Chapter 1

Topic: Overview of basic principles

Four major themes of biochemistry

I.   What are living organism made from?

II.   How do organism acquire and use energy?

III. How does an organism maintain its identity across generation?

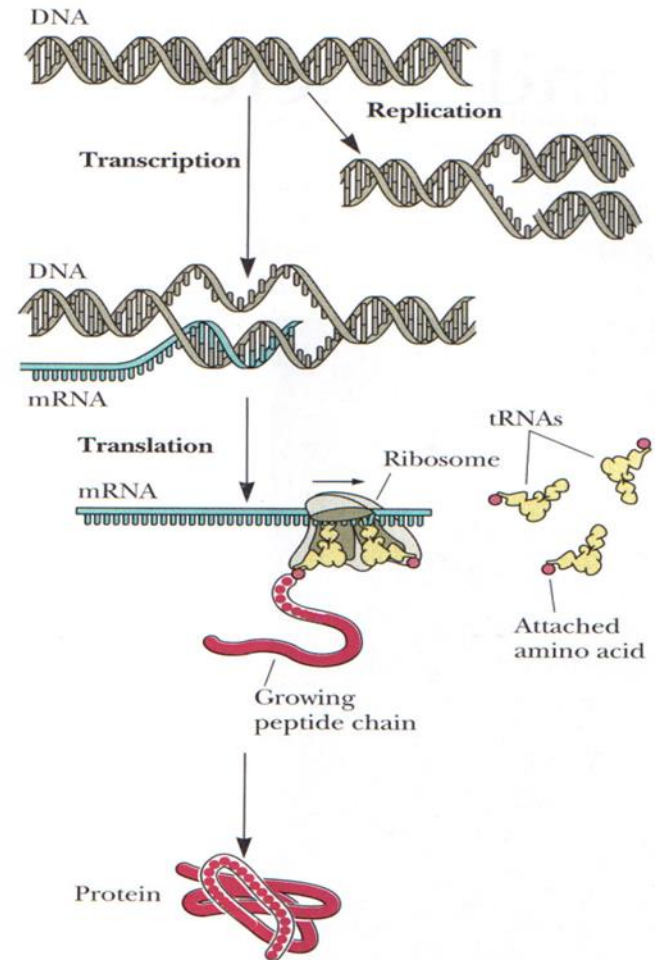IV.   How organism communicate with its environment?

Central dogma of molecular biology

1866 Gregor Mendel:
Plants contains a pair of factors,
one inherited from each parents.

1869 Friedrich Mieschet isolated
nucleic acids

1944 Avery, Mac Leod, Mc Carty –
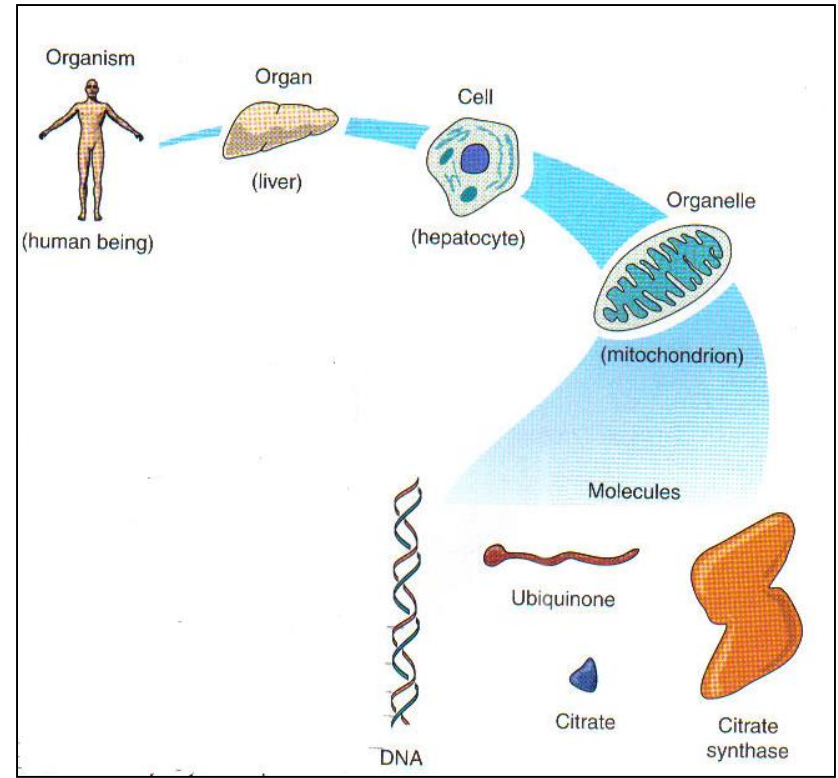DNA carry genetic information.

1958 F. Crieck formulated central
dogma of molecular biology

Biochemistry uses tools of chemistry to explain life on molecular level

Approach : reductionism

Living organism $\Rightarrow$ cells $\Rightarrow$
organelles/membranes $\Rightarrow$ **molecules**
Molecules $\Rightarrow$ composition???
      function ???
      structure (3D) ???
      reaction mechanism

Holistic approach – even complete set of information about all molecules in organism does not reveal how the organism live.
We need to study intact cells and organisms to understand how they live.

Processes of current interest:

Genomics: study of genetic code and its regulation

Proteomics: study or protein function as determined by genetic code

Cloning: insertion of foreign DNA into cell or duplication of an organism through a genetic modification

Epigenetics: the study of heritable changes in gene expression that occur without a change in DNA sequence.
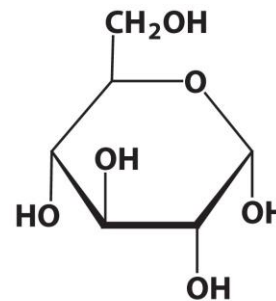
Biochemically important molecules:

Bio-macromolecules
      proteins (various structures and functions)
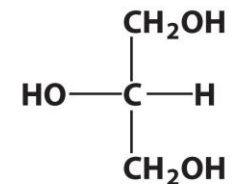   nucleic acids
      membranes

small molecules called metabolites.

Glucose

Glycerol

Unnumbered 1 p2
Biochemistry, Eighth Edition
© 2015 Macmillan Education

Cellular structure

- Viruses – smallest organized particle (nucleic acid and protein)

- Prokaryotic cells- smallest self-replicating organisms

  - Simple structure (bacterial cell, no defined nucleus)

- Eukaryotes – complex organism

  - Plasma membrane, cell wall, cytoplasm, cytosol, organells

All living organism single cell to complex organisms:

viruses (20 – 200nm), *eukaryotic cells* (10 – 100 μm)
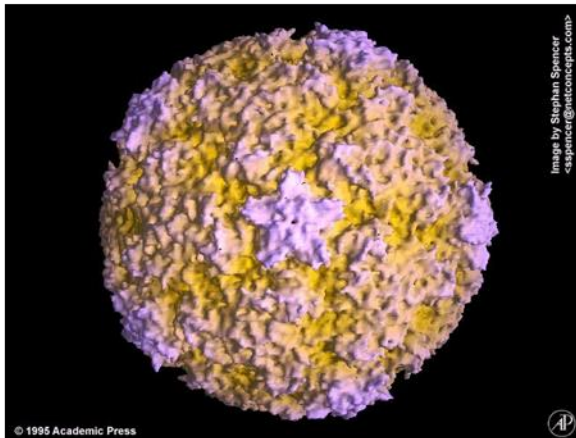
composed of same building blocks

Similar principles in –   replication
                             metabolism
                             ability to organize at the cell level

Key metabolic processes are common to many organisms.

