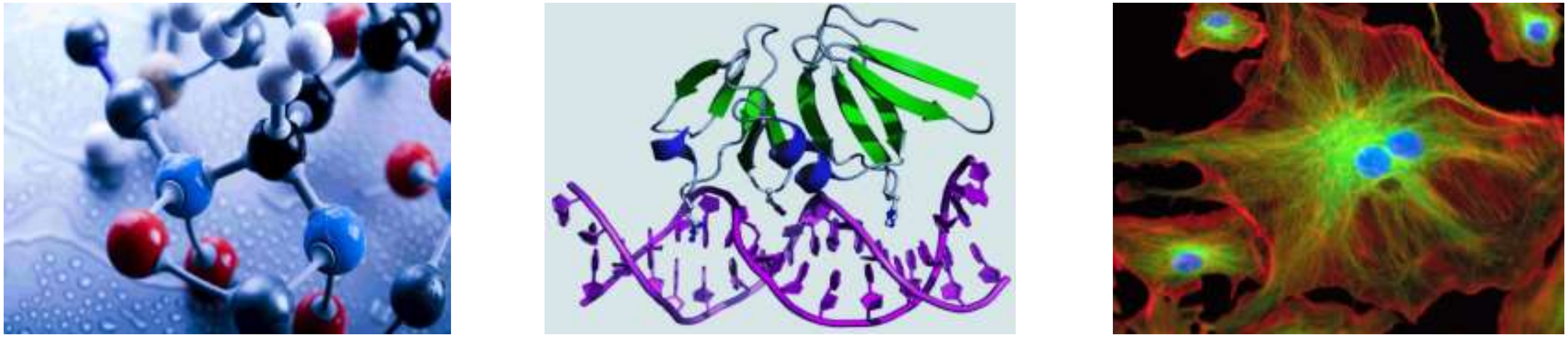
廈門大學生命科學學院
SCHOOL OF LIFE SCIENCES XIAMEN UNIVERSITY

廈門大學
UNIVERSITAS AMOIENSIS

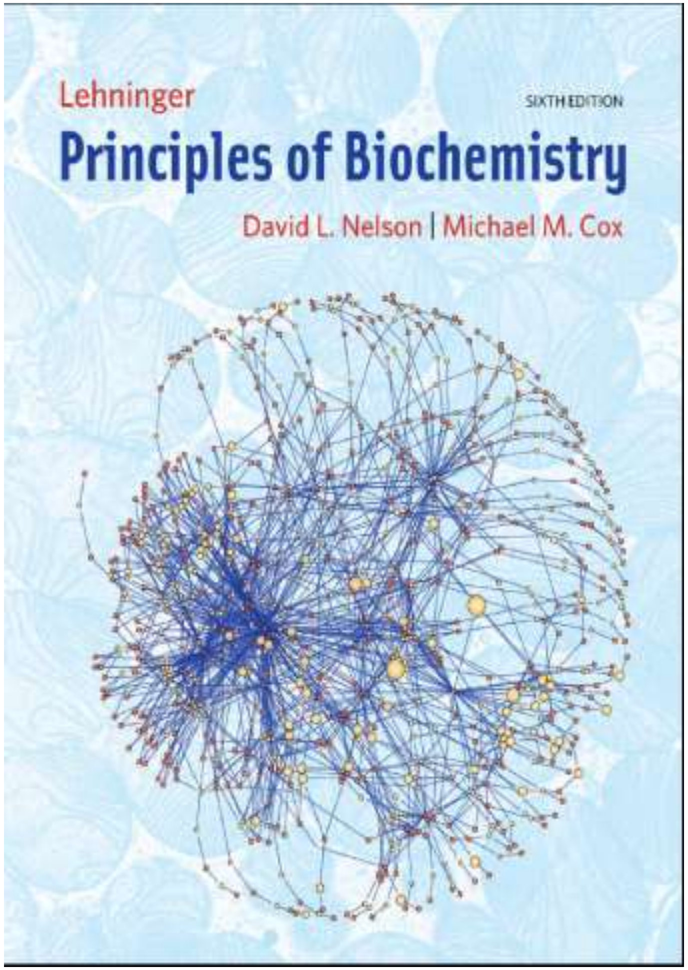
Biochemistry

Science that explores the chemical processes within and related to living organisms.



Reference book

Lehninger
Principles of Biochemistry 6th Ed.



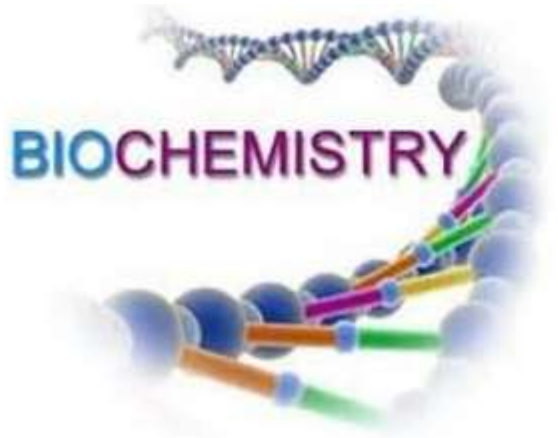
David L. Nelson
Michael M. Cox

LEHNINGER PRINCIPLES OF BIOCHEMISTRY Sixth Edition

CHAPTER 1

The Foundations of Biochemistry

1.1 Cellular Foundations
1.2 Chemical Foundations
1.3 Physical Foundations
1.4 Genetic Foundations



Features of living organisms

- A high degree of chemical complexity and microscopic organization.
- Systems for extracting, transforming, and using energy from the environment.
- Defined functions for each of an organism’s components and regulated interactions among them.
- Mechanisms for sensing and responding to alterations in their surroundings.

Molecular Logic of Life

Wonder of life: diversity and complexity

(Appearance, habitat, and genetic composition……)

The molecular logic of life

Foundations and organizing principles that underlie all diverse life forms.

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

1.1 Cellular foundations

All living organisms are made up of cell(s).

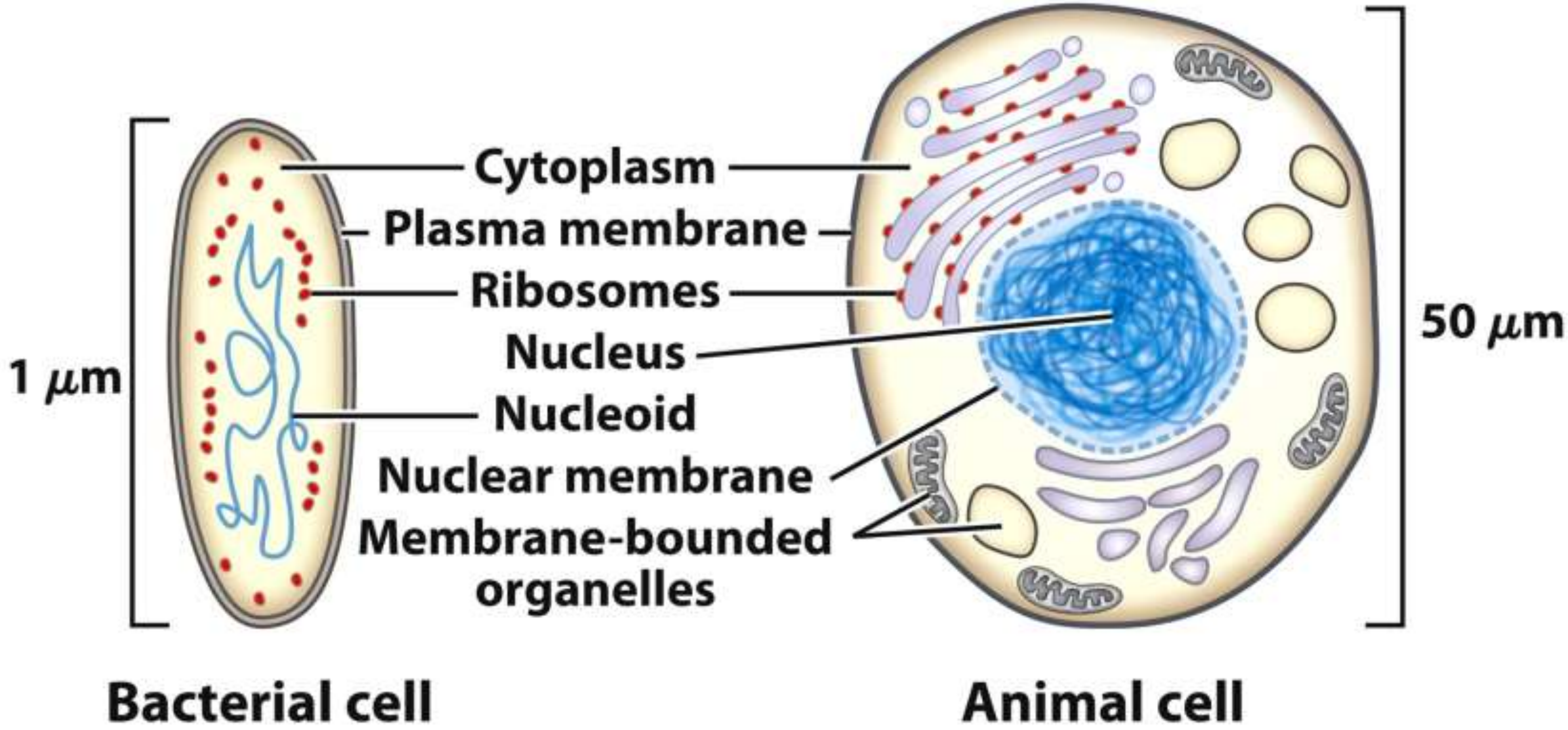


Figure 1-3
Lehninger Principles of Biochemistry, Sixth Edition

1.1 Cellular foundations

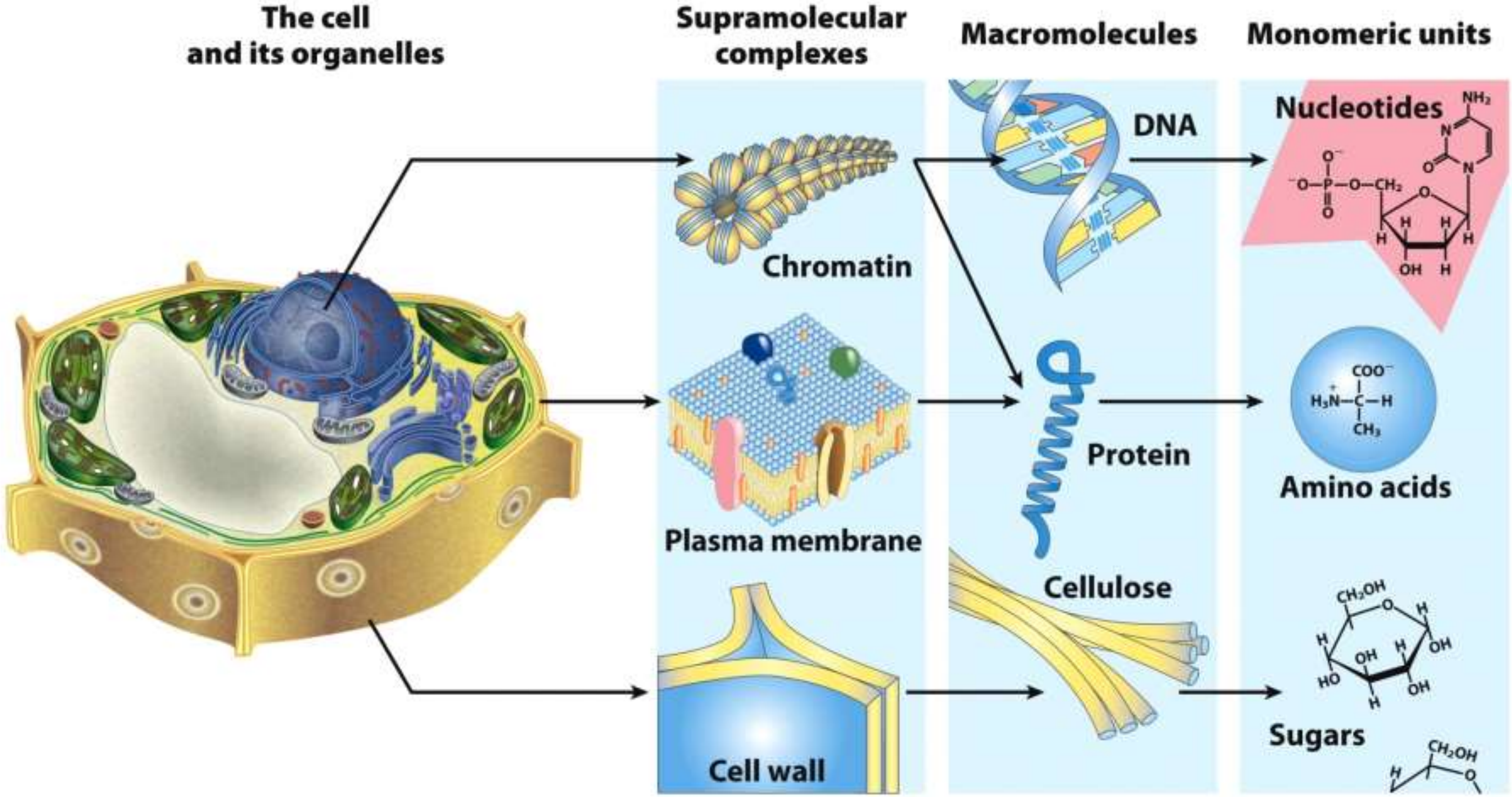


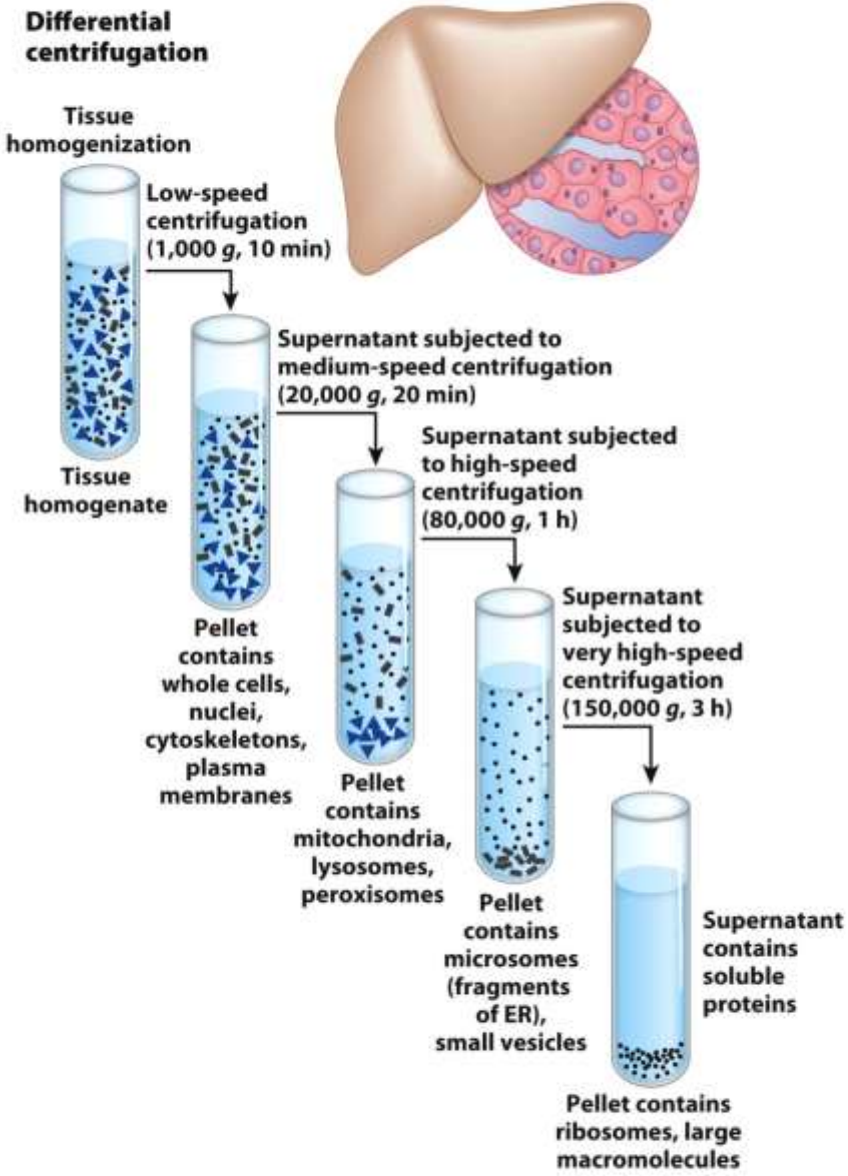
Figure 1-11
Lehninger Principles of Biochemistry, Sixth Edition

1.1 Cellular foundations

Subcellular fractionation of tissue

Cell fractionation:

separating organelles from the cytosol and from each other—an essential step in investigating their structures and functions in biochemistry study.



1.2 Chemical foundations

"THE CHEMISTRY OF LIFE"

All cells are more alike than they are different at the biochemical level.

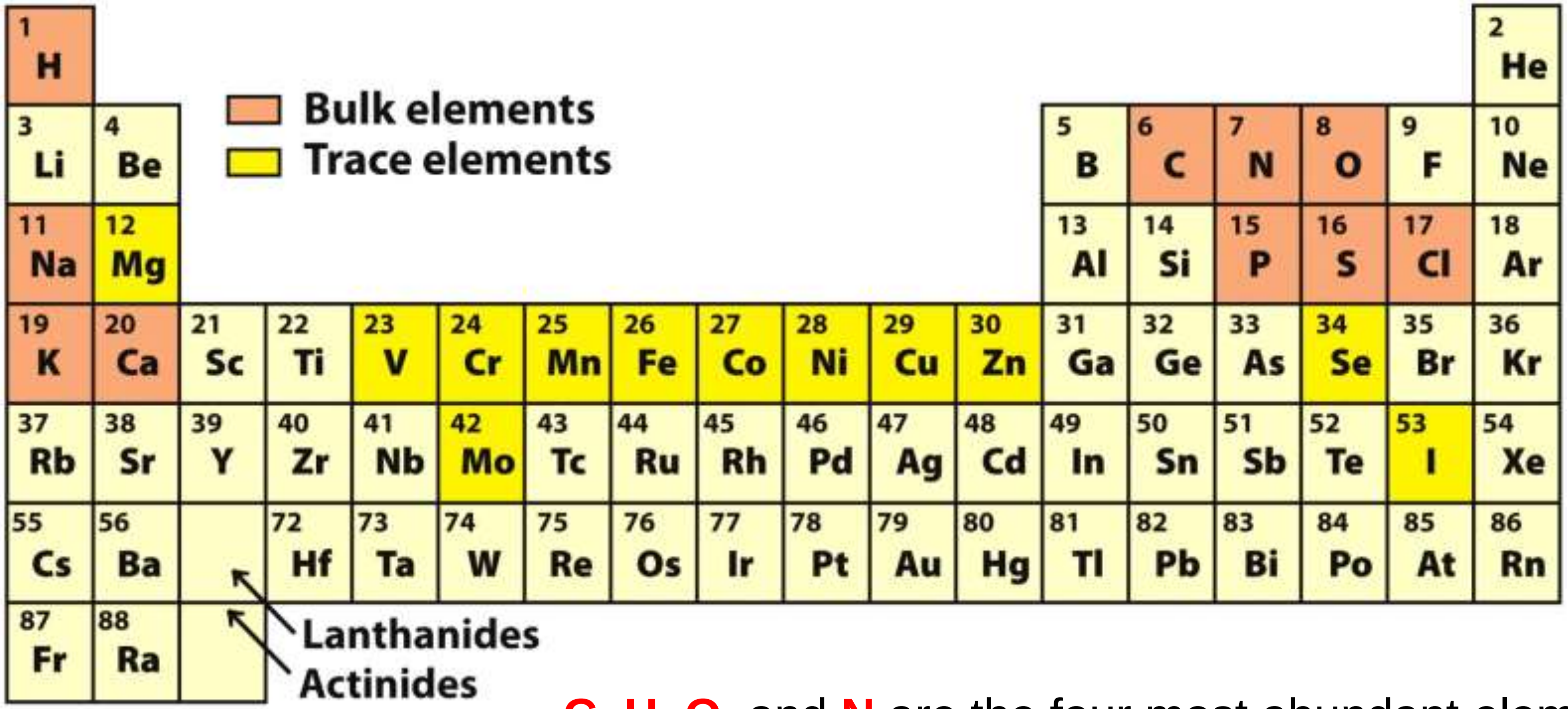


Figure 1-13
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

C, H, O, and N are the four most abundant elements in living organisms, which together make up more than 99% of the mass of most cells.

1.2 Chemical foundations

➢ Biomolecules are compounds of carbon

- Carbon can form covalent ***single***, ***double***, and ***triple*** bonds with other atoms, particularly other carbon atoms.

