

General Biochemistry; BBT-3001-(Semester III)

Unit I: Biomolecules in their Cellular Environment

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Overview

Introduction to Cellular Basis of Life

Cell structures – Prokaryotes and Eukaryotes

Chemical principles in biomolecular structure

Major Classes of biomolecules

Role of water in design of biomolecules



The Central “Dogma” of Biochemistry:

DNA → RNA → Protein

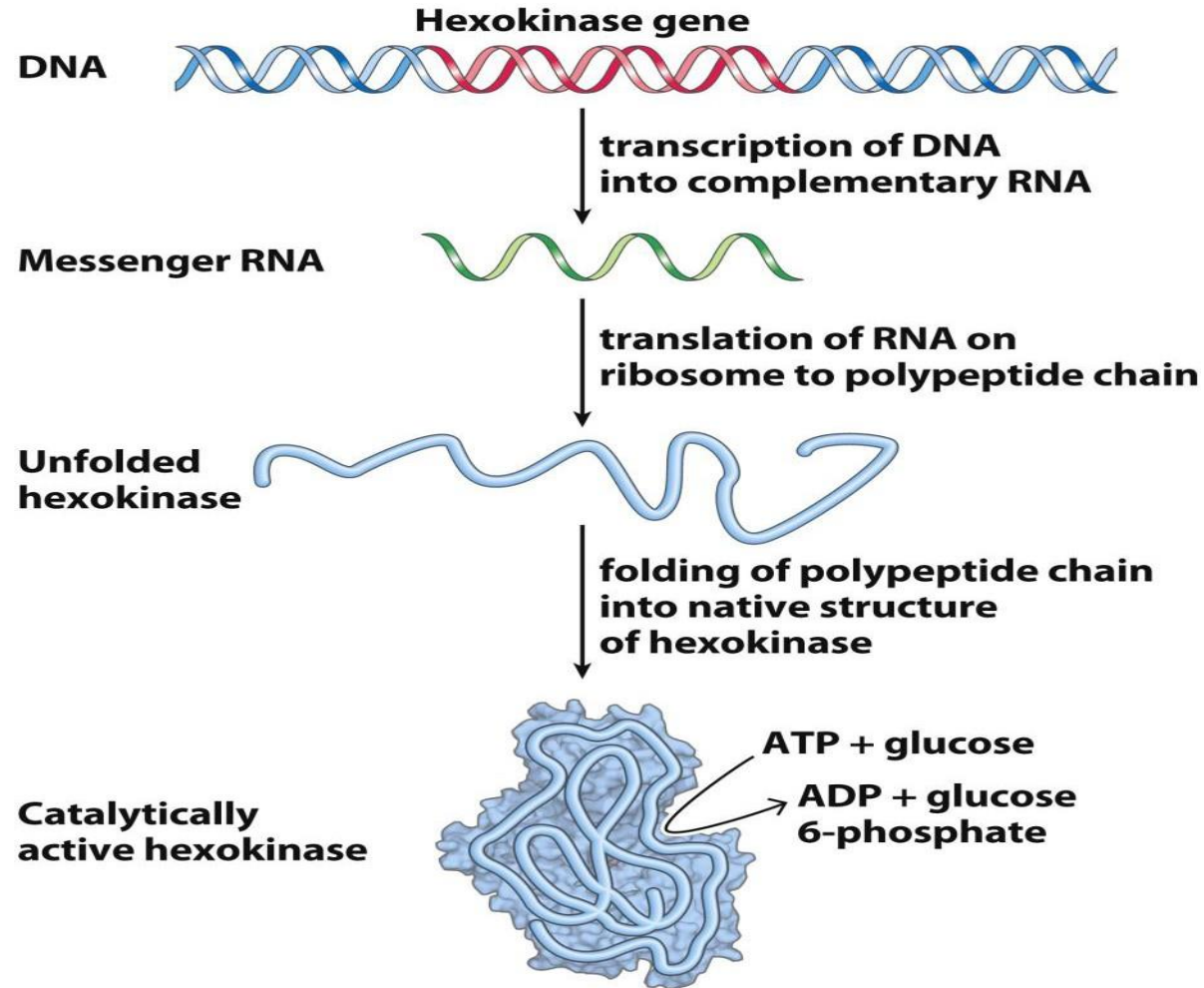


Figure 1-32
Lehninger Principles of Biochemistry, Sixth Edition
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Water

Topics

- ✓ Weak interactions in aqueous systems
- ✓ Ionization of water, weak acids, and weak bases
- ✓ Buffering against pH changes in biological systems
- ✓ Water as a reactant
- ✓ Fitness of the aqueous environment for living organisms

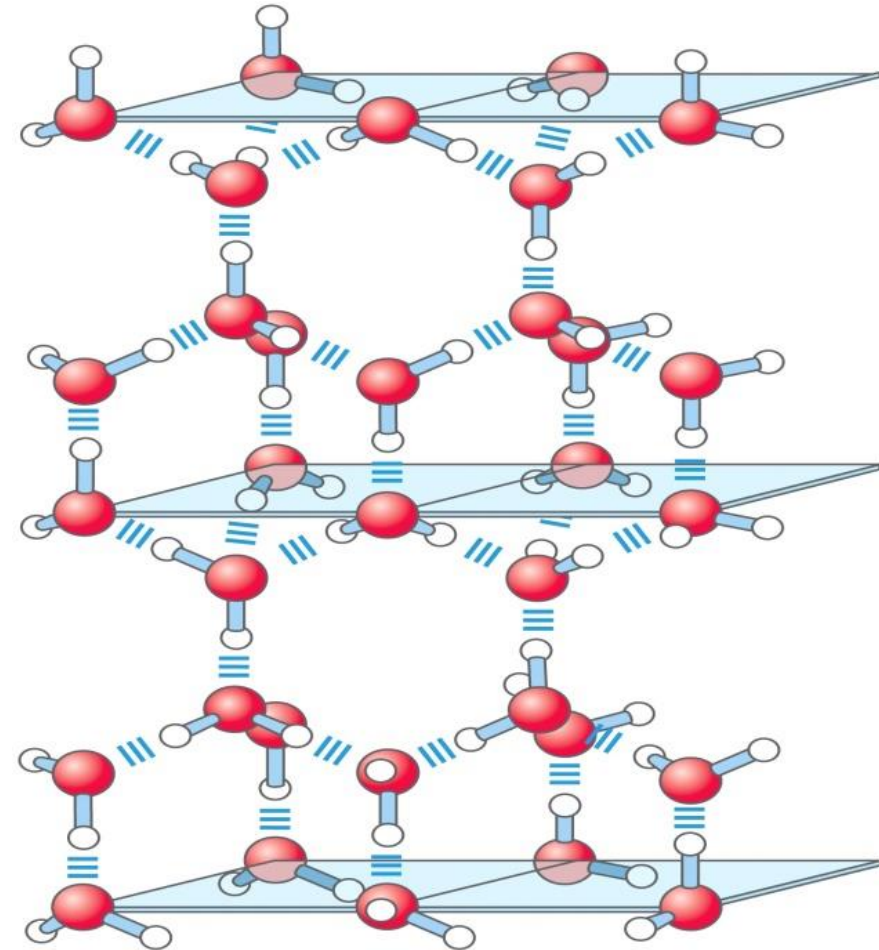


Fig. 2-2. Hydrogen bonding in ice.



Internal Cohesion of Water

Water has a higher melting point, boiling point, and heat of vaporization than most other common solvents. These properties result from the strong attractions that occur between water molecules in liquid and solid (ice) states.

