BME 2901-BIOCHEMISTRY

Introduction to Biochemistry

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- Course objectives: to learn the basic principles of biochemistry, biochemical composition of the body and major biochemical reactions that occur in the body.
- Biochemistry aims to explain biological form and function in chemical terms.

The foundations of biochemistry

- Cellular Foundations
- Chemical Foundations
- Physical Foundations
- Genetic Foundations
- Evolutionary Foundations

Cellular Foundations of Biochemistry

- The smallest organisms consist of single cells and are microscopic.
- Larger, multicellular organisms contain many different types of cells, which vary in size, shape, and specialized function.
- Despite these obvious differences, all cells of the simplest and most complex organisms share certain fundamental properties, which can be seen at the biochemical level.

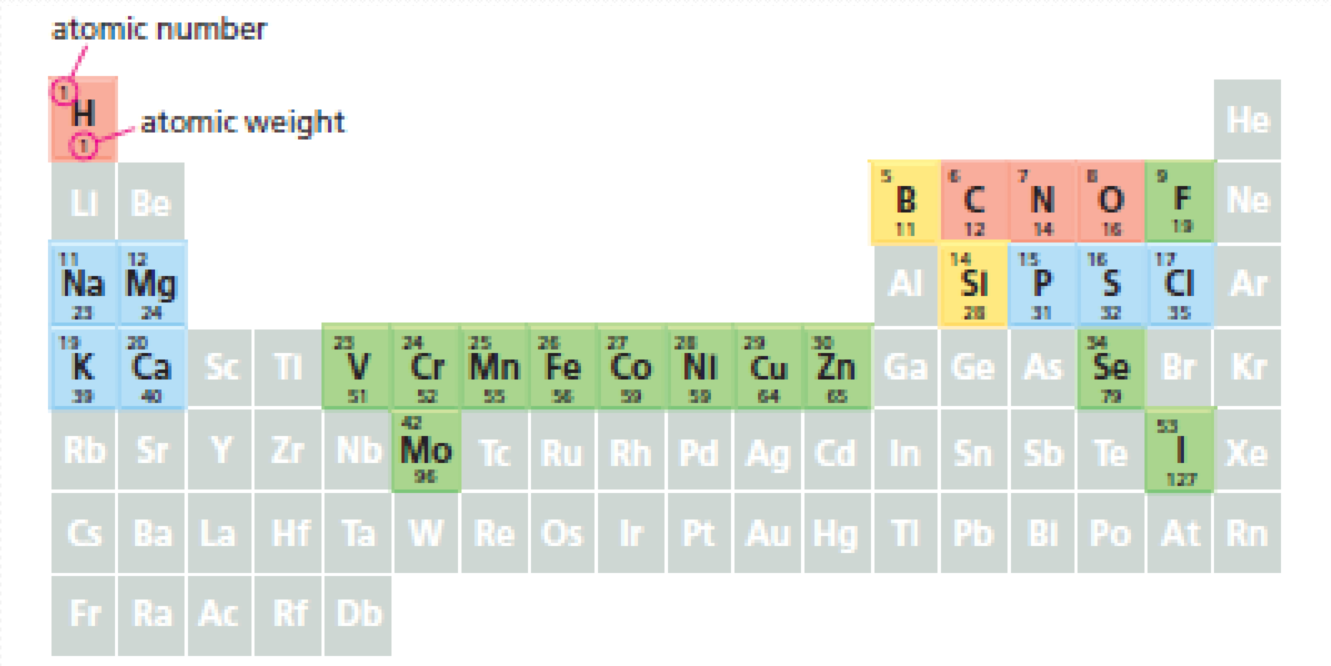
- Plasma membrane
  - Lipids and proteins
  - Flexible
  - Transport and Signaling
- Cytoplasm
  - Metabolites
  - Ribosomes
  - Cytoskeleton
- Nucleus or Nucleoid region
  - Genome
  - Prokaryotes and Eukaryotes

Chemical Foundations of Bichemistry

- Biochemistry aims to explain biological form and function in chemical terms.
- There is the universality of chemical intermediates and transformations in all organisms.

Chemical composition of the body

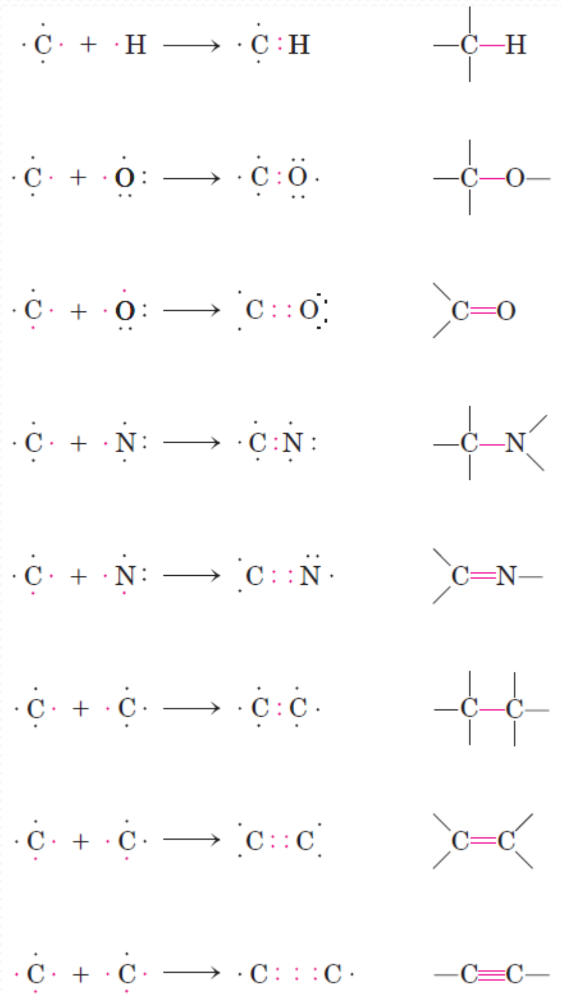
- The four most abundant elements in living organisms, in terms of percentage of total number of atoms, are hydrogen, oxygen, nitrogen, and carbon, which together make up more than 99% of the mass of most cells.
- They are the lightest elements capable of forming one, two, three, and four bonds, respectively.
- The trace elements represent a small fraction of the weight of the human body, but all are essential to life, usually because they are essential to the function of specific proteins, including enzymes.

