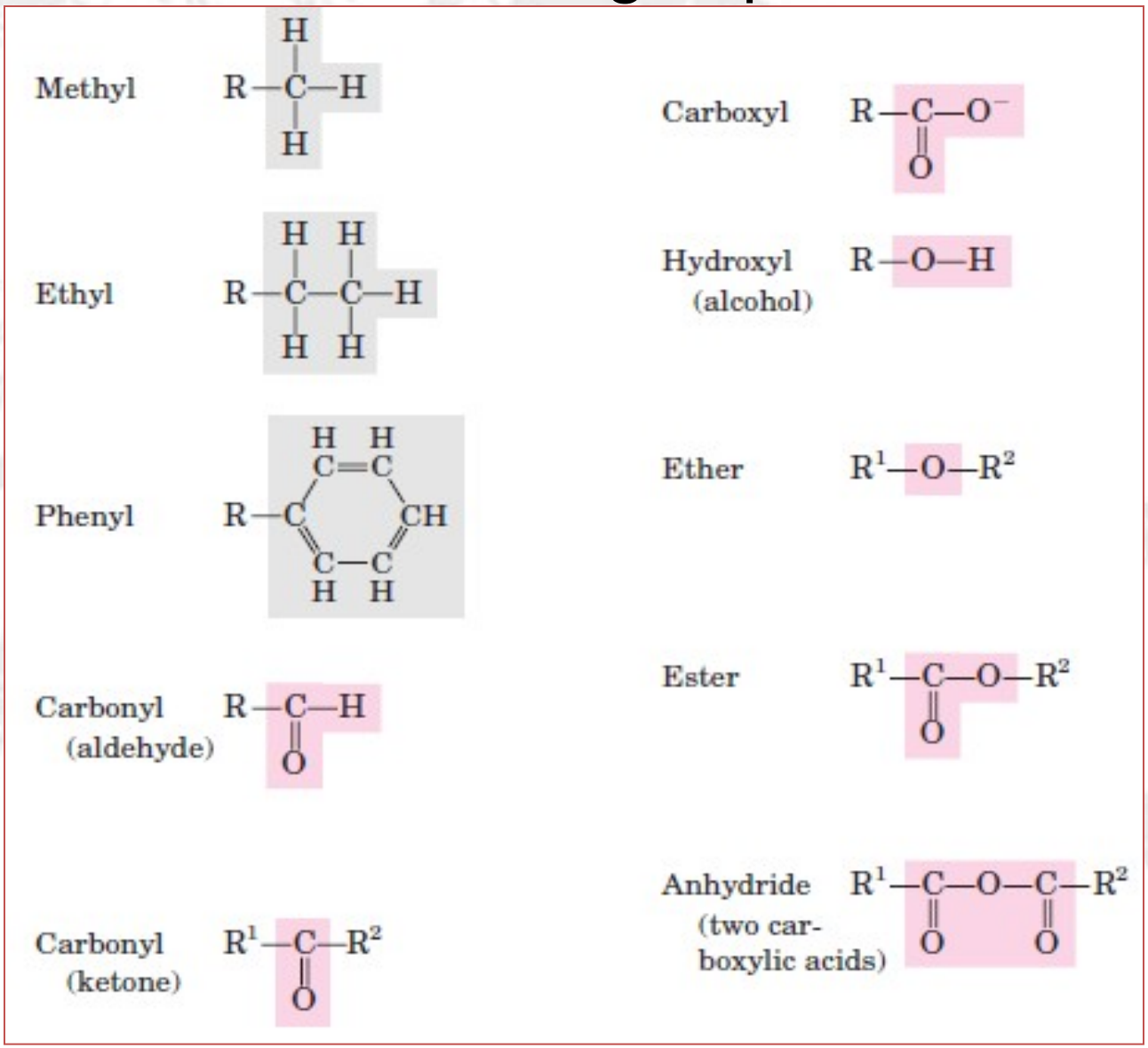




Biomolecules and functional groups

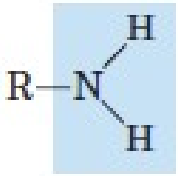
- Most biomolecules = derivatives of hydrocarbons
  - Different families of organic compounds with variety of functional groups
- Some of these families of compounds are:
  - Alcohols
  - Amines
  - Aldehydes and ketones
  - Carboxylic acids
  - Esters
  - Ethers
  - Anhydrides
  - Others

Some common functional groups in biomolecules

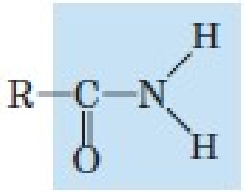


Some common functional groups in biomolecules (cont…)

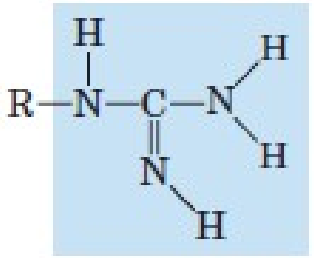
Amino



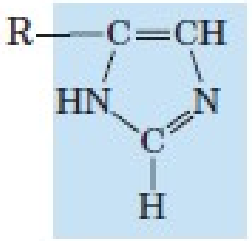
Amido



Guanidino



Imidazole



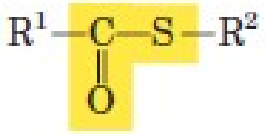
Sulfhydryl



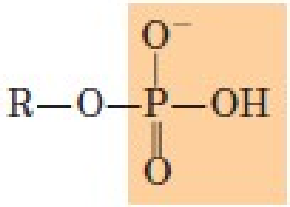
Disulfide



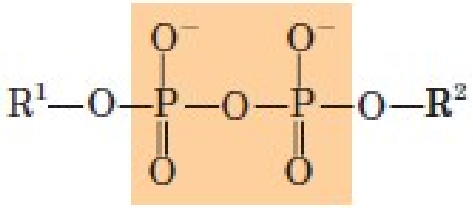
Thioester



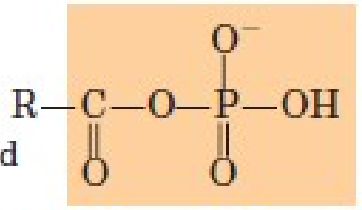
Phosphoryl



Phosphoanhydride



Mixed anhydride
(carboxylic acid and phosphoric acid; also called acyl phosphate)



- Many important biomolecules are polymers

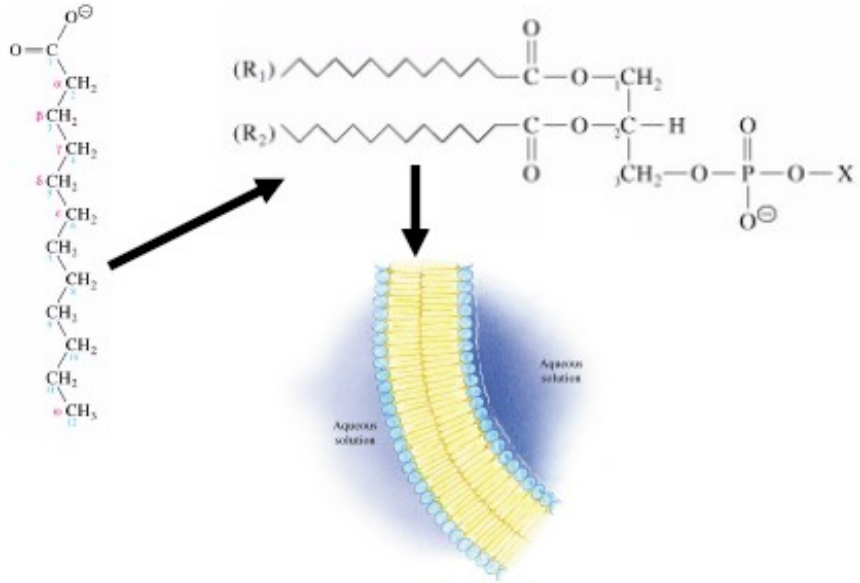
	lipids	proteins	carbo	nucleic acids
monomer	fatty acid	amino acid	glucose	nucleotide
polymer	phospholipid	protein subunit	cellulose	DNA
supramolecular structure	membrane	protein complex	cell wall	chromosome