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

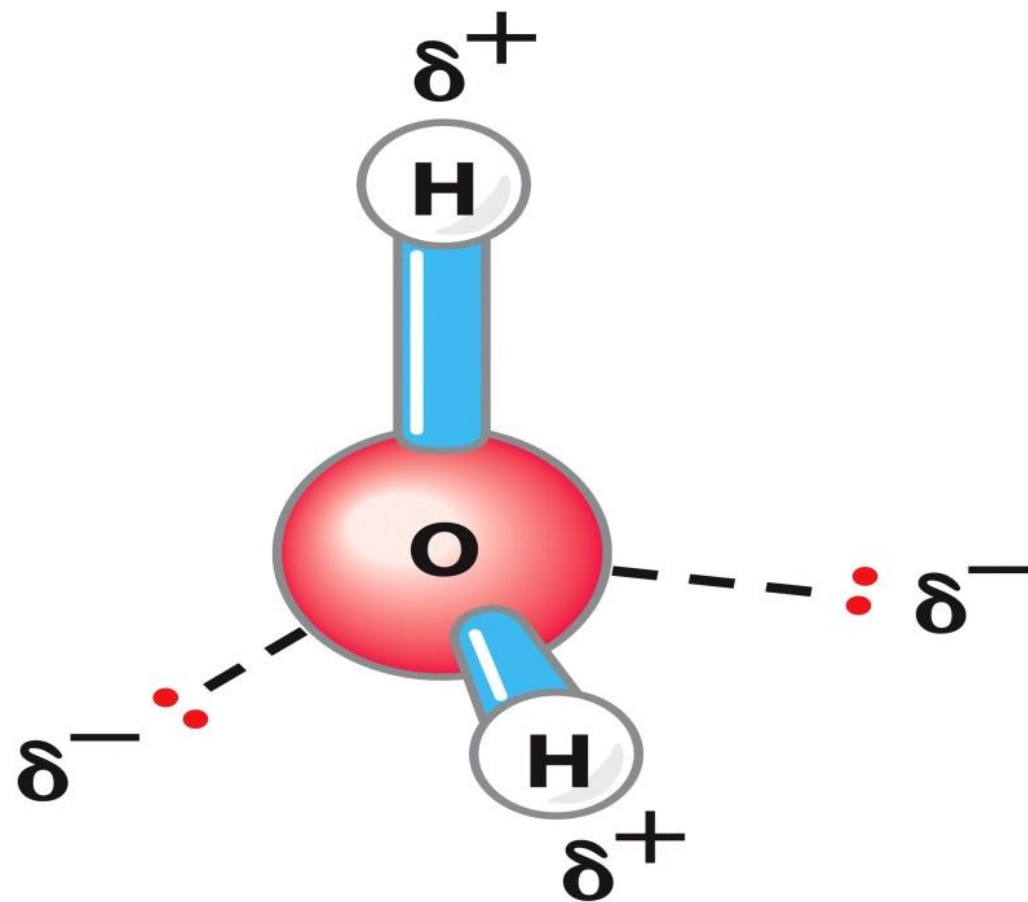
	Melting point (°C)	Boiling point (°C)	Heat of vaporization (J/g)*
Water	0	100	2,260
Methanol (CH ₃ OH)	-98	65	1,100
Ethanol (CH ₃ CH ₂ OH)	-117	78	854
Propanol (CH ₃ CH ₂ CH ₂ OH)	-127	97	687
Butanol (CH ₃ (CH ₂) ₂ CH ₂ OH)	-90	117	590
Acetone (CH ₃ COCH ₃)	-95	56	523
Hexane (CH ₃ (CH ₂) ₄ CH ₃)	-98	69	423
Benzene (C ₆ H ₆)	6	80	394
Butane (CH ₃ (CH ₂) ₂ CH 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.



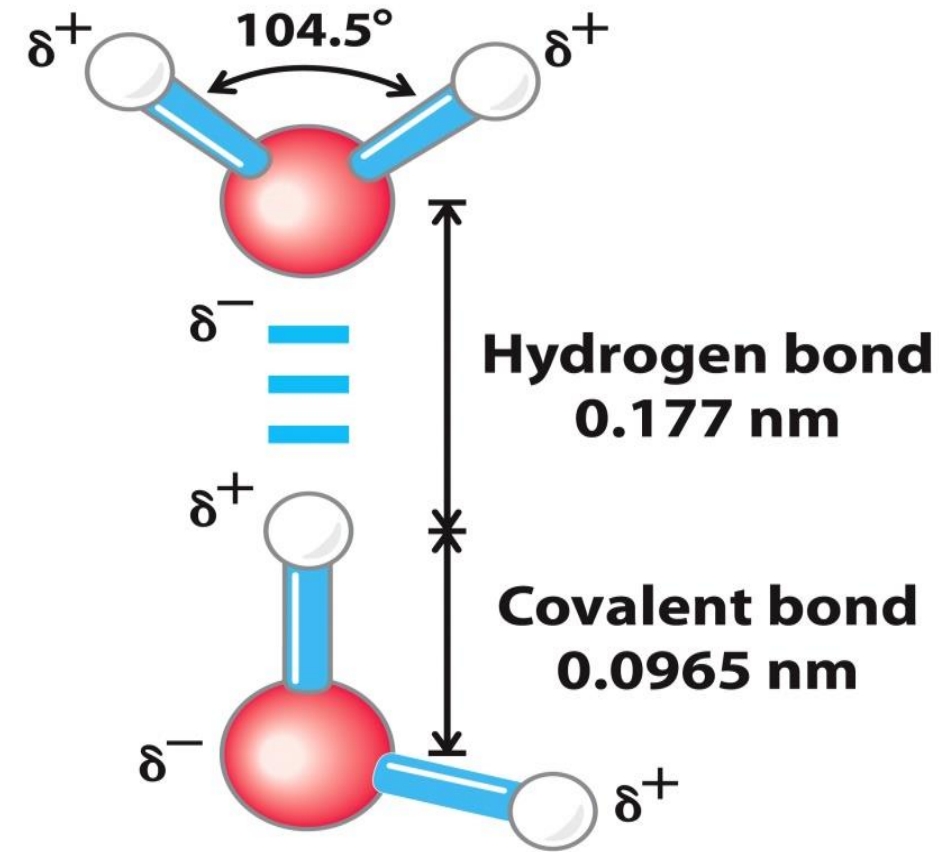
Structure of Water Molecules

- ✓ Water is a **polar solvent**.
- ✓ Water molecules are **polar because hydrogen and oxygen atoms** have substantially different electronegativities (affinities for electrons).
- ✓ Because electrons are shared unequally, the -O-H covalent bonds are dipolar and partial positive and negative charges occur on H and O.
- ✓ This feature plus the fact that 2 unshared pairs of electrons are located within the sp^3 orbitals of O atoms creates a net dipole moment.



