Principles of BIOCHEMISTRY

Water and Its Properties

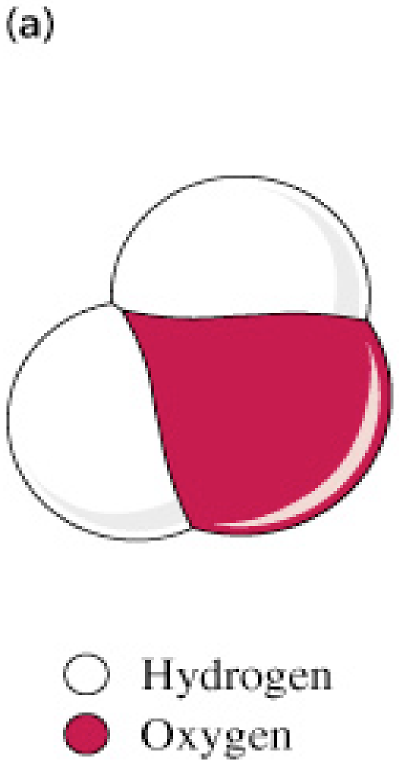
Water

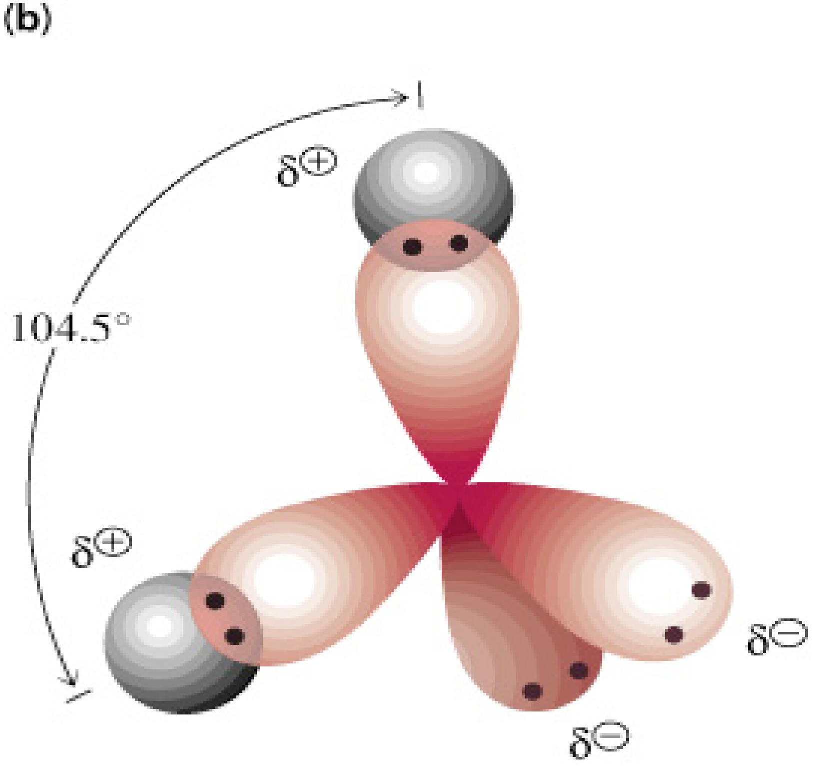
- Water plays a central role in the chemistry of all life
- Proteins, polysaccharides, nucleic acids and membranes all assume their characteristic shapes in response to water
- The chemical properties of water are related to the functions of biomolecules, entire cells,and organisms

The Water Molecule is Polar

- Important properties of water arise from its angled shape
- Angle of 104.5° between two covalent bonds
- Polar O-H bonds due to uneven distribution of charge (oxygen (δ^-), hydrogen (δ^+))
- Angled arrangement of polar bonds creates a permanent dipole for a water molecule