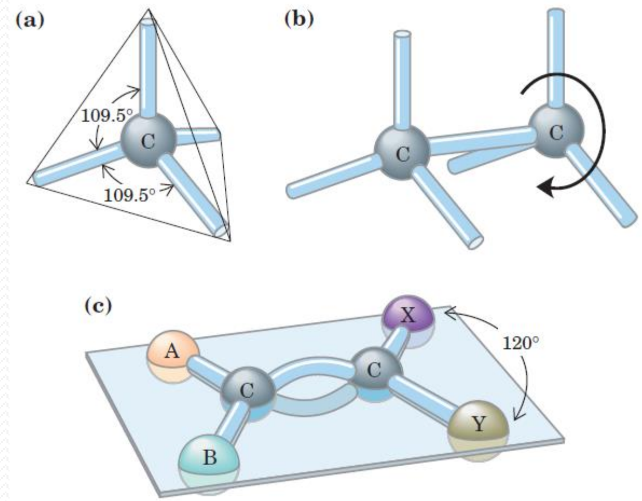


The four elements highlighted in *red* constitute 99% of the total number of atoms present in the human body and about 96% of our total weight. An additional seven elements, highlighted in *blue*, together represent about 0.9% of the total number of atoms. Other elements, shown in *green*, are required in trace amounts by humans. It remains unclear whether those elements shown in *yellow* are essential in humans or not.

Biomolecules Are Compounds of Carbon with a Variety of Functional Groups

- The chemistry of living organisms is organized around carbon, which can form single bonds with hydrogen atoms, and both single and double bonds with oxygen and nitrogen atoms.
- Of greatest significance in biology is the ability of carbon atoms to form very stable carbon–carbon single bonds.
- Each carbon atom can form single bonds with up to four other carbon atoms. Two carbon atoms also can share two (or three) electron pairs, thus forming double (or triple) bonds.





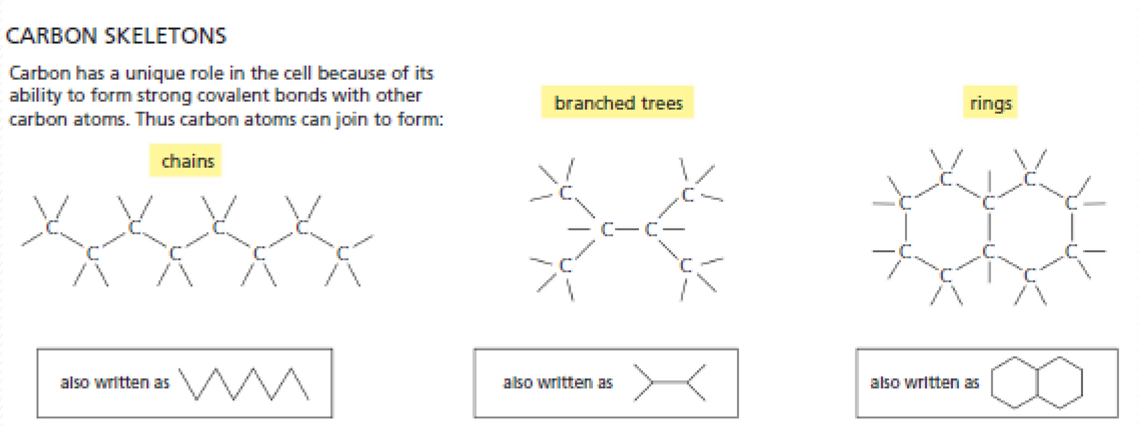
Geometry of carbon bonding.

(a) Carbon atoms have a characteristic tetrahedral arrangement of their four single bonds.

(b) Carbon–carbon single bonds have freedom of rotation.

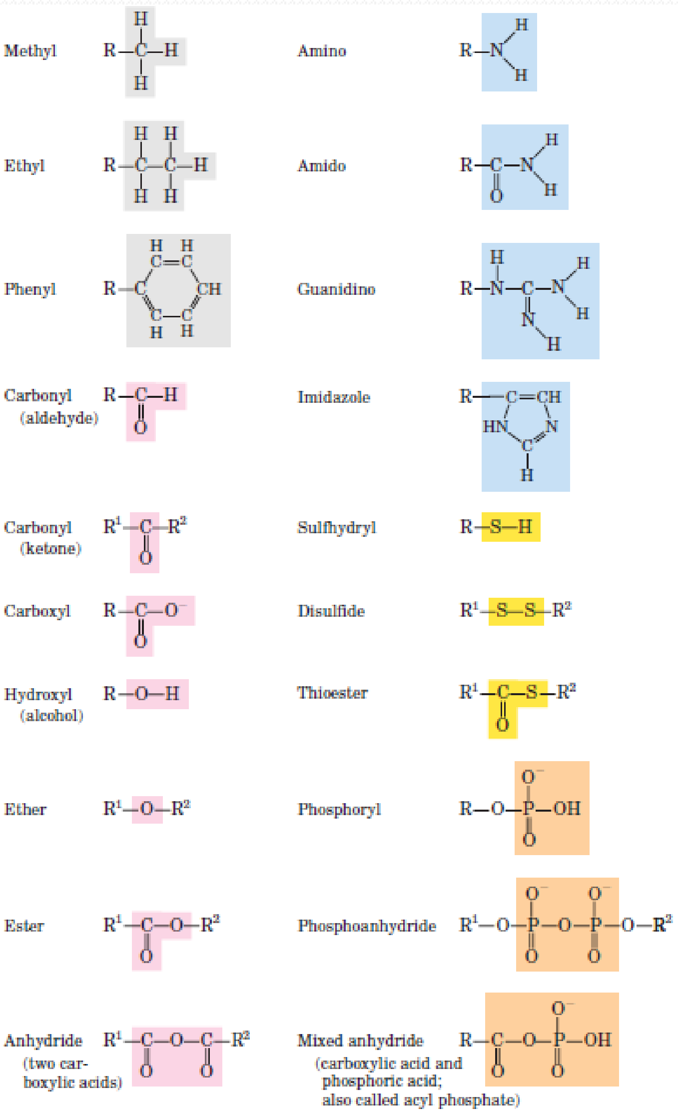
(c) Double bonds are shorter and do not allow free rotation. The two doubly bonded carbons and the atoms designated A, B, X, and Y all lie in the same rigid plane.

- Covalently linked carbon atoms in biomolecules can form linear chains, branched chains, and cyclic structures.



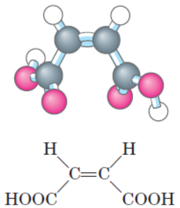
- To these carbon skeletons are added groups of other atoms, called **functional groups**, which confer specific chemical properties on the molecule.

- The bonding versatility of carbon was a major factor in the selection of carbon compounds for the molecular machinery of cells during the origin and evolution of living organisms.
- No other chemical element can form molecules of such widely different sizes and shapes or with such a variety of functional groups.
- Most biomolecules can be regarded as derivatives of hydrocarbons, with hydrogen atoms replaced by a variety of functional groups to yield different families of organic compounds.
- Typical of these are alcohols, which have one or more hydroxyl groups; amines, with amino groups; aldehydes and ketones, with carbonyl groups; and carboxylic acids, with carboxyl groups .
- Many biomolecules are polyfunctional, containing two or more different kinds of functional groups ,each with its own chemical characteristics and reactions.
- The chemical "personality" of a compound is determined not only by the chemistry of its functional groups and also by their disposition in three-dimensional space.