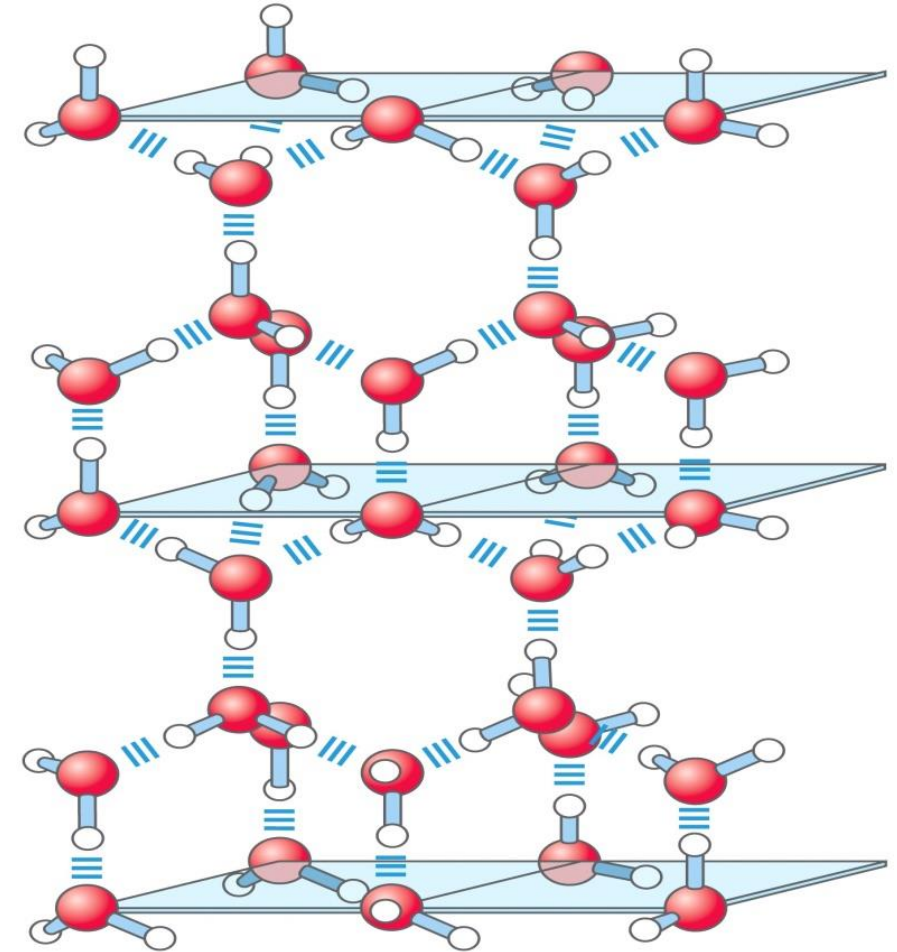
Hydrogen Bonding Between Water Molecules

- ✓ Hydrogen bonds are noncovalent interactions occurring between the H atom of a dipolar molecule such as water, and the unshared electron pair of another atom (i.e., O or N).
- ✓ These bonds represent the primary way in which water molecules interact with themselves (Fig. 2-1b) and many types of biomolecules.
- ✓ The strength of hydrogen bonds is on the same order of magnitude as the thermal energy of an aqueous solution (the kinetic energy of motion of the individual molecules).
- ✓ Thus hydrogen bonds are relatively short-lived (lifetime = 1- to-20 picoseconds).
- ✓ The term “flickering clusters” is used to describe the short-lived groups of water molecules interlinked by hydrogen bonds in liquid water.



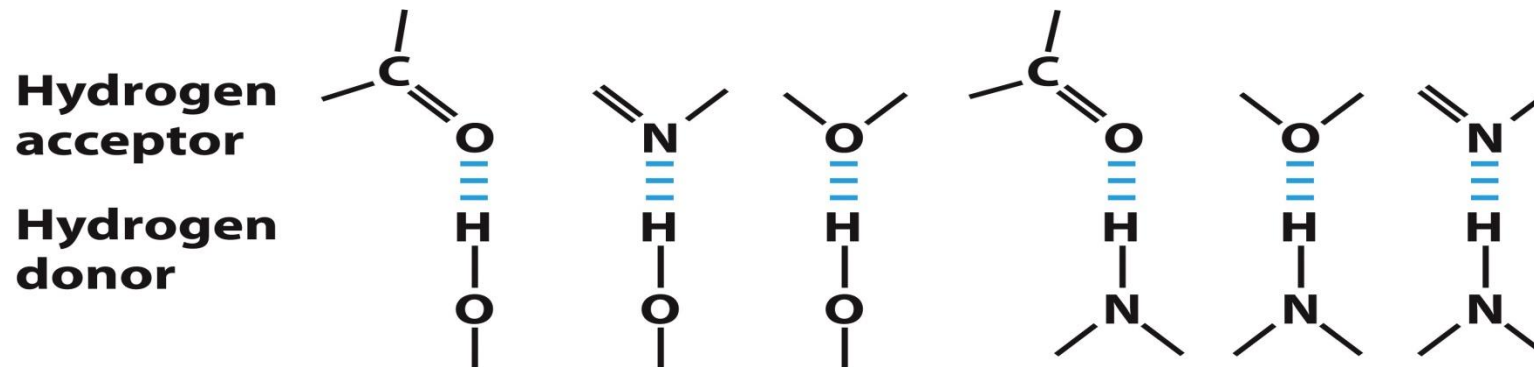
Hydrogen Bonding in Ice

- ✓ Each water molecule in ice forms four hydrogen bonds to its neighbors, creating a regular tetrahedral crystal lattice.
- ✓ In liquid water each water molecule forms hydrogen bonds with an average of 3.4 other water molecules.
- ✓ Due to the more expanded crystal lattice structure of ice, ice is less dense than liquid water, and ice floats on water. Hydrogen bonds account for the relatively high melting point of ice and boiling point of liquid water.



Hydrogen Bonding in Other Molecules (I)

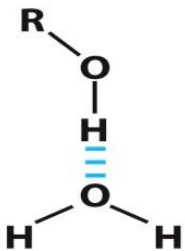
- ✓ Water molecules are not the only molecules that form hydrogen bonds. In fact, hydrogen bonds readily form between an electronegative atom (the hydrogen acceptor, usually oxygen or nitrogen) and a hydrogen atom covalently bonded to another electronegative atom (the hydrogen donor) in the same or another molecule .
- ✓ Because carbon has about the same electronegativity as hydrogen, hydrogen atoms covalently bonded to carbon atoms do not participate in hydrogen bonding.



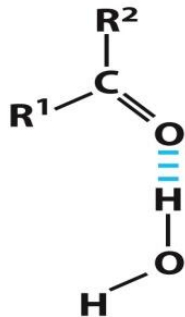
Hydrogen Bonding in Other Molecules (II)

- ✓ Alcohols, aldehydes, ketones, and compounds containing N-H bonds all form hydrogen bonds with water molecules and tend to be soluble in water .
- ✓ Molecules such as sugars and amino acids, which contain these functional groups, commonly are quite soluble in water because of the stabilizing effects hydrogen bonds have on interactions between the solvent and solute. Biologically important hydrogen bonds between Watson-Crick A-T base pairs are illustrated in Fig.