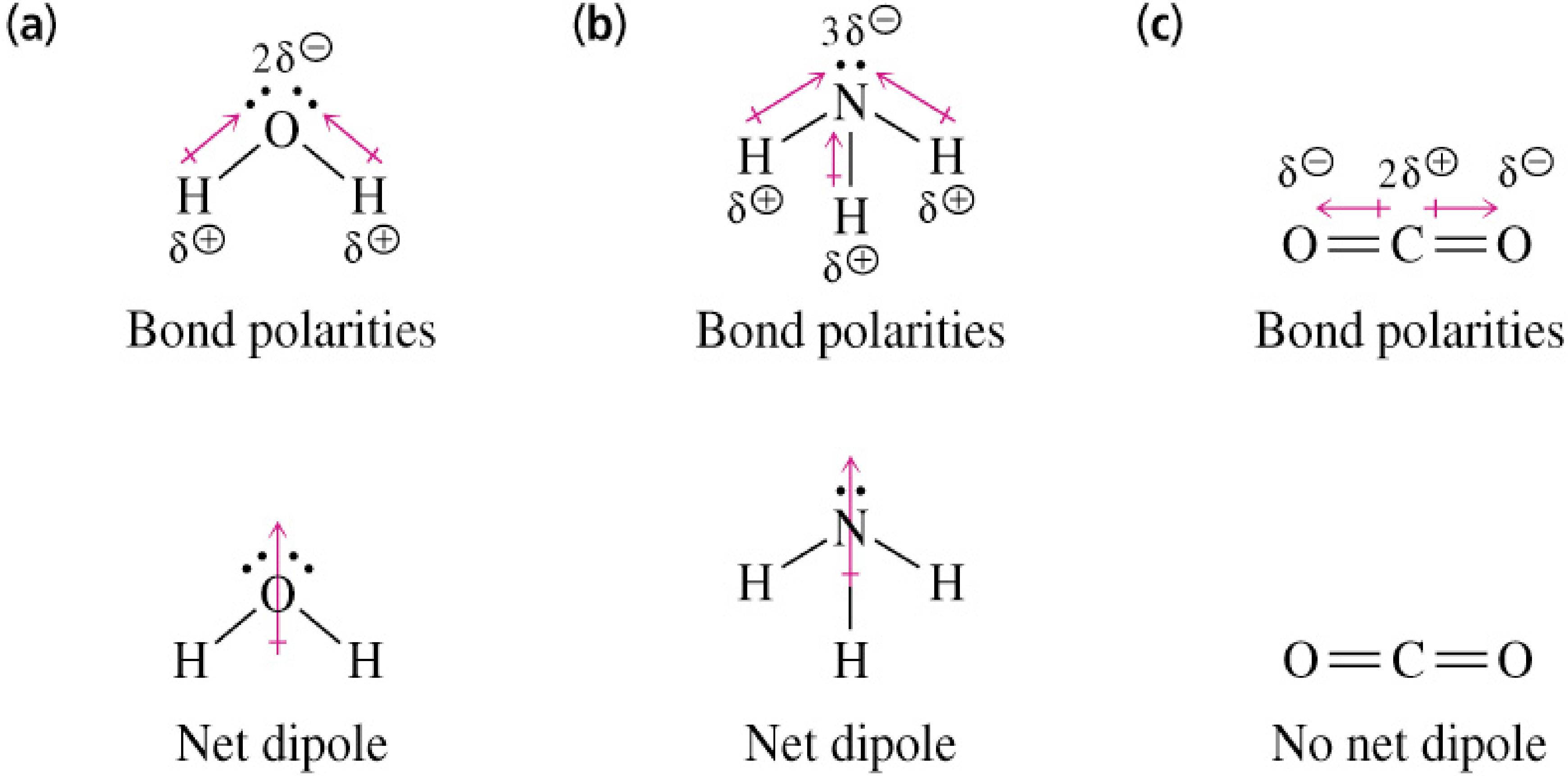
(a) Space-filling structure of water
(b) Covalent bond angle of water