Lipids

monomer: fatty acid

polymer: phospholipid

supramolecular structure: membrane

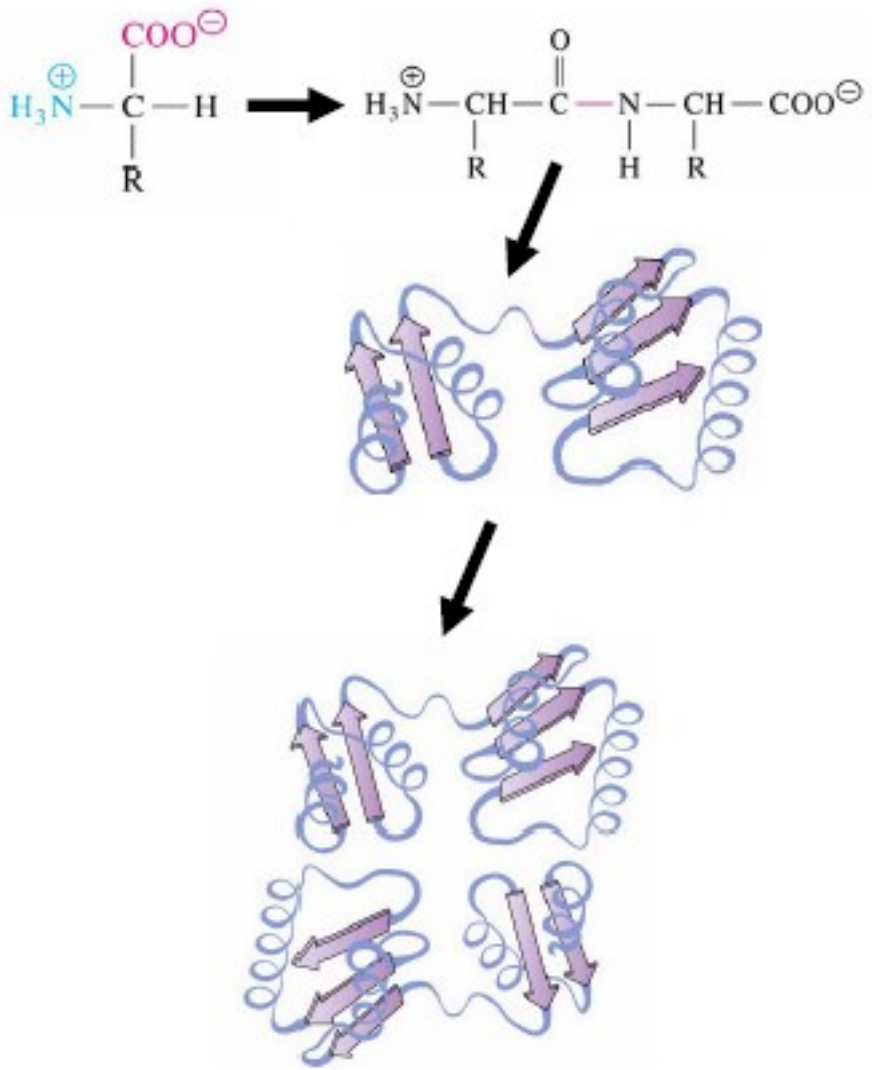


Proteins

monomer — amino acid

polymer — protein subunit

supramolecular structure — Enzyme complex

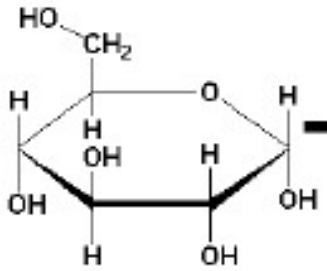


Carbohydrates

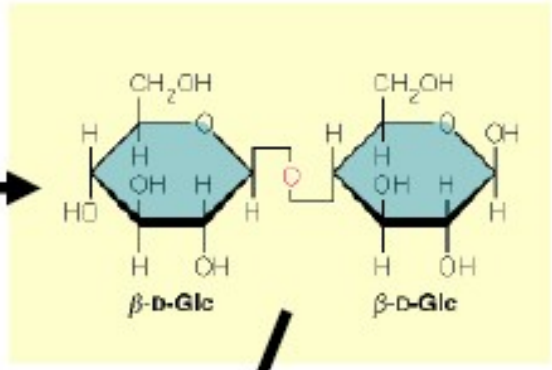
monomer — glucose

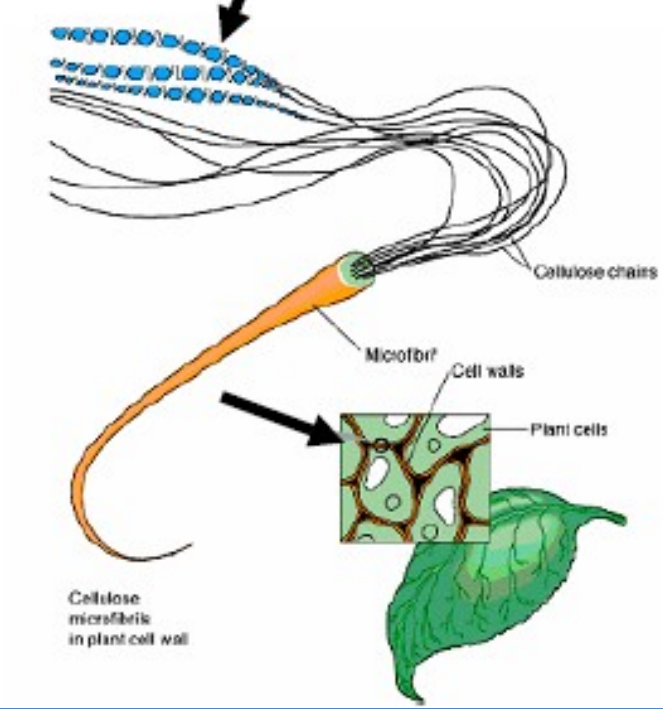
polymer — cellulose

supramolecular structure — cell wall



Glucose



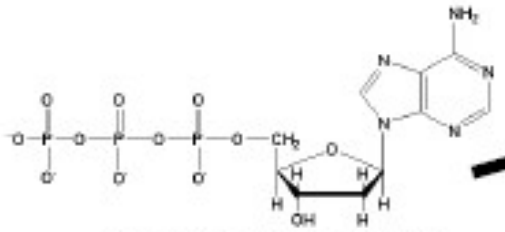


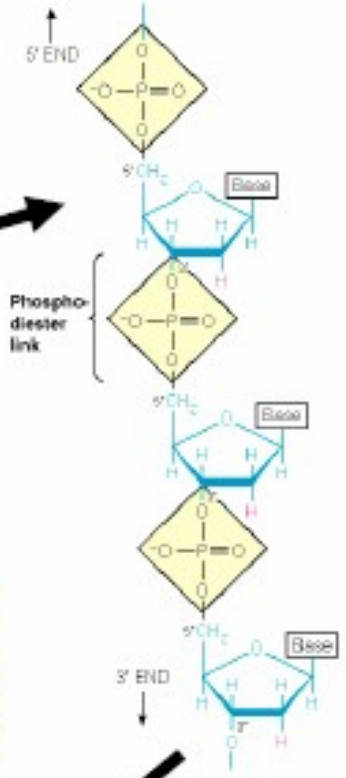
Nucleic acids

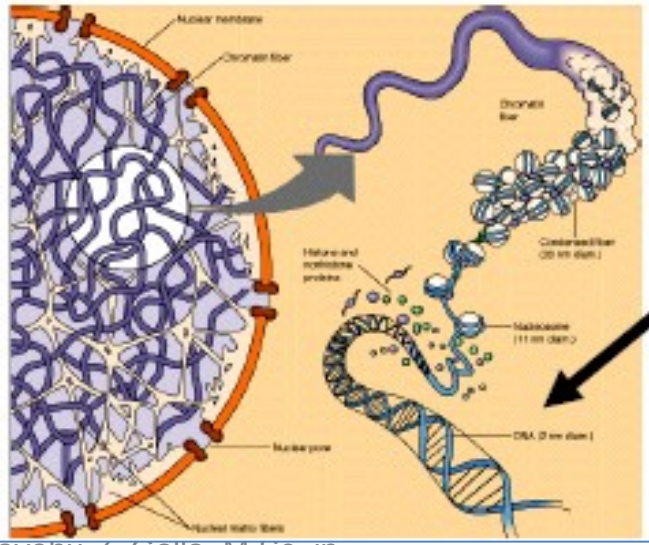
monomer — nucleotide

polymer — DNA

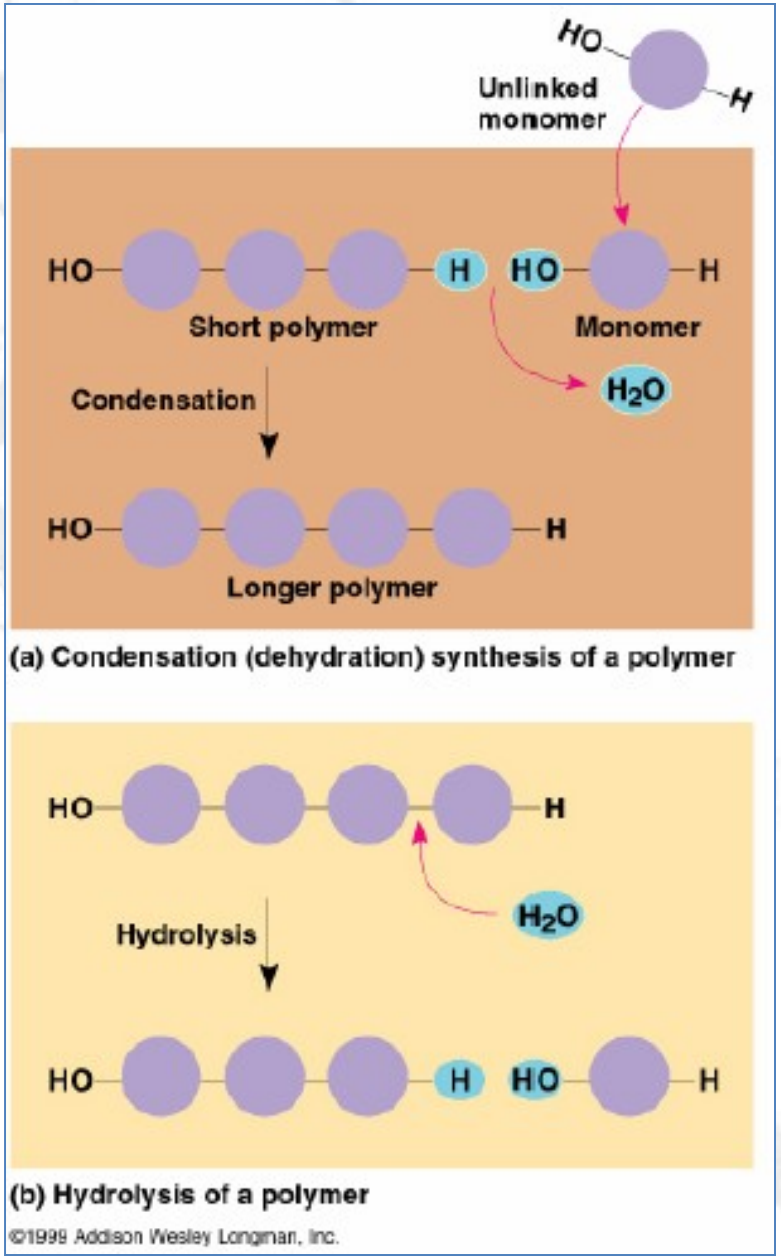
supramolecular structure — chromatin







- Monomers form polymers through condensations
- Polymers are broken down through hydrolysis

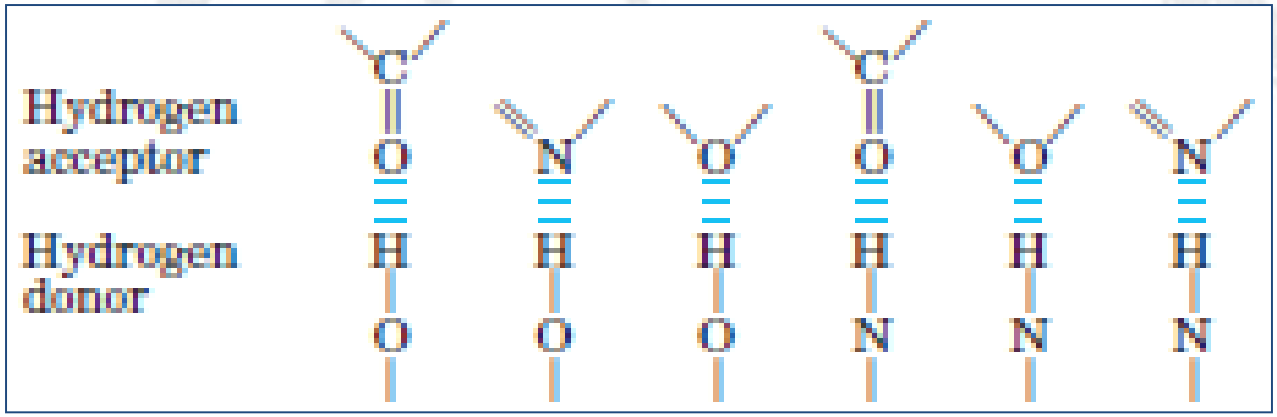


Weak Non-covalent interactions

- Hydrogen bond, Van der Waals force, hydrophobic interactions and ionic interactions