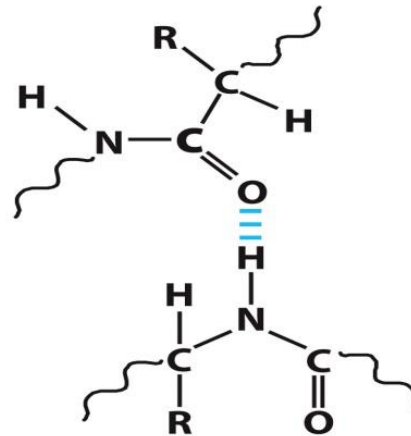
Between the hydroxyl group of an alcohol and water



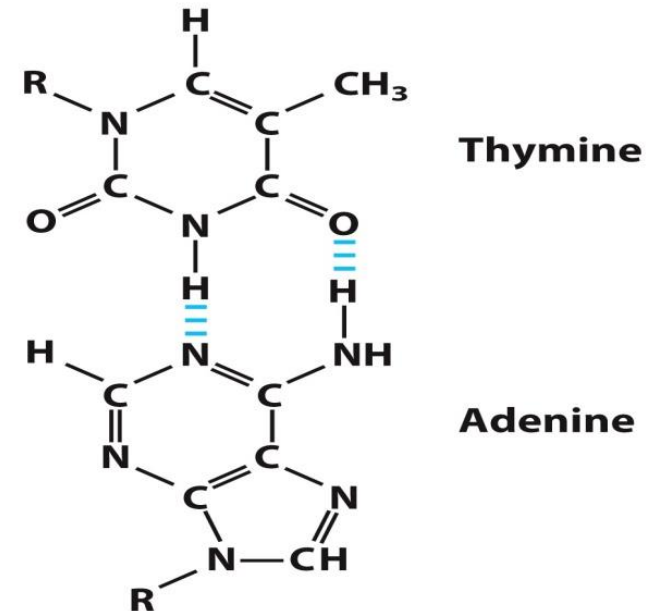
Between the carbonyl group of a ketone and water



Between peptide groups in polypeptides

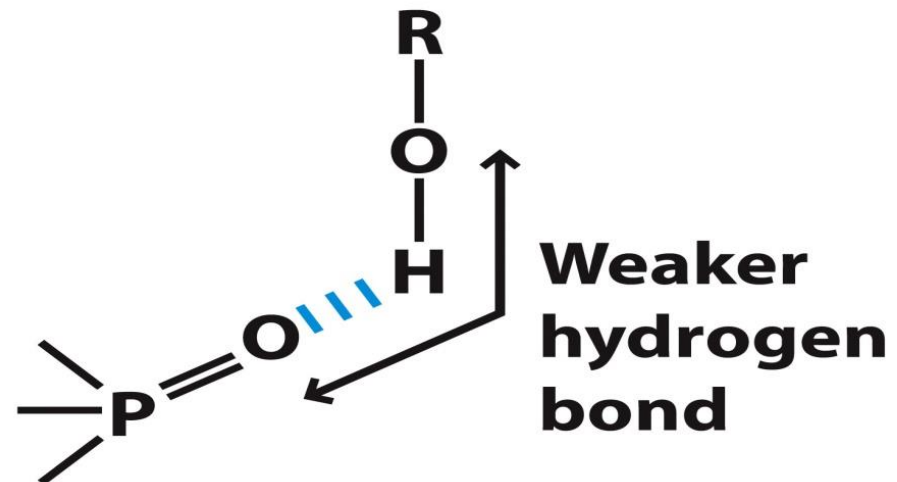
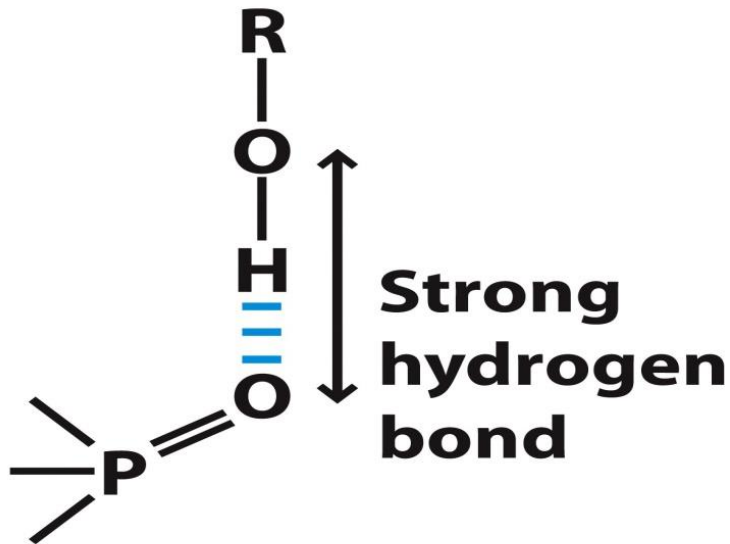


Between complementary bases of DNA



Hydrogen Bond Directionality and Strength

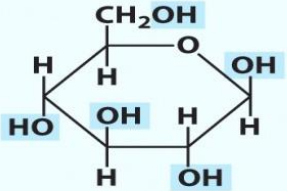
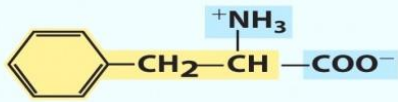

- ✓ Hydrogen bonds are highly directional in that strength depends on the proper alignment of the interacting atoms.
- ✓ The best alignment occurs when the orbital containing the unshared electron pair of the acceptor atom is in line with the covalent bond between the donor atom and H.
- ✓ Directionality confers bonding specificity as with the Watson-Crick hydrogen bonds between the bases of double helical DNA (A-T; G-C), and results in very precise three dimensional structures for nucleic acid and protein molecules.



Classification of Biomolecules Based on Their Interactions with Water

- ✓ Polar biomolecules that dissolve easily in water are referred to as hydrophilic (water-loving).
- ✓ Nonpolar biomolecules that do not dissolve appreciably in water are called hydrophobic (water-fearing).
- ✓ Amphipathic biomolecules have significant amounts of both hydrophilic and hydrophobic structure. Like hydrophobic biomolecules they tend to associate when placed in contact with water molecules.

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

Polar	Nonpolar
Glucose 	Typical wax $\text{CH}_3(\text{CH}_2)_7\text{—CH=CH—}(\text{CH}_2)_6\text{—CH}_2\text{—C(=O)—O—CH}_2$ $\text{CH}_3(\text{CH}_2)_7\text{—CH=CH—}(\text{CH}_2)_7\text{—CH}_2$
Glycine $^+\text{NH}_3\text{—CH}_2\text{—COO}^-$	Amphipathic Phenylalanine 
Aspartate $\text{—OOC—CH}_2\text{—CH(}^+\text{NH}_3\text{)—COO}^-$	Phosphatidylcholine $\text{CH}_3(\text{CH}_2)_{15}\text{CH}_2\text{—C(=O)—O—CH}_2$ $\text{CH}_3(\text{CH}_2)_{15}\text{CH}_2\text{—C(=O)—O—CH—CH}_2\text{—O—P(=O)(O}^-\text{)—O—CH}_2\text{—CH}_2\text{—N}^+(\text{CH}_3)_3$
Lactate $\text{CH}_3\text{—CH(OH)—COO}^-$	
Glycerol $\text{HOCH}_2\text{—CH(OH)—CH}_2\text{OH}$	
	