Polarity of Small Molecules

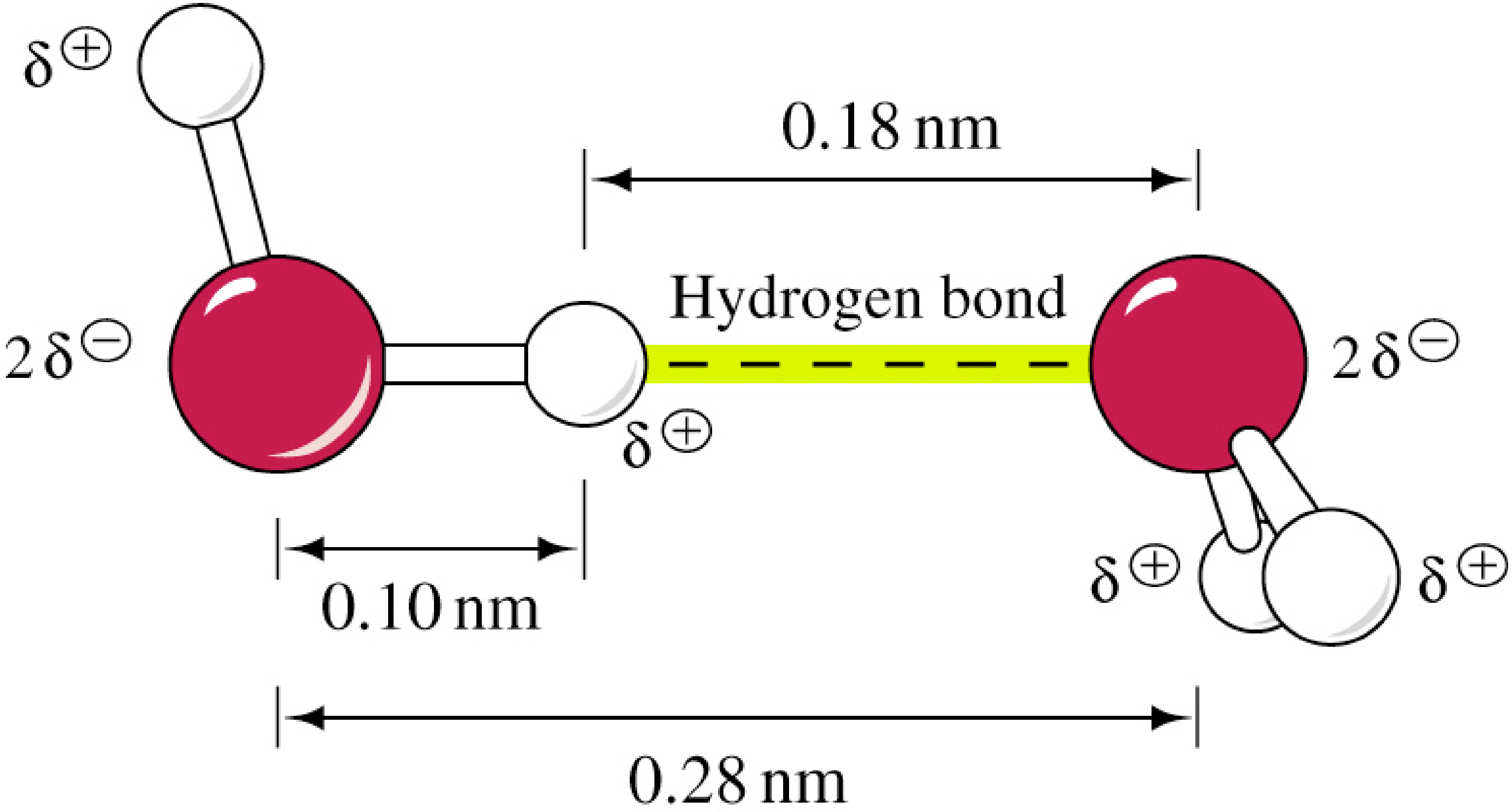
- Water and ammonia each have a permanent dipole while CO_2 does not