- Constantly forming and breaking at physiological temperature
- Individually they are weak, but collectively they have a very significant influence in the 3D structure of proteins, nucleic acids, polysaccharides, and membrane lipids.

Hydrogen bonding:

•H atom bonded to high electronegative elements



- Hydrogen bonds are stronger and mores specific than Van der Waals forces

Van der Waals forces:

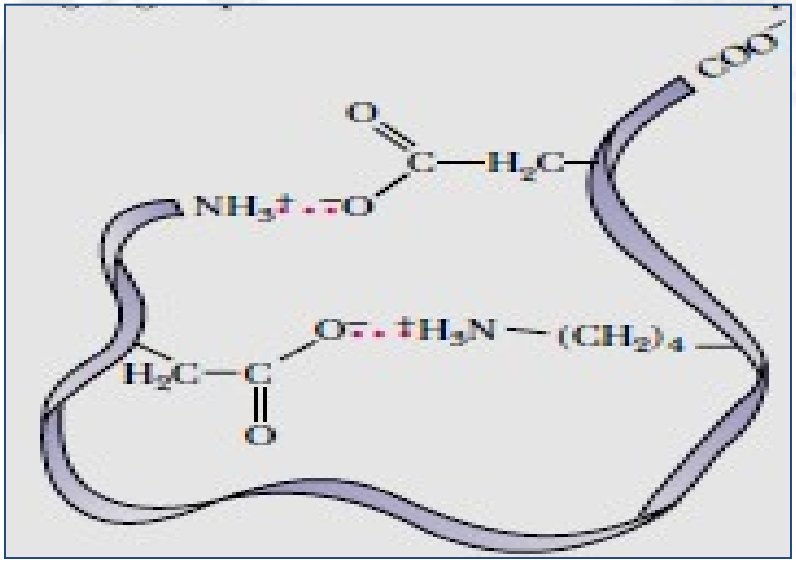
- Arise from attraction between transient dipoles generated by the rapid movement of electrons on all neutral atoms.
- Random variations in the positions of the electrons around one nucleus may create a transient electric dipole, which induces a transient, opposite electric dipole in the nearby atom.
- The strength of van der Waals interaction depends on the relative size of the atoms or molecules and the distance between them.
  - The greater the area of contact the stronger the interaction