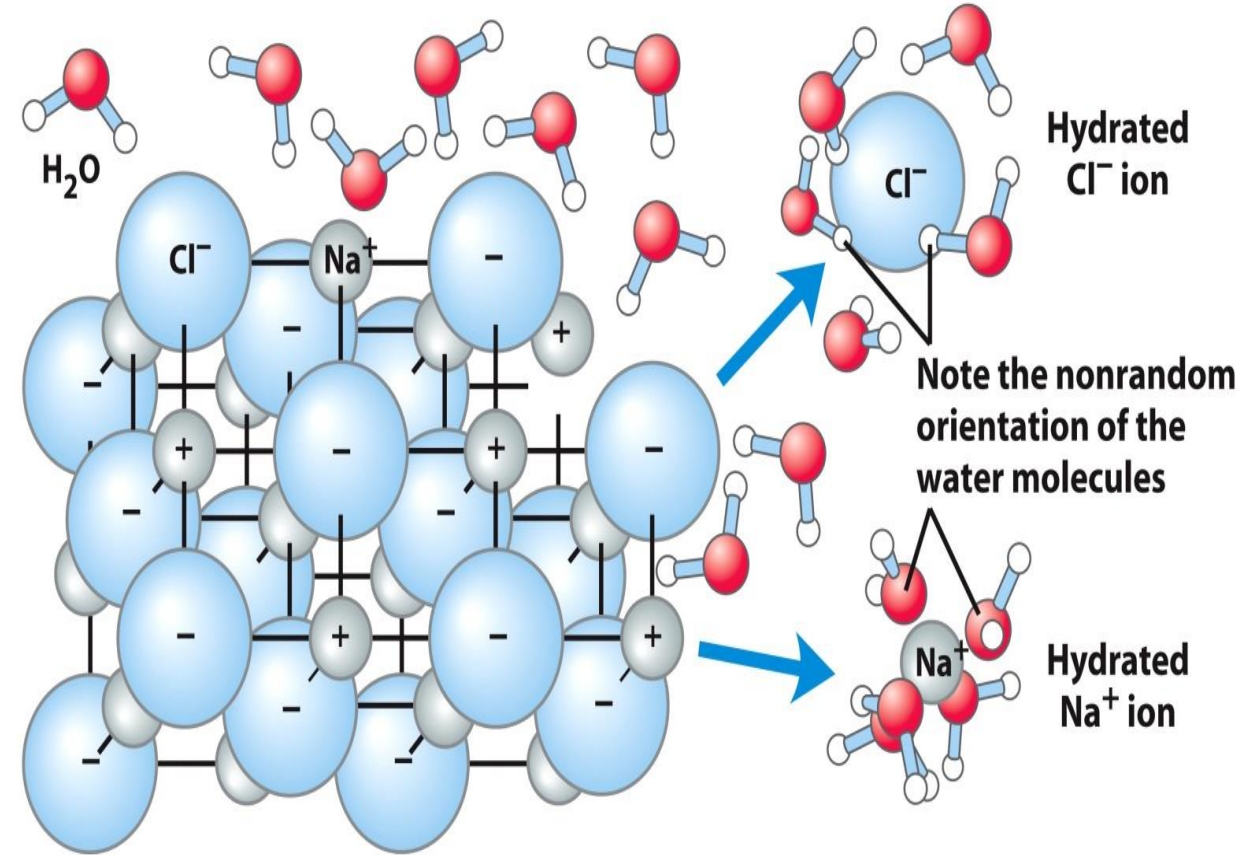
Ionic Interactions and Water

- ✓ Ionic interactions occur between cations and anions.
- ✓ These bonds are non-directional, and strength depends on the distance of separation (r) according to $1/r^2$.
- ✓ Strength also depends on the medium (dielectric constant), and is less in polar than nonpolar solvents.
- ✓ Water is effective at screening the electrostatic interactions between dissolved ions because it has a high dielectric constant, a physical property that reflects the number of dipoles in a solvent.
- ✓ The dielectric constant of water is 78.5 whereas the dielectric constant of benzene, for example, is 4.6.



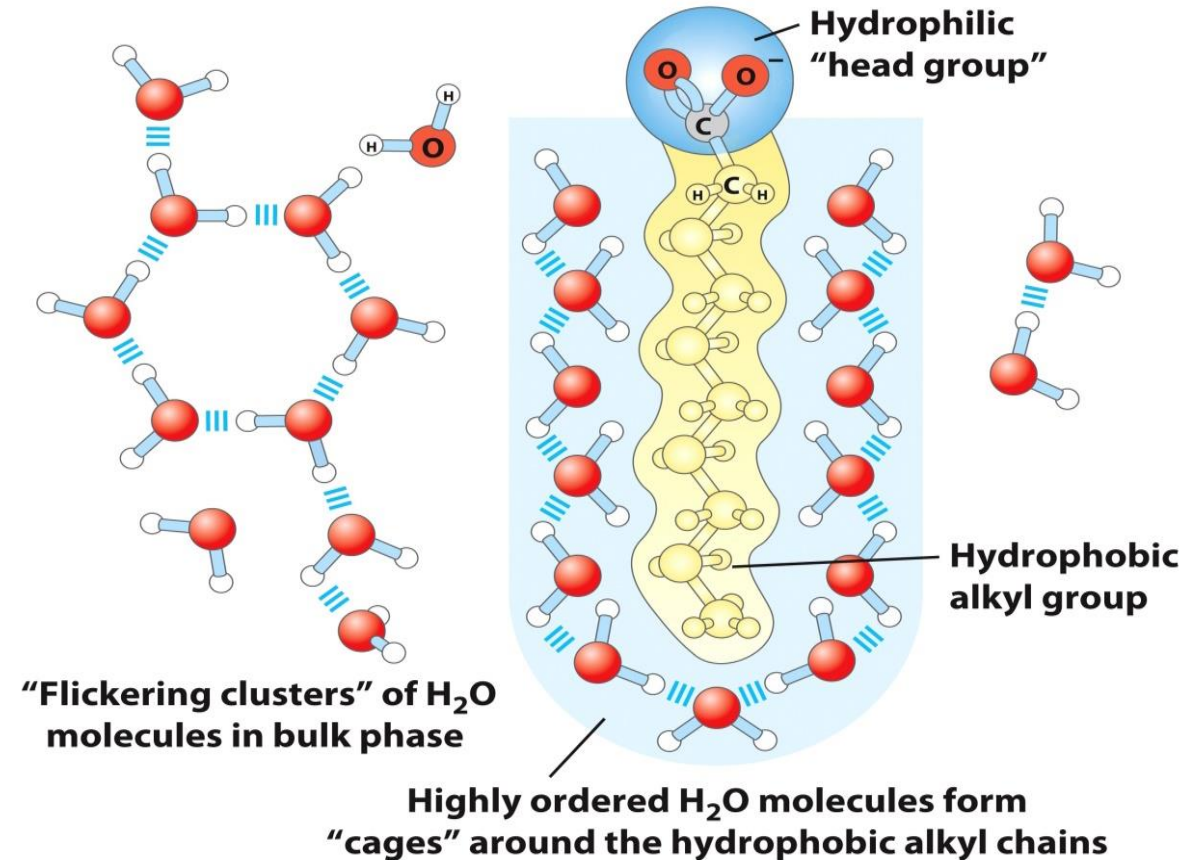
Solvation of Crystalline Substances by H₂O

- ✓ Ionic compounds such as NaCl are readily dissolved in water .
- ✓ Water molecules hydrate and stabilize Na⁺ and Cl⁻ ions, weakening the electrostatic interactions between them and countering their tendency to associate in a crystalline lattice.
- ✓ The resulting increase in entropy (randomness) of the system is largely responsible for the ease of dissolving NaCl in water.
- ✓ Solvation spheres of water molecules surround ions in solutions.
- ✓ Water molecules orient so that the negative ends of their dipoles contact cations and the positive ends contact anions in solution.