Hydrogen Bonding in Water

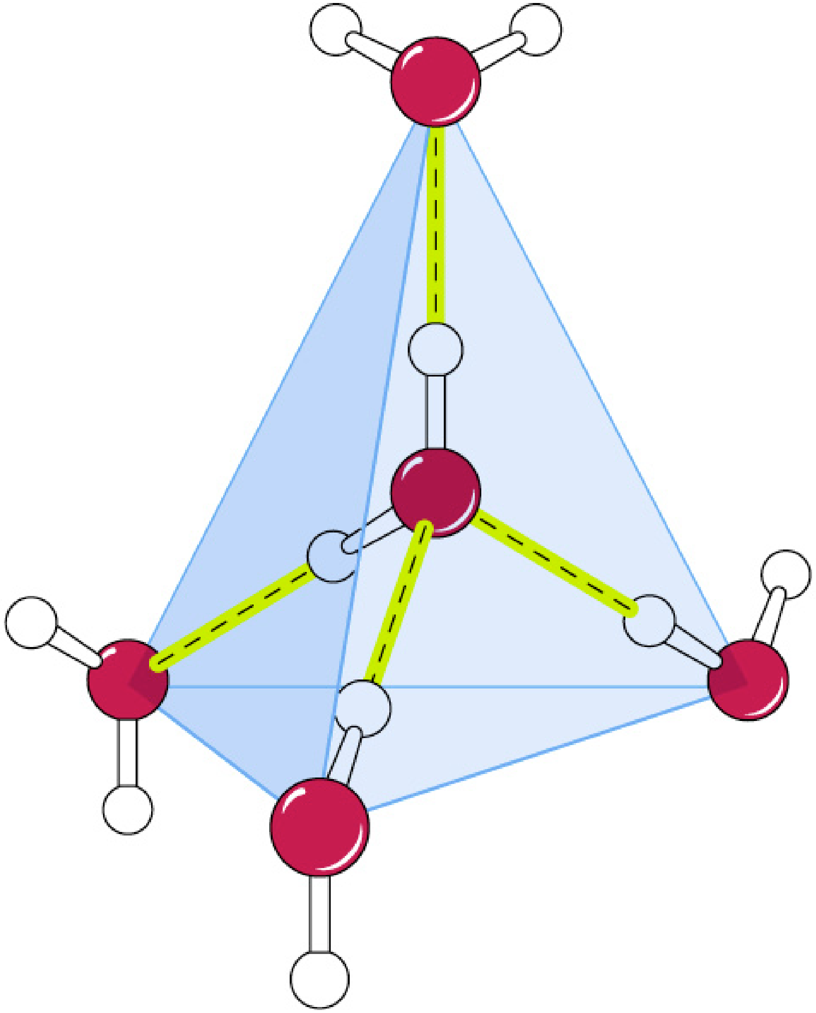
- Water molecules attract each other due to their polarity
- A **hydrogen bond** is formed when a partially positive hydrogen atom attracts the partially negative oxygen atom of a second water molecule
- Hydrogen bonds can form between electronegative atoms and a hydrogen attached to another electronegative atom