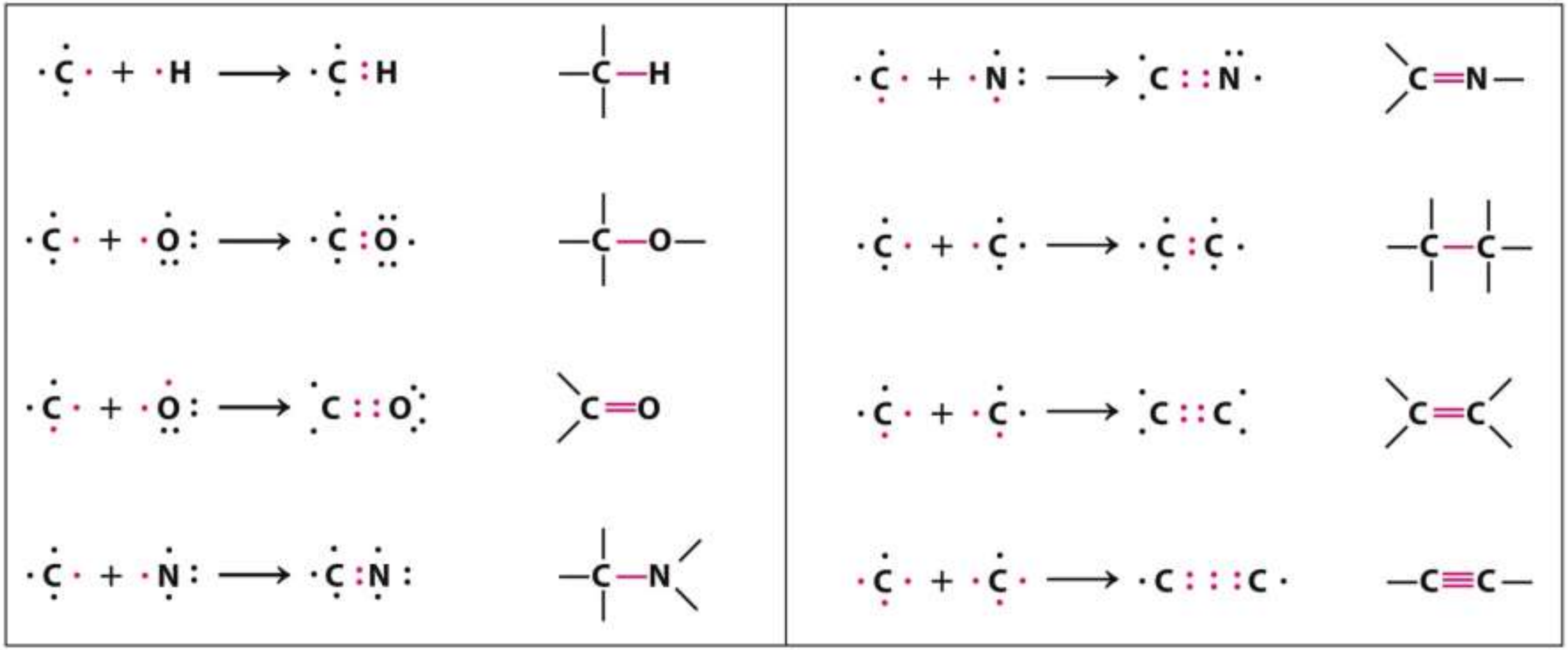


Figure 1-14

Lehninger Principles of Biochemistry, Sixth Edition

1.2 Chemical foundations

- Geometry of carbon bonding

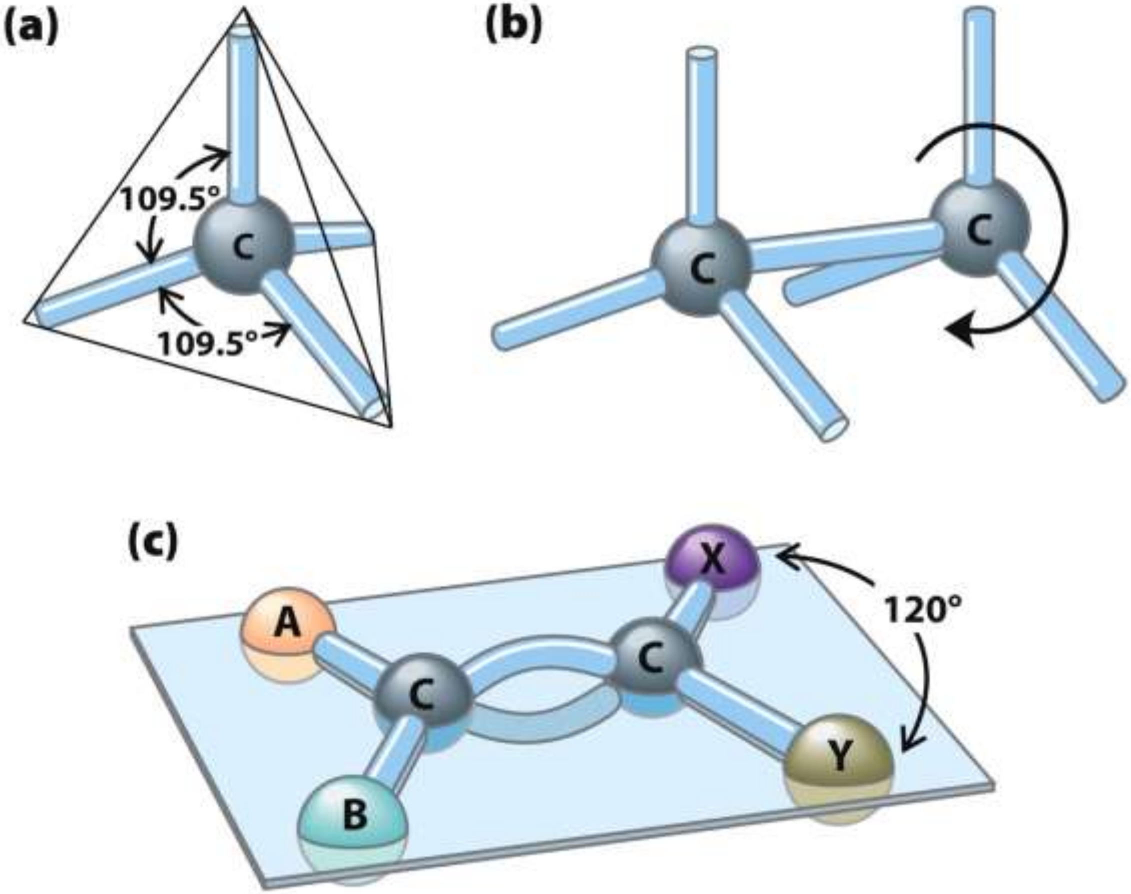


Figure 1-15
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

1.2 Chemical foundations

- Some common functional groups of biomolecules

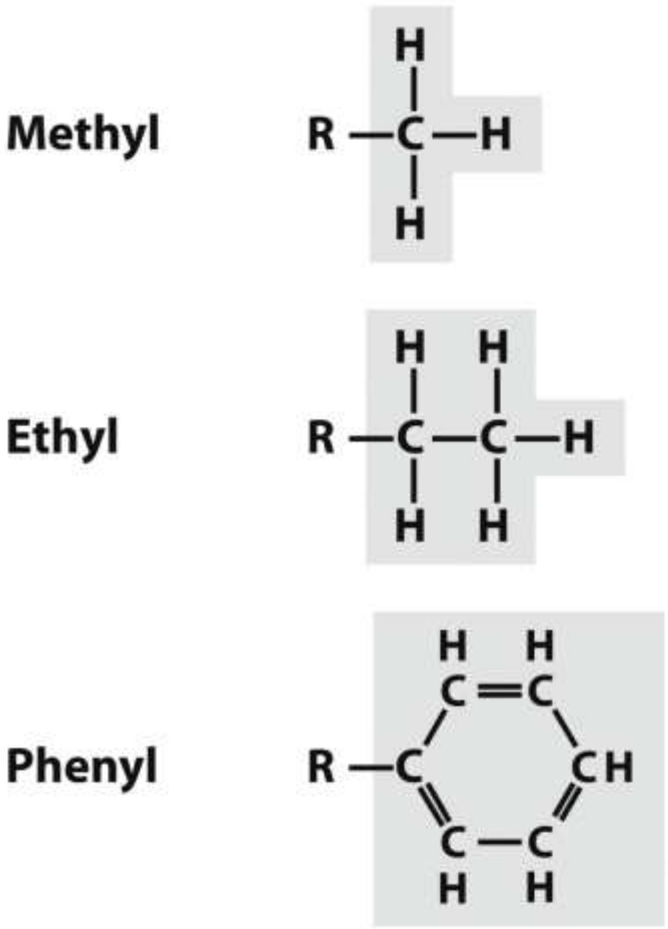


Figure 1-16 part 1
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

1.2 Chemical foundations

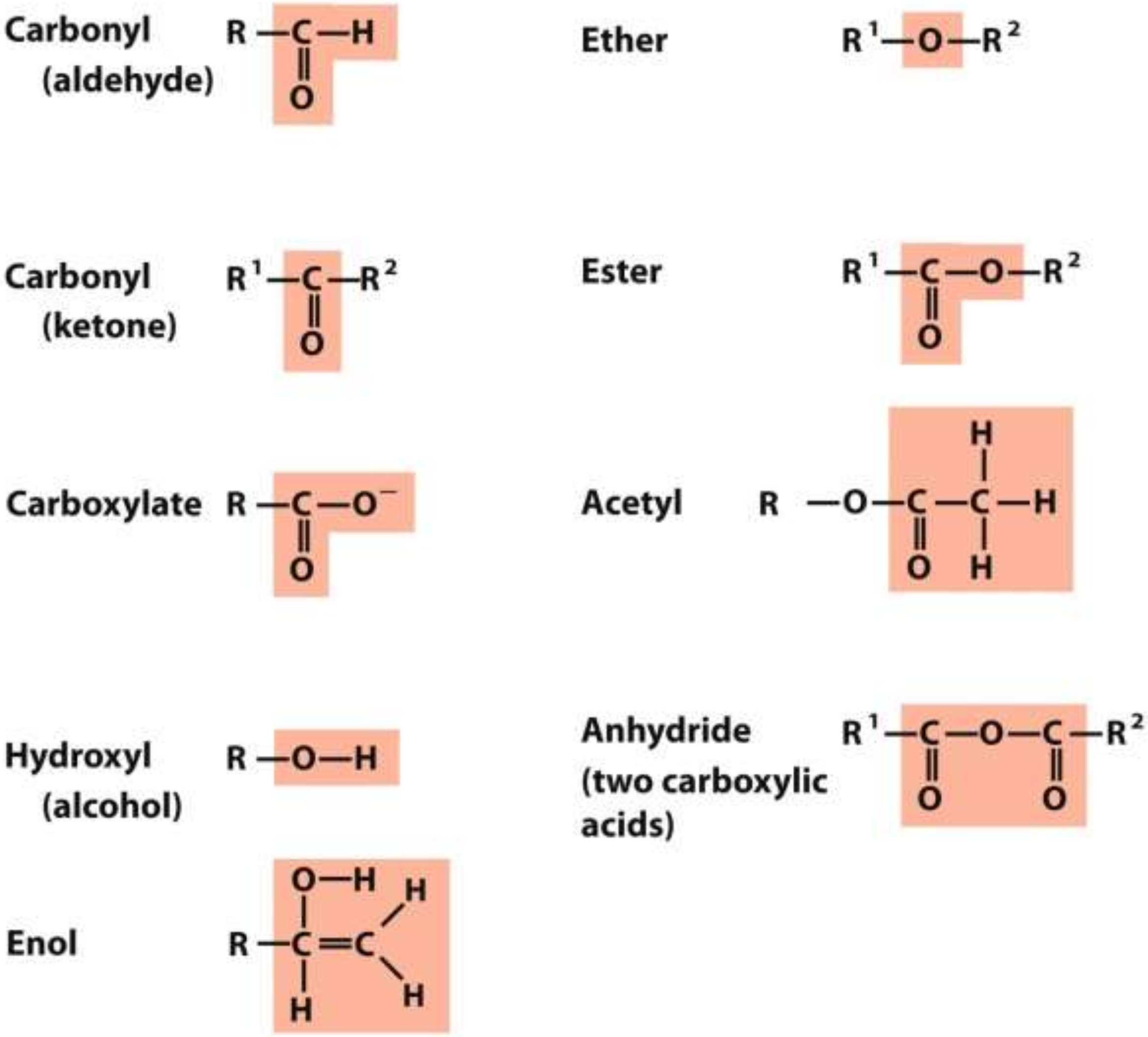


Figure 1-16 part 2
Lehninger Principles of Biochemistry, Sixth Edition

1.2 Chemical foundations

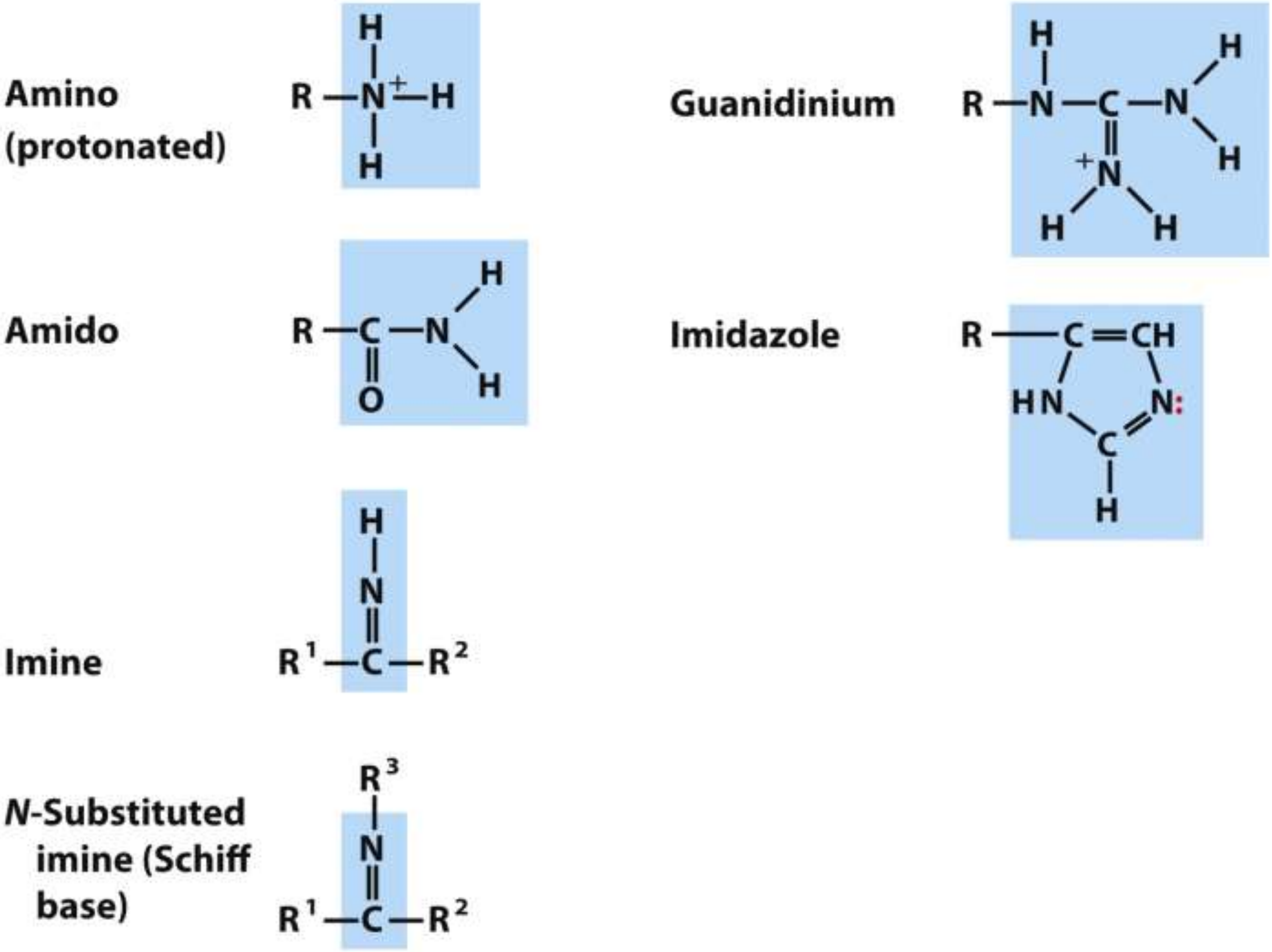


Figure 1-16 part 3
Lehninger Principles of Biochemistry, Sixth Edition

1.2 Chemical foundations

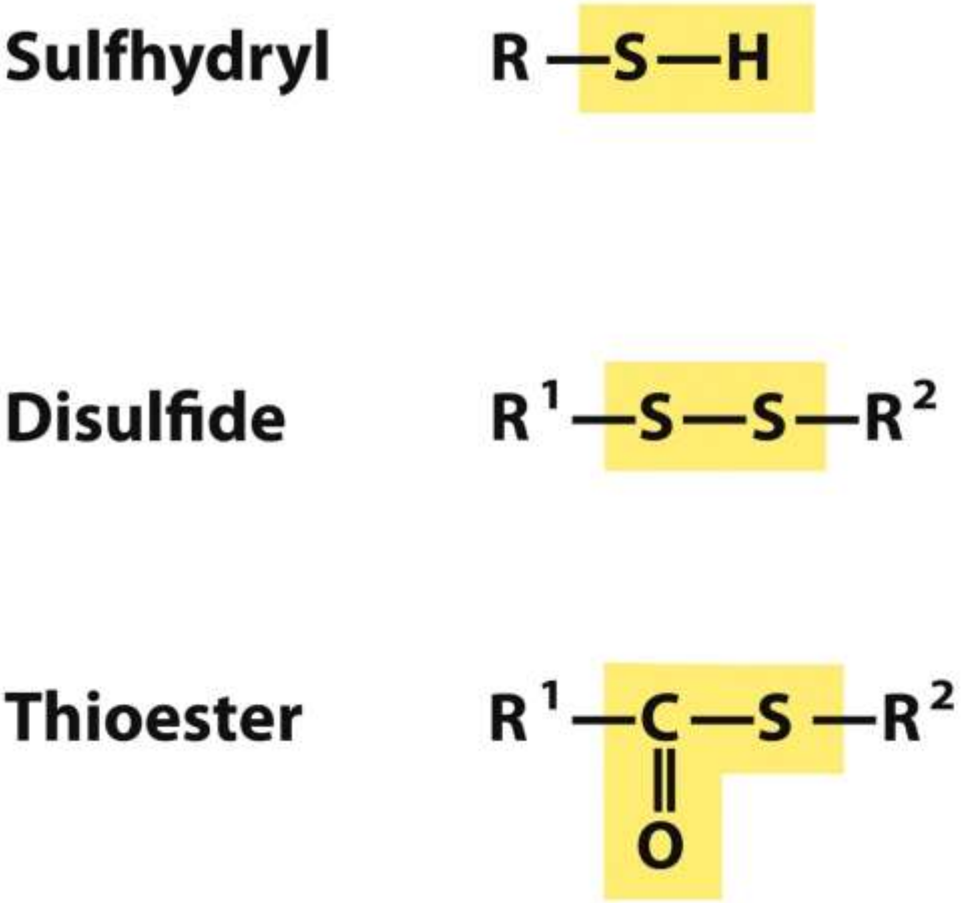
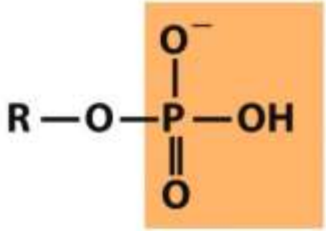


Figure 1-16 part 4
Lehninger Principles of Biochemistry, Sixth Edition

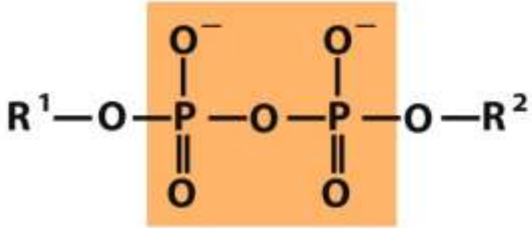
1.2 Chemical foundations

Phosphoryl



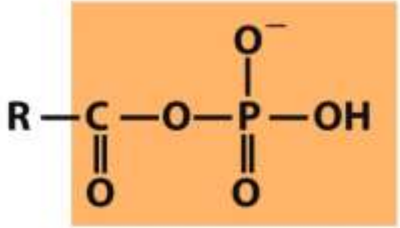
$$R-O-\overset{\overset{\displaystyle O^-}{|}}{\underset{\underset{\displaystyle O}{\|}}{P}}-OH$$

Phosphoanhydride



$$R^1-O-\overset{\overset{\displaystyle O^-}{|}}{\underset{\underset{\displaystyle O}{\|}}{P}}-O-\overset{\overset{\displaystyle O^-}{|}}{\underset{\underset{\displaystyle O}{\|}}{P}}-O-R^2$$

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

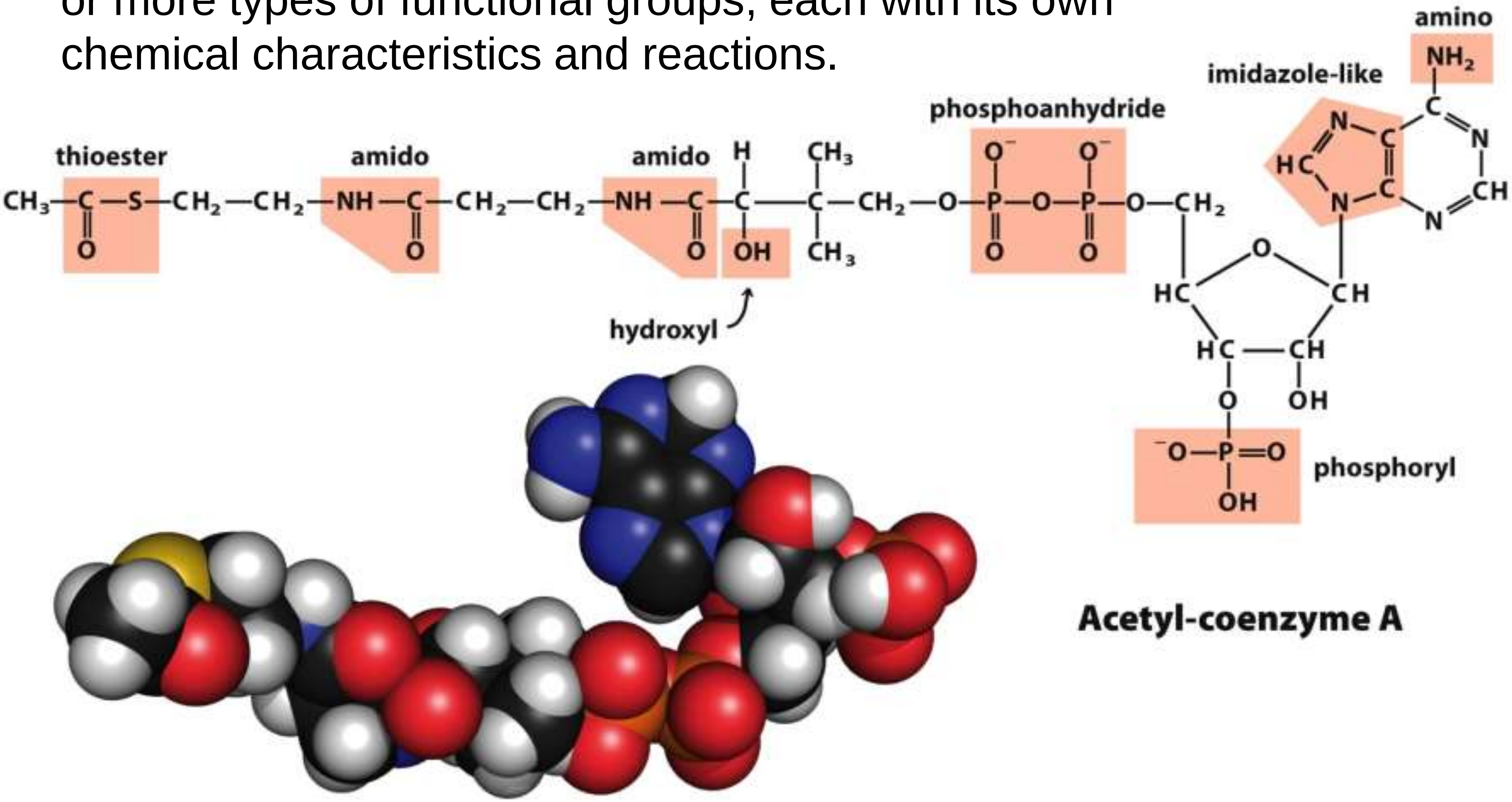


$$R-\underset{\underset{\displaystyle O}{\|}}{C}-O-\overset{\overset{\displaystyle O^-}{|}}{\underset{\underset{\displaystyle O}{\|}}{P}}-OH$$

Figure 1-16 part 5
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

1.2 Chemical foundations

- Many biomolecules are polyfunctional, containing two or more types of functional groups, each with its own chemical characteristics and reactions.