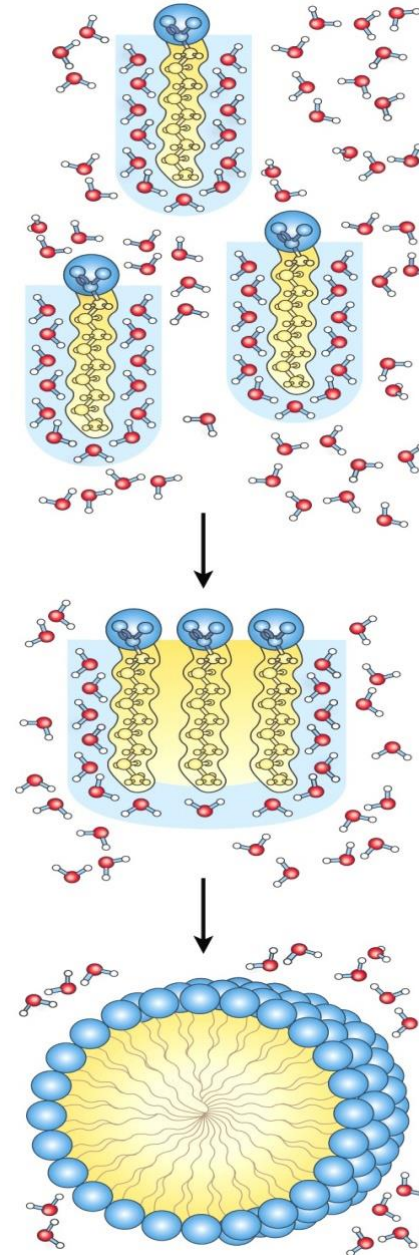
Interaction of Hydrophobic Molecules with Water

- ✓ Hydrophobic molecules, such as hexane, and the nonpolar portions of amphiphiles, such as long-chain fatty acids, lack polar functional groups that can interact with water molecules.
- ✓ This results in a highly ordered cage-like shell (clathrate) of water molecules immediately surrounding the nonpolar molecule.
- ✓ Suspension of a hydrophobic substance in water is thermodynamically unfavorable due to the decreased entropy of water molecules in the cage-like shell.



The Hydrophobic Effect

- ✓ The hydrophobic effect, and the term hydrophobic interactions, refers to the entropy-driven aggregation of nonpolar molecules in aqueous solution that occurs to minimize the ordering of water molecules with which they are in contact.
- ✓ This is not an attractive force, but rather a thermodynamically driven process (Fig. 2-7b).
- ✓ Amphiphiles, such as detergent molecules or long-chain fatty acids form molecular assemblies known as micelles, wherein the hydrophilic portions of the molecules are in contact with water and the hydrophobic regions are sequestered away from water in the interior of the assembly.
- ✓ The hydrophobic effect drives the formation of membranes and contributes to the folding of proteins and the formation of double helical DNA.



Dispersion of lipids in H₂O

Each lipid molecule forces surrounding H₂O molecules to become highly ordered.

Clusters of lipid molecules

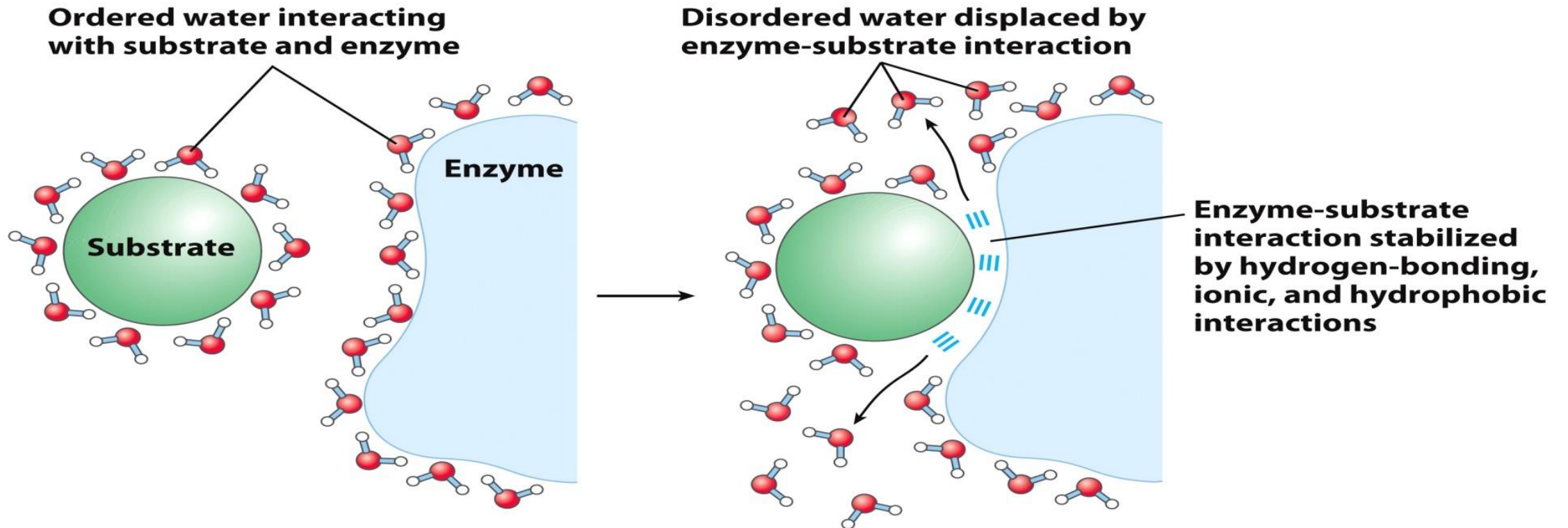
Only lipid portions at the edge of the cluster force the ordering of water. Fewer H₂O molecules are ordered, and entropy is increased.

Micelles

All hydrophobic groups are sequestered from water; ordered shell of H₂O molecules is minimized, and entropy is further increased.

Molecular Interactions Displace Bound Water Molecules

A somewhat ordered layer of water molecules occurs around all solutes, even polar ones, in liquid water. In enzyme-substrate interactions, ordered water molecules are displaced due to binding. The entropically favorable release of these water molecules provides a thermodynamic push towards formation of the enzyme-substrate complex.



van der Waals Interactions

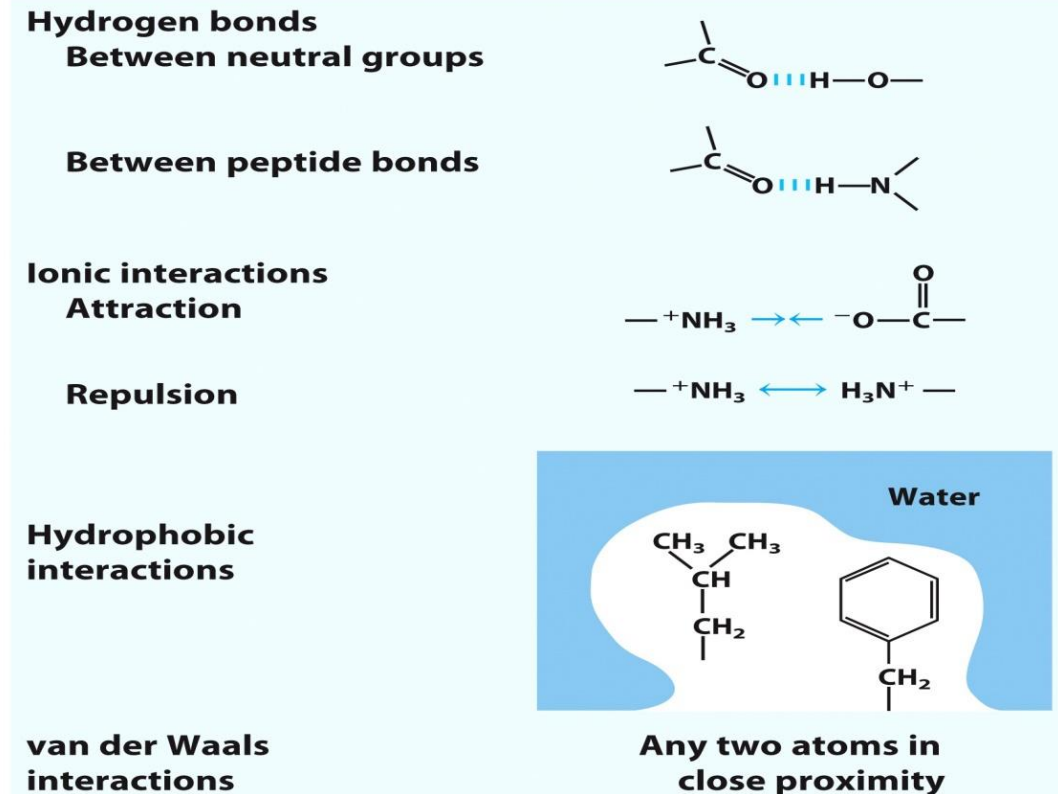
- ✓ van der Waals interactions are bonds between fluctuating, induced dipoles within the electron clouds of interacting molecules. These bonds can occur between nonpolar or polar molecules.
- ✓ van der Waals bonds are extremely dependent on the distance of separation between molecules, and are significant only when the electron clouds of the molecules are just touching.
- ✓ Values for van der Waals radii and covalent radii of some common elements are listed in In the “space-filling” molecular models shown throughout the Lehninger textbook, atoms are depicted in sizes proportional to their van der Waals radii.