Different organisms have macromolecules of similar structure and common biochemical processes suggest that all organisms evolved from a common ancestor.
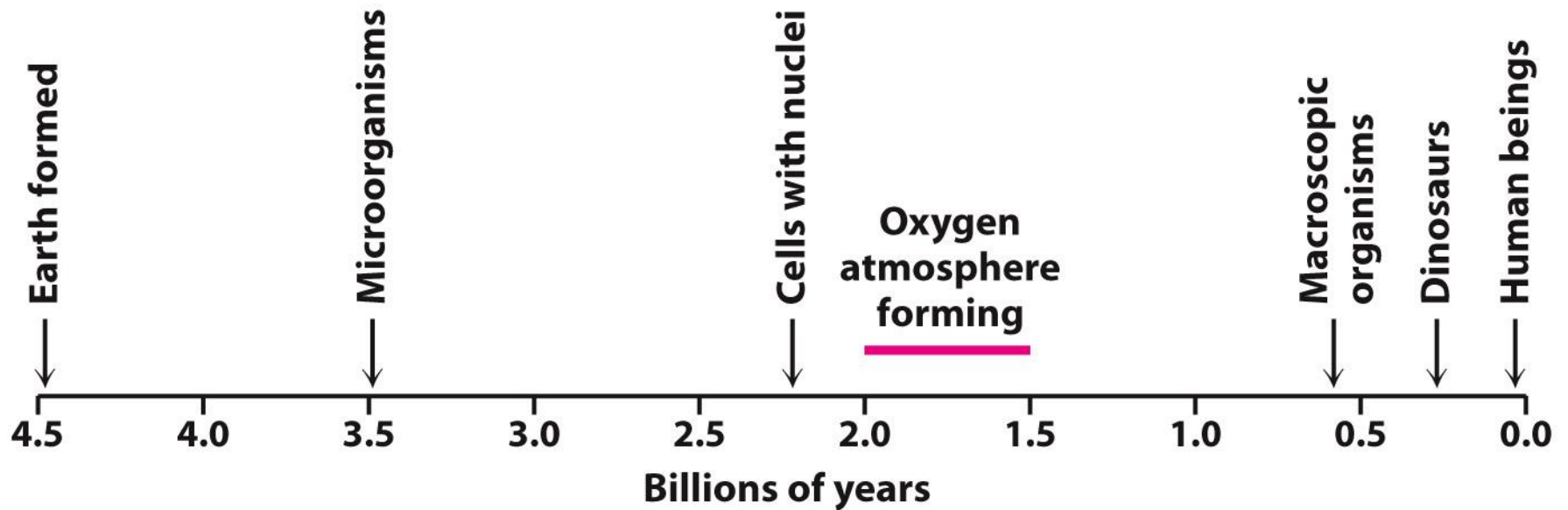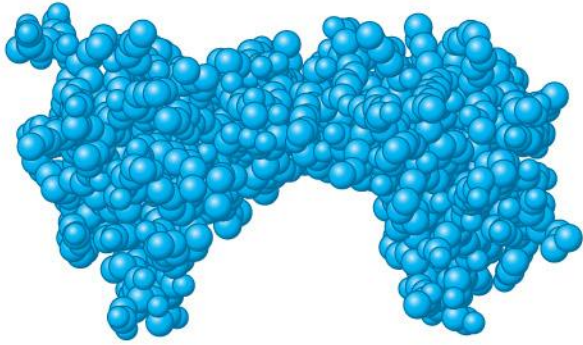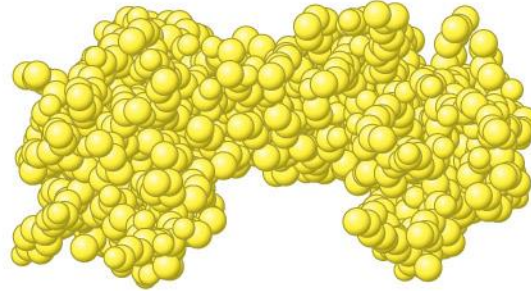

Figure 1.2
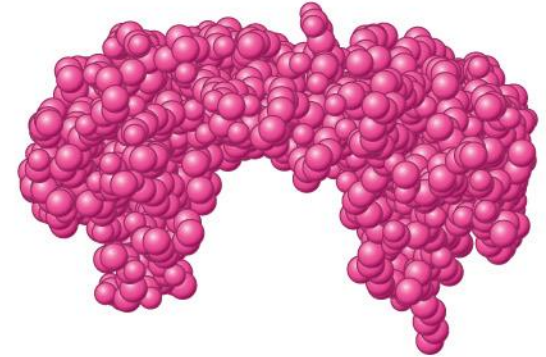*Biochemistry*, Eighth Edition
© 2015 Macmillan Education

TATA box binding protein

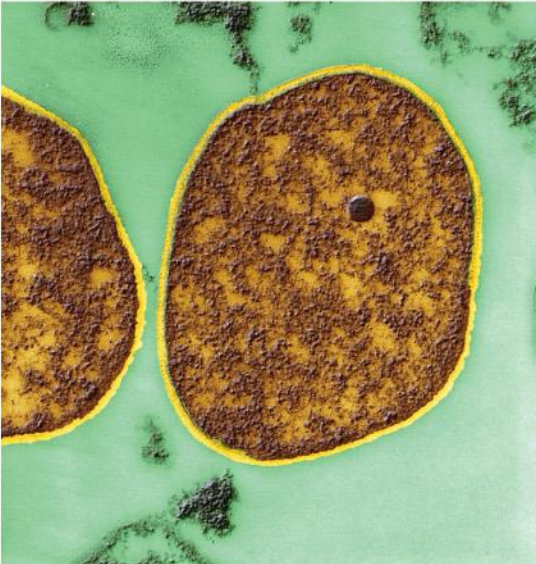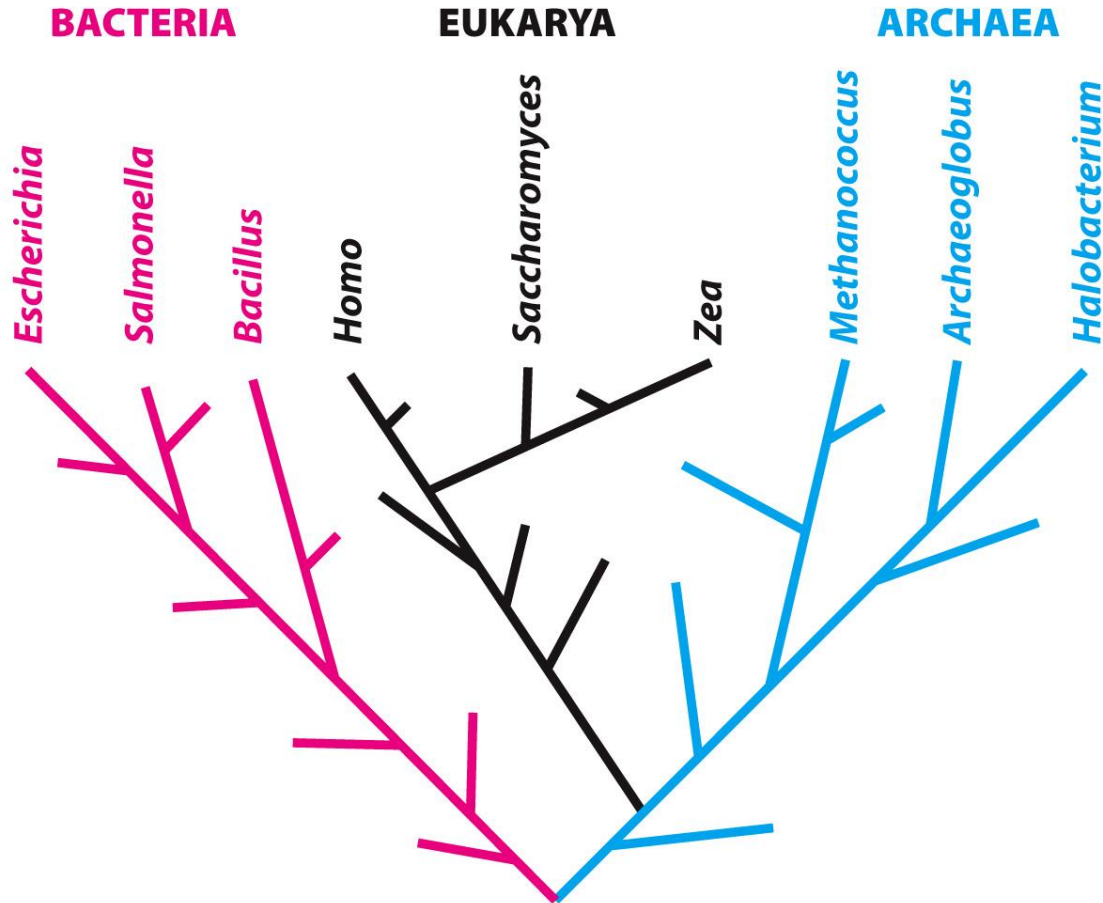Sulfolobus archaea   Arabidopsis thaliana   Homo sapiens