Acetyl-coenzyme A

Figure 1-17
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

1.2 Chemical foundations

Macromolecules are major constituents of cells

- Many biological molecules are **macromolecules**, polymers with molecular weights above ~5,000 that are assembled from relatively simple precursors.

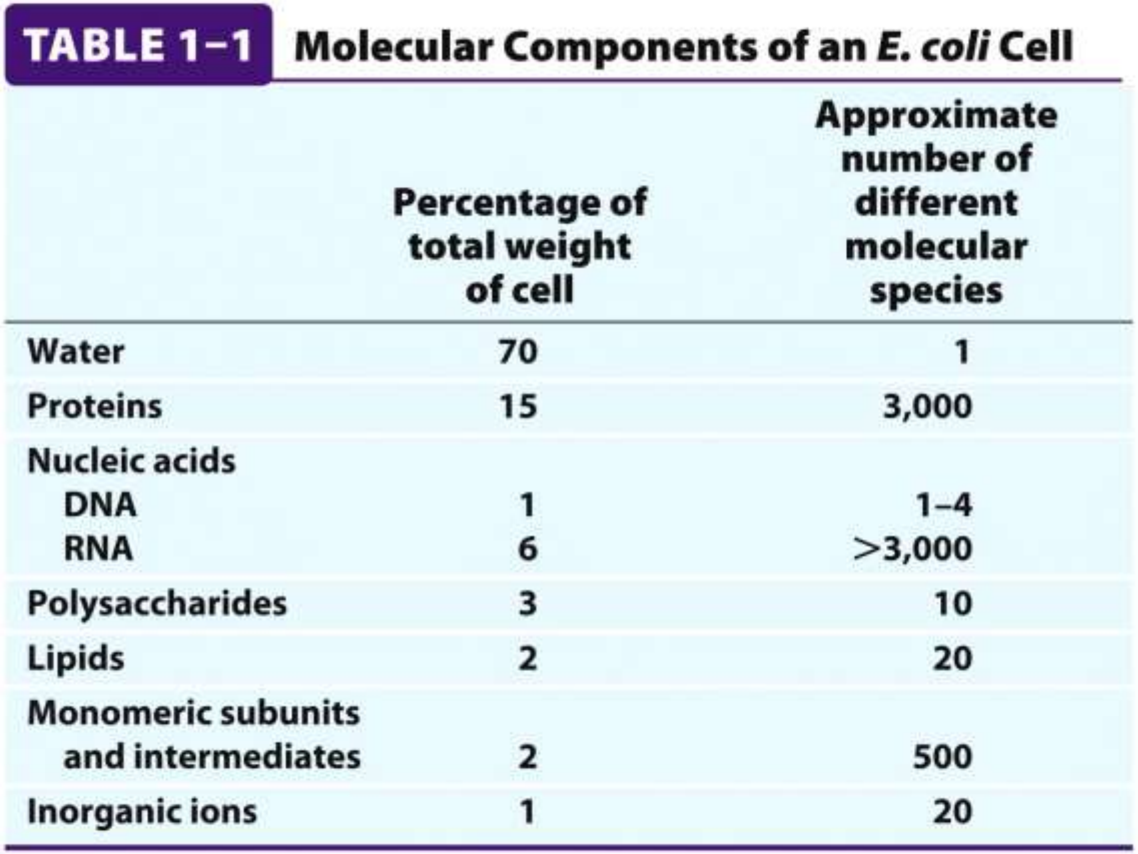


TABLE 1–1 Molecular Components of an *E. coli* Cell

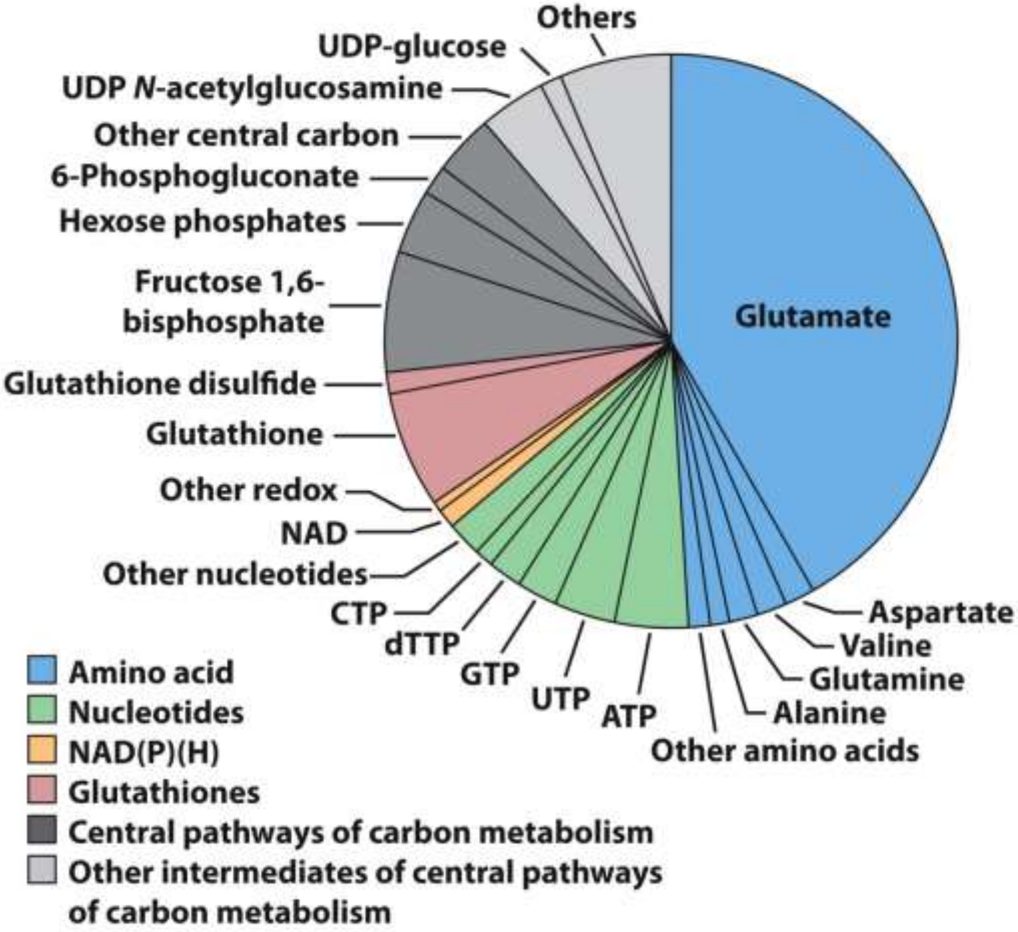
	Percentage of total weight of cell	Approximate number of different molecular species
Water	70	1
Proteins	15	3,000
Nucleic acids		
DNA	1	1–4
RNA	6	>3,000
Polysaccharides	3	10
Lipids	2	20
Monomeric subunits and intermediates	2	500
Inorganic ions	1	20

Table 1-1
Lehninger Principles of Biochemistry, Sixth Edition

1.2 Chemical foundations

- **Cells contain a universal set of small molecules**

There are ~1000 different small organic molecules (M_r ~100 to ~500), with intracellular concentrations ranging from nanomolar to millimolar. The entire collection of these small molecules in a given cell under a specific set of conditions has been called the **metabolome**.



The metabolome of *E. coli* growing on glucose

1.2 Chemical foundations

- **Carbon-containing compounds commonly exist as stereoisomers**
  - The constituent atoms of a biomolecule are arranged in three-dimensional space—its stereochemistry.

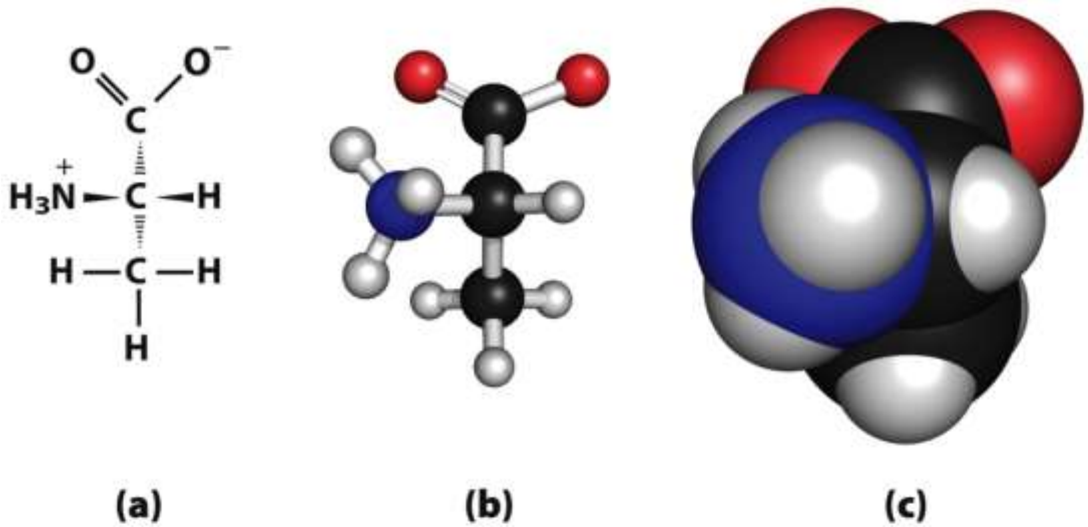


Figure 1-18
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

Interactions between biomolecules are stereospecific!

1.2 Chemical foundations

- Three-dimensional structure is described by **configuration** and **conformation**

Configuration, the fixed spatial arrangement of atoms in a stereoisomer. The identifying characteristic of the stereoisomer cannot be interconverted without temporarily breaking one or more covalent bonds.

Conformation, the spatial arrangement of substituent groups are free to assume different positions in space without breaking any bonds because of the freedom of rotation about single bonds.

1.2 Chemical foundations

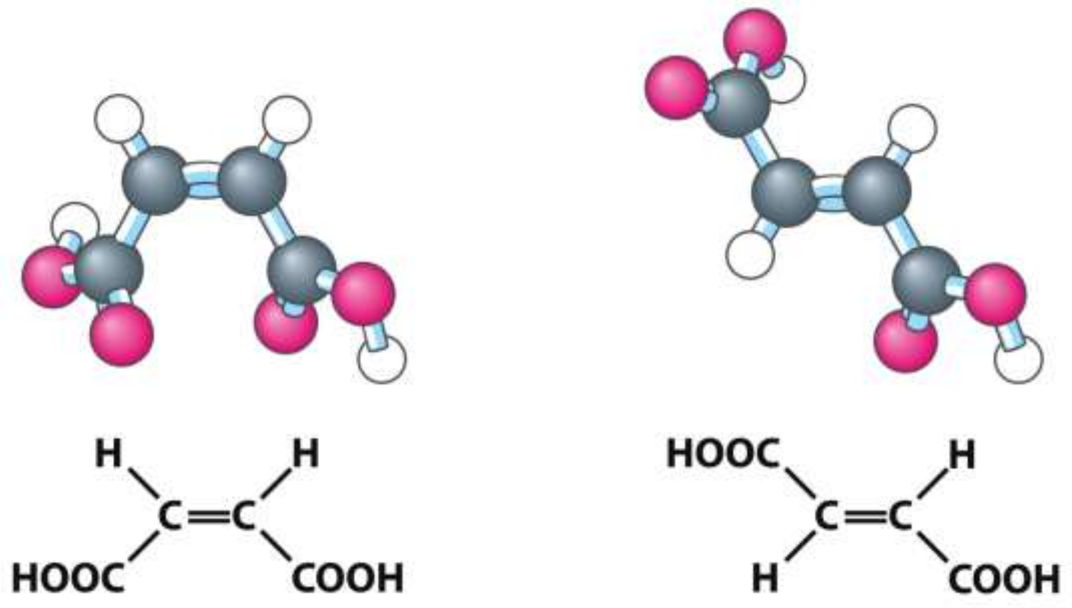
Causes of configuration

(1) double bonds, around which there is little or no freedom of rotation

Geometric isomers
(or ***cis-trans* isomers**)

cis, “on this side”—
groups on the same
side of the double
bond

trans, “across”—
groups on opposite
sides of the double
bond)



Maleic acid (cis) **Fumaric acid (trans)**

Figure 1-19a
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

1.2 Chemical foundations

Causes of configuration

(2) **chiral centers**, around which substituent groups are arranged in a specific orientation.

chiral centers, a carbon atom with four different substituents is said to be asymmetric, and asymmetric carbons are called chiral centers.

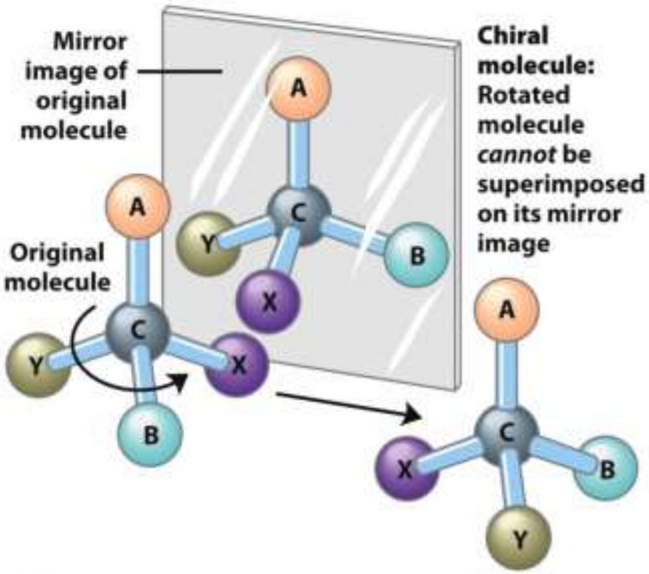


Figure 1-20a
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

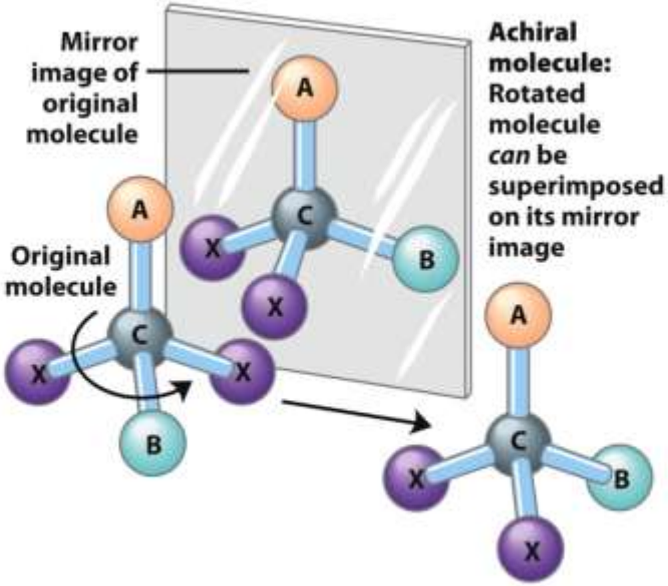


Figure 1-20b
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

1.2 Chemical foundations

RS system of nomenclature

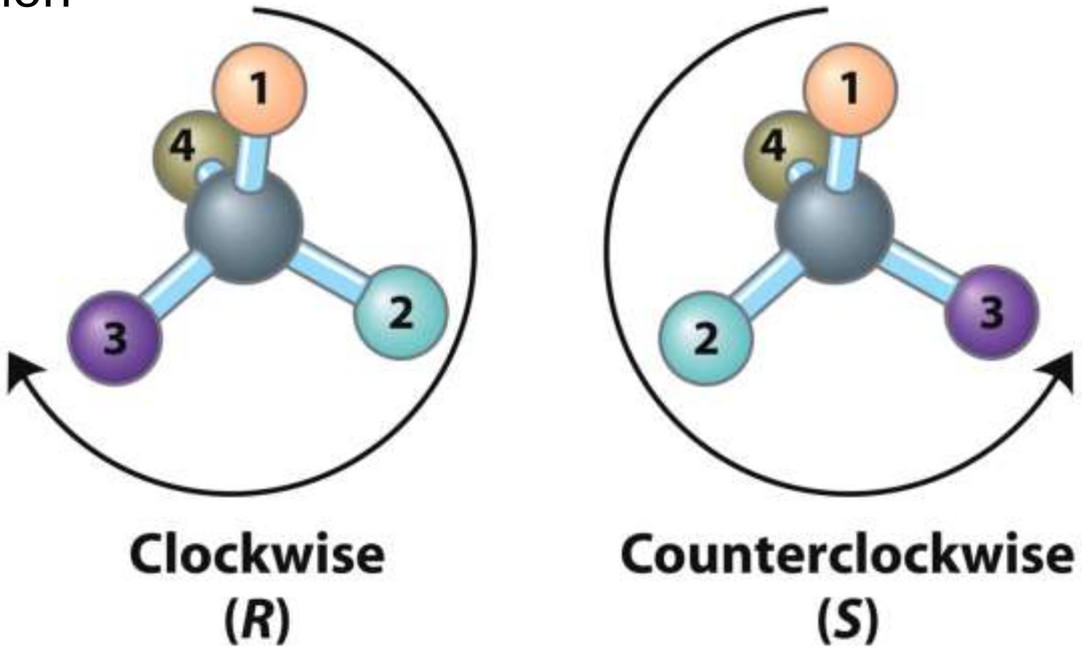
The priorities of some common substituents are：

$-OCH_3 > -OH >$

$-NH_2 > -COOH >$

$-CHO > -CH_2OH >$

$-CH_3 > -H$



Clockwise
(*R*)

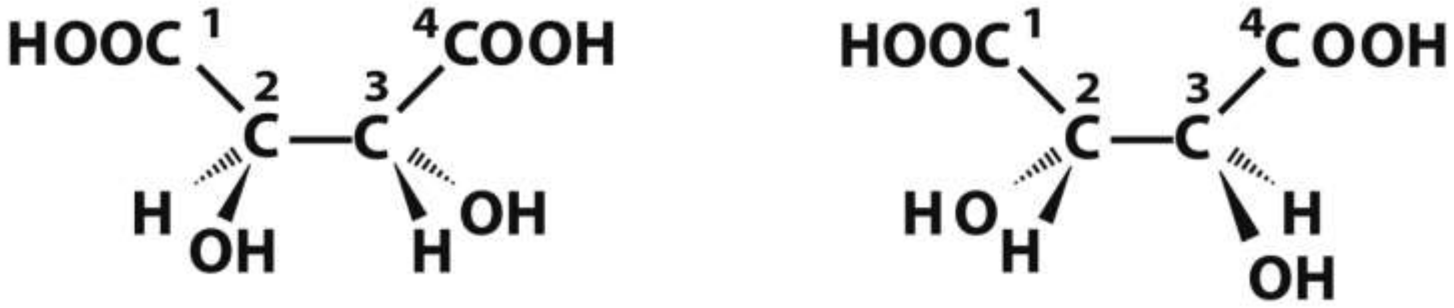
Counterclockwise
(*S*)

Unnumbered 1 p18a
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

The group of lowest priority (4) pointing away from the viewer

1.2 Chemical foundations

Each chiral carbon is designated either (*R*) or (*S*)



(2*R*,3*R*)-Tartaric acid
(dextrorotatory)

(2*S*,3*S*)-Tartaric acid
(levorotatory)

Box 1-2 figure 1
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

1.2 Chemical foundations

DL system of nomenclature

Stereoisomers having a configuration related to that of L-glyceraldehyde are designated **L**, and stereoisomers related to D-glyceraldehyde are designated **D**.

L-Glyceraldehyde D-Glyceraldehyde

L-Glyceraldehyde (*S*)-Glyceraldehyde

Unnumbered 1 p18b
Lehninger Principles of Biochemistry, Sixth Edition

1.2 Chemical foundations

A molecule with only one chiral carbon can have two stereoisomers; when two or more (*n*) chiral carbons are present, there can be 2^n stereoisomers.