Hydrophobic interaction:

- The tendency of nonpolar compounds to self-associate in an aqueous environment.
- Arises from the need to minimize energetically unfavorable interactions between nonpolar groups and water. That is hydrophobic interactions arise not because of any intrinsic affinity of nonpolar substances for one another, but because water molecules prefer the stronger interactions that they share with one another, compared to their interaction with nonpolar molecules.

Ionic interaction

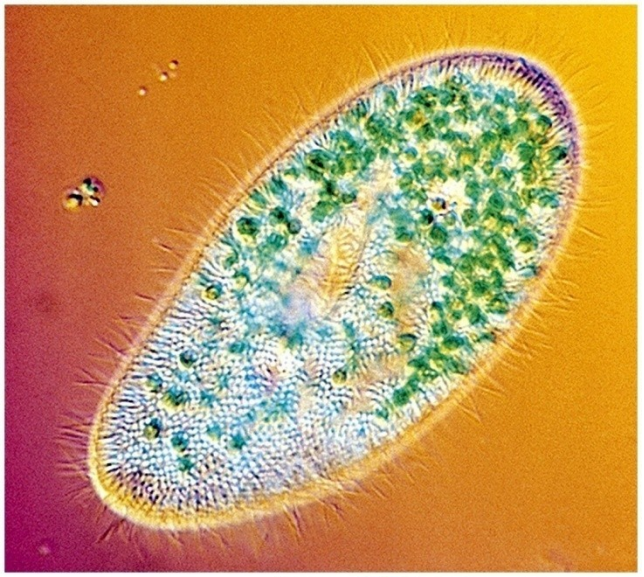
- Results from attractive forces between oppositely charged functional groups
  - Negatively charged carboxyl groups and positively charged amino groups.
- The strength of ionic interactions is highly dependent on the nature of the interacting species and the distance between them



- Weak non-covalent interactions are for recognition and interaction among biomolecules in very specific ways
- Structural complementarity is the very essence of biomolecular recognition.
  - Most precise recognition and interaction occurs if the structure of one is complementary to the structure of the other, as in a lock and its key.
- The biomolecular recognition are mediated by weak non-covalent forces of attractions
  - The binding of an antigen to a specific antibody
  - The binding of a hormone or a neurotransmitter to cellular receptor protein
  - The binding of a substrate to a specific enzyme

Cells

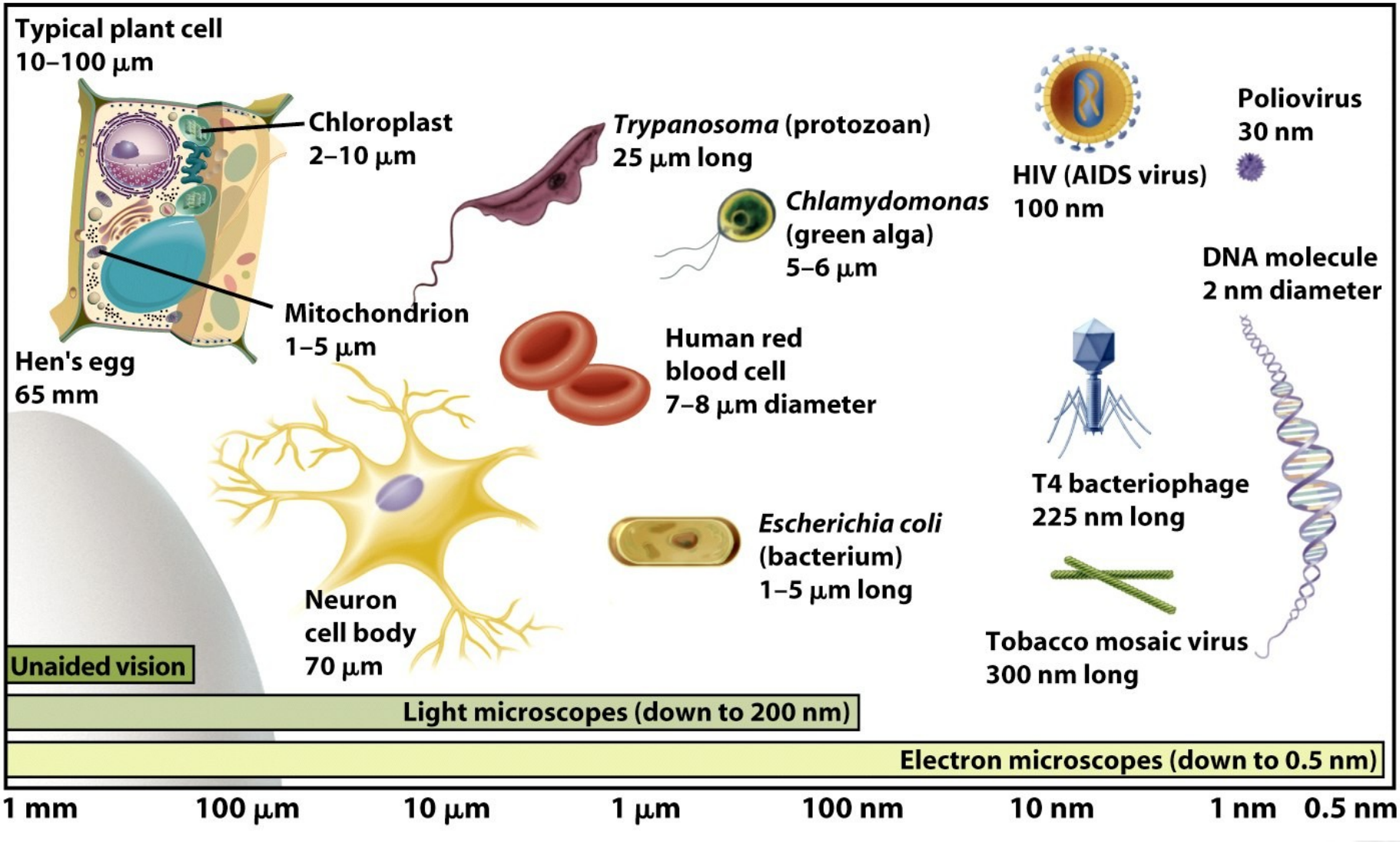
- Smallest living unit of structure and function of all organisms is the cell
- Most are microscopic
- Cell theory
  - All living things are made of cells – Theodor Schwann & Matthias Schleiden in 1839
  - All cells arise from preexisting cells – Rudolf Virchow (50 years later)