Noncovalent Interactions and Macromolecular Structure

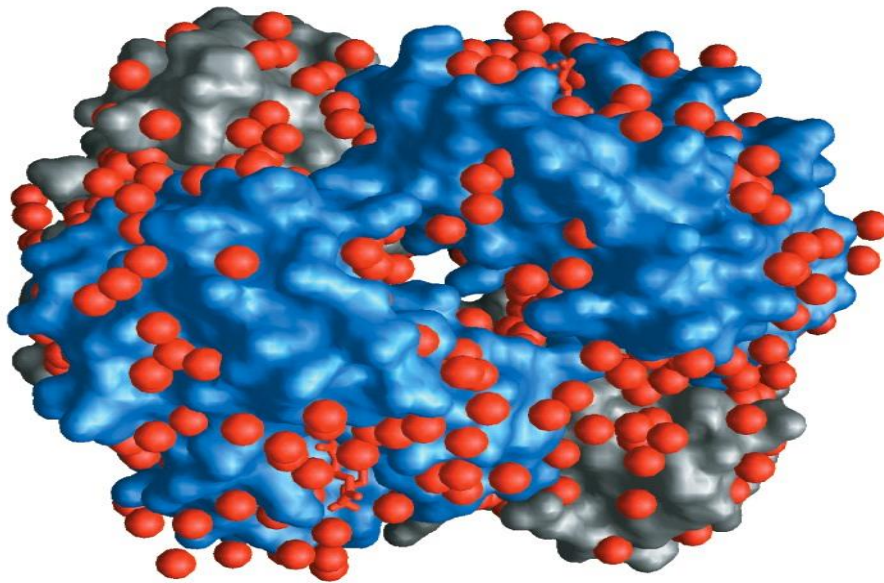
- ✓ As summarized above, noncovalent interactions are weak electrical bonds between molecules. The types of noncovalent interactions are 1) hydrogen bonds, 2) ionic (electrostatic) bonds, and 3) van der Waals interactions.
- ✓ Noncovalent interactions (1-5 kcal/mol) are typically ~100-fold weaker than covalent bonds.
- ✓ Their stability is only slightly greater than thermal energy in biological systems.
- ✓ Nonetheless, noncovalent interactions play important roles in protein and nucleic acid stabilization because they are collectively strong.
- ✓ Note that the hydrophobic effect drives molecular interactions, but is not a noncovalent bond per se.

TABLE 2-5 Four Types of Noncovalent (“Weak”) Interactions among Biomolecules in Aqueous Solvent

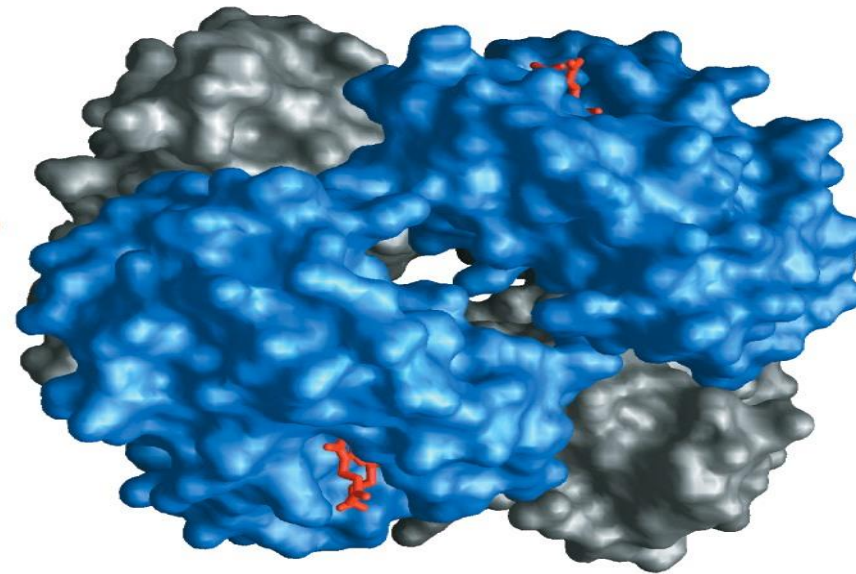


Binding of Water Molecules to Proteins

- ✓ Structural analysis indicates that some water molecules are tightly bound to proteins.
- ✓ These water molecules have different properties from those of the bulk water of the solvent.
- ✓ In certain proteins, tightly bound water molecules play roles in catalysis and roles in ligand binding.



(a)



(b)