Stereoisomers that are mirror images of each other are called **enantiomers(对映异构体).** Pairs of stereoisomers that are not mirror images of each other are called **diastereomers (非对映异构体).**

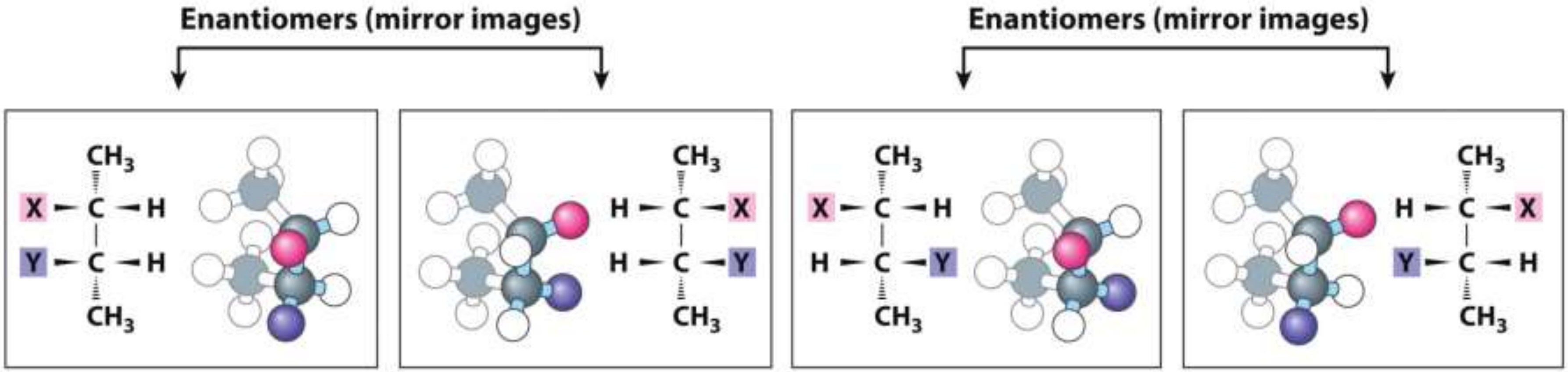
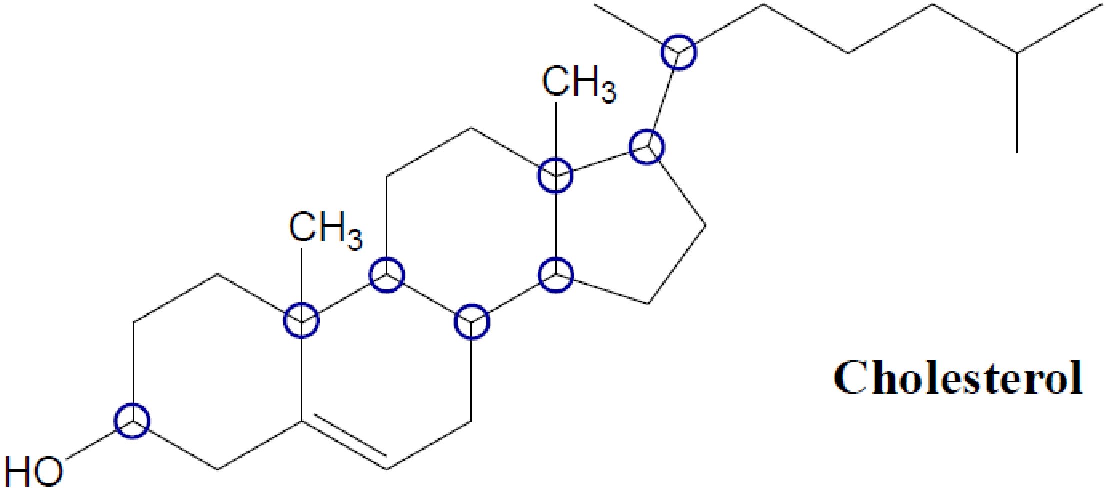


Figure 1-21
Lehninger Principles of Biochemistry, Sixth Edition

1.2 Chemical foundations

Examples: Number of Stereoisomers

What is the maximum number of possible stereo-isomers of the following compounds?



Cholesterol

$2^8 = 256$ possible stereoisomers.

But Nature makes only one!

1.2 Chemical foundations

What’s so great about chiral molecules?

Many biologically important molecules are chiral and optically active. Often, living systems contain **only one** of the possible stereochemical forms of a compound, or they are found in separate systems.

– L-lactic acid is found in living muscles; D-lactic acid is present in sour milk.

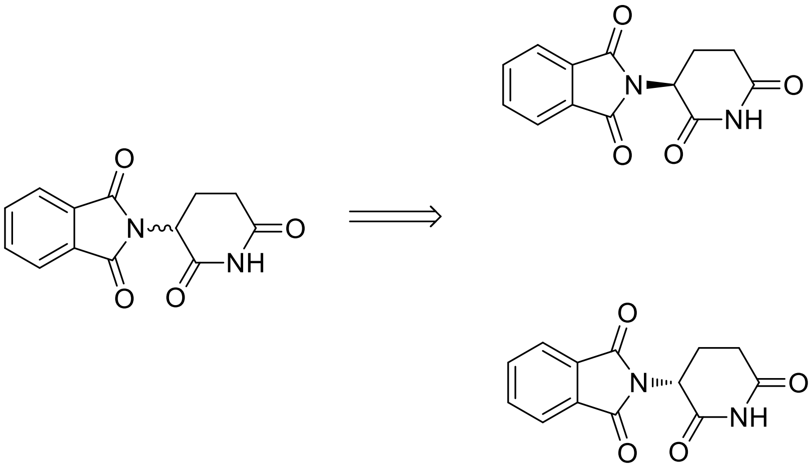
– In some cases, one form of a molecule is beneficial, and the enantiomer is a poison (e.g., **thalidomide**).

– Humans can metabolize D-monosaccharides but not L-isomers; only L-amino acids are used in protein synthesis.

1.2 Chemical foundations

Thalidomide （反应停事件）

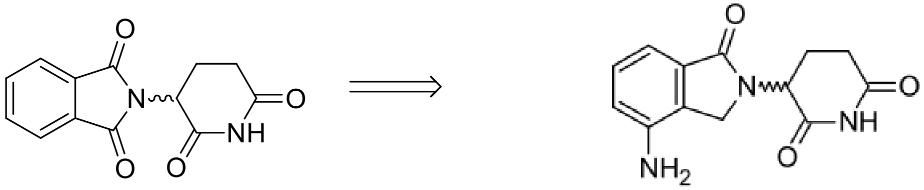
In the late 1950s and early 1960s, more than 10,000 children in 46 countries were born with deformities such as **phocomelia** as a consequence of thalidomide use.



Phocomelia
(海豹肢症畸形儿)

1.2 Chemical foundations

Thalidomide analog



Lenalidomide

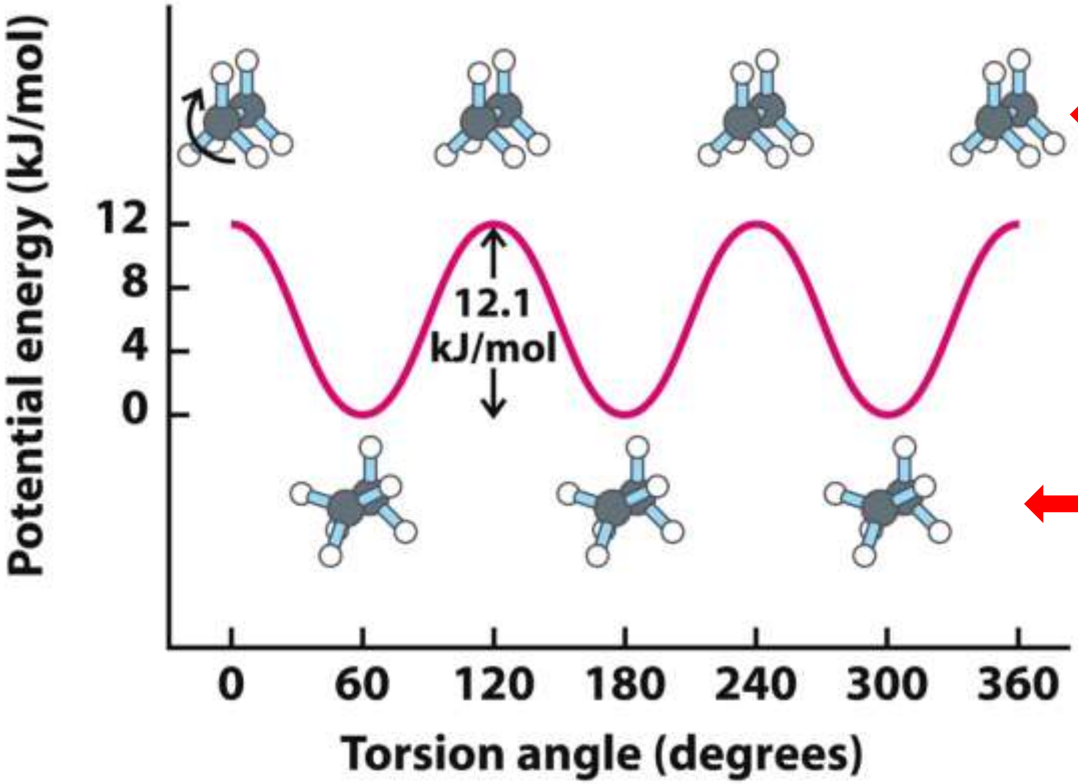
Use for :

- Multiple myeloma （**多发性骨髓瘤**）
- Myelodysplastic syndrome （**骨质增生异常综合症**）
- Other cancer treatment in clinical trial.

1.2 Chemical foundations

Cause of conformation

Freedom of rotation around the C—C bond



eclipsed, least stable

staggered, more stable

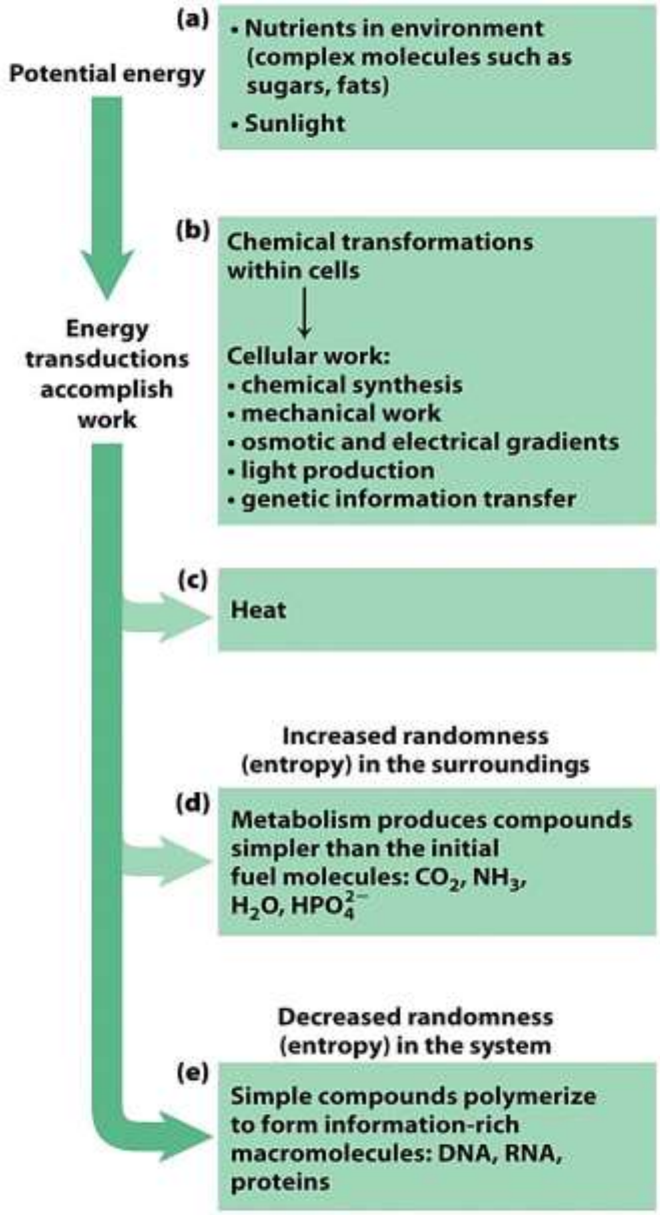
Figure 1-22
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

1.3 Physical foundations

The first law of thermodynamics: *in any physical or chemical change, the total amount of energy in the universe remains constant, although the form of the energy may change*.

- Organisms transform energy and matter from their surroundings
- Living organisms exist in a dynamic steady state, never at equilibrium with their surroundings
- The flow of electrons provides energy for organisms

All reactions involved in electron flow are **oxidation-reduction reactions**:
one reactant is oxidized (loses electrons) as another is reduced (gains electrons).



Potential energy

(a)
- Nutrients in environment (complex molecules such as sugars, fats)
- Sunlight

Energy transductions accomplish work

(b) Chemical transformations within cells

Cellular work:
- chemical synthesis
- mechanical work
- osmotic and electrical gradients
- light production
- genetic information transfer

(c) Heat

Increased randomness (entropy) in the surroundings

(d) Metabolism produces compounds simpler than the initial fuel molecules: CO_2, NH_3, H_2O, HPO_4^{2-}

Decreased randomness (entropy) in the system

(e) Simple compounds polymerize to form information-rich macromolecules: DNA, RNA, proteins

1.3 Physical foundations

The second law of thermodynamics: *the total entropy of the universe is continually increasing*, the tendency in nature is toward ever-greater disorder in the universe.

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

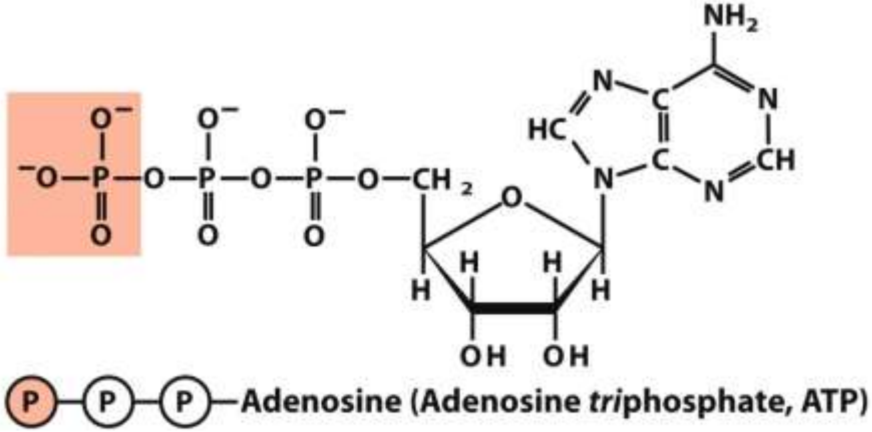
ΔG, free-energy (自由能) change
ΔH, enthalpy (焓) change
ΔS, entropy (熵) change
T, absolute temperature

J. Williard Gibbs, 1839–1903

A process tends to occur spontaneously only if **ΔG is negative** (if free energy is *released* in the process).

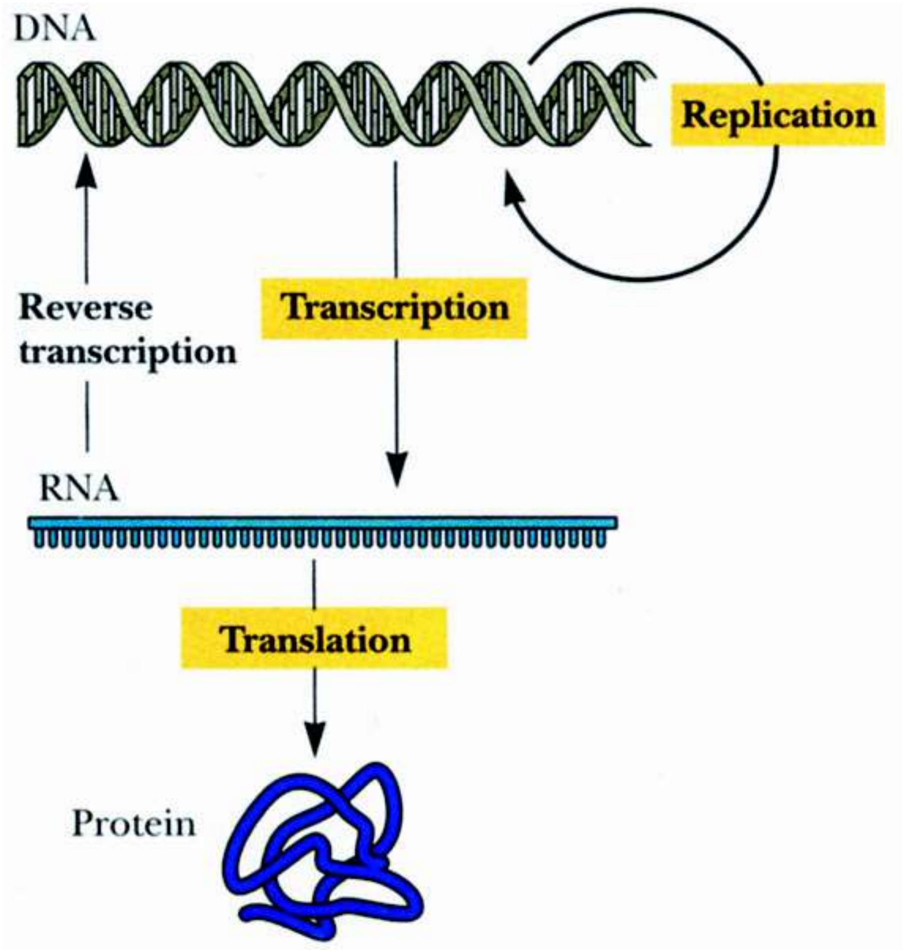
Creating and maintaining order requires work and energy!

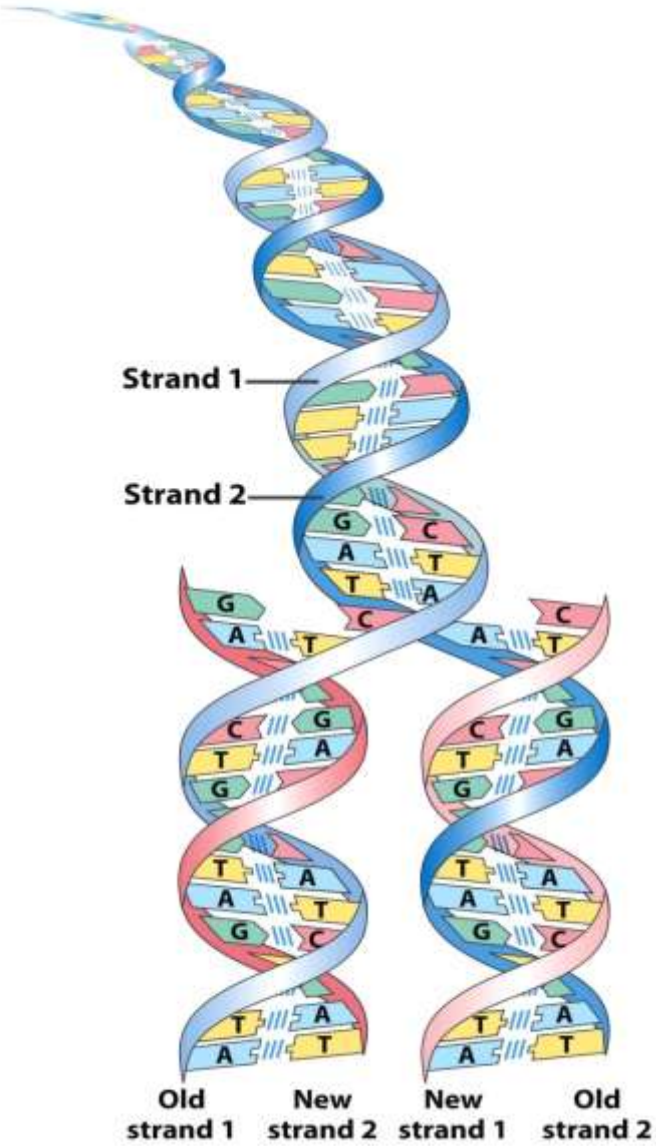
To synthesize macromolecules from their monomeric units, free energy must be supplied to the system.



1.4 Genetic foundations

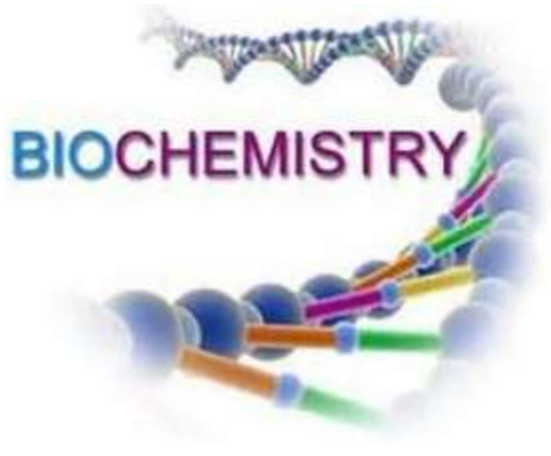
Genetic information is encoded in DNA





CHAPTER 2

Water



Water — H_2O

Water is the most abundant substance in living systems, making up **70%** or more of the weight of most organisms.

Vital for life, water is by far the most abundant component of every cell.

Water, Water, Everywhere

2.1 Weak Interactions in Aqueous Systems

I. Hydrogen bond

- The electrostatic interaction between the hydrogen atom of one water molecule and the oxygen atom of another yields the **hydrogen bond**.

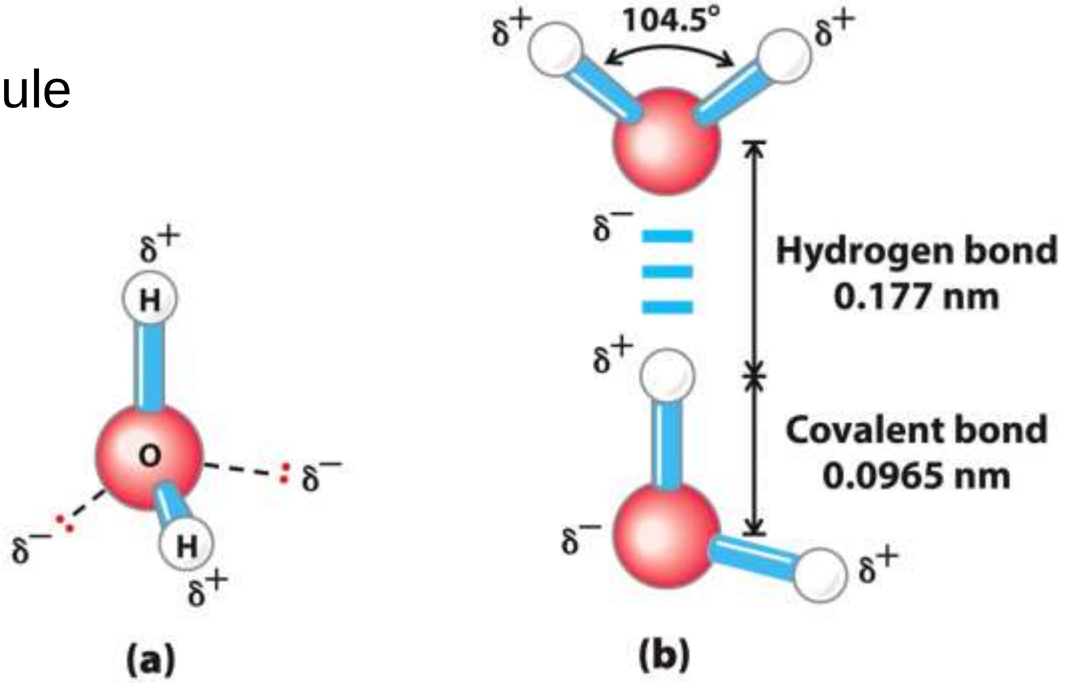


Figure 2-1
Lehninger Principles of Biochemistry, Sixth Edition

2.1 Weak Interactions in Aqueous Systems

- Hydrogen bonds can form between an electronegative atom (the hydrogen acceptor, usually oxygen or nitrogen) and a hydrogen atom covalently bonded to another electronegative atom (the hydrogen donor) in the same or another molecule.