Cell …

- Cell size



Cells …

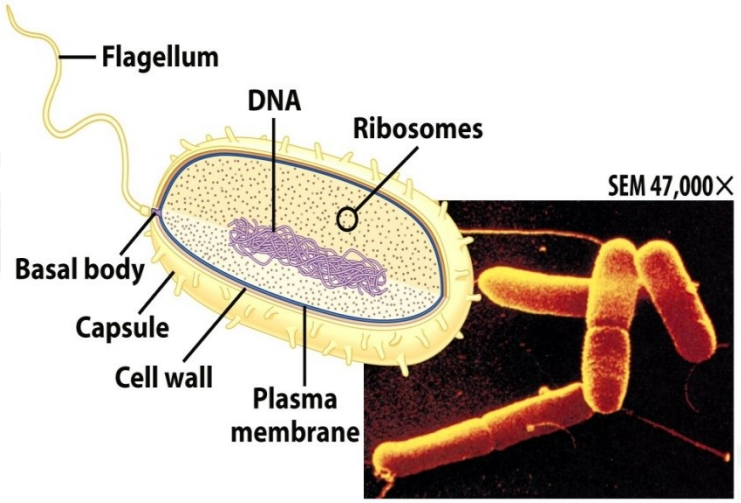
- Components of cells
  - Cell membrane
  - Cytoplasm – surrounded by the cell membrane
  - Organelles – structures for cell function
  - Control center with DNA

- Cell types
  - Prokaryotic – cells that lack true nucleus
  - Eukaryotic – cell with membrane-bound nucleus

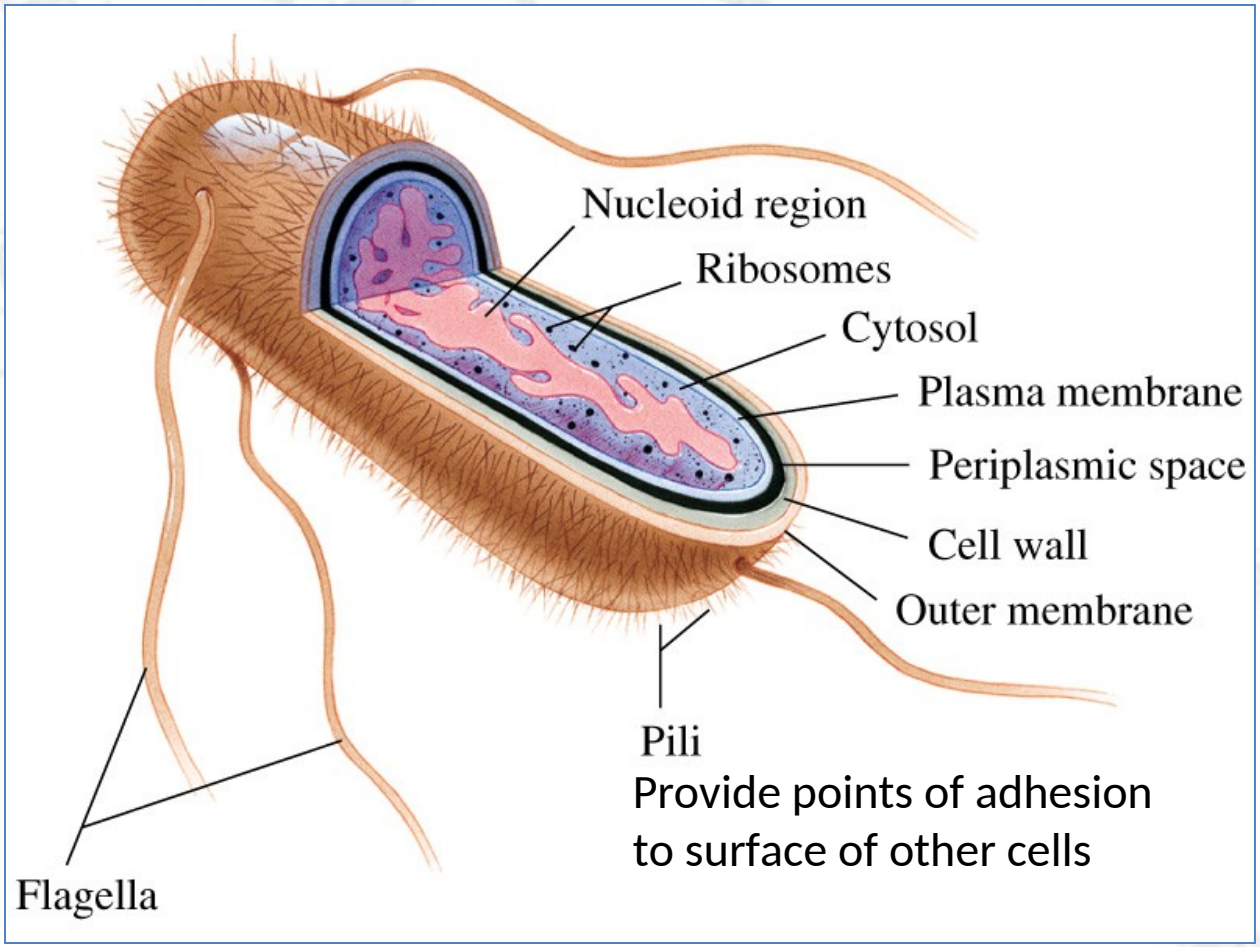
Cells …

1. Prokaryote cells: cells that does not contain membrane-bound nucleus. Example, bacteria and blue-green algae (cyanobacteria)

- **Plasma membrane:** encloses the cytoplasm
- Lack the membranous subcellular organelles
- **The nucleoid:** contain prokaryotic ‘chromosome’
- **Flagella:** tail-like appendages used for movement of the bacteria through its surrounding



- **Bacterial cell wall:** Peptidoglycan (complex of oligosaccharides and protein) cell wall protects the cell from mechanical and osmotic pressure



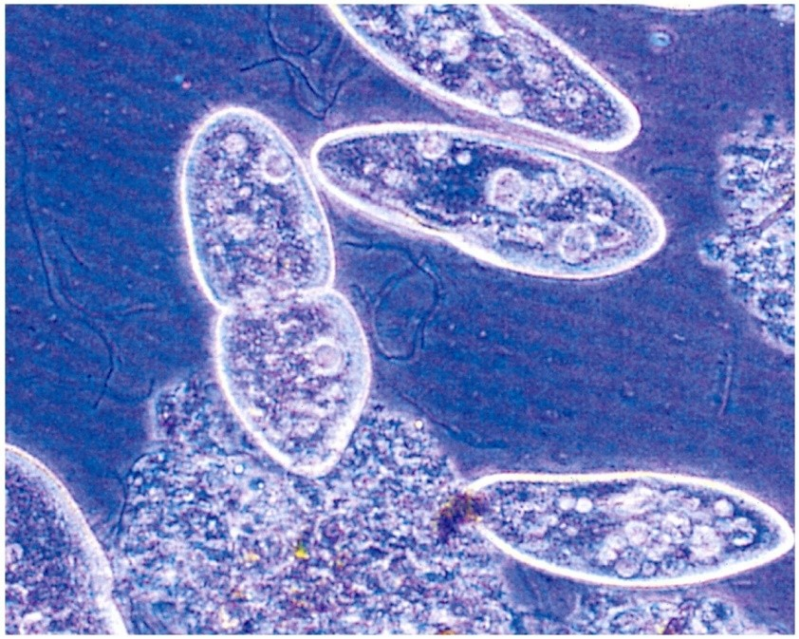
Provide points of adhesion to surface of other cells