Hydrogen bonding between two water molecules



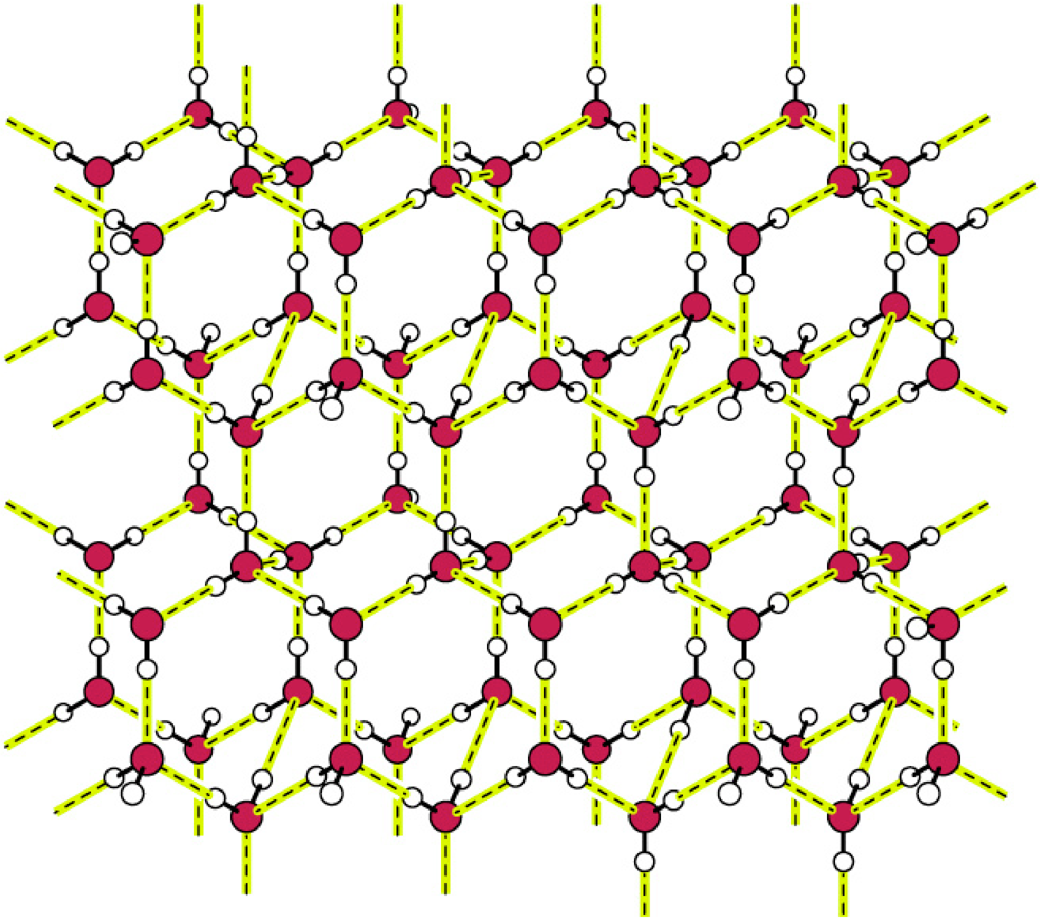
Hydrogen bonding by a water molecule

- A water molecule can form up to four hydrogen bonds
- Hydrogen bonds shown in yellow



Structure of ice.

- Hexagonal lattice structure
- Every water molecule is H - bonded to 4 others



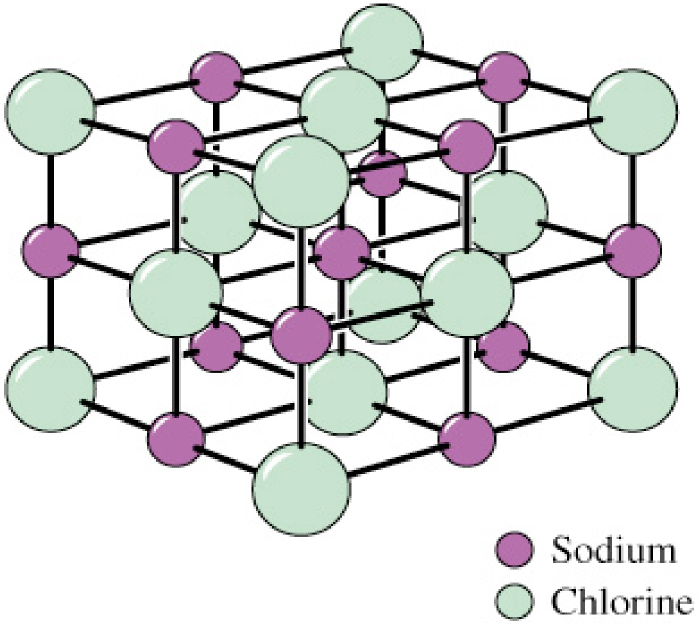
Ionic and Polar Substances Dissolve in Water

- **Hydrophilic** (water-loving) substances (polar and ionic (**electrolytes**)) readily dissolve in H_2O
- Polar water molecules align themselves around ions or other polar molecules
- A molecule or ion surrounded by solvent molecules is **solvated**
- When the solvent is water the molecules or ions are **hydrated**

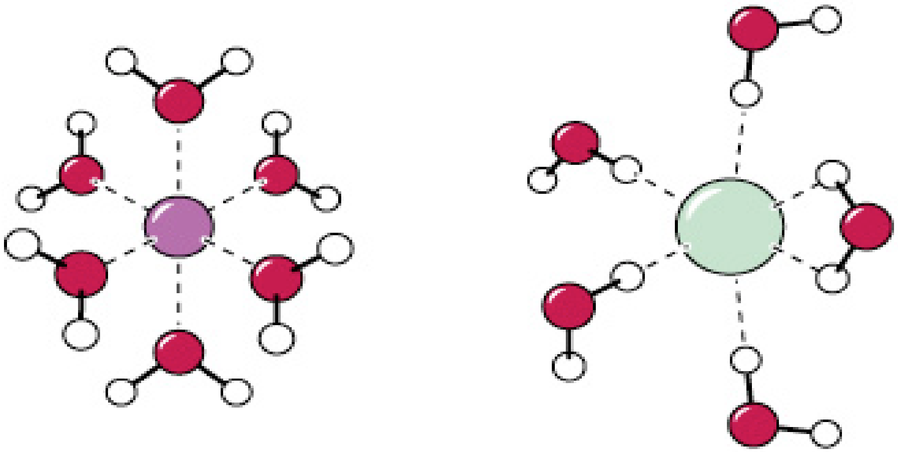
Dissolution of NaCl in water

(a) Electrostatic forces hold ions together in crystalline sodium

(b) Water molecules form solvation spheres around Na$^+$ and Cl$^-$



(a) NaCl crystal



(b)