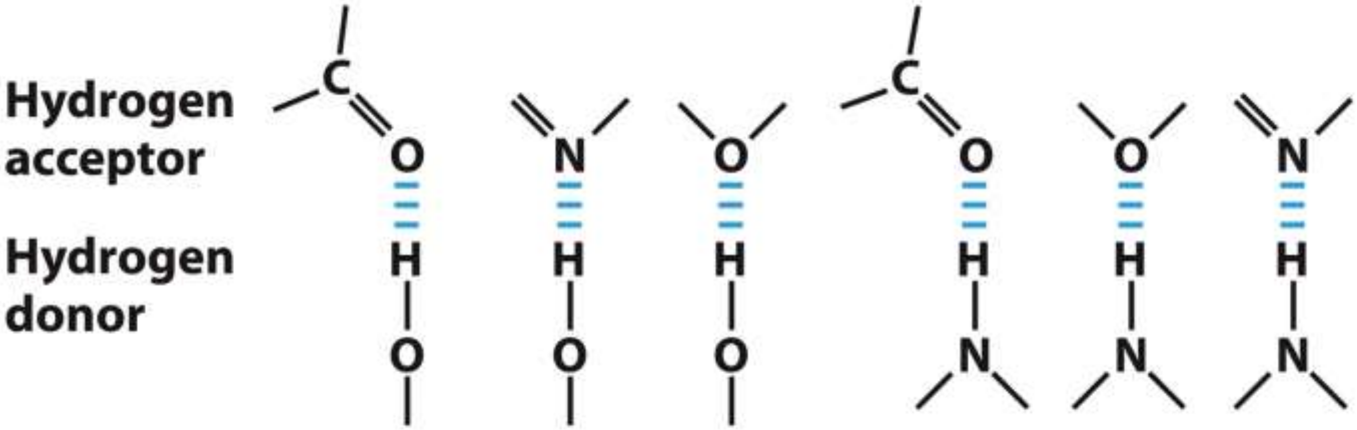


Figure 2-3
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

Hydrogen atoms covalently bonded to carbon atoms do not participate in hydrogen bonding.

2.1 Weak Interactions in Aqueous Systems

- Some biologically important hydrogen bonds

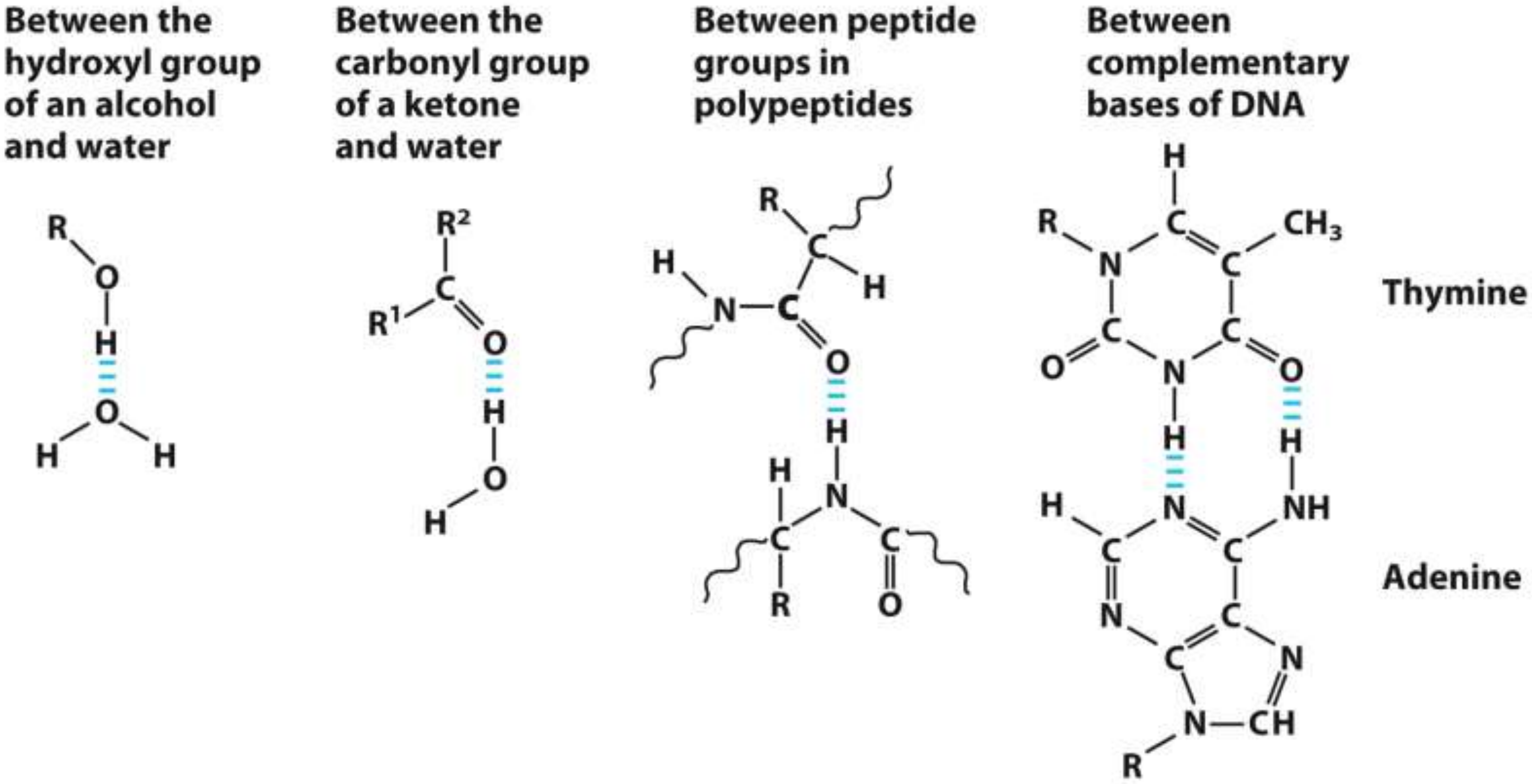


Figure 2-4
Lehninger Principles of Biochemistry, Sixth Edition

2.1 Weak Interactions in Aqueous Systems

➢ Property of hydrogen bonds

- **Hydrogen bonds** are relatively weak with bond dissociation energies of about **23 kJ/mol** compared to **470 kJ/mol** for a covalent O─H bond and **348 kJ/mol** for a covalent C─C bond .

- **Hydrogen bonds** can be easily broken – particularly if bent (e.g. DNA replication).

- **Hydrogen bonds** have directionalities.

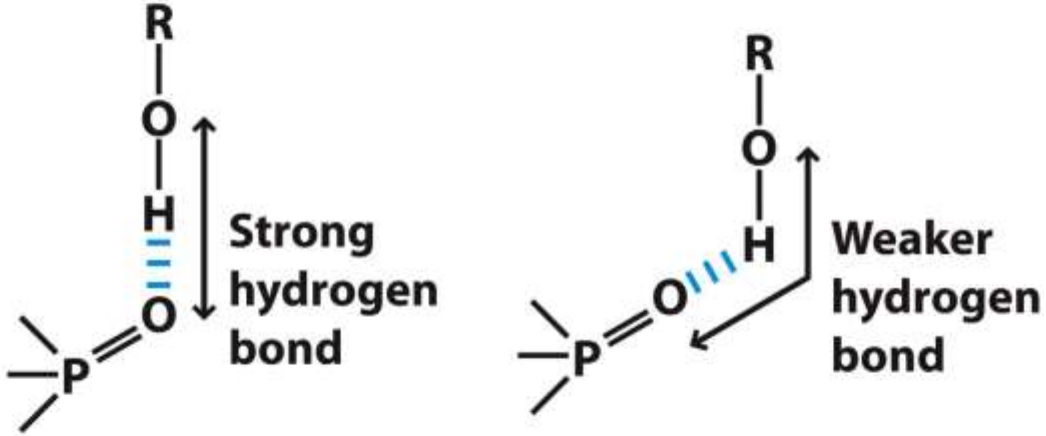


Figure 2-5
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

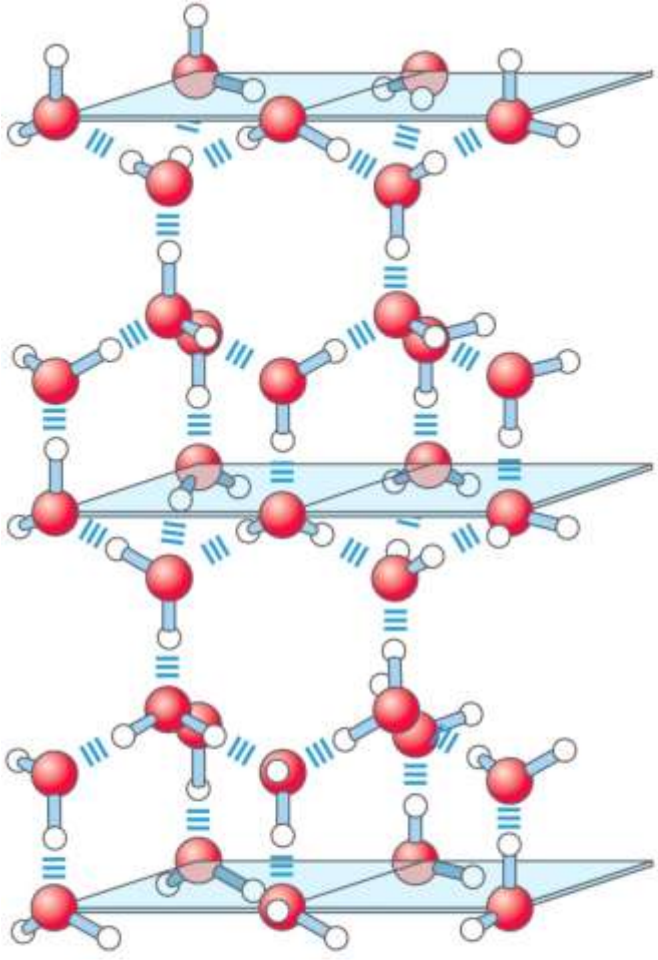
2.1 Weak Interactions in Aqueous Systems

➢ Hydrogen bonding gives water its unusual properties

- The tetrahedral arrangement of the water molecule gives each molecule the potential to form 4 hydrogen bonds (1 for each hydrogen and 2 for the oxygen).

- In the liquid state, the disorganization of the molecules yields an average of 3.4 bonds per molecule.

- In the solid state, the fixed nature of the molecule in the crystal lattice yields the full hydrogen bonding compliment.



Hydrogen bonding in ice

2.1 Weak Interactions in Aqueous Systems

- The hydrogen bonds in water exert a significant attractive force, causing water to cling to itself (**Cohesion**) and to other surfaces (**Adhesion**).

- Together, adhesion and cohesion enable water molecules to move upwards through narrow tubes against the force of gravity ─ a property of water known as **capillarity**. Water moves up a plant stem through cohesion-tension in the xylem ─ *only possible because of the hydrogen bonds*.

- Water must gain or lose a large amount of energy for its temperature to change – which makes it a stable environment to live in (**homeostasis**). Water's ability to absorb large amounts of energy (= high specific heat capacity) helps to keep cells at an even temperature despite changes to the external temperature.

2.1 Weak Interactions in Aqueous Systems

- Hydrogen bonds result in the high melting and boiling points for water

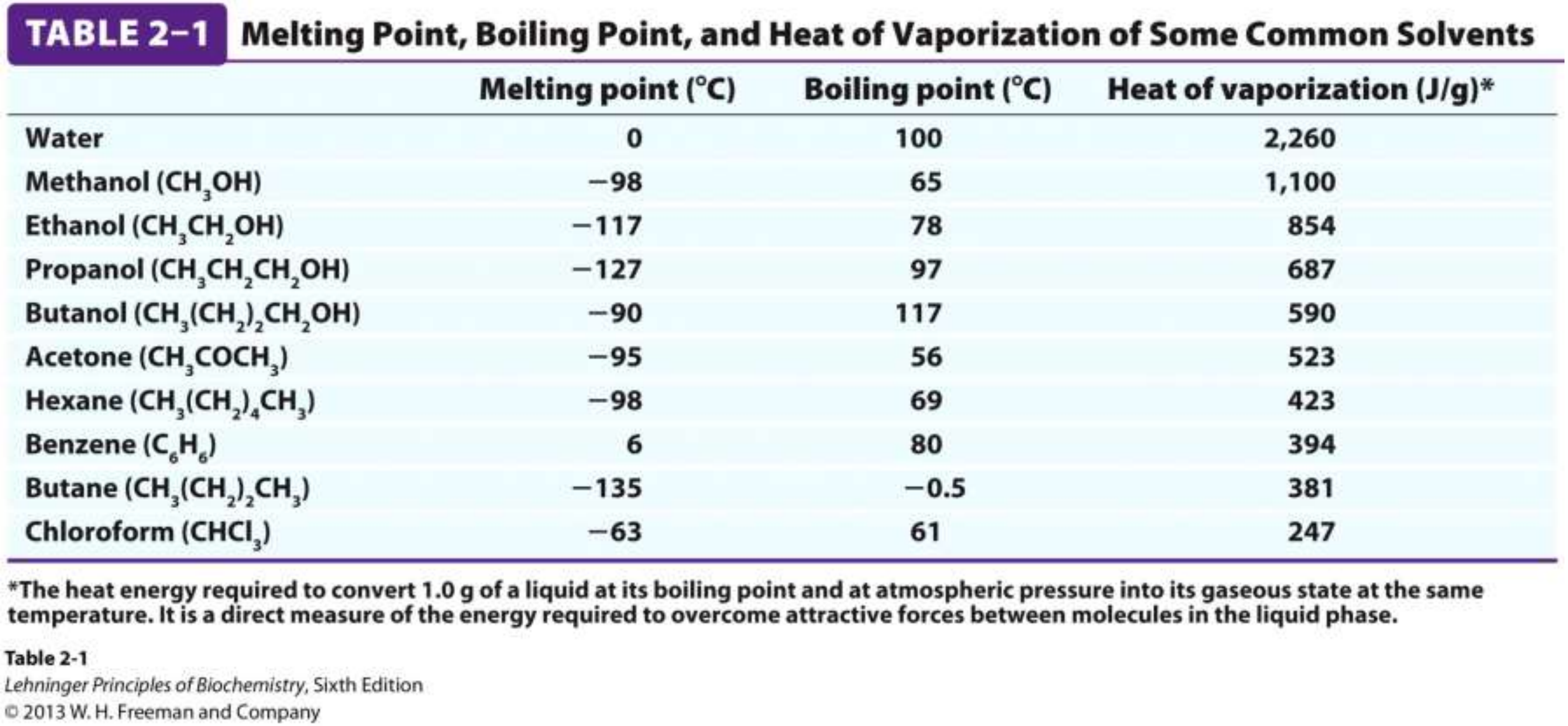


TABLE 2–1 Melting Point, Boiling Point, and Heat of Vaporization of Some Common Solvents

	Melting point (°C)	Boiling point (°C)	Heat of vaporization (J/g)*
Water	0	100	2,260
Methanol (CH_3OH)	−98	65	1,100
Ethanol (CH_3CH_2OH)	−117	78	854
Propanol ($CH_3CH_2CH_2OH$)	−127	97	687
Butanol ($CH_3(CH_2)_2CH_2OH$)	−90	117	590
Acetone (CH_3COCH_3)	−95	56	523
Hexane ($CH_3(CH_2)_4CH_3$)	−98	69	423
Benzene (C_6H_6)	6	80	394
Butane ($CH_3(CH_2)_2CH_3$)	−135	−0.5	381
Chloroform ($CHCl_3$)	−63	61	247

*The heat energy required to convert 1.0 g of a liquid at its boiling point and at atmospheric pressure into its gaseous state at the same temperature. It is a direct measure of the energy required to overcome attractive forces between molecules in the liquid phase.

Table 2-1
Lehninger Principles of Biochemistry, Sixth Edition

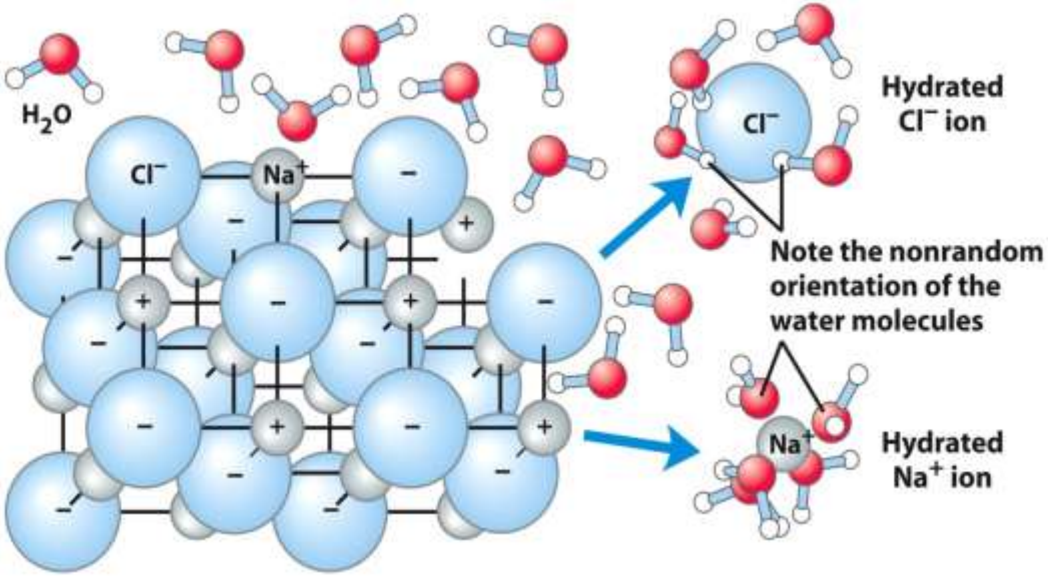
Though a small molecule, water is powerful …

2.1 Weak Interactions in Aqueous Systems

II. Ionic (or Charge-Charge) Interactions

- Ionic interactions are about 5-10% the strength of a C─C bond (20-40 vs. 350 kJ/mole)

- Charged or polar compounds (like NaCl) that dissolve easily in water are **hydrophilic** (亲水的), nonpolar molecules (like lipids and waxes) that poorly dissolve in water are **hydrophobic** (疏水的).



Note the nonrandom orientation of the water molecules

- The anions (Cl^-) are surrounded by the positively charged **hydrogens** on water.
- The cations (Na^+) are surrounded by the negatively charged **oxygen** on water.

2.1 Weak Interactions in Aqueous Systems

- Water readily dissolves biomolecules containing charged functional groups like carboxylic acids ($-COO^{-}$) and amines ($-NH_3^{+}$)

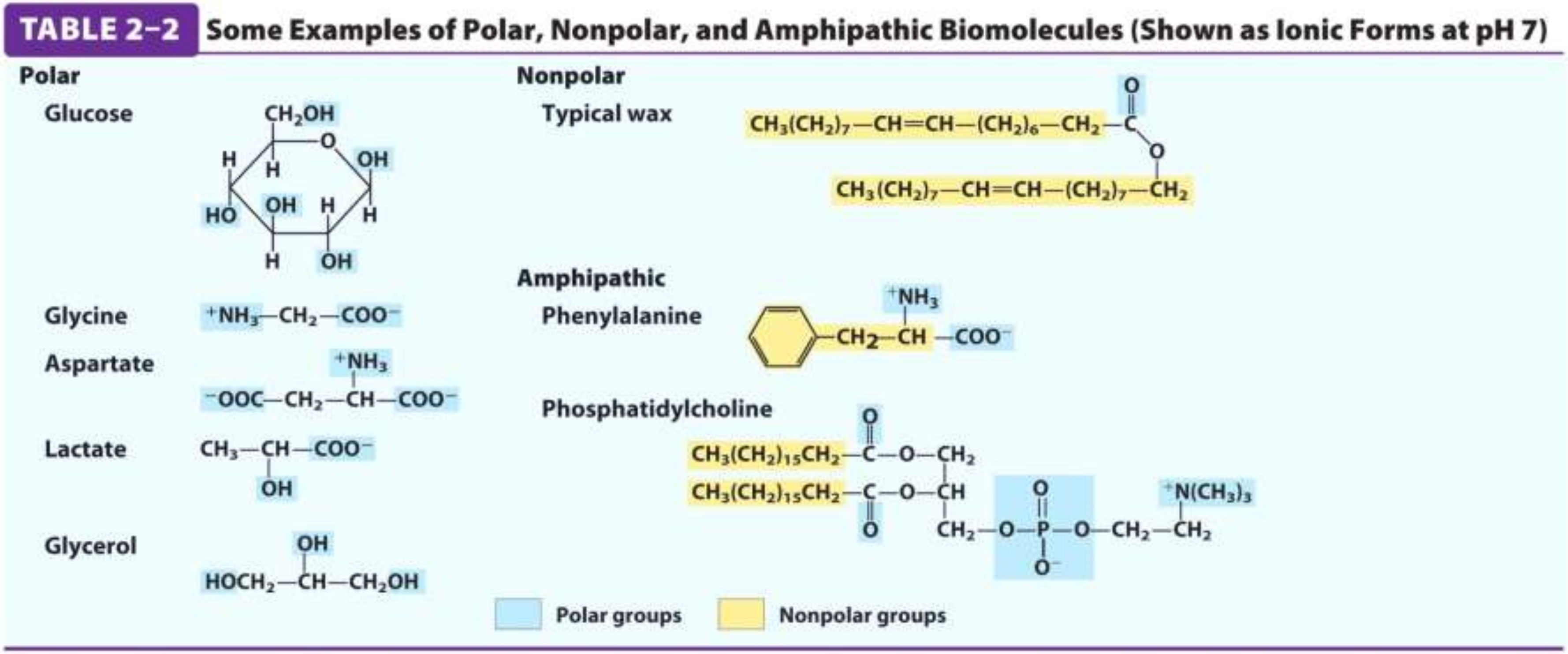


TABLE 2-2 **Some Examples of Polar, Nonpolar, and Amphipathic Biomolecules (Shown as Ionic Forms at pH 7)**

Polar

Glucose

Glycine $^{+}NH_3-CH_2-COO^{-}$

Aspartate $^{-}OOC-CH_2-\overset{^{+}NH_3}{\overset{|}{C}H}-COO^{-}$

Lactate $CH_3-\underset{\underset{OH}{|}}{CH}-COO^{-}$

Glycerol $HOCH_2-\overset{OH}{\overset{|}{C}H}-CH_2OH$

Nonpolar

Typical wax

$CH_3(CH_2)_7-CH=CH-(CH_2)_6-CH_2-\overset{O}{\overset{\|}{C}}-O-CH_2-(CH_2)_7-CH=CH-(CH_2)_7CH_3$

Amphipathic

Phenylalanine

Phosphatidylcholine

🟦 Polar groups 🟨 Nonpolar groups

Table 2-2

Lehninger Principles of Biochemistry, Sixth Edition

2.1 Weak Interactions in Aqueous Systems

III. Hydrophobic Interactions

The forces that hold the nonpolar regions of the molecules together are called **hydrophobic interactions**.