Figure 1.1
Biochemistry, Eighth Edition
© 2015 Macmillan Education [Photos: (Left) Eye of Science/Science Source; (middle) Holt Studios/Photo Researchers; (right) Time Life Pictures/Getty Images]

On the basis of biochemical characteristics, all organisms can be placed in one of three domains:
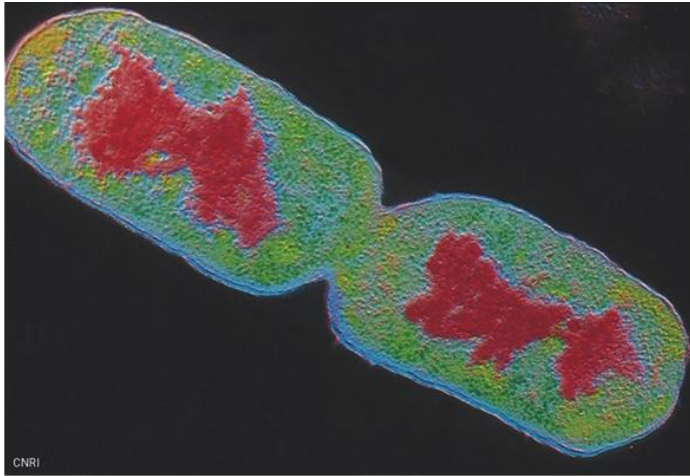

BACTERIA   **EUKARYA**   **ARCHAEA**

Escherichia   *Salmonella*   *Bacillus*   *Homo*   *Saccharomyces*   *Zea*   *Methanococcus*   *Archaeoglobus*   *Halobacterium*
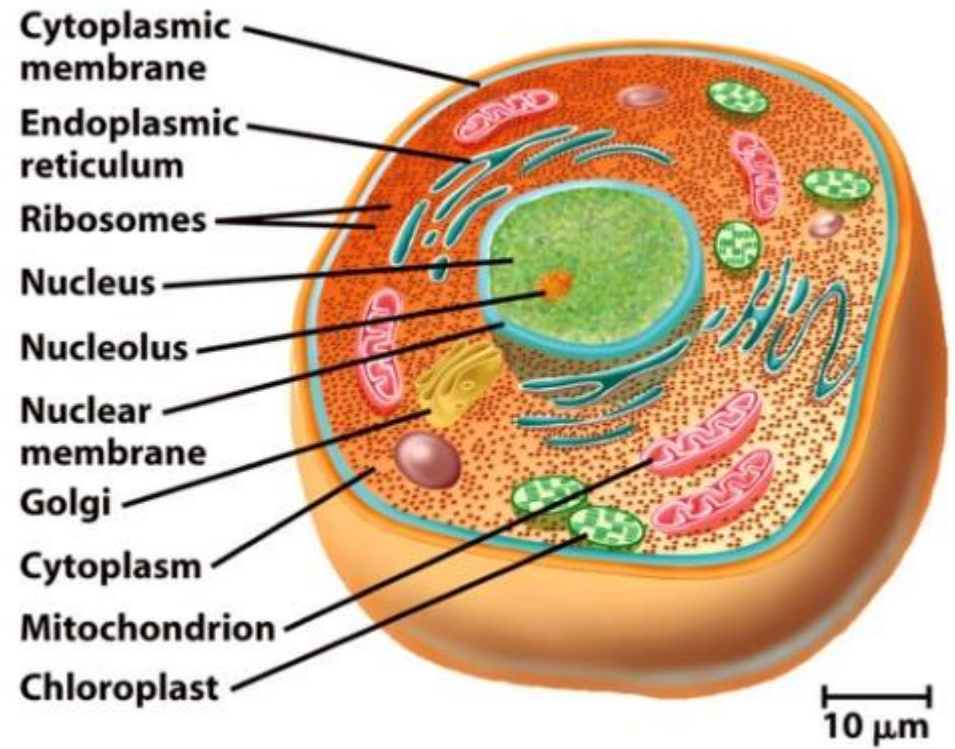
Prokaryotes:
Bacteria and Archaea
Single cell organism
Missing organelles

Archaea: metabolic pathways similar to those of eukaryotes (enzymes involved in transcription and translation.)
Often organism that lives in harsh condiditions

Electron micrographs of *E. coli* cells. Condensed DNA (**nucleoid** is shown in red)

Cytoplasmic membrane
Endoplasmic reticulum
Ribosomes
Nucleus
Nucleolus
Nuclear membrane
Golgi
Cytoplasm
Mitochondrion
Chloroplast

10 μm

Small molecules

- ATP, AMP. NADH –coenzymes
- sacharides
- Ions
- lipids

Covalent and non-covalent interactions are important for the structure and stability of biological molecules
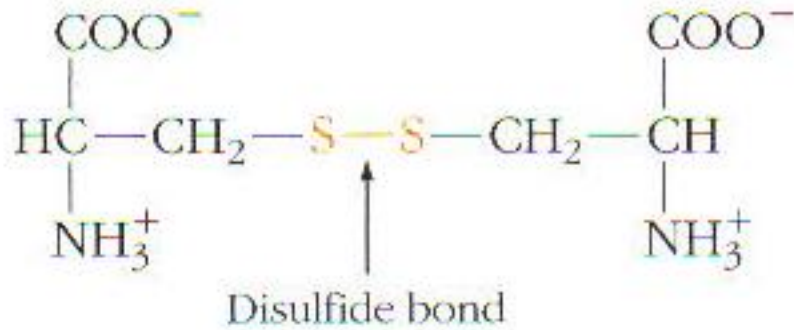
Covalent bonds, formed by electron sharing between two adjacent atoms, are the strongest bonds.