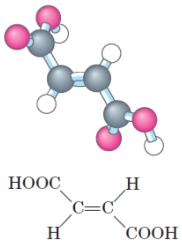


Stereochemistry

- The covalent bonds and functional groups of a biomolecule are central to its function, but the arrangement of the molecule's constituent atoms in three-dimensional space, **stereochemistry**, is also important.
- A carbon-containing compound commonly exists as **stereoisomers**, molecules with the same chemical bonds but different stereochemistry—that is, different **configuration**, the fixed spatial arrangement of atoms. Interactions between biomolecules are invariably **stereospecific**, requiring specific stereochemistry in the interacting molecules.

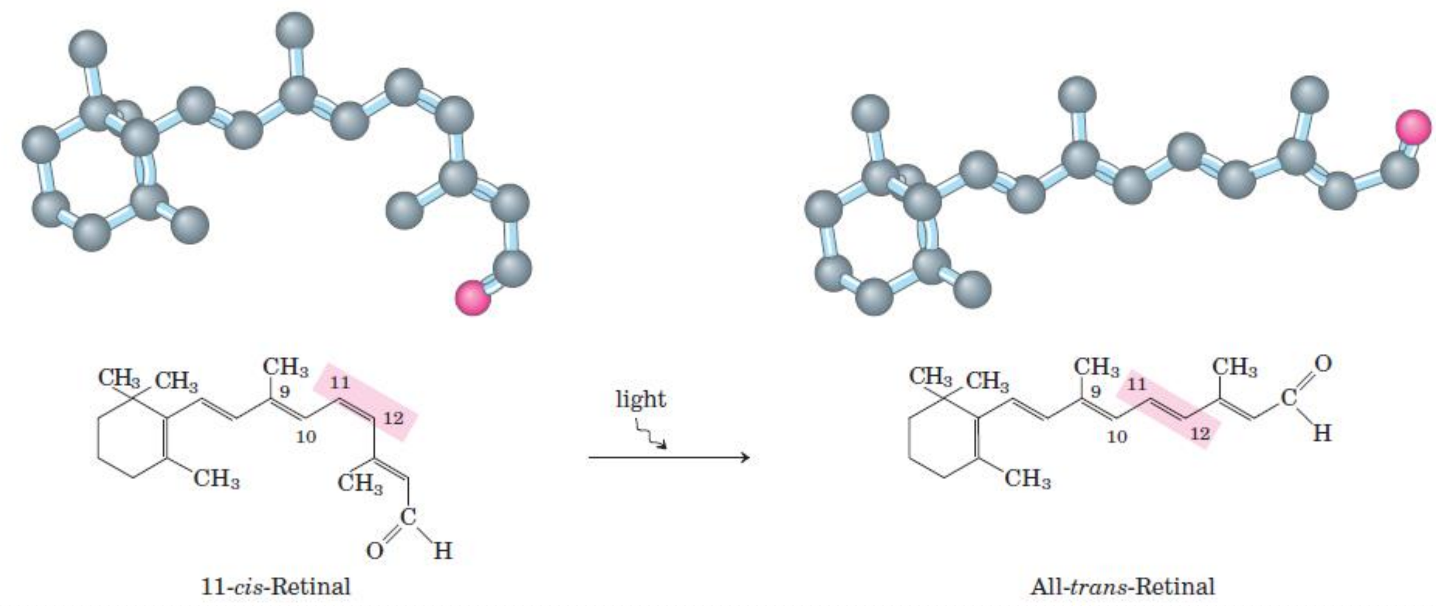


Maleic acid (cis)



Fumaric acid (trans)

Configuration can change biological function of a molecule



In the vertebrate retina, the initial event in light detection is the absorption of visible light by 11-*cis*-retinal. The energy of the absorbed light (about 250 kJ/mol) converts 11-*cis*-retinal to all-*trans*-retinal, triggering electrical changes in the retinal cell that lead to a nerve impulse.

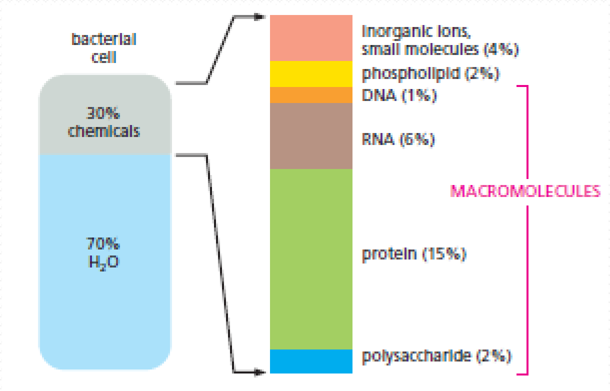
Cells Contain a Universal Set of Small Molecules

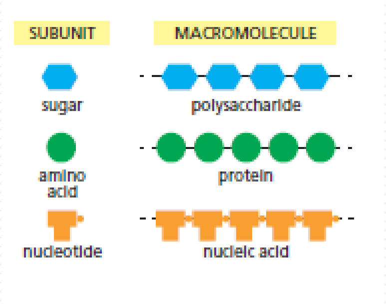
- This collection of molecules includes the common amino acids, nucleotides, sugars and their phosphorylated derivatives, and a number of mono-, di-, and tricarboxylic acids.
- The molecules are polar or charged, water soluble, and present in micromolar to millimolar concentrations.
- They are trapped within the cell because the plasma membrane is impermeable to them—although specific membrane transporters can catalyze the movement of some molecules into and out of the cell or between compartments in eukaryotic cells.
- The universal occurrence of the same set of compounds in living cells is a manifestation of the universality of metabolic design, reflecting the evolutionary conservation of metabolic pathways that developed in the earliest cells.
- Macromolecules are the major constituents of the cells.

Cells Contain Four Major Families of Macromolecules

- **Proteins**, **Nucleic acids**, **Carbohydrates**, **Lipids**
- All organic molecules are synthesized from—and are broken down into—the same set of simple compounds.
- Both their synthesis and their breakdown occur through sequences of simple chemical changes that are limited in variety and follow step-by-step rules that make up the **metabolism**.

- Macromolecules are the principal building blocks from which a cell is constructed and also the components that confer the most distinctive properties on living things.
- Macromolecules are constructed simply by covalently linking small organic monomers, or *subunits*, into long chains, or polymers.