- Hydrophobic (“Water Hating”) interactions are ~ 2% the strength of a C─C bond (8 vs. 350 kJ/mole).
- Water becomes highly ordered around hydrophobic groups (-ΔS)
- Greasy chains stay together to minimize entropy loss by water.
- The hydrophobic effect is the exclusion of non-polar substances by water.

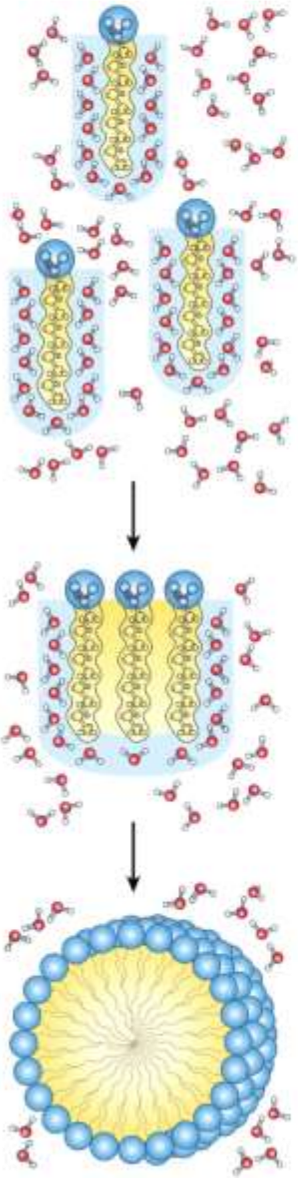
Figure 2-7a
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

2.1 Weak Interactions in Aqueous Systems

Amphipathic compounds in water form **micelles** to achieve stable structures that the nonpolar regions of the molecules cluster together to present the smallest hydrophobic area to the aqueous solvent, and the polar regions are arranged to maximize their interaction with the solvent.

The strength of hydrophobic interactions is not due to any intrinsic attraction between nonpolar moieties. Rather, it results from the system’s achieving the greatest thermodynamic stability by minimizing the number of ordered water molecules required to surround hydrophobic portions of the solute molecules.

Same idea results in the structure of biological membranes!



Dispersion of lipids in H_2O

Each lipid molecule forces surrounding H_2O molecules to become highly ordered.

Clusters of lipid molecules

Only lipid portions at the edge of the cluster force the ordering of water. Fewer H_2O molecules are ordered, and entropy is increased.

Micelles

All hydrophobic groups are sequestered from water; ordered shell of H_2O molecules is minimized, and entropy is further increased.

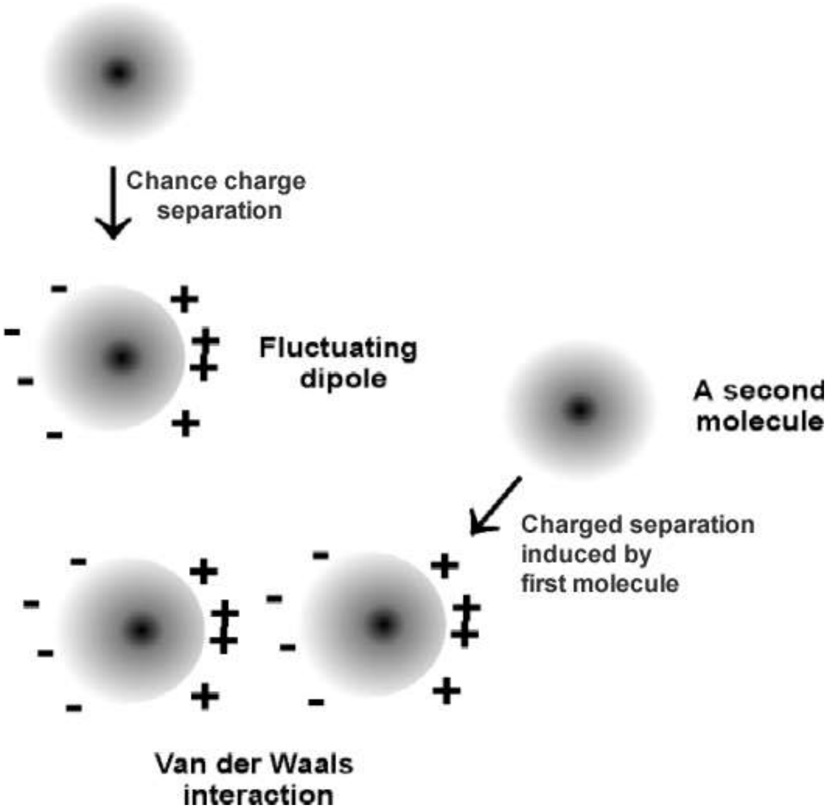
2.1 Weak Interactions in Aqueous Systems

IV. van der Waals Interactions

- In a molecule, electrons are constantly orbiting the nucleus and a region may become temporarily electron poor and slightly positive while another region becomes slightly negative. This creates a temporary dipole and two molecules with temporary dipoles are attracted to each other.

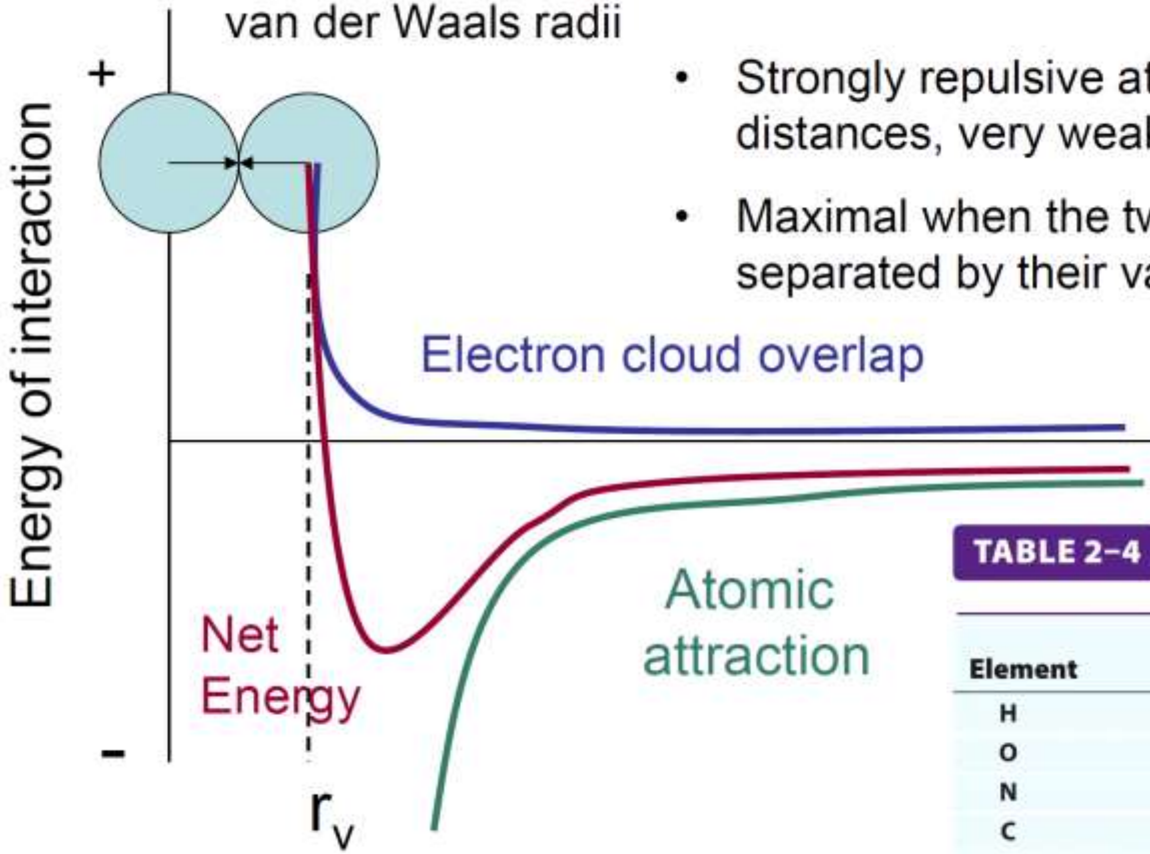
- **van der Waals** interactions result from the formation of instantaneous, temporary dipoles in non-polar molecules due to electron motion.

- They are ~ 1% the strength of a carbon-carbon bond (4 vs. 350 kJ/mole)



2.1 Weak Interactions in Aqueous Systems

- **van der Waal radius**
  A measure of how close that atom will allow another to approach



- Strongly repulsive at short internuclear distances, very weak at long distances
- Maximal when the two atoms are separated by their van der Waals radii

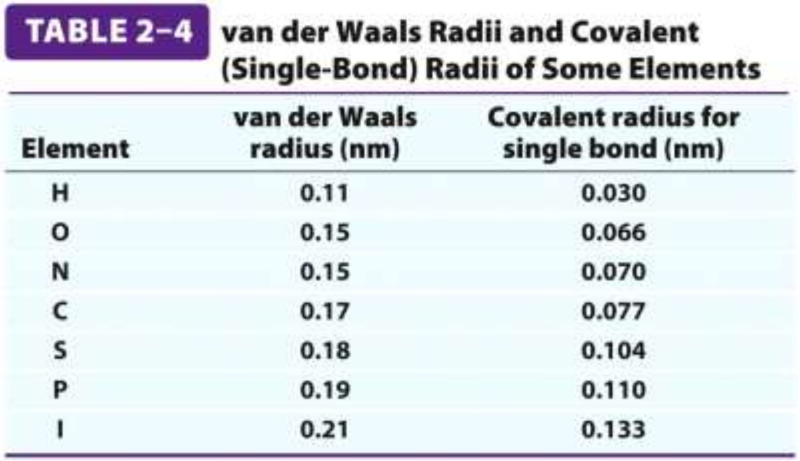


TABLE 2-4 van der Waals Radii and Covalent (Single-Bond) Radii of Some Elements

Element	van der Waals radius (nm)	Covalent radius for single bond (nm)
H	0.11	0.030
O	0.15	0.066
N	0.15	0.070
C	0.17	0.077
S	0.18	0.104
P	0.19	0.110
I	0.21	0.133

2.1 Weak Interactions in Aqueous Systems

Summary

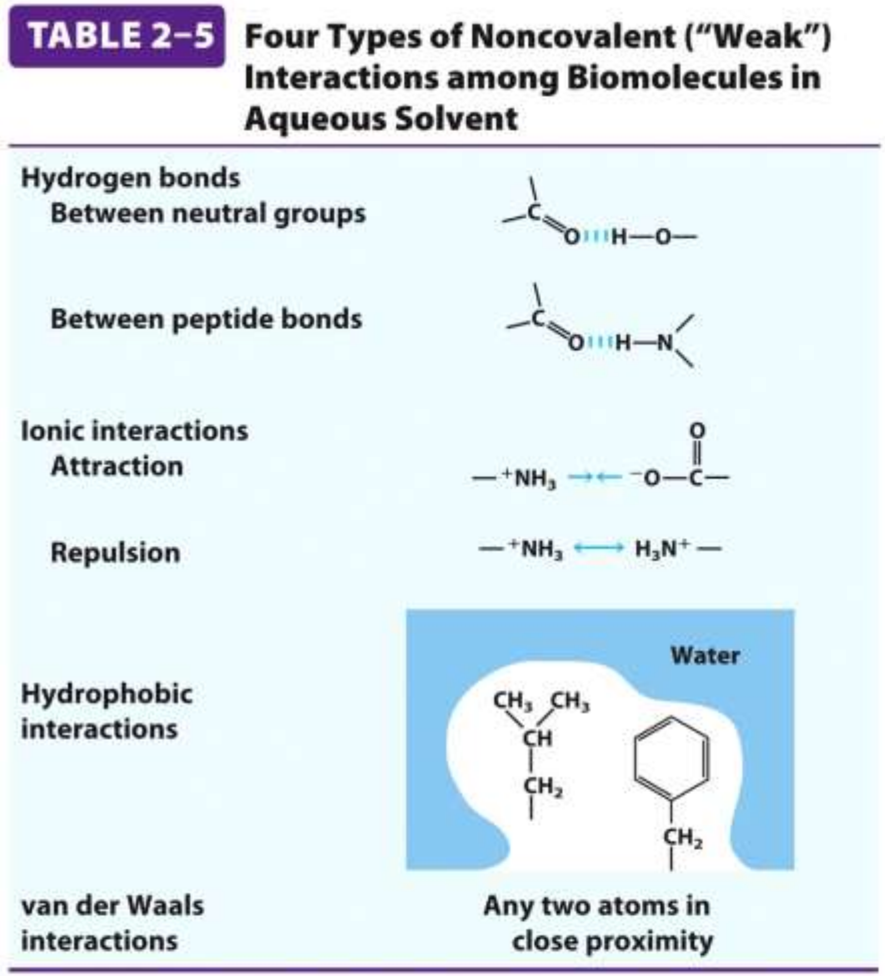


TABLE 2–5 **Four Types of Noncovalent ("Weak") Interactions among Biomolecules in Aqueous Solvent**

Hydrogen bonds	
Between neutral groups	$-C=O \cdots H-O-$
Between peptide bonds	$-C=O \cdots H-N<$
Ionic interactions	
Attraction	$-{}^{+}NH_3 \rightarrow\leftarrow {}^{-}O-\overset{O}{\overset{\Vert}{C}}-$
Repulsion	$-{}^{+}NH_3 \longleftrightarrow H_3N^{+}-$
Hydrophobic interactions	
van der Waals interactions	**Any two atoms in close proximity**

Table 2-5
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

Approx. energy

~ 20 kJ/mole

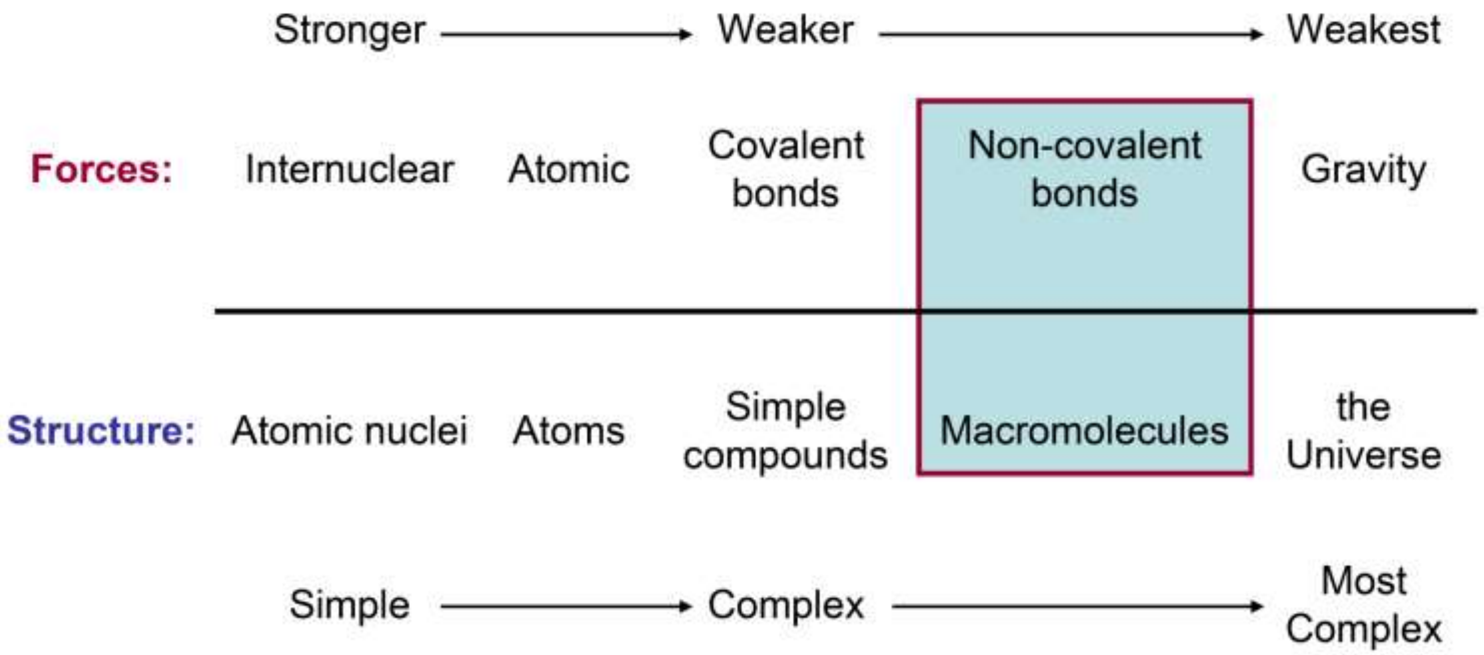
20 - 40 kJ/mole

~ 8 kJ/mole

~ 4 kJ/mole

2.1 Weak Interactions in Aqueous Systems

- **Weak interactions are crucial to macromolecular structure and function**



Stronger → Weaker → Weakest

Forces:	Internuclear	Atomic	Covalent bonds	Non-covalent bonds	Gravity
Structure:	Atomic nuclei	Atoms	Simple compounds	Macromolecules	the Universe

Simple → Complex → Most Complex

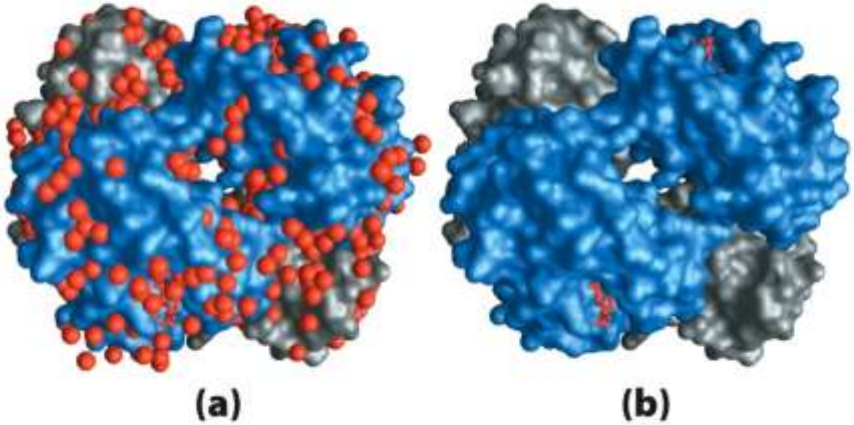
"The more complex the system, the weaker are the forces that govern its behavior"

- J. R. Platt

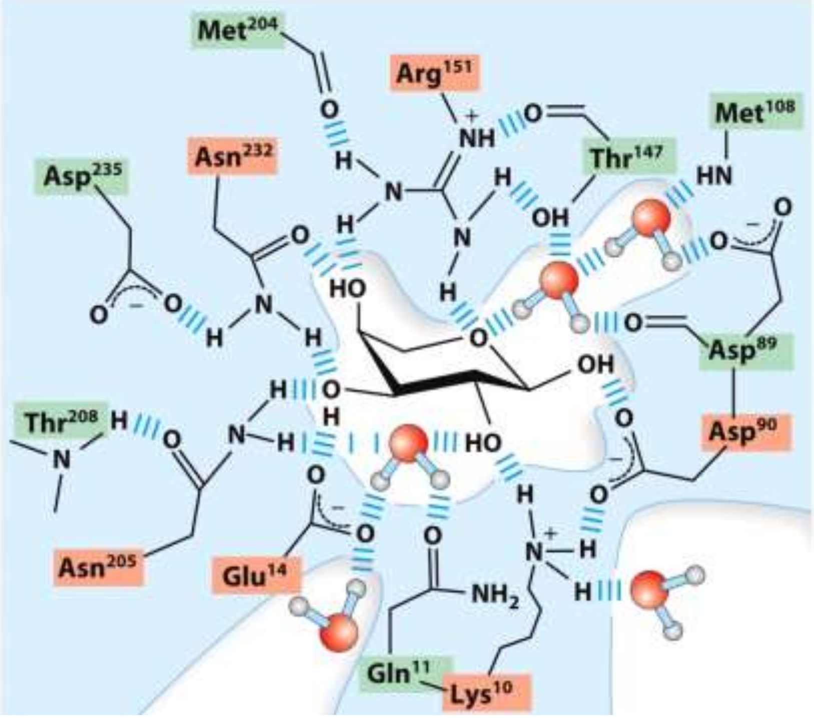
2.1 Weak Interactions in Aqueous Systems

- **Water as “part” of proteins**

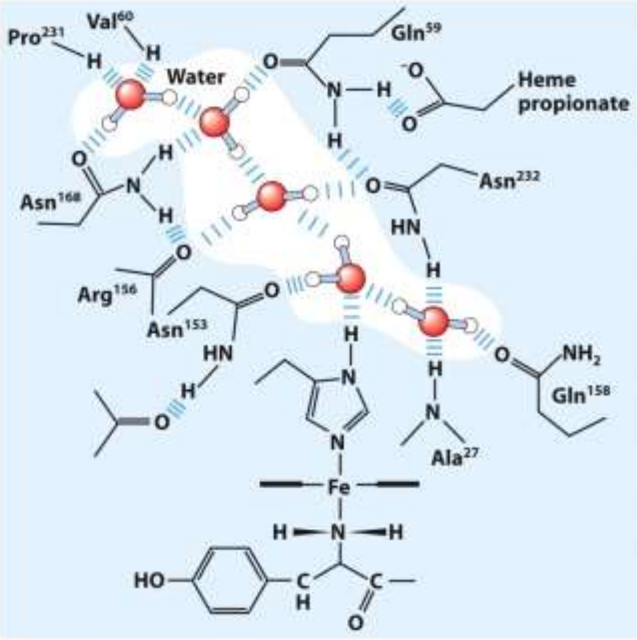
Same in DNA and RNA!