Solubilities of molecules in water

- Solubility in water depends upon the ratio of polar to nonpolar groups in a molecule
- The larger the portion of nonpolar groups the less soluble the molecule is in water
- The larger the portion of polar groups (e.g. hydroxyl groups (-OH)) the more soluble the molecule is in water

Solubilities of short-chain alcohols in water

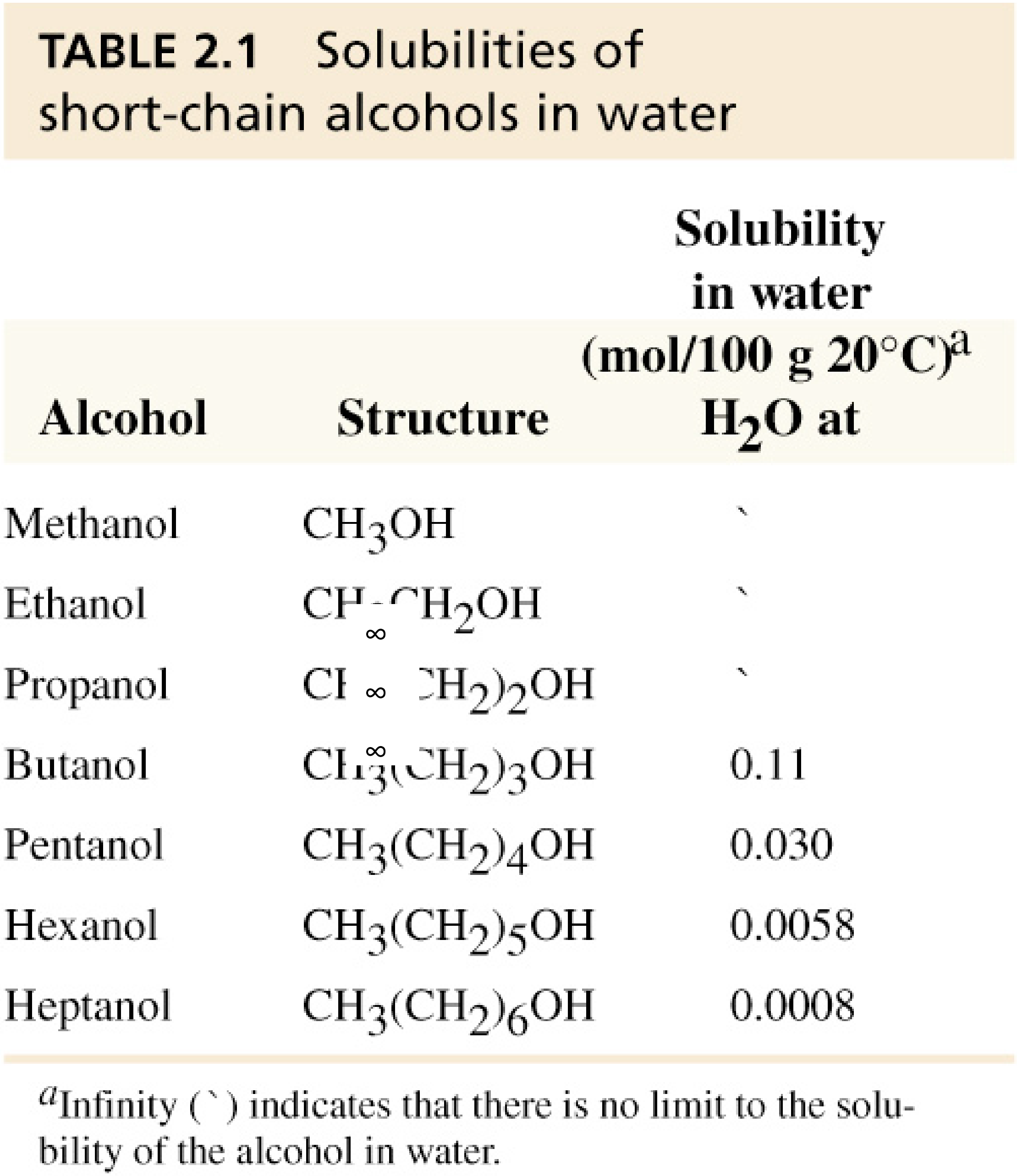


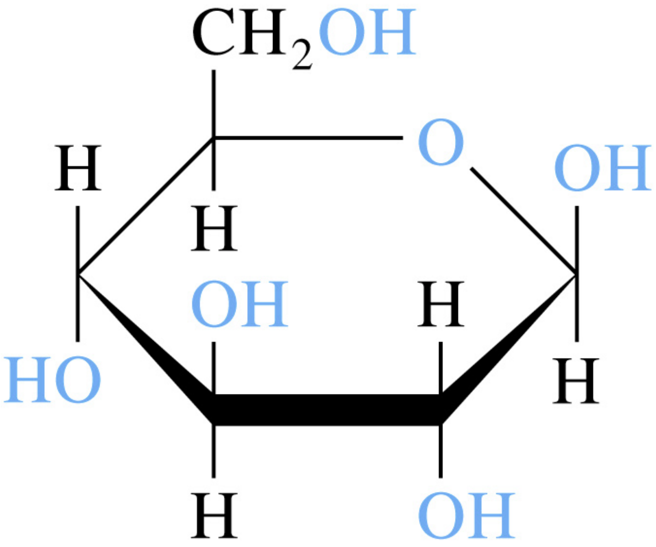
TABLE 2.1 Solubilities of short-chain alcohols in water

Alcohol	Structure	Solubility in water (mol/100 g H_2O at 20°C)[a]
Methanol	CH_3OH	`
Ethanol	CH_3CH_2OH ∞	`
Propanol	$CH_3(CH_2)_2OH$ ∞	`
Butanol	$CH_3(CH_2)_3OH$ ∞	0.11
Pentanol	$CH_3(CH_2)_4OH$	0.030