Major Features of Prokaryotic Cells

Structure	Molecular Composition	Function
Cell wall	Peptidoglycan: a rigid framework of polysaccharide cross-linked by short peptide chains. Some bacteria possess a lipopolysaccharide- and protein-rich outer membrane.	Mechanical support, shape, and protection against swelling in hypotonic media. The cell wall is a porous nonselective barrier that allows most small molecules to pass.
Cell membrane	The cell membrane is composed of about 45% lipid and 55% protein. The lipids form a bilayer that is a continuous nonpolar hydrophobic phase in which the proteins are embedded.	The cell membrane is a highly selective permeability barrier that controls the entry of most substances into the cell. Important enzymes in the generation of cellular energy are located in the membrane.
Nuclear area or nucleoid	The genetic material is a single tightly coiled DNA molecule 2 nm in diameter but over 1 mm in length (molecular mass of *E. coli* DNA is 3×10^9 daltons; 4.64×10^6 nucleotide pairs).	DNA is the blueprint of the cell, the repository of the cell's genetic information. During cell division, each strand of the double-stranded DNA molecule is replicated to yield two double-helical daughter molecules. Messenger RNA (mRNA) is transcribed from DNA to direct the synthesis of cellular proteins.
Ribosomes	Bacterial cells contain about 15,000 ribosomes. Each is composed of a small (30S) subunit and a large (50S) subunit. The mass of a single ribosome is 2.3×10^6 daltons. It consists of 65% RNA and 35% protein.	Ribosomes are the sites of protein synthesis. The mRNA binds to ribosomes, and the mRNA nucleotide sequence specifies the protein that is synthesized.
Storage granules	Bacteria contain granules that represent storage forms of polymerized metabolites such as sugars or β-hydroxybutyric acid.	When needed as metabolic fuel, the monomeric units of the polymer are liberated and degraded by energy-yielding pathways in the cell.
Cytosol	Despite its amorphous appearance, the cytosol is now recognized to be an organized gelatinous compartment that is 20% protein by weight and rich in the organic molecules that are the intermediates in metabolism.	The cytosol is the site of intermediary metabolism, the interconnecting sets of chemical reactions by which cells generate energy and form the precursors necessary for biosynthesis of macromolecules essential to cell growth and function.

Cells …

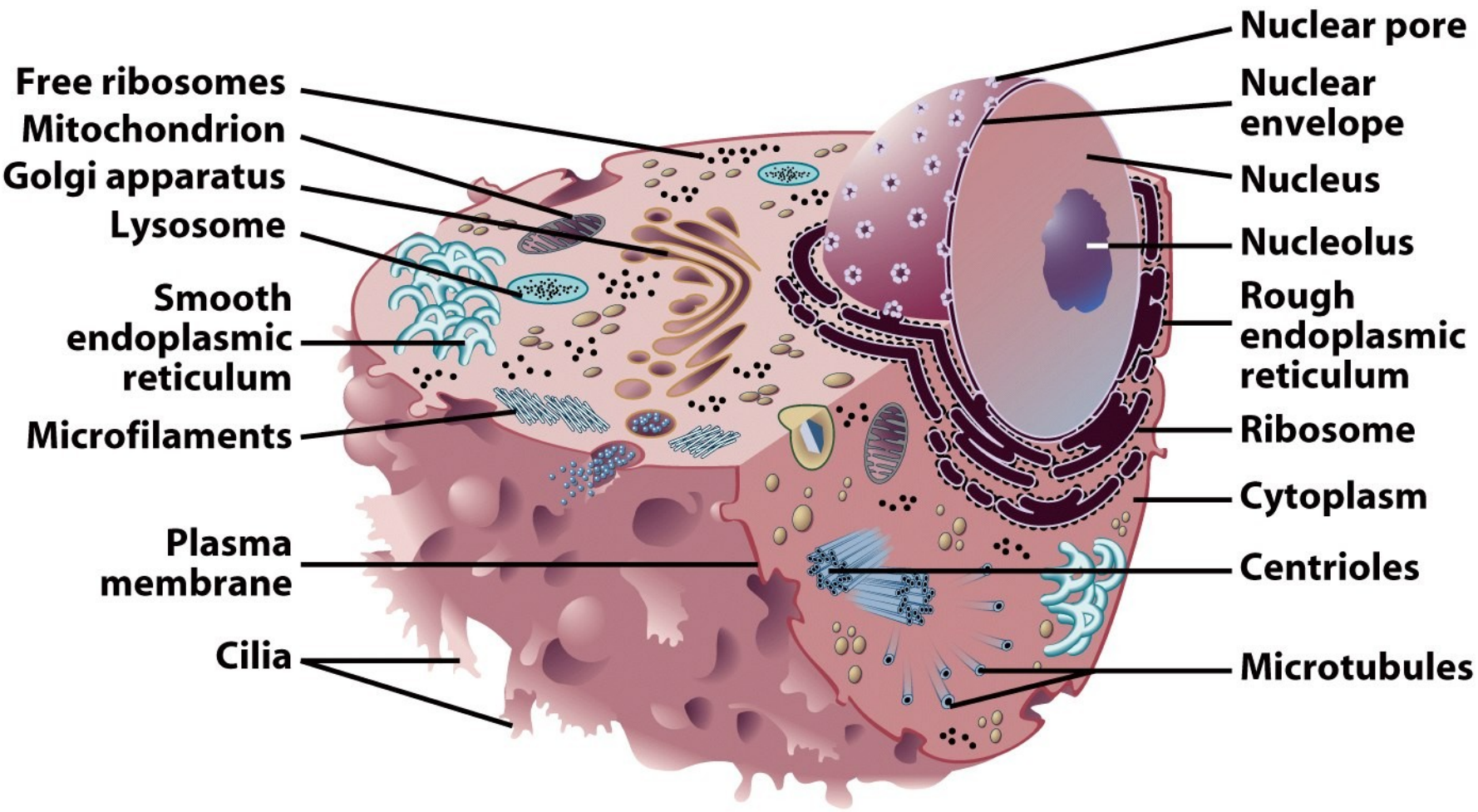
2. Eukaryotes
   - Cells with membrane-bound nucleus
   - Have a number of membrane-bound subcellular organelles, each of which has a specific function.
     - Example: animal cells, plant cells, fungi, protists