Water binding in hemoglobin



Hydrogen-bonded water as part of a protein's sugar binding site



Water chain in cytochrome *f*

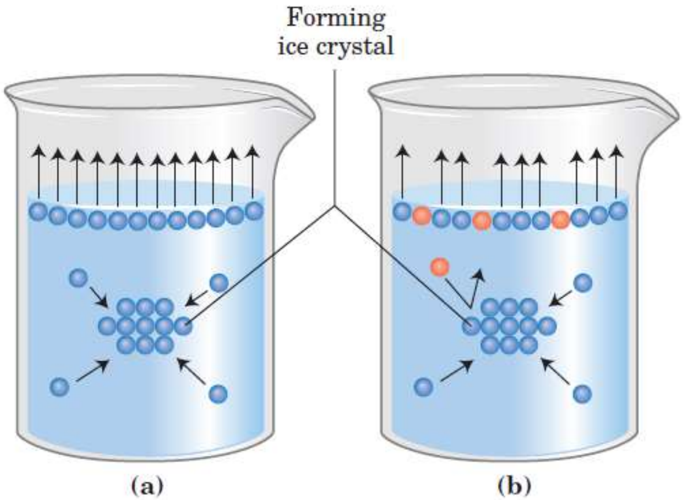
2.1 Weak Interactions in Aqueous Systems

➢ Colligative Properties of Water

Colligative Properties: properties of solutions that depend **ONLY** on the number of solute particles in solution, **NOT** on the identity of the solute.

- Solutes affect properties of the solvent by lowering the effective concentration of the solvent, so that
  - Vapor pressure lowering
  - Freezing point depression
  - Boiling point elevation
  - Osmotic pressure

- For water, the presence of a solute disrupts the hydrogen bonding network.



In **pure water,** every molecule at the surface is H_2O, and all contribute to the vapor pressure. Every molecule in the bulk solution is H_2O, and can contribute to formation of ice crystals.

In this **solution,** the effective concentration of H_2O is reduced; only 3 of every 4 molecules at the surface and in the bulk phase are H_2O. The vapor pressure of water and the tendency of liquid water to enter a crystal are reduced proportionately.

2.1 Weak Interactions in Aqueous Systems

➢ Osmotic pressure

Water molecules diffusing from the region of higher water concentration to the region of lower water concentration produce **osmotic pressure**.

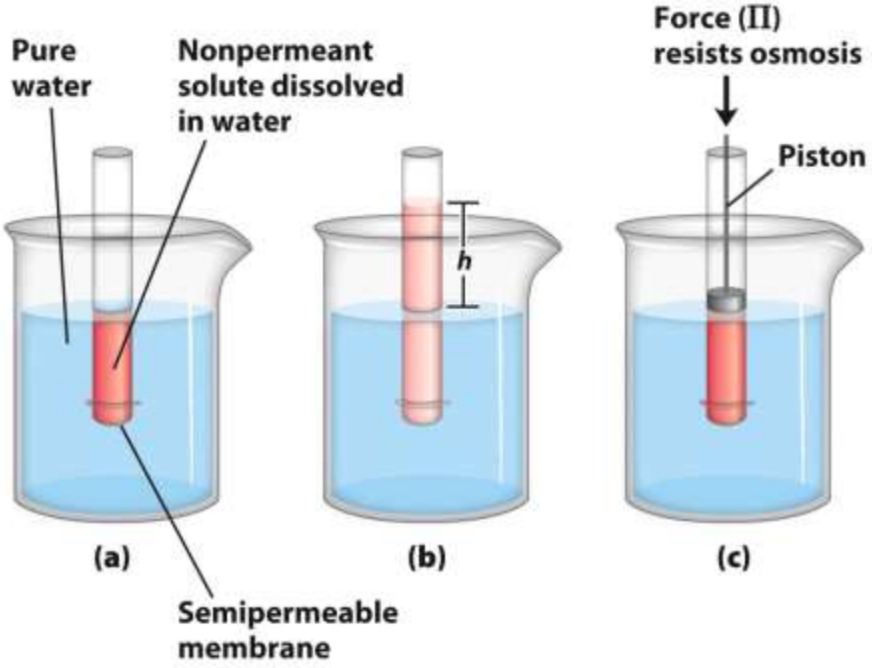


Figure 2-12
Lehninger Principles of Biochemistry, Sixth Edition

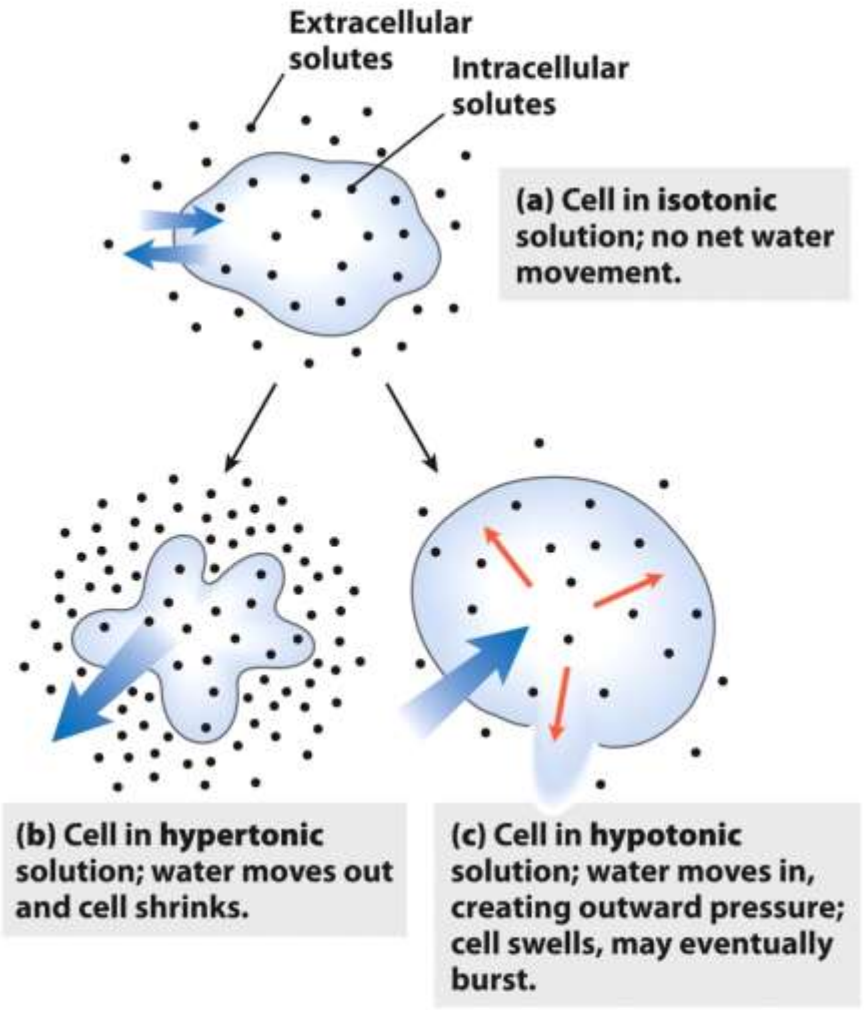


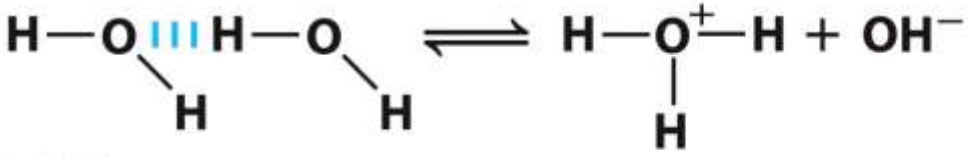
Figure 2-13
Lehninger Principles of Biochemistry, Sixth Edition

2.2 Ionization of Water, Weak Acids, and Weak Bases

➢ Pure Water Is Slightly Ionized

Water molecules have a slight tendency to undergo reversible ionization to yield a hydrogen ion (a proton) and a hydroxide ion

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



Unnumbered 2 p58
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

Although we commonly show the dissociation product of water as H^+, free protons do not exist in solution; hydrogen ions formed in water are immediately hydrated to form **hydronium ions** (H_3O^+).

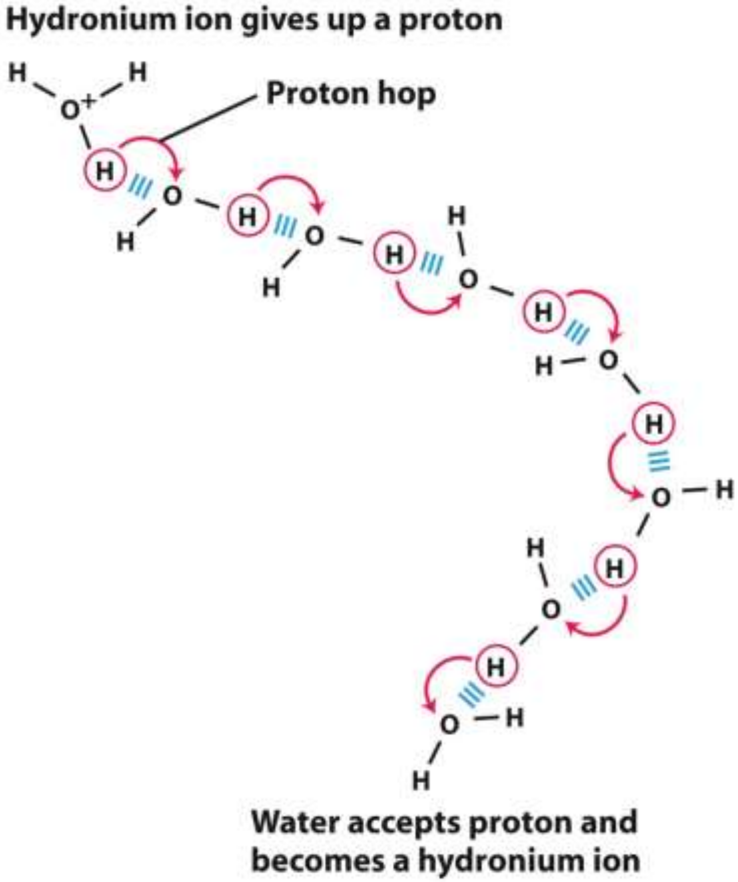


Figure 2-14
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

2.2 Ionization of Water, Weak Acids, and Weak Bases

➢ Equilibrium Constant K_{eq} of water

Equilibrium constant K_{eq}

The equilibrium constant is **fixed** and **characteristic** for any given chemical reaction at a specified temperature.

$$A + B \rightleftharpoons C + D \qquad K_{eq} = \frac{[C][D]}{[A][B]}$$

K_{eq} of water

$$H_2O \rightleftharpoons H^+ + OH^- \qquad K_{eq} = \frac{[H^+][OH^-]}{[H_2O]}$$

Concentration of pure water is 55.5 M —(1,000 g/L)/(18.015 g/mol) →

$$K_{eq} = \frac{[H^+][OH^-]}{[55.5\ \mathrm{M}]}$$

25°C

Ion product constant of water, K_w

$$(55.5\ \mathrm{M})(K_{eq}) = [H^+][OH^-] = K_w$$

K_{eq}= 1.8 x 10^{-16} M (measured)

$$\boxed{\begin{aligned} K_w &= [H^+][OH^-] = (55.5\ \mathrm{M})(1.8 \times 10^{-16}\ \mathrm{M}) \\ &= 1.0 \times 10^{-14}\ \mathrm{M}^2 \end{aligned}}$$

@ neutral pH ($[H^+] = [OH^-]$)

$$K_w = [H^+][OH^-] = [H^+]^2 = [OH^-]^2$$

$$[H^+] = \sqrt{K_w} = \sqrt{1 \times 10^{-14}\ \mathrm{M}^2}$$

$$[H^+] = [OH^-] = 10^{-7}\ \mathrm{M}$$

2.2 Ionization of Water, Weak Acids, and Weak Bases

- **pH** designates the H^+ and OH^- Concentrations

$$\boxed{\mathrm{pH} = \log \frac{1}{[\mathrm{H}^+]} = -\log\,[\mathrm{H}^+]}$$

TABLE 2-6 **The pH Scale**

$[H^+]$ (M)	pH	$[OH^-]$ (M)	pOH*
10^0 (1)	0	10^{-14}	14
10^{-1}	1	10^{-13}	13
10^{-2}	2	10^{-12}	12
10^{-3}	3	10^{-11}	11
10^{-4}	4	10^{-10}	10
10^{-5}	5	10^{-9}	9
10^{-6}	6	10^{-8}	8
10^{-7}	7	10^{-7}	7
10^{-8}	8	10^{-6}	6
10^{-9}	9	10^{-5}	5
10^{-10}	10	10^{-4}	4
10^{-11}	11	10^{-3}	3
10^{-12}	12	10^{-2}	2
10^{-13}	13	10^{-1}	1
10^{-14}	14	10^0 (1)	0

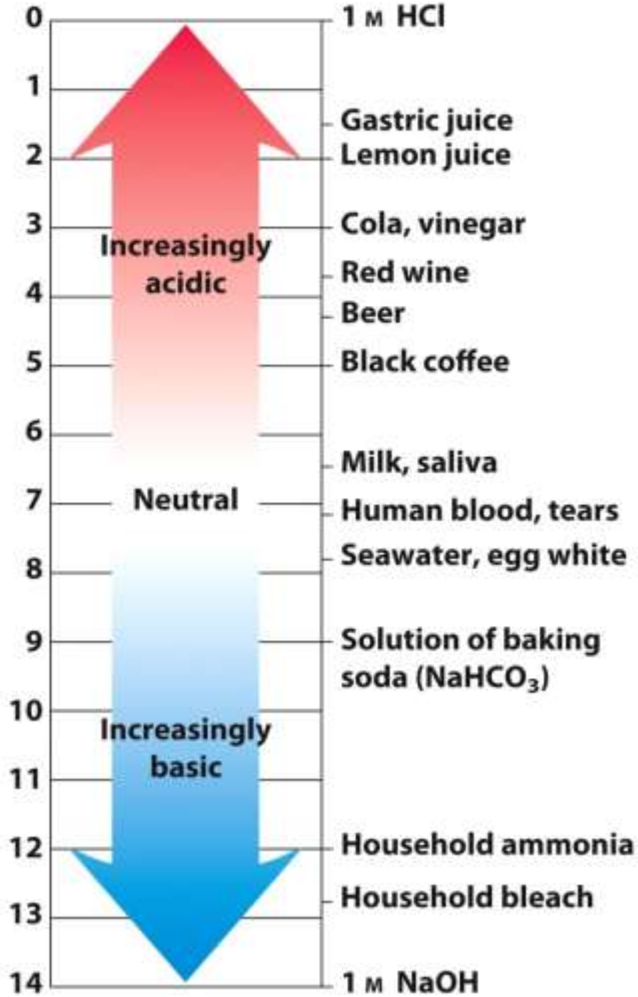


Figure 2-15
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

2.2 Ionization of Water, Weak Acids, and Weak Bases

➢ Weak acids & weak bases

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

A^-, conjugate base

Acids, proton donors
Bases, proton acceptors

- Weak acids and bases—those not completely ionized when dissolved in water. Weak acids have only a modest tendency to shed their protons.
- For biological systems, protons are necessary for numerous cellular processes, therefore, a source of protons are need:
  - ✗ Ionization of a strong acid is too big
  - ✗ Ionization of water itself is way too little
  - ✓ Ionization of a weak acid is just right

Water: $K_{eq} = 1.8 \times 10^{-16}$
Acetic acid: $K_{eq} = 1.7 \times 10^{-5}$

A 100 billion-fold difference…

$$HAc \rightleftharpoons H^+ + Ac^-$$

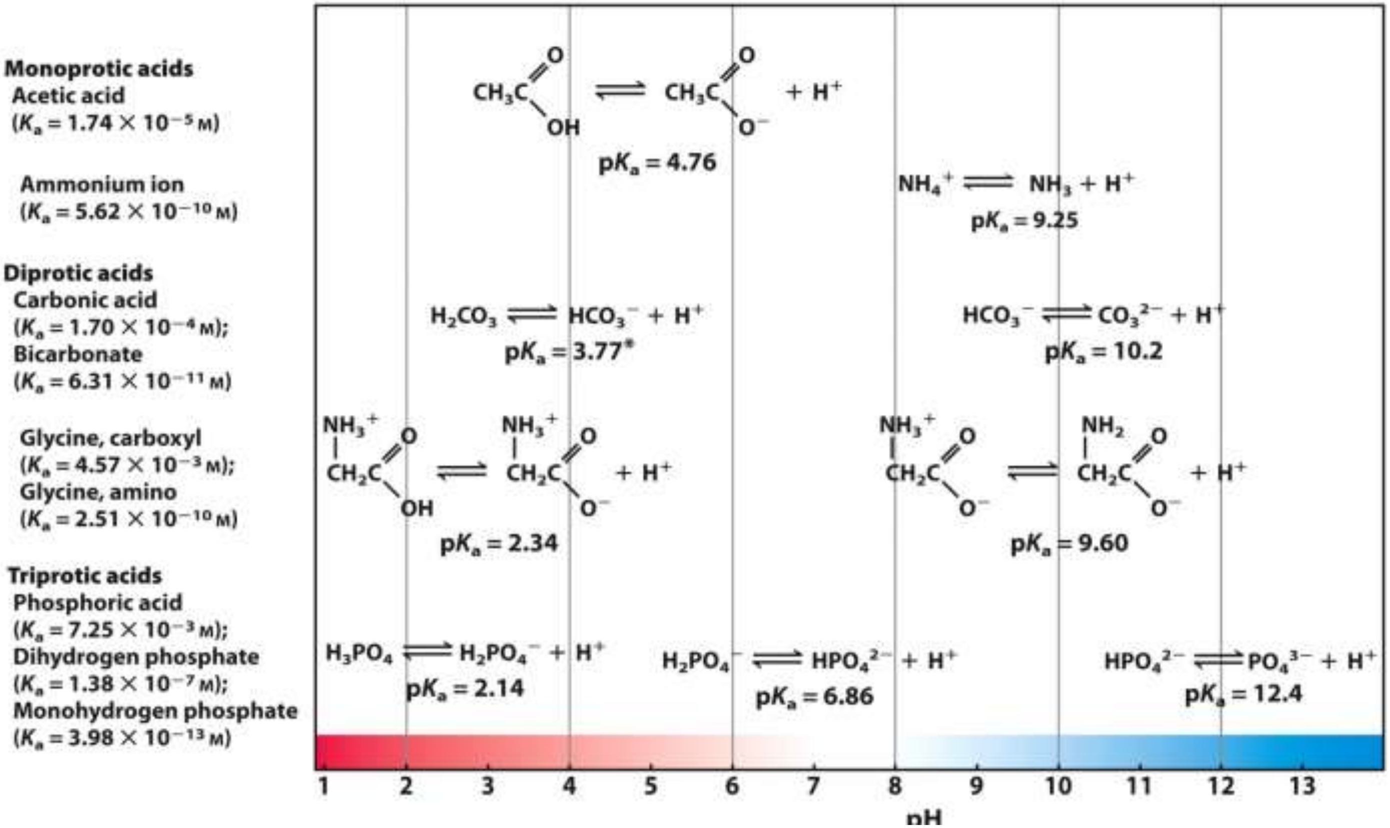
$$K_a = \frac{[H^+][Ac^-]}{[HAc]} = 1.74 \times 10^{-5}\ \text{M}$$

2.2 Ionization of Water, Weak Acids, and Weak Bases

- **p*K*$_a$**

Equilibrium constant K_{eq} for ionization reactions is usually called **ionization constants** or **acid dissociation constants**, often designated K_a.

$$\boxed{\begin{aligned} pK_a &= \log \frac{1}{K_a} \\ &= -\log K_a \end{aligned}}$$



Weak acids and bases have characteristic acid dissociation constants

2.2 Ionization of Water, Weak Acids, and Weak Bases

➢ Titration curves for weak acids

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

$$K_{eq} = \frac{[H^+][A^-]}{[HA]} = K_a$$

- On the titration curve graph, it is the inflection point at which:

  $[HA] = [A^-]$

- The pK_a is equal to the pH at which the acid and its conjugate base exist at same concentration.