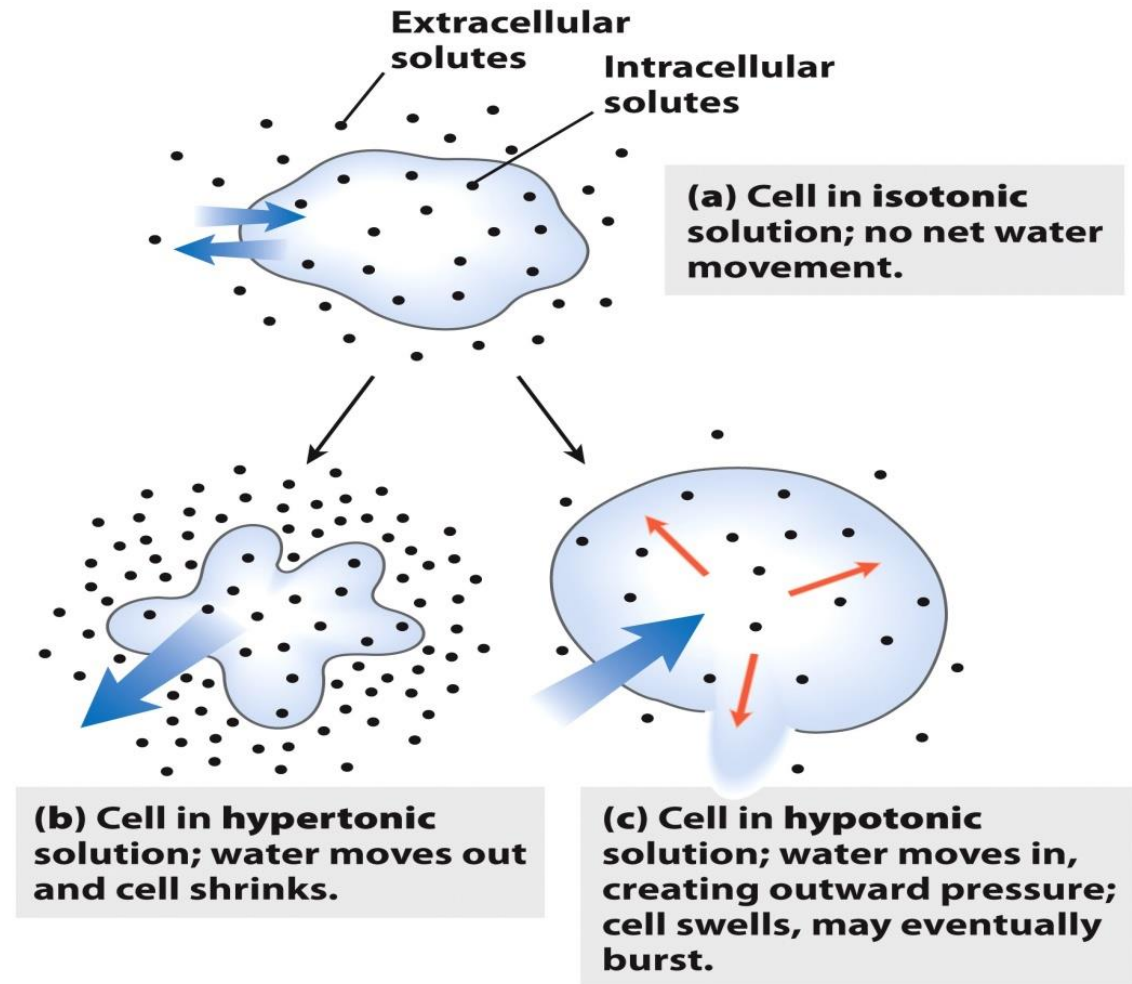
Colligative Properties of H₂O

- ✓ Solutes alter the vapor pressure, boiling point, melting point, and osmotic pressure of aqueous solutions (i.e., the colligative properties of water).
- ✓ In all cases, these physical properties change due to the fact that the concentration of water is lower in solutions than it is in pure water.
- ✓ The effect of solute concentration on the colligative properties of water is independent of the chemical properties of the solute and depends only on the number of solute components dissolved in the sample of water.

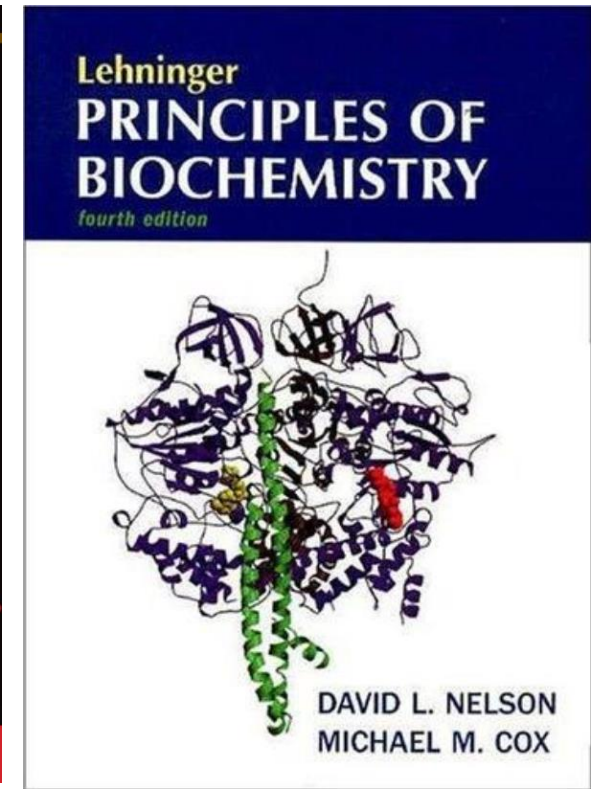
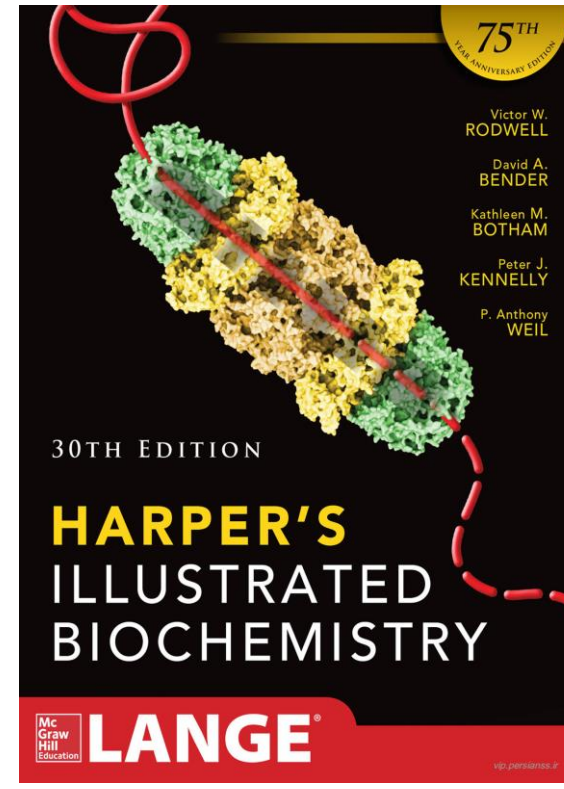
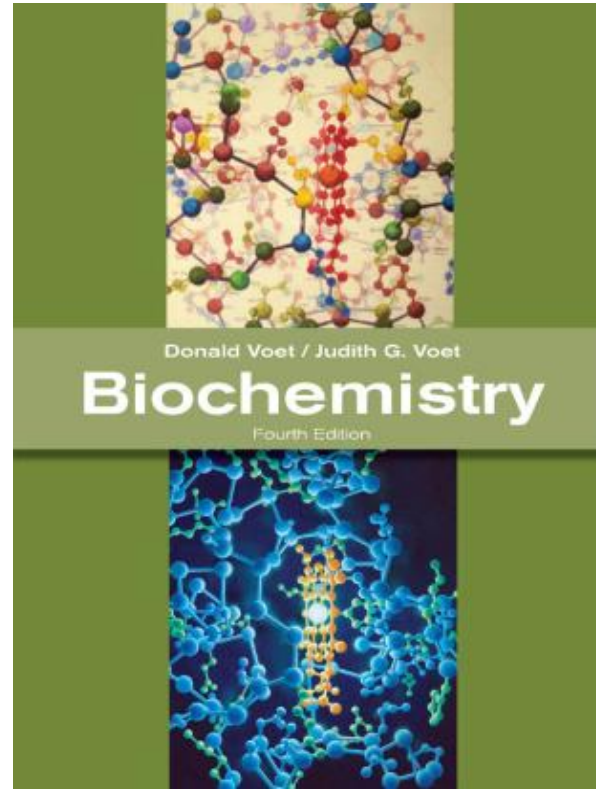


Movement of Water Across Plasma Membranes

- ✓ Osmosis is the movement of water across a semipermeable membrane in response to osmotic pressure differences across the membrane.
- ✓ Most isolated cells have a high concentration of dissolved solutes within their cytoplasm. Thus, they are prone to damage by water uptake-induced cell lysis.
- ✓ The terms isotonic, hypertonic, and hypotonic refer to the relative concentrations of solutes in a cell's cytoplasm and the concentration of solutes in the water in which the cell is suspended.
- ✓ Water will always move toward the side of the membrane with the higher solute concentration.



Acknowledgement



For Query

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