Protozoan

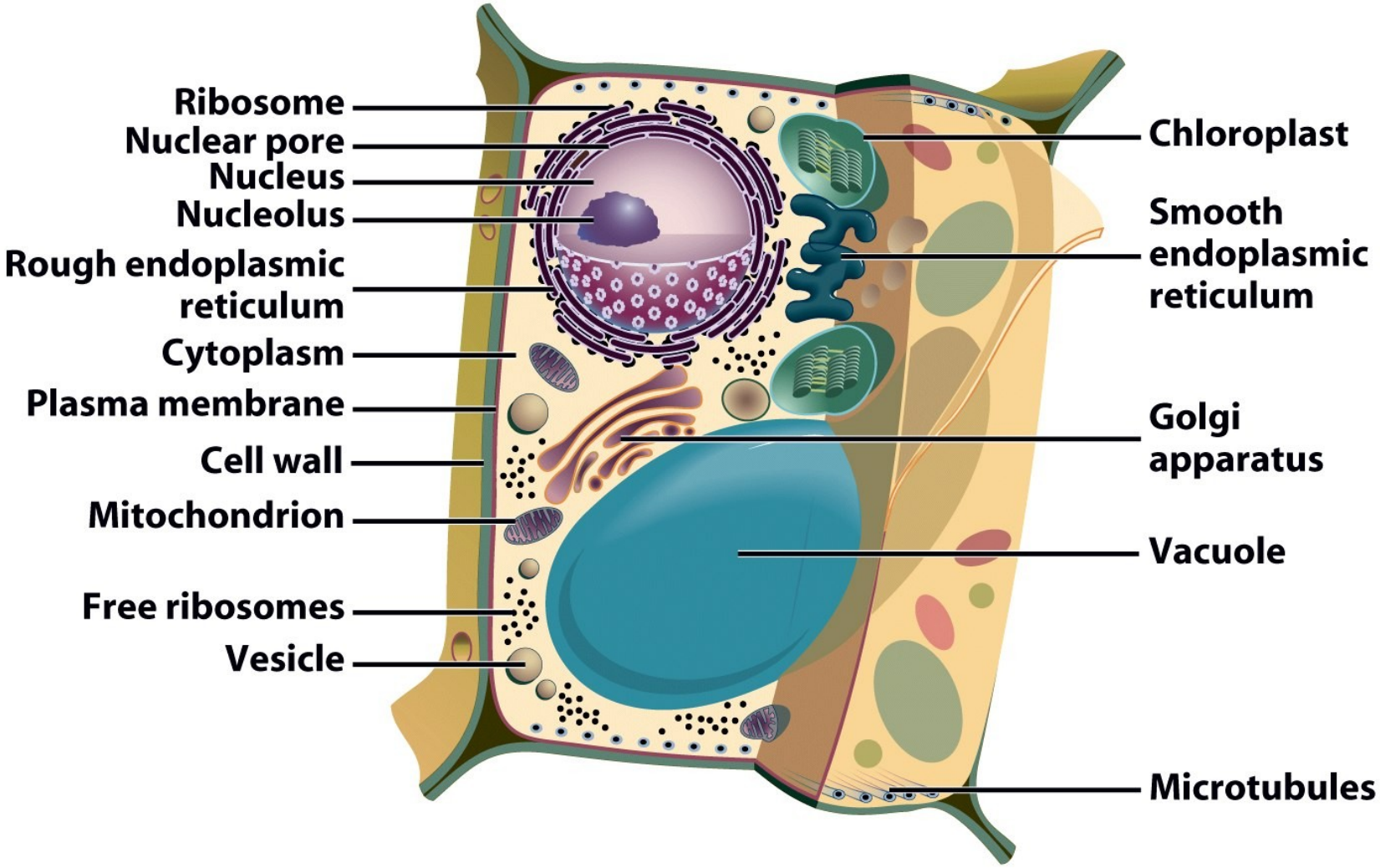
Cells …

- **Representative Animal Cell**



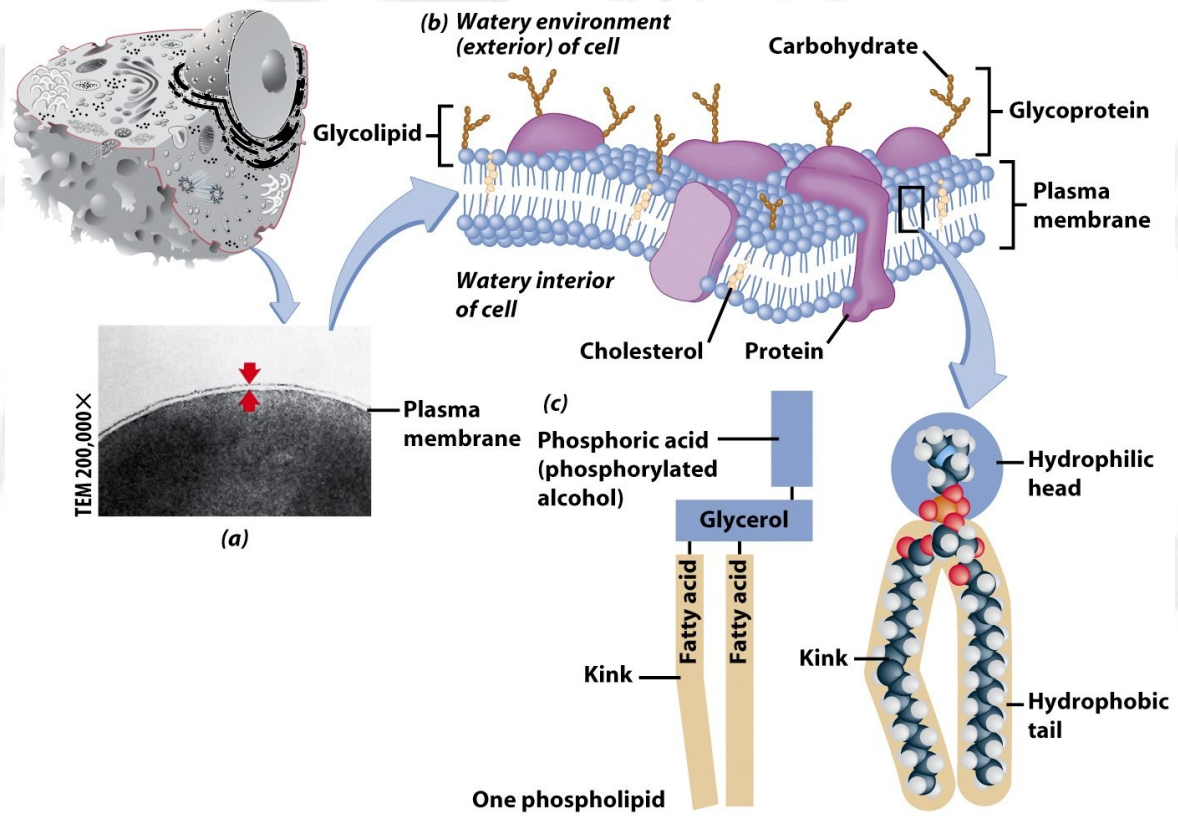
Cells …

- **Representative Plant Cell**



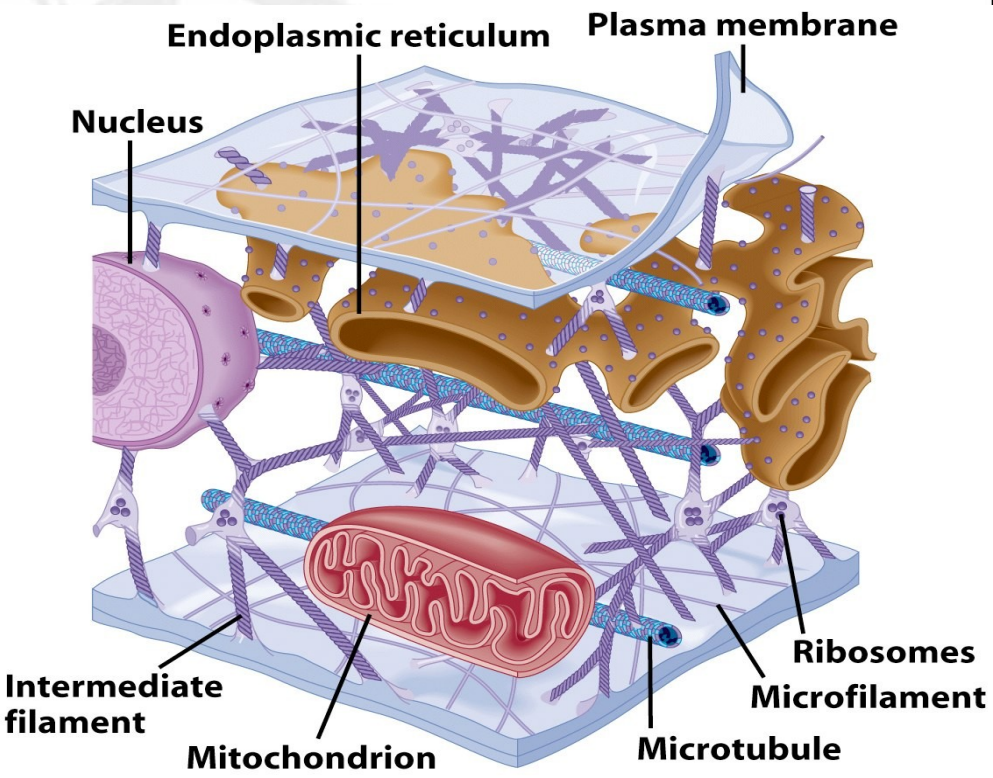
Cells …

- **Plasma membrane:** defines the periphery of the cell, separating its contents from the surroundings and regulates movement of materials into and out of cell
- Double layer of phospholipids, sterols & proteins