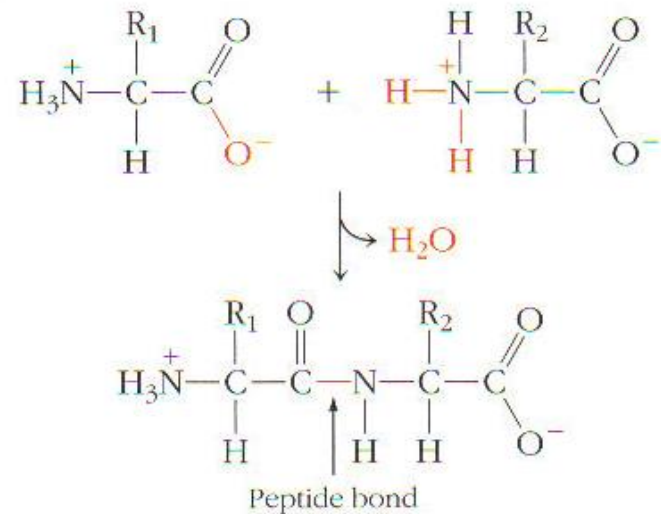A typical C-C covalent bond has a distance of 1.54 Å and a bond energy of 355 kJ mol^{-1} (85 kcal mol^{-1}).

Energy units: Joules (J) 1J is the energy that is required to move 1 meter against a force of 1 N.
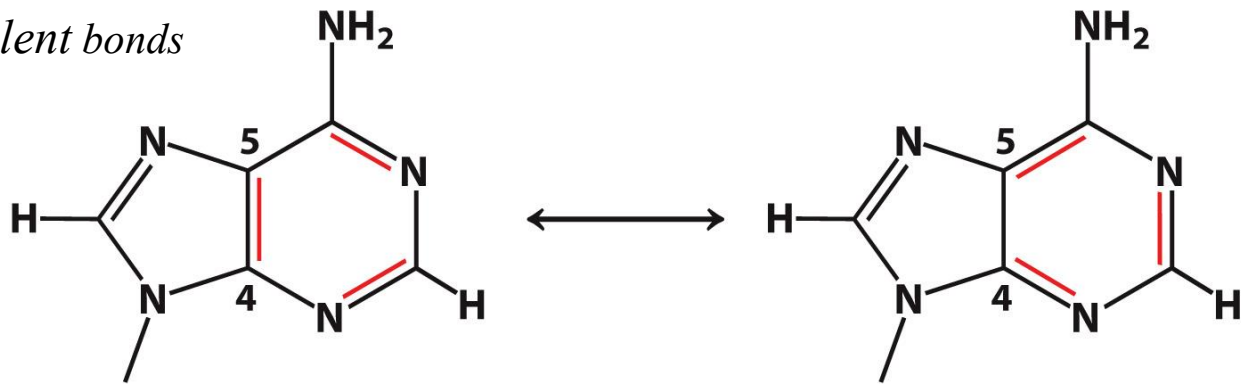Distances: 1 Angstrom is 0.1 nm or 10^{-10} m.

I. Disulfide bond:

I. Peptide bond:

Resonance structures.

Covalent bonds

Resonance structures of adenine
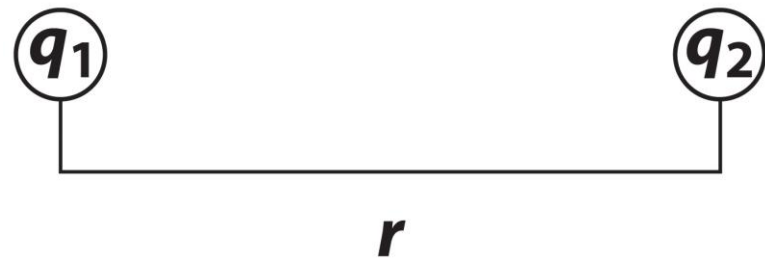
Noncovalent bonds
Ionic interactions.

Ionic interactions, also called electrostatic interactions, occur between oppositely charged molecules.

Electrostatic interactions in water have a bond distance of ≈3 Å and a bond energy, given by Coulomb energy, of 5.86 kJ mol^{-1} (1.4 kcal mol^{-1})

$$E = kq_1q_2/Dr$$

D dielectric constant
A measure of a substance's ability to insulate charges from each other.

q_1 ———— q_2

r

Unnumbered 1 p7b
Biochemistry, Eighth Edition
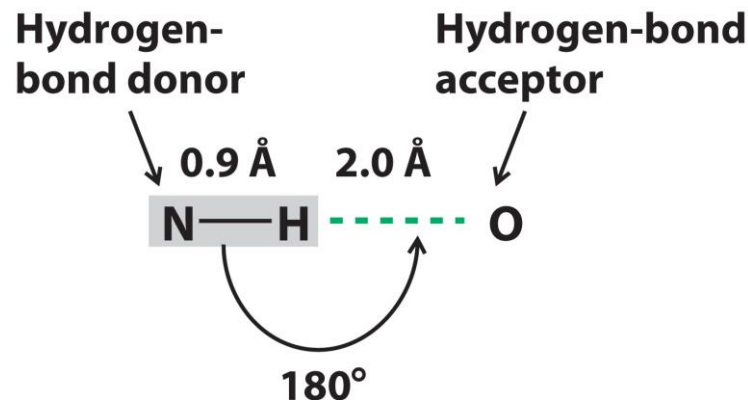© 2015 Macmillan Education

Noncovalent bonds

Hydrogen bonds.

Hydrogen bonds occur between an electronegative atom and a hydrogen covalently bonded to another electronegative atom.

Hydrogen bonds vary in bond distance from 1.5 Å to 2.6 Å with bond energies from 4-20 kJ mol^{-1} (1-5 kcal mol^{-1})

Unnumbered 1 p8a
Biochemistry, Eighth Edition
© 2015 Macmillan Education

Hydrogen-bond donor

Hydrogen-bond acceptor

$$N\!\!-\!\!H - - - - - - - N$$
$$\delta^- \quad\ \delta^+ \qquad\qquad\qquad \delta^-$$

$$N\!\!-\!\!H - - - - - - - O$$

$$O\!\!-\!\!H - - - - - - - N$$

$$O\!\!-\!\!H - - - - - - - O$$

Figure 1.9
Biochemistry, Eighth Edition
© 2015 Macmillan Education

van der Waal interactions.

Van der Waals interactions occur between two molecules that sufficiently close (the van der Walls contact distance) such that transient electronic asymmetries in one molecule induce complementary interaction in the partner molecule.