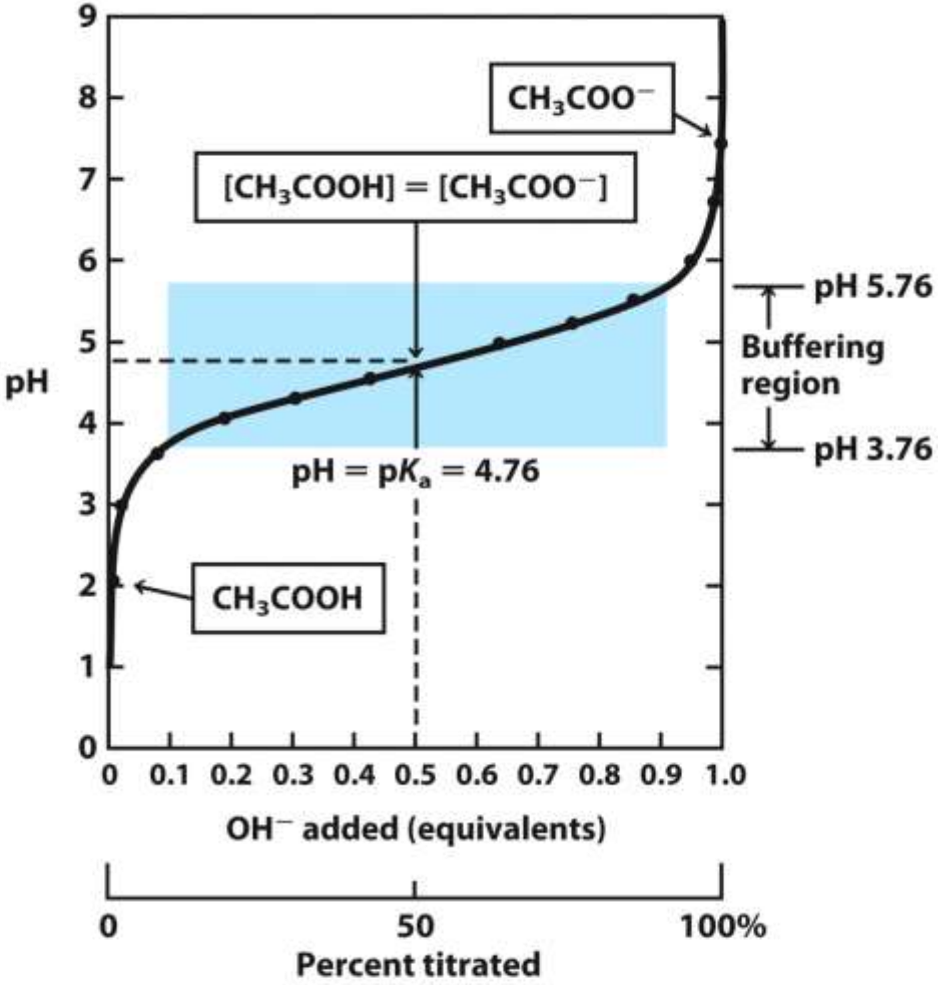


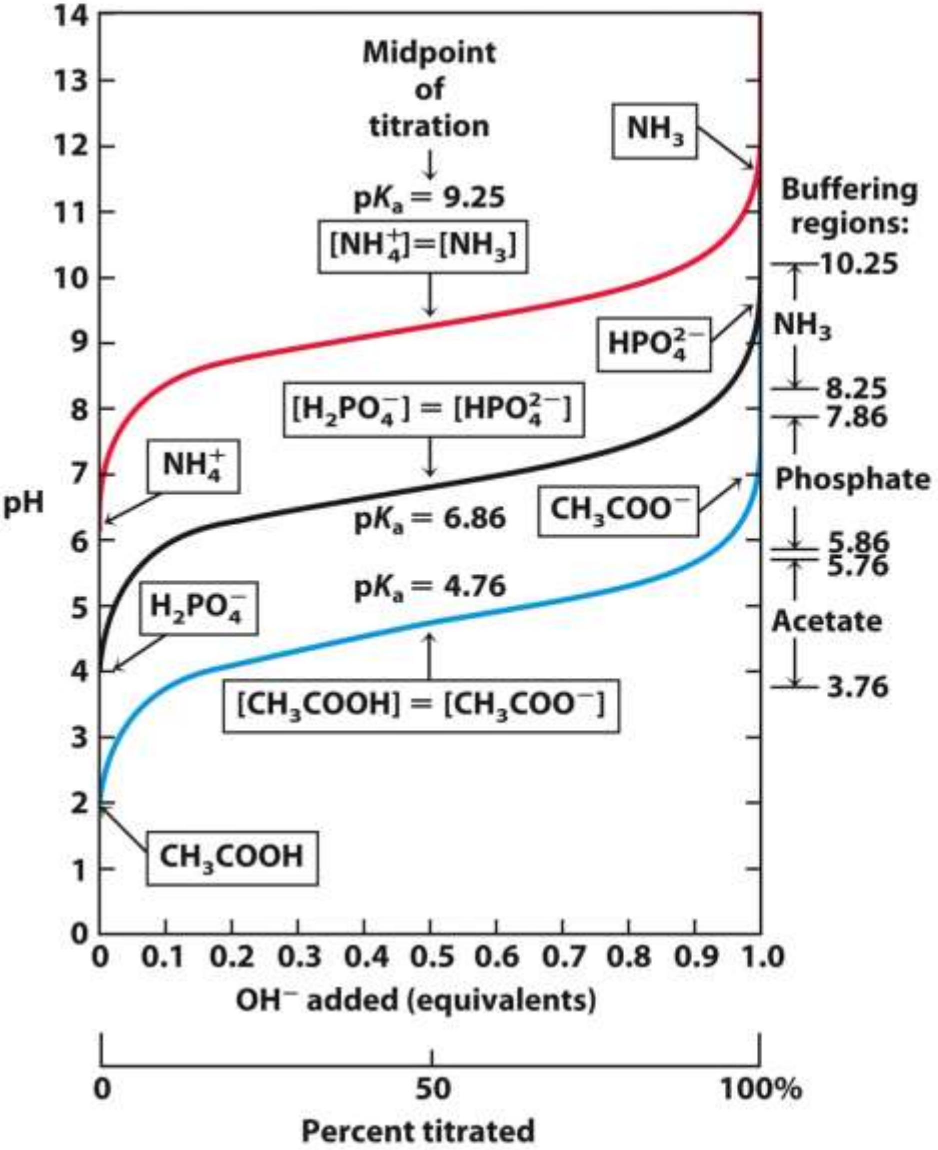
Figure 2-17
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

2.2 Ionization of Water, Weak Acids, and Weak Bases

- The larger the pK_a, the weaker the acid

The stronger the acid, the smaller its pK_a; the stronger the base, the larger its pK_a.

The pK_a can be determined experimentally; it is the pH at the midpoint of the titration curve for the acid or base.



2.3 Buffering against pH Changes in Biological Systems

➢ Buffers

- **Buffers** are mixtures of weak acids and their conjugate bases
- Buffers are aqueous systems that tend to **resist changes in pH** when small amounts of acid (H^+) or base (OH^-) are added.
- The effective buffering region is usually at pH values equal to the $pK_a \pm 1$
- The **buffer capacity** is the solution's ability to resist pH change, which is determined by:

  1° the pK_a of the weak acid

  2° the total concentration of the weak acid plus its conjugate base

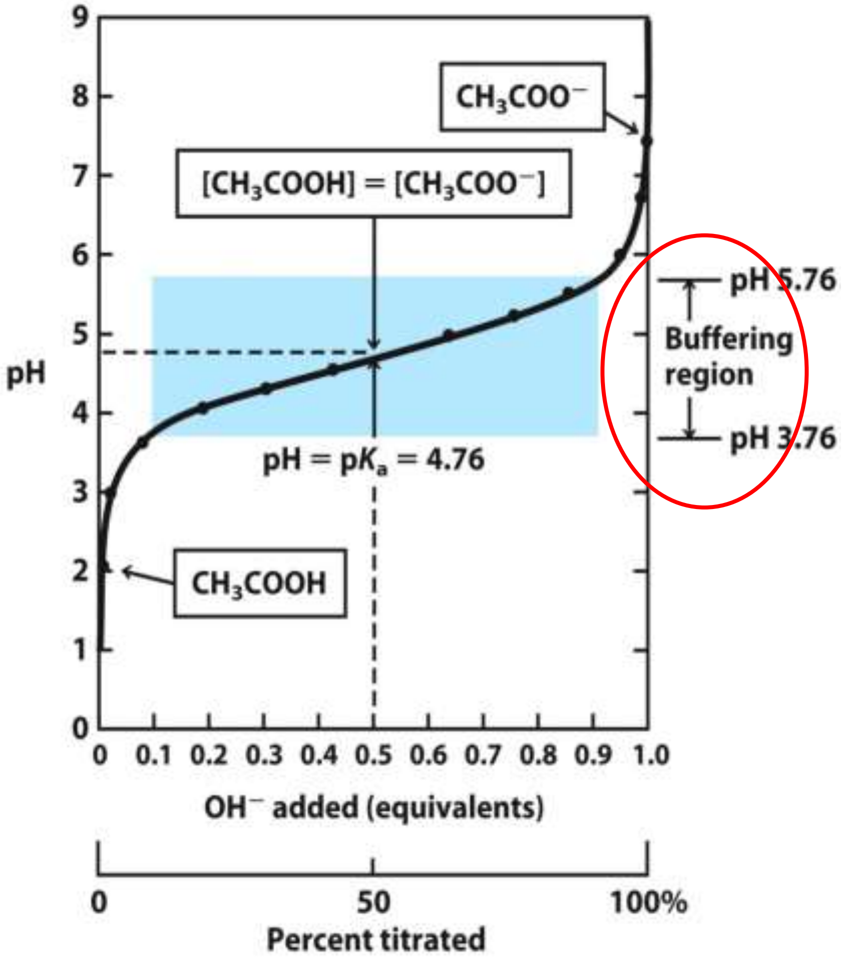


Figure 2-17
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

2.3 Buffering against pH Changes in Biological Systems

➢ Why buffering system?

- Almost every biological process is **pH dependent**; a small change in pH produces a large change in the rate of the process.

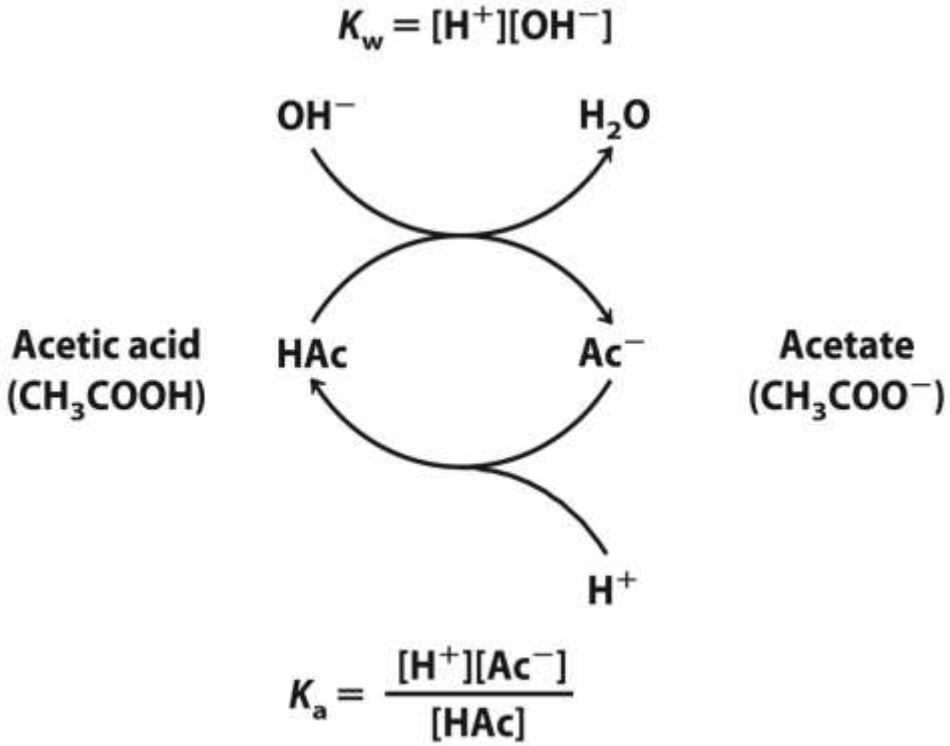
- Cells and organisms maintain a specific and constant cytosolic pH, keeping biomolecules in their optimal ionic state, usually near pH 7. In multicellular organisms, the pH of extracellular fluids is also tightly regulated.

- Constancy of pH is achieved primarily by **biological buffers**: mixtures of weak acids and their conjugate bases.

2.3 Buffering against pH Changes in Biological Systems

➢ How do buffers work?

- Whenever H^+ or OH^- is added to a buffer, the result is a small change in the ratio of the relative concentrations of the weak acid and its anion and thus a small change in pH.
- The decrease in concentration of one component of the system is balanced exactly by an increase in the other. The sum of the buffer components does not change, only their ratio.



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

$$K_a = \frac{[H^+][Ac^-]}{[HAc]}$$

- Buffering action is simply the consequence of two reversible reactions taking place simultaneously and reaching their points of equilibrium as governed by their equilibrium constants, K_w and K_a.

2.3 Buffering against pH Changes in Biological Systems

➢ Henderson-Hasselbalch equation

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

$$[H^+] = K_a \frac{[HA]}{[A^-]}$$

$$-\log[H^+] = -\log K_a - \log \frac{[HA]}{[A^-]}$$

$$pH = pK_a - \log \frac{[HA]}{[A^-]}$$

$$\boxed{pH = pK_a + \log \frac{[A^-]}{[HA]}}$$

Henderson-Hasselbalch equation

Usage of Henderson-Hasselbalch equation:

(1) calculate pK_a, given pH and the molar ratio of proton donor and acceptor;

(2) calculate pH, given pK_a and the molar ratio of proton donor and acceptor;

(3) calculate the molar ratio of proton donor and acceptor, given pH and pK_a.

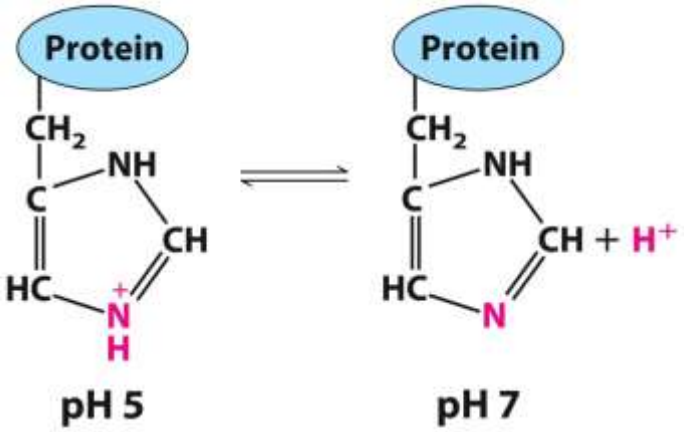
For example

When $[HA] = [A^-]$

$$pH = pK_a + \log 1 = pK_a + 0 = pK_a$$

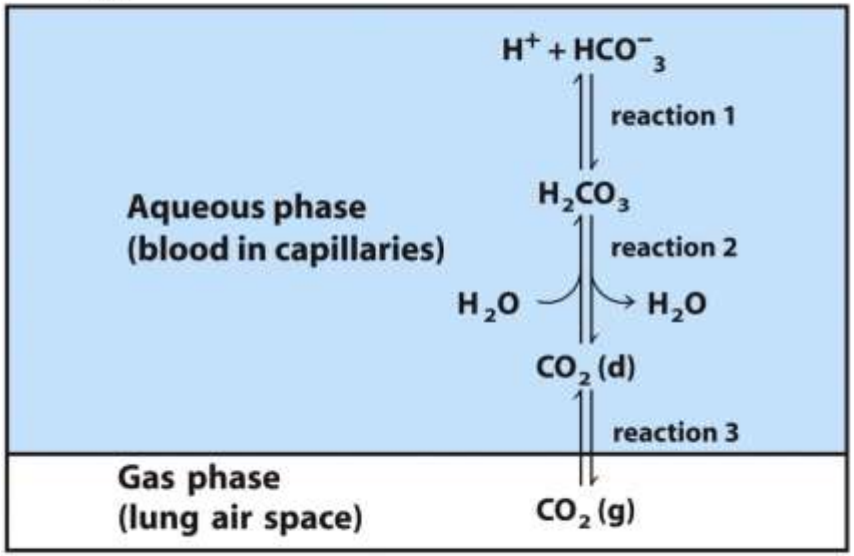
2.3 Buffering against pH Changes in Biological Systems

- **Weak acids or bases buffer cells and tissues against pH changes**
  - Many amino acids with functional groups that are weak acids or weak bases



  - Two especially important biological buffers are the **phosphate** and **bicarbonate** systems.

$$H_2PO_4^- \rightleftharpoons H^+ + HPO_4^{2-}$$



The bicarbonate buffer system

2.3 Buffering against pH Changes in Biological Systems

pH optimum

Enzymes typically show maximal catalytic activity at a characteristic pH, called the **pH optimum.**

- The catalytic activity of enzyme is especially sensitive to pH values, just above or below the optimum can lead to a drastic drop off in activity.
- Many aspects of cell structure and function are dependent on pH.
- Biological systems must be able to finely control the pH in order to maintain metabolic and cellular functions.

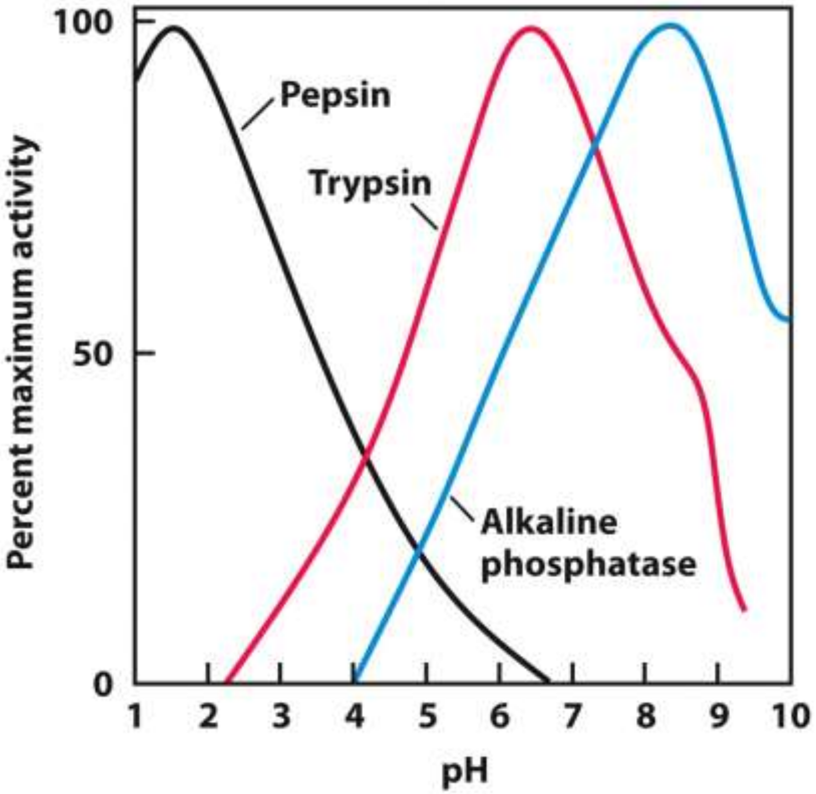
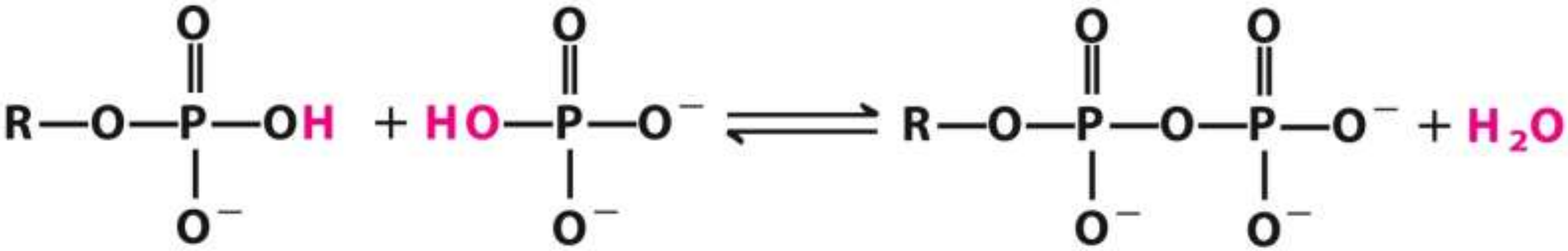


Figure 2-22
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

2.4 Water as a Reactant

Water is not just the solvent in which the chemical reactions of living cells occur; it is very often a **direct participant** in those reactions.

- **Condensation reaction**



$$\mathrm{R{-}O{-}\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O^-}{|}}{P}}{-}OH} + \mathrm{HO{-}\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O^-}{|}}{P}}{-}O^-} \rightleftharpoons \mathrm{R{-}O{-}\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O^-}{|}}{P}}{-}O{-}\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O^-}{|}}{P}}{-}O^-} + \mathrm{H_2O}$$

(ADP)

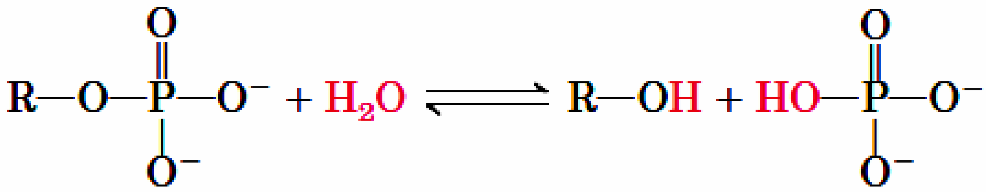
(ATP)

Phosphoanhydride

Figure 2-23
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

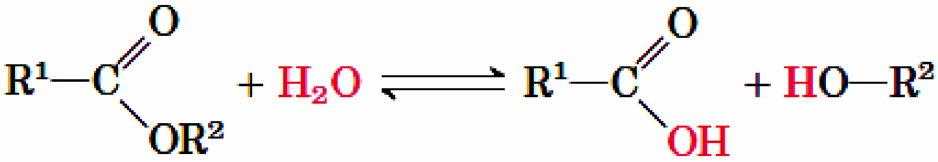
2.4 Water as a Reactant

- **Hydrolysis reaction**

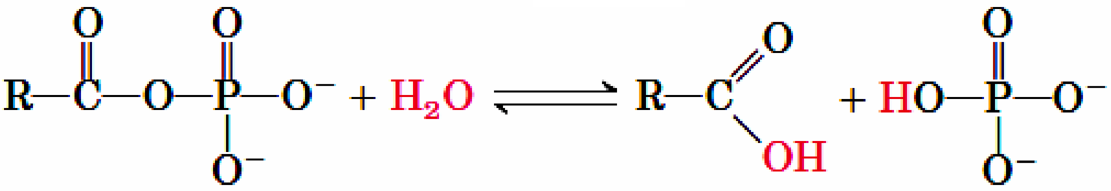


$$R{-}O{-}\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O^-}{|}}{P}}{-}O^- + H_2O \rightleftharpoons R{-}OH + HO{-}\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O^-}{|}}{P}}{-}O^-$$

Phosphate ester



Carboxylate ester



Acyl phosphate

2.4 Water as a Reactant

- **Oxidation-reduction reaction**

$$\underset{\text{Glucose}}{C_6H_{12}O_6} + 6O_2 \longrightarrow 6CO_2 + 6H_2O$$

The “**metabolic water**” formed by oxidation of foods and stored fats is actually enough to allow some animals in very dry habitats (gerbils, kangaroo rats, camels) to survive for extended periods without drinking water.

Take home messages …

✓ **Geometry of carbon bond**

Single, double bonds

✓ **Three-dimensional structure**

Configuration & conformation

✓ **Stereoisomers**

Geometric isomers, chirality

✓ **Oxidation-reduction reactions**

Lose electrons vs. gain electrons

Take home messages …

- ✓ **Weak Interactions in Aqueous Systems**

  Hydrogen bonding , Ionic interactions , Hydrophobic interactions, van der Waals Interactions …

- ✓ **Ionization of Water, Weak Acids, and Weak Bases**

  Equilibrium constant, K_{eq} , pK_a

- ✓ **Buffering against pH Changes in Biological Systems**

  Buffer system, pH Optimum

Further Reading …

Nicolls, P. (2000) Introduction: the biology of the water molecule. *Cell. Mol. Life Sci.* **57**, 987–992.

Pace, N.R. (2001) The universal nature of biochemistry. *Proc. Natl. Acad. Sci. USA* **98**, 805–808.