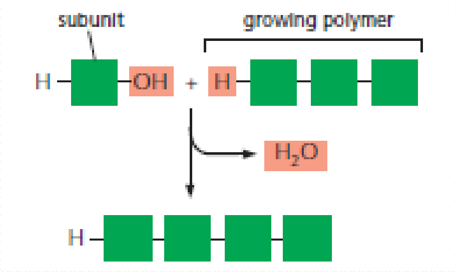




Macromolecules

- **Proteins,** long polymers of amino acids, constitute the largest fraction (besides water) of cells. Some proteins have catalytic activity and function as enzymes; others serve as structural elements, signal receptors, or transporters that carry specific substances into or out of cells. Proteins are perhaps the most versatile of all biomolecules.
- The **nucleic acids,** DNA and RNA, are polymers of nucleotides. They store and transmit genetic information, and some RNA molecules have structural and catalytic roles in supramolecular complexes.
- The **polysaccharides,** polymers of simple sugars such as glucose, have two major functions: as energy-yielding fuel stores and as extracellular structural elements with specific binding sites for particular proteins. Shorter polymers of sugars (oligosaccharides) attached to proteins or lipids at the cell surface serve as specific cellular signals.
- The **lipids,** greasy or oily hydrocarbon derivatives, serve as structural components of membranes, energy-rich fuel stores, pigments, and intracellular signals.

- Although the chemical reactions for adding subunits to each polymer are different in detail for proteins, nucleic acids, and polysaccharides, they share important features:
  - Each polymer grows by the addition of a monomer onto one end of the polymer chain via a condensation reaction, in which a molecule of water is lost with each subunit added.
  - In all cases, the reactions are catalyzed by specific enzymes, which ensure that only the appropriate monomer is incorporated.



- In a sense, the process resembles the repetitive operation of a machine in a factory—with some important differences:
  - First, most macromolecules are made from a set of monomers that are slightly different from one another; for example, proteins are constructed from 20 different amino acids.
  - Second, and most important, the polymer chain is not assembled at random from these subunits; instead the subunits are added in a particular order, or sequence.

Sequence of the subunits is the key

- The biological functions of proteins, nucleic acids, and many polysaccharides are absolutely dependent on the particular sequence of subunits in the linear chains.
- By varying the sequence of subunits, the cell can make an enormous diversity of the polymeric molecules.
- Thus, for a protein chain 200 amino acids long, there are 20^{200} possible combinations, while for a DNA molecule 10,000 nucleotides long, with its four different nucleotides, there are $4^{10,000}$ different possibilities.
- Thus the machinery of polymerization must be subject to a sensitive control that allows it to specify exactly which subunit should be added next to the growing polymer end.

- Many biological molecules are **macromolecules**, polymers of high molecular weight assembled from relatively simple precursors (**monomeric units** or **subunits**).
- Proteins, nucleic acids, and polysaccharides are produced by the polymerization of relatively small compounds.
- Synthesis of macromolecules is a major energy-consuming activity of cells. Macromolecules themselves may be further assembled into **supramolecular complexes** which then form the cell and its compartments.

Structural hierarchy in the molecular organization of cells

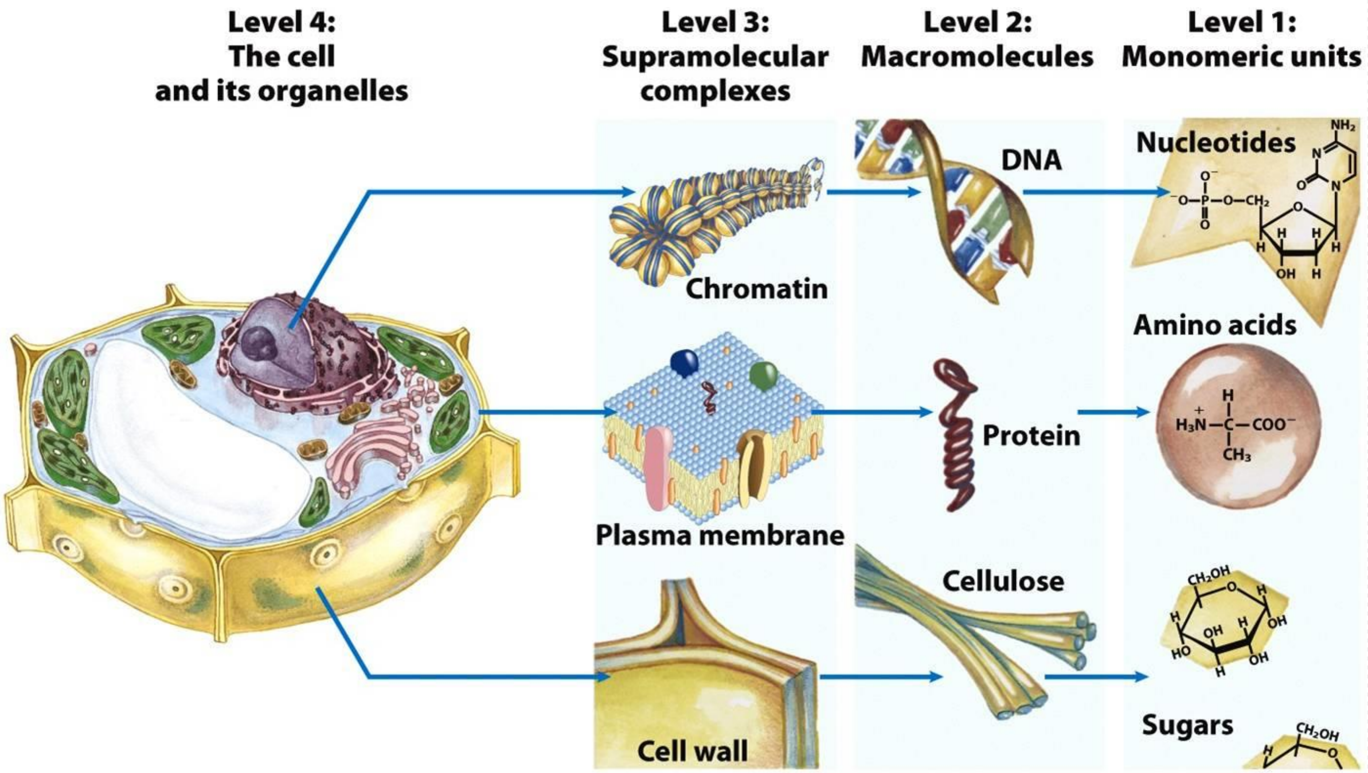
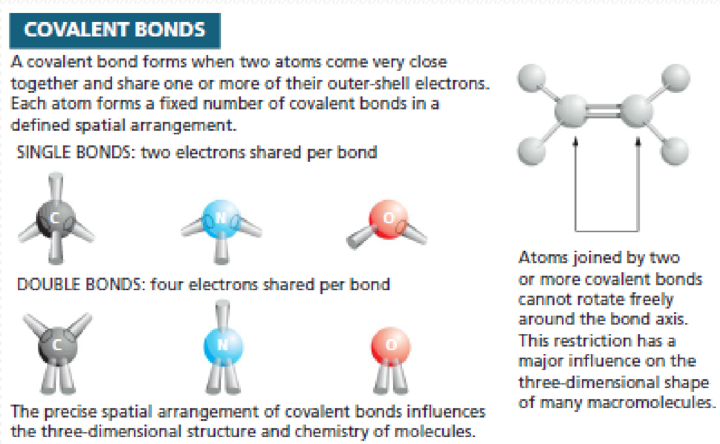