Van der Waals interactions have bond energies from 2-4 kJ mol^{-1} (0.5-1.0 kcal mol^{-1})
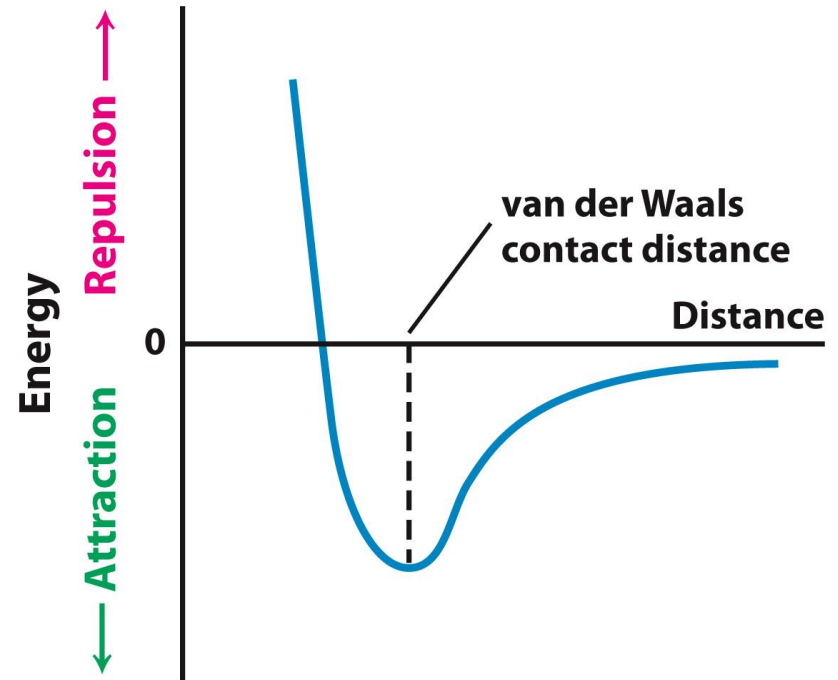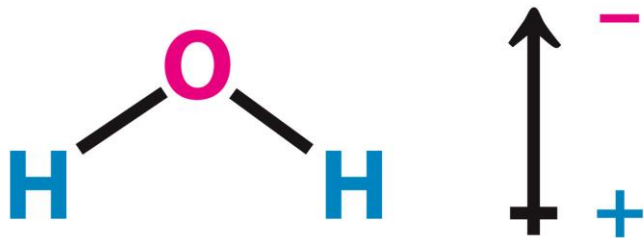

Figure 1.10
Biochemistry, Eighth Edition
© 2015 Macmillan Education

Water is a polar molecule. The charges on the molecule are not evenly distributed.
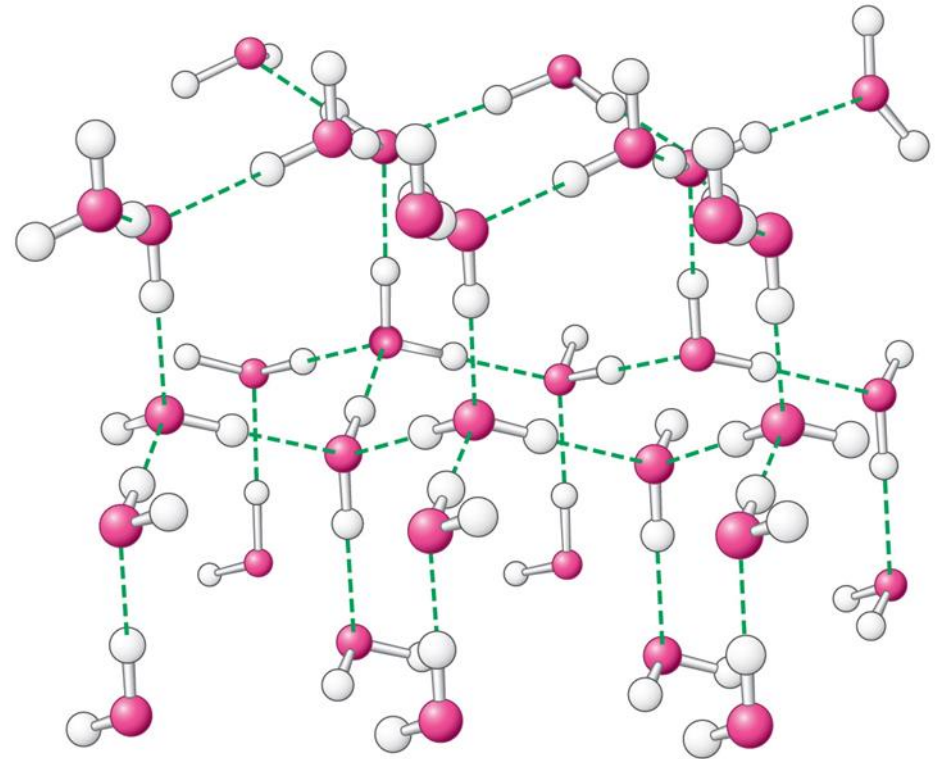
Electric dipole

−

+

H O H

Figure 1.11
Biochemistry, Eighth Edition
© 2015 Macmillan Education

Water molecules solvate proteins and ions in the solutions
Water molecules also form a channels through protein
structure necessary for proton transport

The hydrophobic effect.

Nonpolar molecules in water can be driven together by the hydrophobic effect which is powered by the increase in entropy of water. The associated interactions are called hydrophobic interaction.
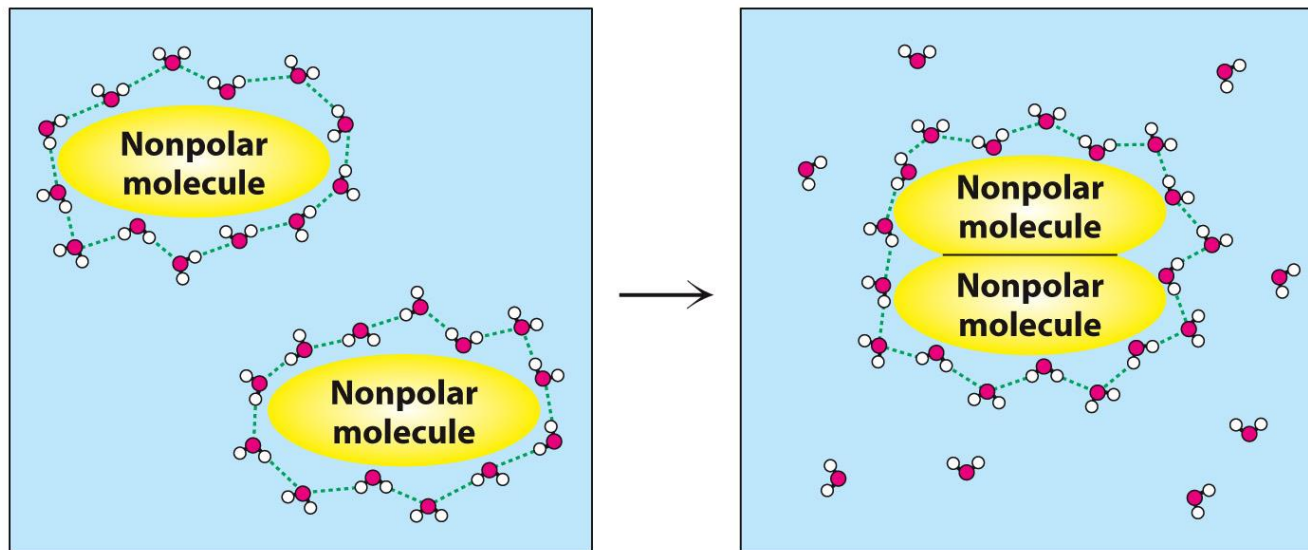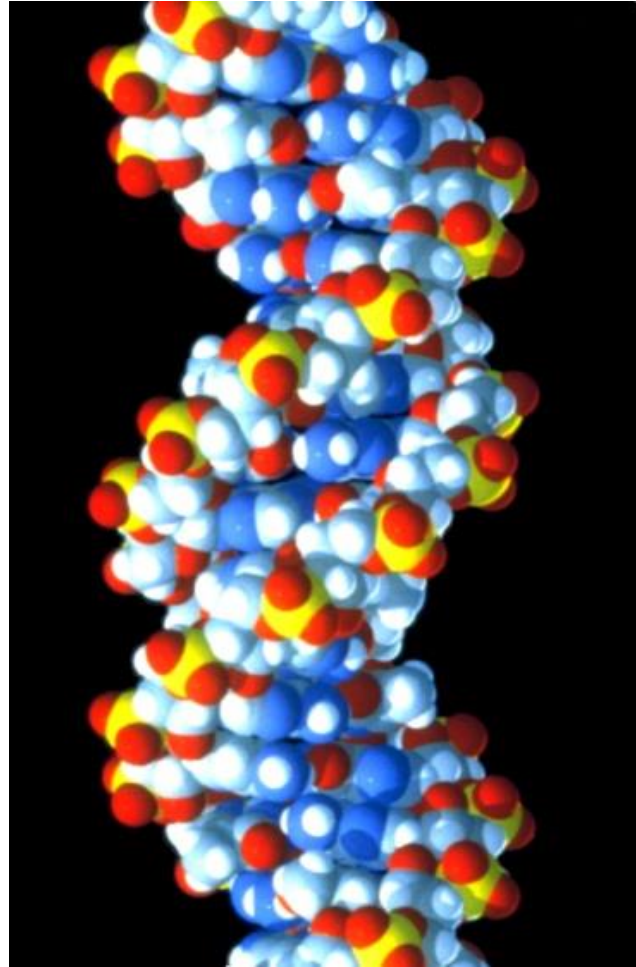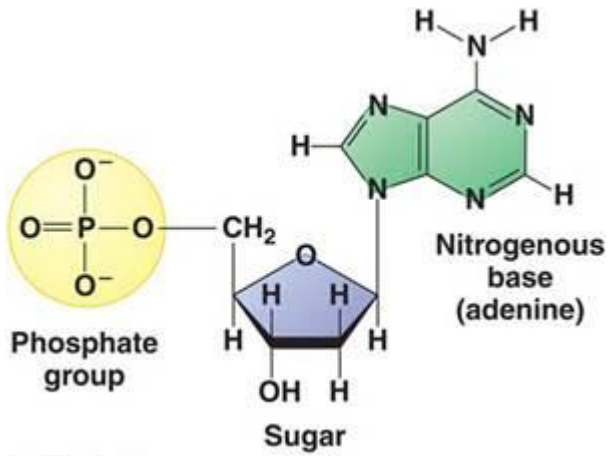