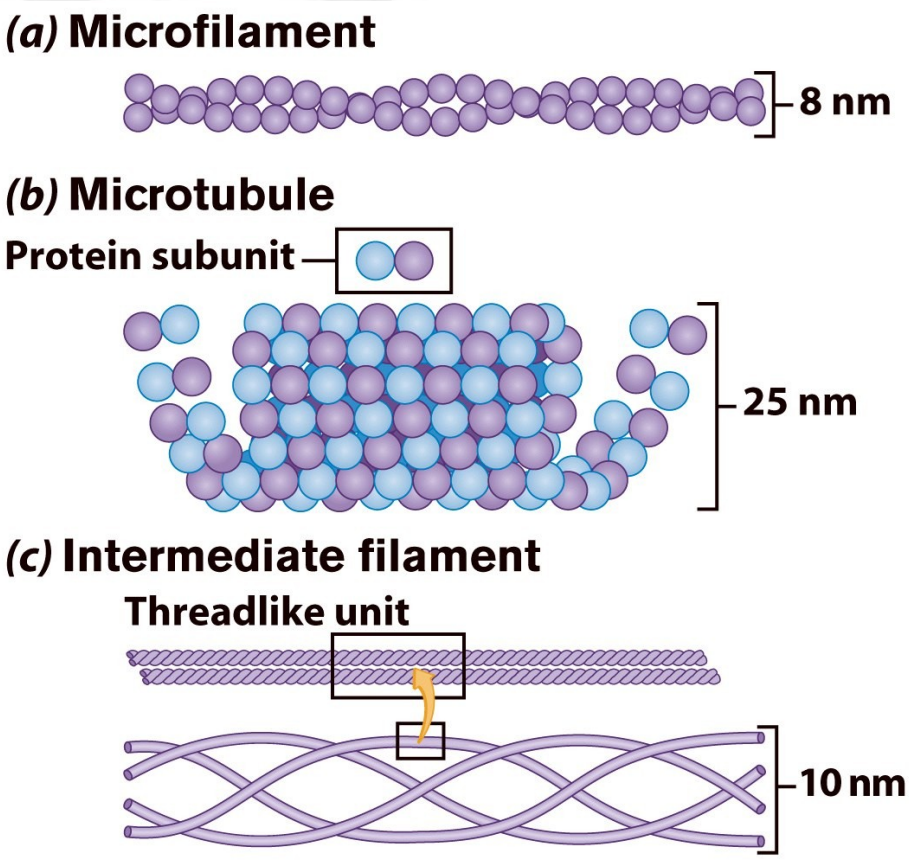
Cells …

- **Cytoplasm:** The internal volume bounded by the plasma membrane
  - Viscous fluid containing organelles
  - components of cytoplasm
    - Interconnected filaments & fibers
    - Fluid = cytosol
    - Organelles (not nucleus)
    - Storage substances



Cells …

- Cytoskeleton
  - Filaments & fibers
  - Made of 3 fiber types
    - Microfilaments
    - Microtubules
    - Intermediate filaments
  - 3 functions:
    - mechanical support
    - anchor organelles
    - help move substances



Major Features of a Typical Animal Cell

Structure	Molecular Composition	Function
Extracellular matrix	The surfaces of animal cells are covered with a flexible and sticky layer of complex carbohydrates, proteins, and lipids.	This complex coating is cell-specific, serves in cell – cell recognition and communication, creates cell adhesion, and provides a protective outer layer.
Cell membrane (plasma membrane)	Roughly 50:50 lipid:protein as a 5-nm-thick continuous sheet of lipid bilayer in which a variety of proteins are embedded.	The plasma membrane is a selectively permeable outer boundary of the cell, containing specific systems—pumps, channels, transporters—for the exchange of nutrients and other materials with the environment. Important enzymes are also located here.
Nucleus	The nucleus is separated from the cytosol by a double membrane, the nuclear envelope. The DNA is complexed with basic proteins (histones) to form chromatin fibers, the material from which chromosomes are made. A distinct RNA-rich region, the nucleolus, is the site of ribosome assembly.	The nucleus is the repository of genetic information encoded in DNA and organized into chromosomes. During mitosis, the chromosomes are replicated and transmitted to the daughter cells. The genetic information of DNA is transcribed into RNA in the nucleus and passes into the cytosol where it is translated into protein by ribosomes.
Mitochondria	Mitochondria are organelles surrounded by two membranes that differ markedly in their protein and lipid composition. The inner membrane and its interior volume, the matrix, contain many important enzymes of energy metabolism. Mitochondria are about the size of bacteria, ≈1 μm. Cells contain hundreds of mitochondria, which collectively occupy about one-fifth of the cell volume.	Mitochondria are the power plants of eukaryotic cells where carbohydrates, fats, and amino acids are oxidized to CO_2 and H_2O. The energy released is trapped as high-energy phosphate bonds in ATP.
Golgi apparatus	A system of flattened membrane-bounded vesicles often stacked into a complex. Numerous small vesicles are found peripheral to the Golgi and contain secretory material packaged by the Golgi.	Involved in the packaging and processing of macromolecules for secretion and for delivery to other cellular compartments.

Major Features of Typical Animal Cell (continued)

Endoplasmic reticulum (ER) and ribosomes	Flattened sacs, tubes, and sheets of internal membrane extending throughout the cytoplasm of the cell and enclosing a large interconnecting series of volumes called *cisternae*. The ER membrane is continuous with the outer membrane of the nuclear envelope. Portions of the sheetlike areas of the ER are studded with ribosomes, giving rise to *rough ER*. Eukaryotic ribosomes are larger than prokaryotic ribosomes.	The endoplasmic reticulum is a labyrinthine organelle where both membrane proteins and lipids are synthesized. Proteins made by the ribosomes of the rough ER pass through the outer ER membrane into the cisternae and can be transported via the Golgi to the periphery of the cell. Other ribosomes unassociated with the ER carry on protein synthesis in the cytosol.
Lysosomes	Lysosomes are vesicles 0.2–0.5 μm in diameter, bounded by a single membrane. They contain hydrolytic enzymes such as proteases and nucleases which, if set free, could degrade essential cell constituents. They are formed by budding from the Golgi apparatus.	Lysosomes function in intracellular digestion of materials entering the cell via phagocytosis or pinocytosis. They also function in the controlled degradation of cellular components.
Peroxisomes	Like lysosomes, peroxisomes are 0.2–0.5 μm single-membrane–bounded vesicles. They contain a variety of oxidative enzymes that use molecular oxygen and generate peroxides. They are formed by budding from the smooth ER.	Peroxisomes act to oxidize certain nutrients, such as amino acids. In doing so, they form potentially toxic hydrogen peroxide, H_2O_2, and then decompose it to H_2O and O_2 by way of the peroxide-cleaving enzyme catalase.
Cytoskeleton	The cytoskeleton is composed of a network of protein filaments: actin filaments (or microfilaments), 7 nm in diameter; intermediate filaments, 8–10 nm; and microtubules, 25 nm. These filaments interact in establishing the structure and functions of the cytoskeleton. This interacting network of protein filaments gives structure and organization to the cytoplasm.	The cytoskeleton determines the shape of the cell and gives it its ability to move. It also mediates the internal movements that occur in the cytoplasm, such as the migration of organelles and mitotic movements of chromosomes. The propulsion instruments of cells—cilia and flagella—are constructed of microtubules.

References

1. Lehninger, Nelson Principles of Biochemistry. 4th ed
2. Robert K. Murray, Harper's Illustrated Biochemistry, 28th ed.
3. U. Satyanarayana, Biochemistry 3rd ed
4. Colleen Smith, Allen D. Marks, and Michael Lieberman, Marks' Medical Biochemistry: A clinical approach. 4th ed.

Thank You