Figure 1-11
Lehninger Principles of Biochemistry, Fifth Edition

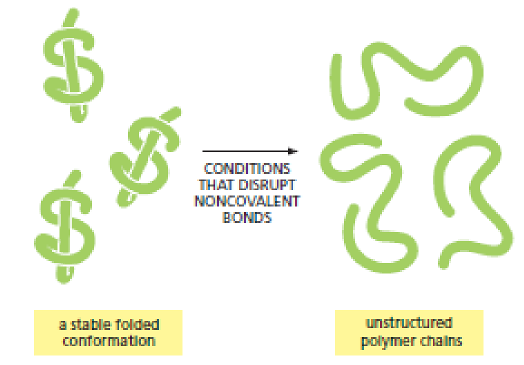
Covalent Bonds

- The monomeric subunits in proteins, nucleic acids, and polysaccharides are joined by covalent bonds.
- Most of the single covalent bonds that link together the subunits in a macromolecule allow rotation of the atoms they join; thus the polymer chain has great flexibility.
- In principle, this allows a single-chain macromolecule to adopt an almost unlimited number of shapes, or **conformations** under the influence of random thermal energy.



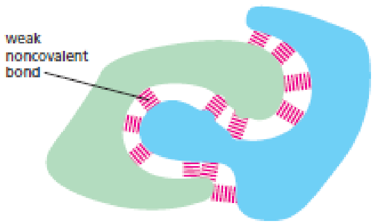
Non-covalent Bonds

- However, the shapes of most biological macromolecules are highly constrained because of weaker, noncovalent bonds that form between different parts of the molecule.
- These noncovalent interactions include **hydrogen bonds** (between polar groups), **ionic interactions** (between charged groups), **hydrophobic interactions** (among nonpolar groups in aqueous solution), and **van der Waals interactions**.
- These weaker interactions ensure that the polymer chain preferentially adopts one particular **conformation**, determined by the linear sequence of monomers in the chain.
- Most protein molecules and many of the RNA molecules found in cells fold tightly into one highly preferred conformation in this way.
- Although energies of those noncovalent interactions are smaller than those of covalent bonds, weak interactions between macromolecules can promote strong and specific binding and stabilize macro- and supramolecular complexes, producing their unique structures.



WEAK NONCOVALENT CHEMICAL BONDS

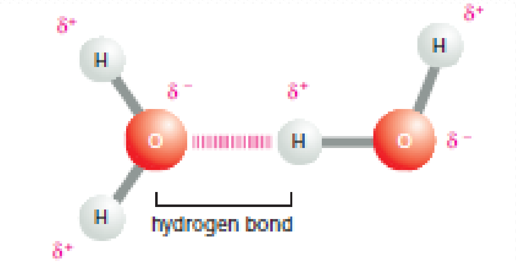
Organic molecules can interact with other molecules through three types of short-range attractive forces known as *noncovalent bonds*: van der Waals attractions, electrostatic attractions, and hydrogen bonds. The repulsion of hydrophobic groups from water is also important for these interactions and for the folding of biological macromolecules.



Weak noncovalent bonds have less than 1/20 the strength of a strong covalent bond. They are strong enough to provide tight binding only when many of them are formed simultaneously.

Hydrogen Bonds

- In each molecule of water (H_2O), the two H atoms are linked to the O atom by covalent bonds.
- The two H–O bonds are highly polar because the O is strongly attractive for electrons, whereas the H is only weakly attractive.
- Thus, there is an unequal distribution of electrons in a water molecule, with a preponderance of positive charge on the two H atoms and negative charge on the O.
- When a positively charged region of one water molecule (that is, one of its H atoms) comes close to a negatively charged region (that is, the O) of a second water molecule, the electrical attraction between them can establish a weak bond called a hydrogen bond.



Hydrogen Bonds

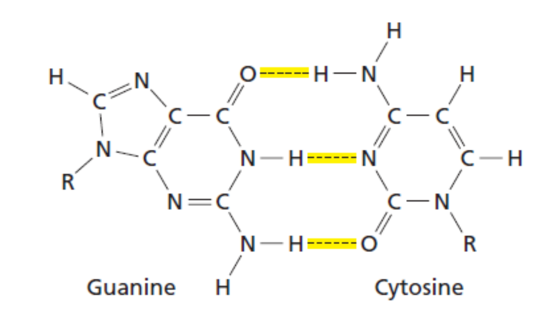
- These bonds are much weaker than covalent bonds and are easily broken by random thermal motions.
- However, the combined effect of many weak bonds is huge.
- Each water molecule can form hydrogen bonds through its two H atoms to two other water molecules, producing a network in which hydrogen bonds are being continually broken and formed. It is because of these interlocking hydrogen bonds that water at room temperature is a liquid—with a high boiling point and high surface tension—and not a gas.
- Without hydrogen bonds, life, as we know it, could not exist.

WATER STRUCTURE

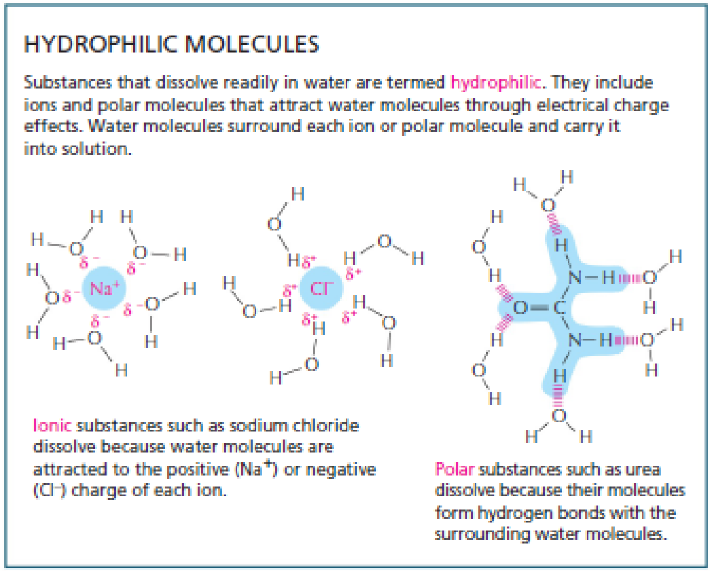
Molecules of water join together transiently in a hydrogen-bonded lattice.

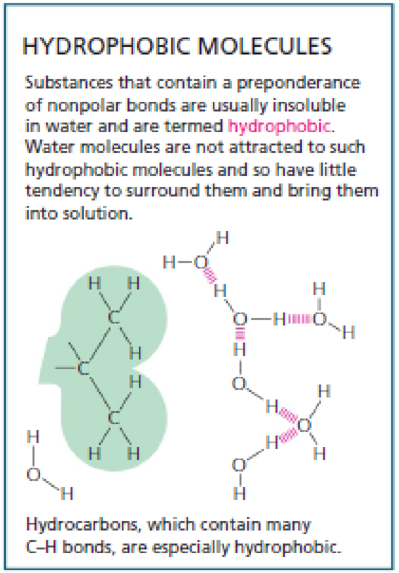
The cohesive nature of water is responsible for many of its unusual properties, such as high surface tension, high specific heat, and high heat of vaporization.