Figure 1.12
Biochemistry, Eighth Edition
© 2015 Macmillan Education

Noncovalent forces and DNA molecule

Phosphate group

Nitrogenous base (adenine)

Sugar

Stability of DNA double helix

When a double helix forms, charge repulsion occurs between the negatively charged phosphates of the backbone.

These repulsive forces are reduced by the high dielectric constant of water and interaction of positively charged ions with the phosphate groups.
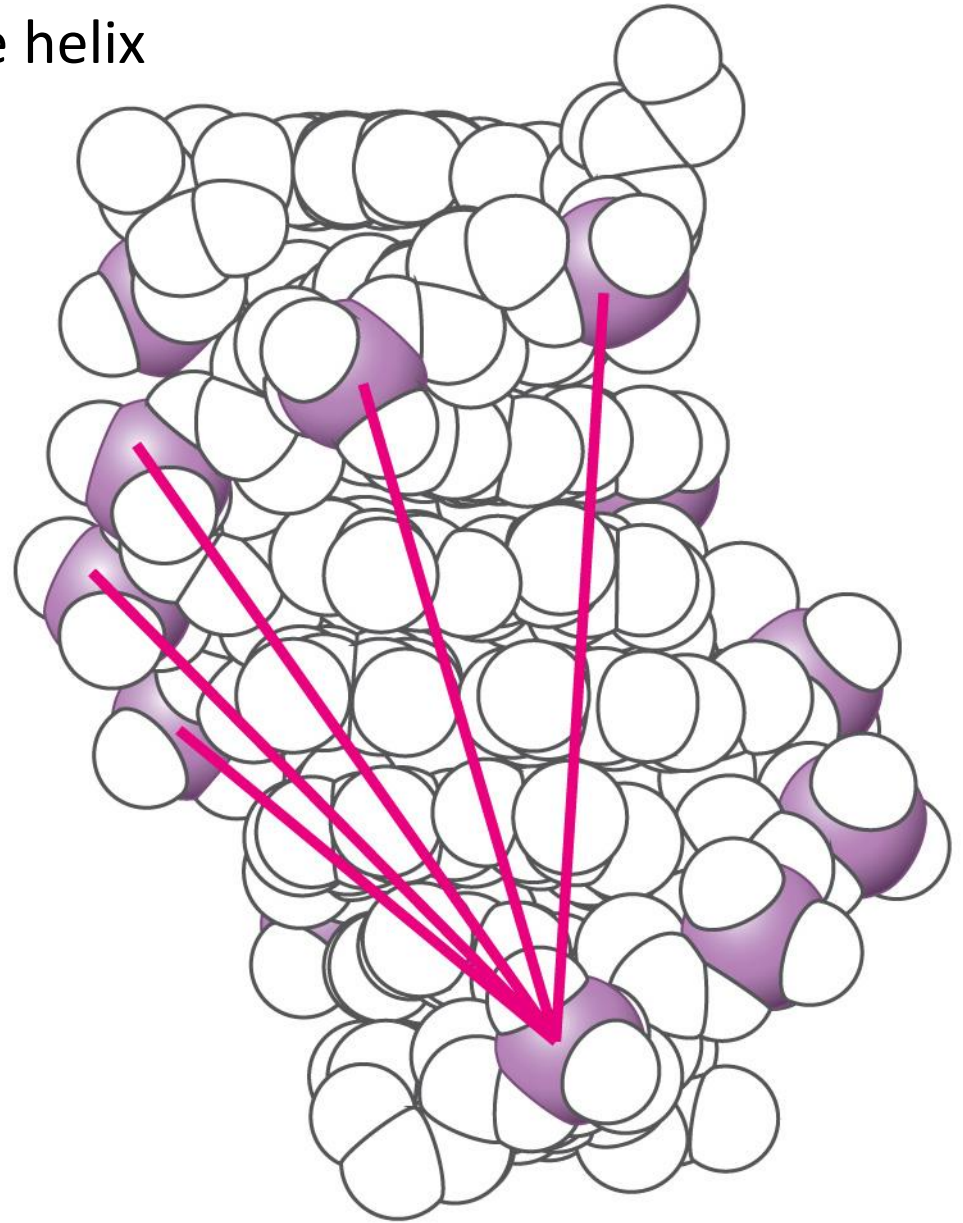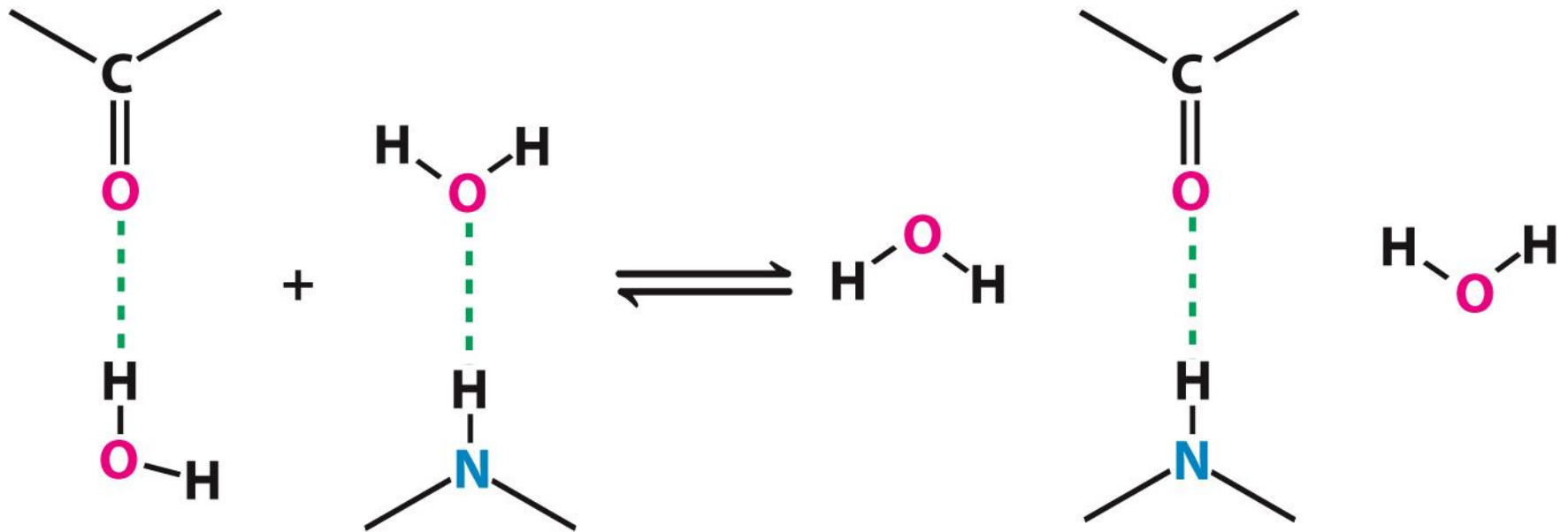

Figure 1.13
Biochemistry, Eighth Edition
© 2015 Macmillan Education

Hydrogen bonds form between bases, which are in the hydrophobic interior away from the disrupting effects of water.

In the interior of the helix, bases are stacked and interact with one another through van der Waals interactions.
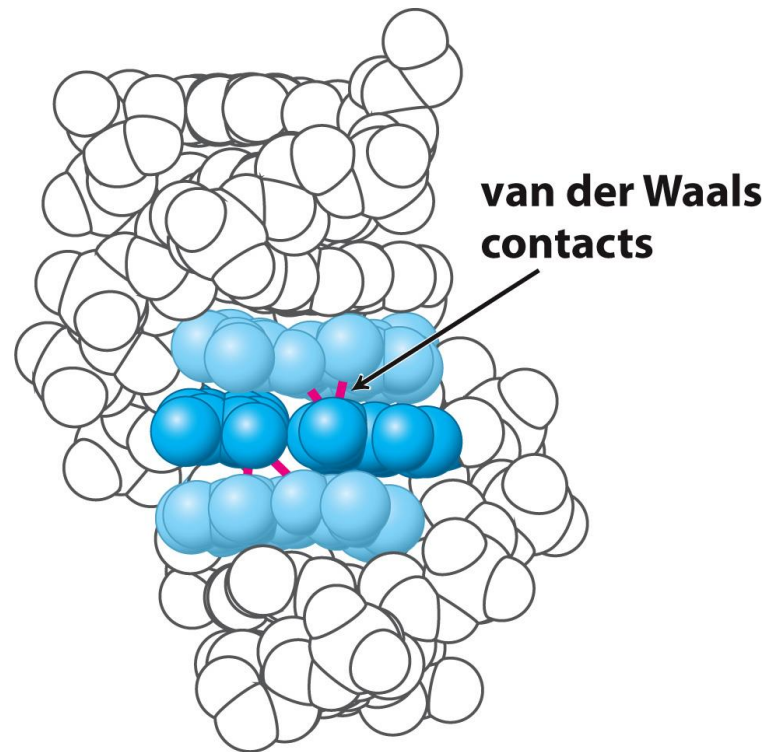

van der Waals contacts

Figure 1.14
Biochemistry, Eighth Edition
© 2015 Macmillan Education

The First Law of Thermodynamics states the the total energy of a system and its environment is constant.

The Second Law of Thermodynamics states the total entropy of a system plus that of its surroundings <u>always increases.</u>

Entropy can decrease locally in the system if there is a corresponding increase in entropy in the surroundings.

Thermodynamic of chemical reactions:

$$\Delta G = \Delta H - T\Delta S$$

ΔG – change in the free energy

ΔH – change in the enthalpy,

ΔS – change in the entropy of the system

Spontaneous reaction, nonspontaneous reaction

Comparing to simple chemical reaction – entropy contribution is significant in biological reactions.

Chemical equilibrium and standard state

$\Delta G = \Delta G\,° + RT\ln K_{eq}$

K_{eq} equilibrium constant

equilibrium

$\Delta G = 0$ => $\Delta G\,'° = -RT\ln K_{eq}$

$\Delta G\,'°$ free energy change
at standard conditions

Equilibrium constant of reaction
can be calculated from the standard free energy and vice versa

Living organism – high organization of structures => low entropy
Organism maintain this thermodynamically unfavorable state as long
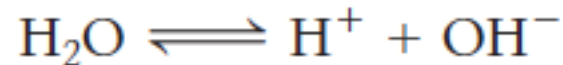*As they are obtaining free energy from food.*

Acid–base reactions are central in many
biochemical processes

Acid-base reactions involve the addition or removal of a H^+ ion.
Such reactions are important in biochemistry.

pH is a measure of the H^+ concentration and is defined by

$$pH = -\log[H^+]$$

H^+ and OH^- ions are formed upon the dissociation of H_2O.