- Hydrogen bonds are not limited to water. In general, a hydrogen bond can form whenever a positively charged H atom held in one molecule by a polar covalent linkage comes close to a negatively charged atom—typically an oxygen or a nitrogen—belonging to another molecule.
- Hydrogen bonds can also occur between different parts of a single large molecule, where they often help the molecule fold into a particular shape, for example proteins and DNA.



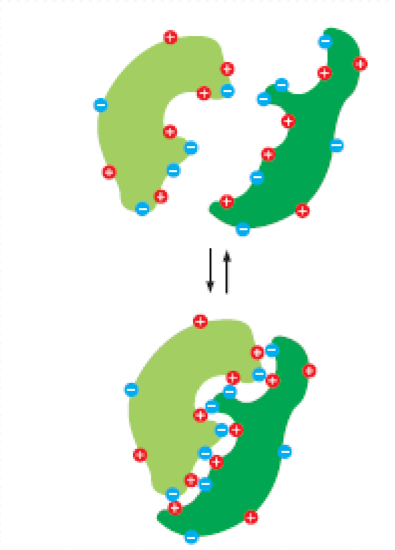
- Molecules, such as alcohols, that contain polar bonds and that can form hydrogen bonds mix well with water.
- Molecules carrying positive or negative charges (ions) likewise dissolve readily in water.
- Such molecules are termed **hydrophilic**, meaning that they are "water-loving." A large proportion of the molecules in the aqueous environment of a cell fall into this category, including sugars, DNA, RNA, and a majority of proteins.
- **Hydrophobic** ("water-fearing") molecules, by contrast, are uncharged and form few or no hydrogen bonds, and they do not dissolve in water.





Ionic Interactions

- Ionic interactions are extremely important in biology because they allow molecules to interact through electrical forces.
- Any large molecule with many polar groups will have a pattern of partial positive and negative charges on its surface. When such a molecule encounters a second molecule with a complementary set of charges, the two will be attracted to each other by **electrostatic attraction.**
- Ionic interactions are important in biology: an enzyme that binds a positively charged substrate will often use a negatively charged amino acid side chain to guide its substrate into the proper position.

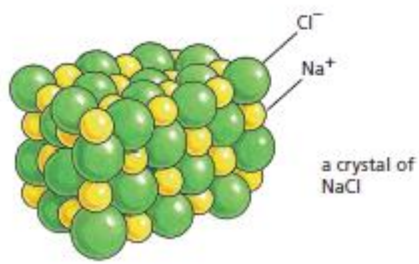


ELECTROSTATIC ATTRACTIONS

Attractive interactions occur both between fully charged groups (ionic bond) and between partially charged groups on polar molecules.

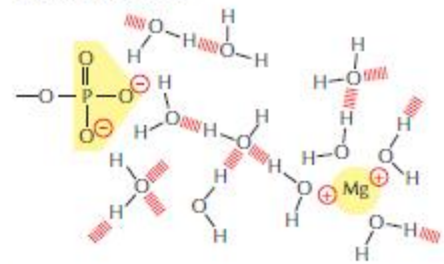
The force of attraction between the two partial charges, δ+ and δ−, falls off rapidly as the distance between the charges increases.

In the absence of water, ionic bonds are very strong. They are responsible for the strength of such minerals as marble and agate, and for crystal formation in common table salt, NaCl.

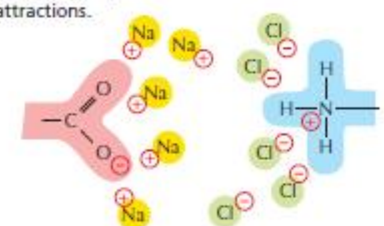


ELECTROSTATIC ATTRACTIONS IN AQUEOUS SOLUTIONS

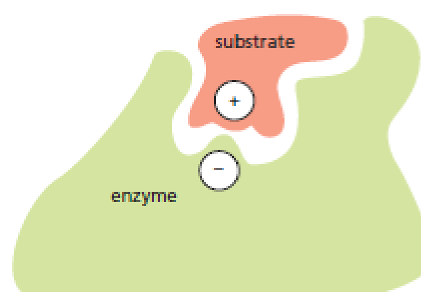
Charged groups are shielded by their interactions with water molecules. Electrostatic attractions are therefore quite weak in water.



Inorganic ions in solution can also cluster around charged groups and further weaken these electrostatic attractions.

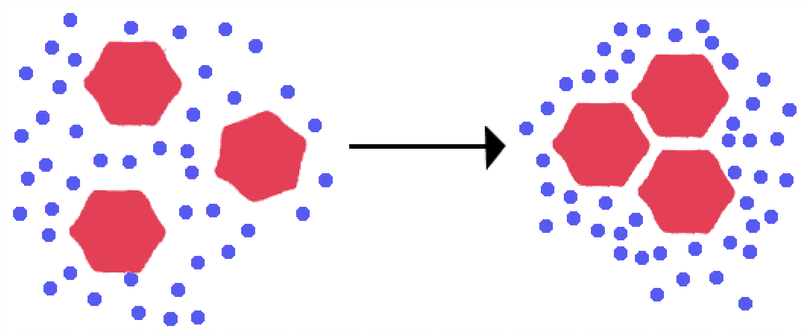


Despite being weakened by water and inorganic ions, electrostatic attractions are very important in biological systems. For example, an enzyme that binds a positively charged substrate will often have a negatively charged amino acid side chain at the appropriate place.



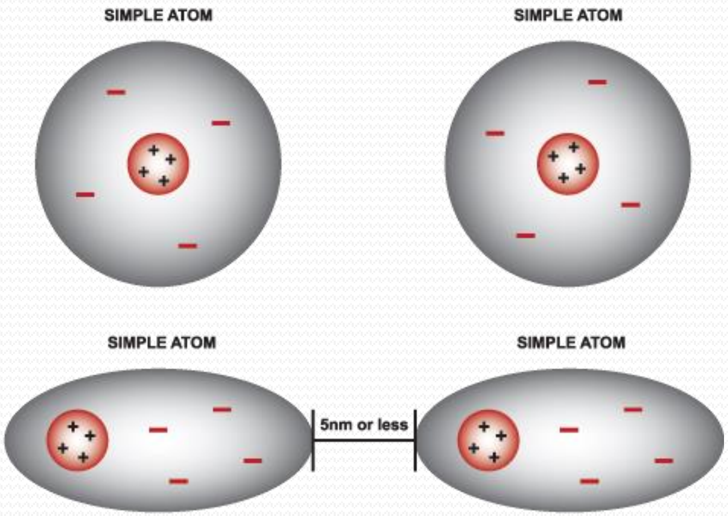
Hydrophobic Interactions

- Three-dimensional structure of water forces the hydrophobic portions of dissolved molecules together in order to minimize their disruptive effect on the hydrogen-bonded network of water molecules.
- This expulsion from the aqueous solution generates hydrophobic interaction.
- It describes the segregation of water and nonpolar substances, which maximizes hydrogen bonding between molecules of water and minimizes the area of contact between water and nonpolar molecules.