$$H_2O \rightleftharpoons H^+ + OH^-$$

The equilibrium constant K_{eq} for the dissociation of water is given by

$$K_{eq} = [H^+][OH^-]/[H_2O]$$

K_w, the ion constant of water is given by

$$K_w = K_{eq} \times [H_2O]$$

This can be simplified to

$$K_w = [H^+][OH^-]$$

$$K_w = [H^+][OH^-]$$

$$K_w = [H^+][OH^-] = 1.0 \times 10^{-14}\,M^2$$

From this, we can

$$[OH^-] = 10^{-14}/[H^+] \quad \text{and} \quad [H^+] = 10^{-14}/[OH^-]$$

At pH 7, $[H^+] = [OH^-] = 10^{-7}$

Acid–base reactions can disrupt the double helix

As base is added to a solution of double helical DNA, the helix is disrupted or denatured.
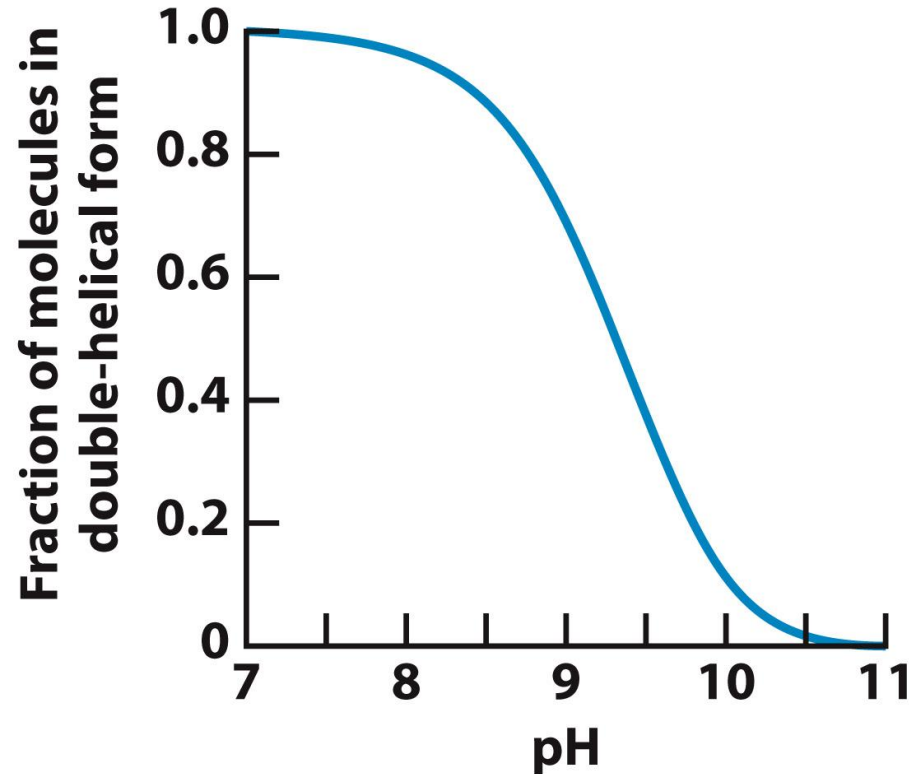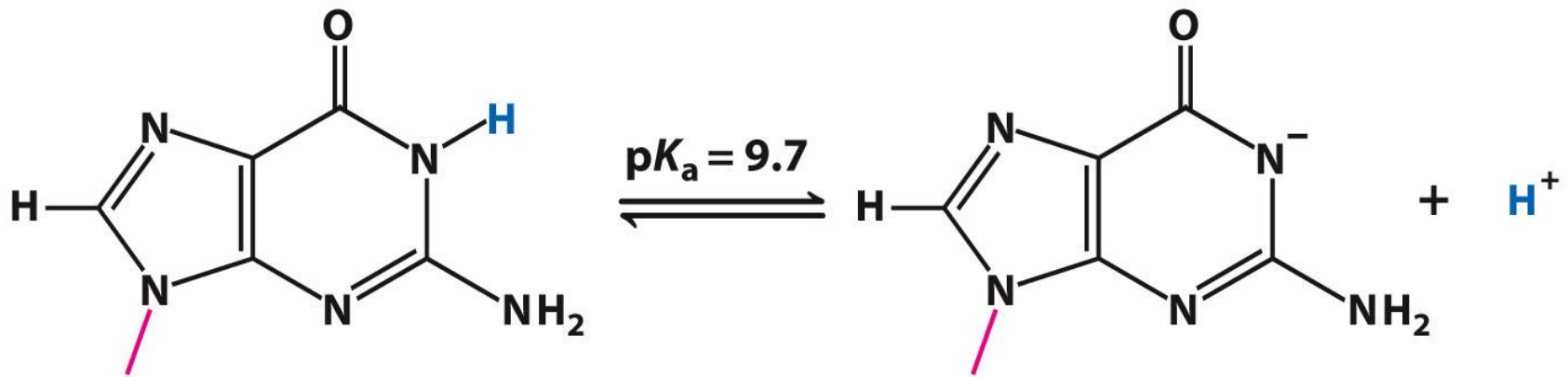
Figure 1.16
Biochemistry, Eighth Edition
© 2015 Macmillan Education

The chemical basis of the denaturation is the disruption of base-pairing. For example, the loss of a proton by the base guanine prevents base pairing with cytosine.

Guanine (G)

More generally, proton removal from any molecule HA is described by

$$K_a = [H^+][A^-]/[HA]$$

The pK_a value indicates the susceptibility of proton removal.

$$pK_a = -\log(K_a)$$

When $pH = pK_a$

$$-\log[H^+] = -\log([H^+][A^-]/[HA])$$

and

$$[H^+] = [H^+][A^-]/[HA]$$

$$1 = [A^-]/[HA] \qquad \text{or} \qquad [A^-] = [HA]$$

Thus, when the pH is equal to the pK_a, the concentration of the protonated form of HA (the acid) is equal to the deprotonated form A⁻ (the base).

The N-1 proton of guanine has a pK_a of 9.7. When the pH is near or exceeds this value, the proton is lost, base pairing is disrupted and the helix is denatured.

Buffers regulate pH in organisms and in the laboratory

0.1 mM Na⁺CH₃COO⁻

Gradual pH change

Water

Figure 1.17
Biochemistry, Eighth Edition
© 2015 Macmillan Education

An acid-base conjugate pair resists changes in the pH of a solution.

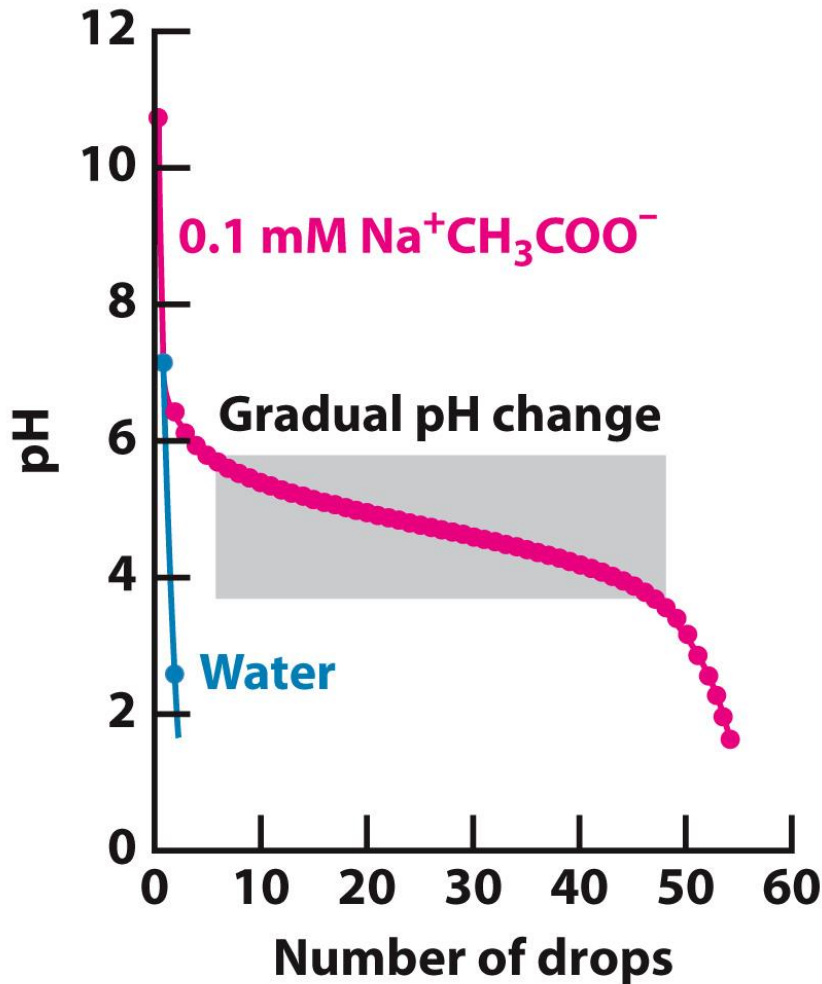In other words, it acts as a buffer. A buffer is most effective at a pH near its pK_a.

The ionization reaction of a weak acid is given by

$$HA \rightleftharpoons H^+ + A^-$$

The equilibrium constant for this reaction is

$$K_a = [H^+][A^-]/[HA]$$

Taking the logarithms of both sides yields

$$\log(K_a) = \log([H^+]) + \log([A^-]/[HA])$$

Substituting pK_a and pH and rearranging yield the Henderson-Hasselbalch equation

$$pH = pK_a + \log([A^-]/[HA])$$

Consideration of this equation reveals that weak acids are most effective as buffers at pH near their pK_a.