Van der Waals Interactions

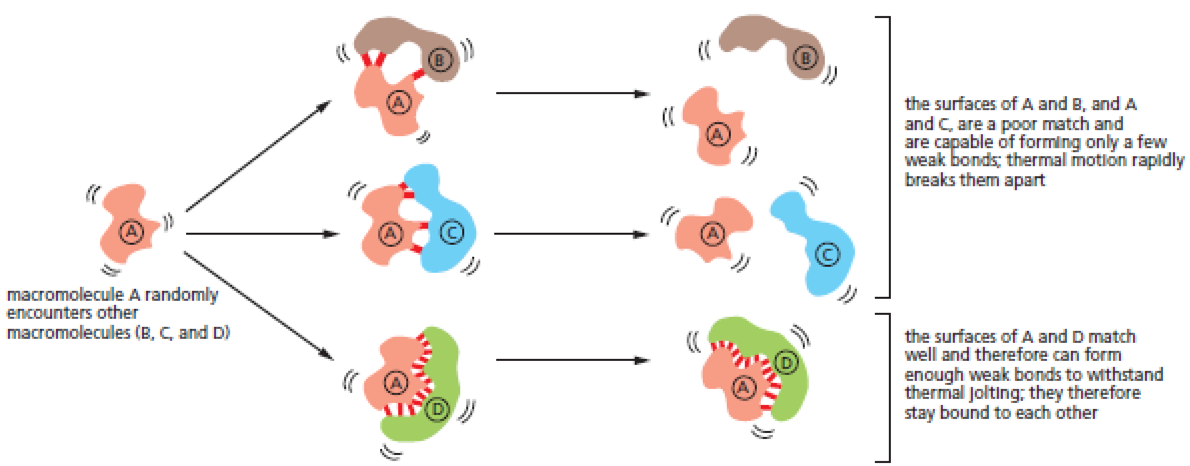
- Form of electrical attraction caused by fluctuating electric charges that arise whenever two atoms come within a very short distance of each other.



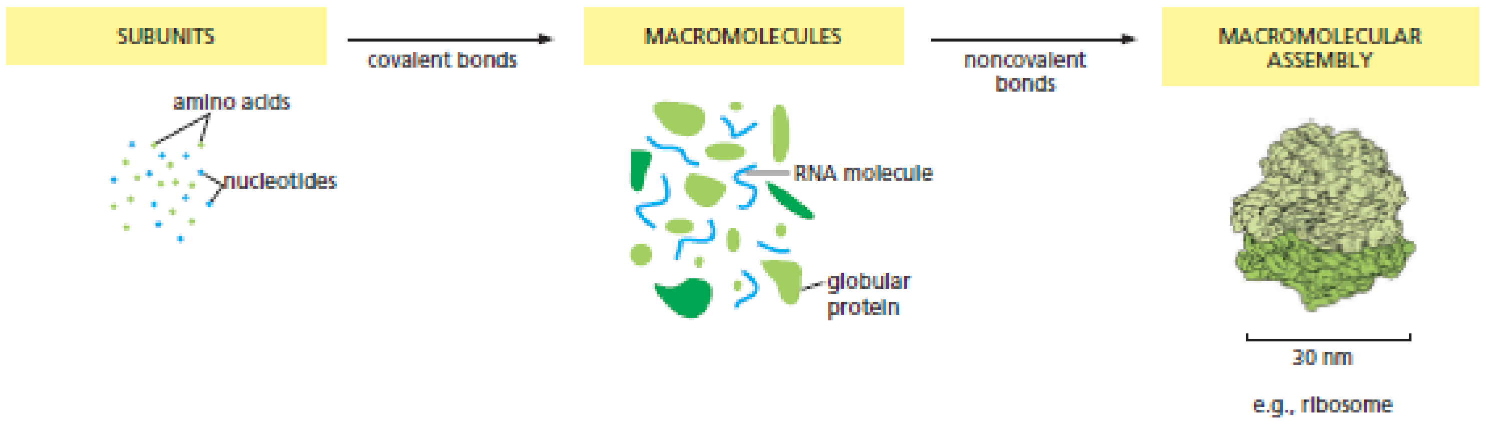
When two atoms come within 5 nanometers of each other, there will be a slight interaction between them, thus causing polarity and a slight attraction.

Noncovalent Bonds Allow a Macromolecule to Bind Other Selected Molecules

- Although noncovalent bonds are individually weak, they can add up to create a strong attraction between two molecules when these molecules fit together very closely so that many noncovalent bonds can occur between them.
- This form of molecular interaction provides for great specificity in the binding of a macromolecule to other small and large molecules, because the multipoint contacts required for strong binding make it possible for a macromolecule to select just one of the many thousands of different molecules present inside a cell.



- Binding of this type makes it possible for proteins to function as enzymes.
- It can also stabilize associations between any macromolecules, as long as their surfaces match closely.
- Noncovalent bonds thereby allow macromolecules to be used as building blocks for the formation of much larger structures.



The biological functions of macromolecules are dependent on:

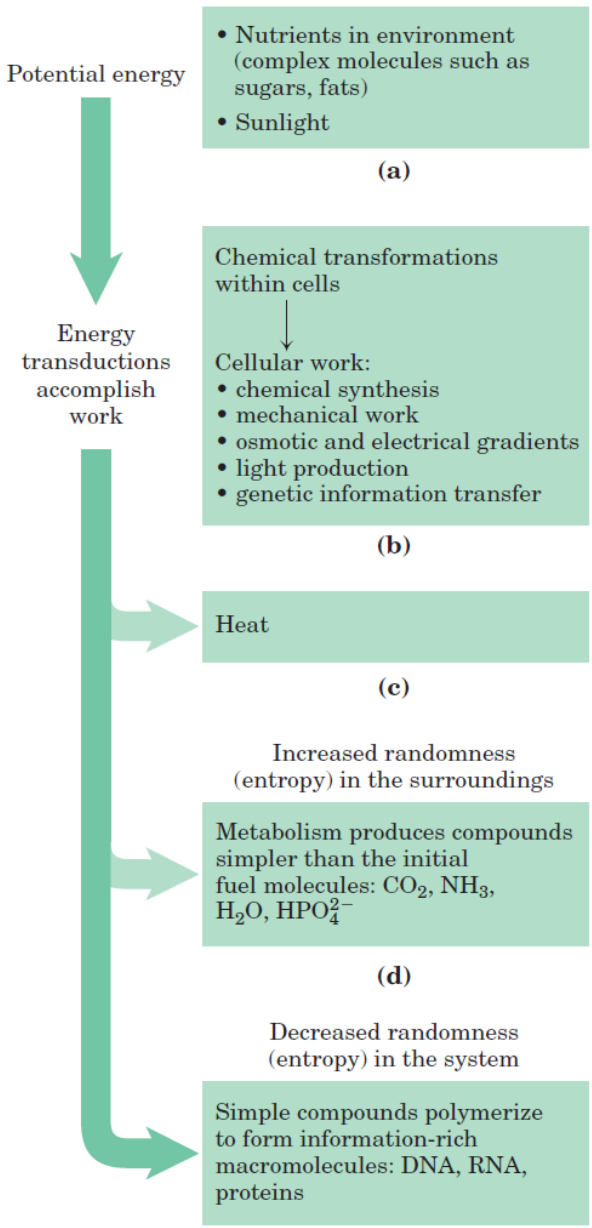
- Type of subunits
- Sequence of subunits
- Configuration of the molecule
- Conformation of the molecule

Physical Foundations of Biochemistry

- Living cells and organisms must perform work to stay alive and to reproduce themselves.
- The synthetic reactions that occur within cells, like the synthetic processes in any factory, require the input of energy.
- Energy is also consumed in the motion and the storage and expression of information without which structures rich in information inevitably become disordered and meaningless.

- In the course of evolution, cells have developed highly efficient mechanisms for coupling the energy obtained from sunlight or fuels to the many energyconsuming processes they must carry out.
- One goal of biochemistry is to understand, in quantitative and chemical terms, the means by which energy is extracted, channeled, and consumed in living cells. We can consider cellular energy conversions—like all other energy conversions—in the context of the laws of thermodynamics.

- Nearly all living organisms derive their energy, directly or indirectly, from the radiant energy of sunlight, which arises from thermonuclear fusion reactions carried out in the sun.
- Photosynthetic cells absorb light energy and use it to drive electrons from water to carbon dioxide, forming energy-rich products such as glucose ($C_6H_{12}O_6$), starch, and sucrose and releasing O_2 into the atmosphere.
- Nonphotosynthetic cells and organisms obtain the energy they need by oxidizing the energy-rich products of photosynthesis and then passing electrons to atmospheric O2 to form water, carbon dioxide, and other end products, which are recycled in the environment.
- Virtually all energy transductions in cells can be traced to this flow of electrons from one molecule to another, in a "downhill" flow from higher to lower electrochemical potential.

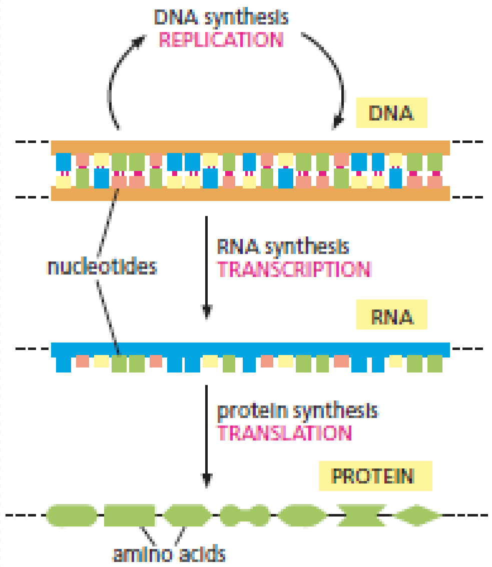


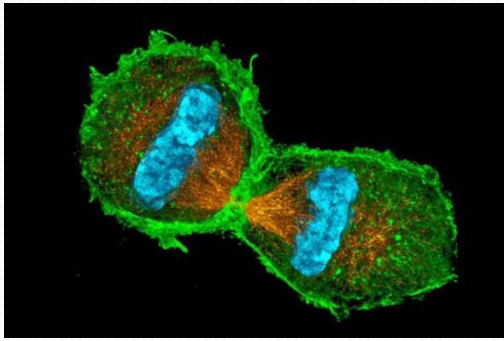
- To form covalent bonds between subunits to synthesize a biomolecule requires energy.
- The cell must invest energy to order the subunits in their correct sequence.
- Amino acids in a mixture do not spontaneously condense into a single type of protein, with a unique sequence.
- This would represent increased order in a population of molecules; but according to the second law of thermodynamics, the tendency in nature is toward ever-greater disorder in the universe: *the total entropy of the universe is continually increasing.*
- To bring about the synthesis of macromolecules from their monomeric units, free energy must be supplied to the system.

- The required free energy is supplied by the catabolism and coupled to a cell's energy-requiring reactions by the help of high energy compounds such as ATP.
- In living organisms, an exergonic reaction (liberating free energy) can be coupled to an endergonic (energy-requiring) reaction to drive otherwise unfavorable reactions.
- Enzymes reduces the activation energy for the reaction and greatly increases the reaction rate.

Genetic Foundations of Biochemistry

- Living cells and organisms have the ability to reproduce themselves for countless generations with nearly perfect fidelity.
- The sequence of the nucleotides, in DNA encodes the instructions for forming all other cellular components and provides a template for the production of identical DNA molecules to be distributed to progeny when a cell divides.
- The continued existence of a biological species requires its genetic information to be maintained in a stable form, expressed accurately in the form of gene products, and reproduced with a minimum of errors.
- Effective storage, expression, and reproduction of the genetic message defines individual species, distinguishes them from one another, and assures their continuity over successive generations.





Evolutionary Foundations of Biochemistry

- All modern organisms share a common evolutionary progenitor and were derived from it by a series of small changes (mutations), each of which conferred a selective advantage to some organism in some ecological niche.
- Occasional inheritable mutations yield an organism that is better suited for survival in an ecological niche and progeny that are preferentially selected.
- This process of mutation and selection is the basis for the Darwinian evolution that led from the first cell to all the organisms that now exist, and it explains the fundamental similarity of all living organisms.

structure
reaction
rate
enzyme
energy
living
properties
water
chemical
organisms
information
experiment
function
molecules
bond
substrate
affect
characteristics
activity
biological
catalytic
active
altering
enzymes
explain
describe
effect
functioning
initial
identify
extract
reactions
temperature
unique
relate
logic
product
adhesion
action
activation
abilities
carbohydrates
biomolecules
anabolism
alter
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capacity
compound
catalysts
concentration
cohesion
coenzyme
control
covalent
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denature
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design
earth
different
demonstrate
dehydration
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concerning
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determined
factors
enzymatic
group
heated
free
formation
formed
found
increasing
hydrolysis
hydrophilic
hydrogen
lab
levels
induced-fit
inhibition
hydrophobic
influence
intervals
isolated
investigate
oligosaccharide
ionic
organic
polypeptide
mixed
molecule
nucleic
particular
physical/chemical
parts/monomers
protein
related
responsible
repeating
tissue
system
triglyceride
possible
phospholipid
progress
nature
place
relationship
model
need
nomenclature
select
proteins
speeds
synthesis
sterol
substance
work