Hexanol	$CH_3(CH_2)_5OH$	0.0058
Heptanol	$CH_3(CH_2)_6OH$	0.0008

[a] Infinity (`) indicates that there is no limit to the solubility of the alcohol in water.

Structure of glucose

- Glucose has five hydroxyl groups and a ring oxygen which can hydrogen bond
- Glucose is very soluble in water

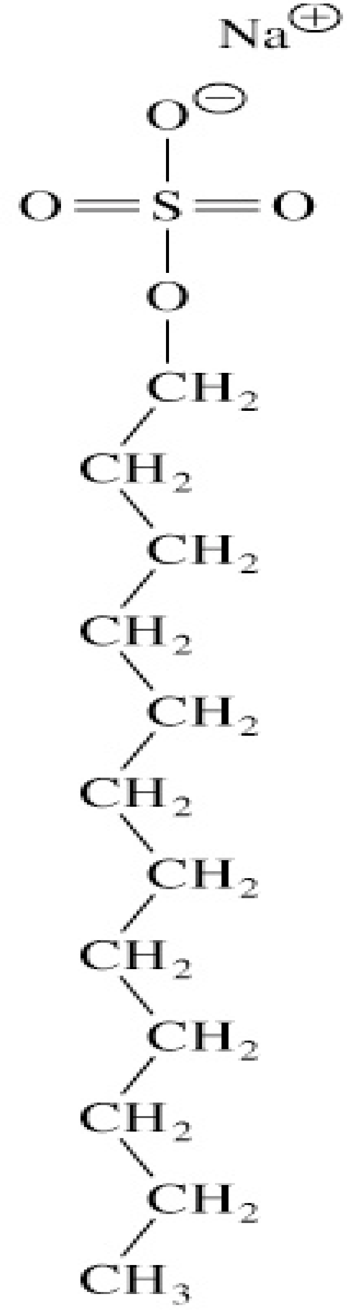


Nonpolar Substances Are Insoluble in Water

- **Hydrophobic** (water-fearing) molecules are nonpolar
- **Hydrophobic effect** - the exclusion of nonpolar substances by water (critical for protein folding and self-assembly of biological membranes)
- **Amphipathic molecules** have hydrophobic chains and ionic or polar ends. Detergents (surfactants) are examples.

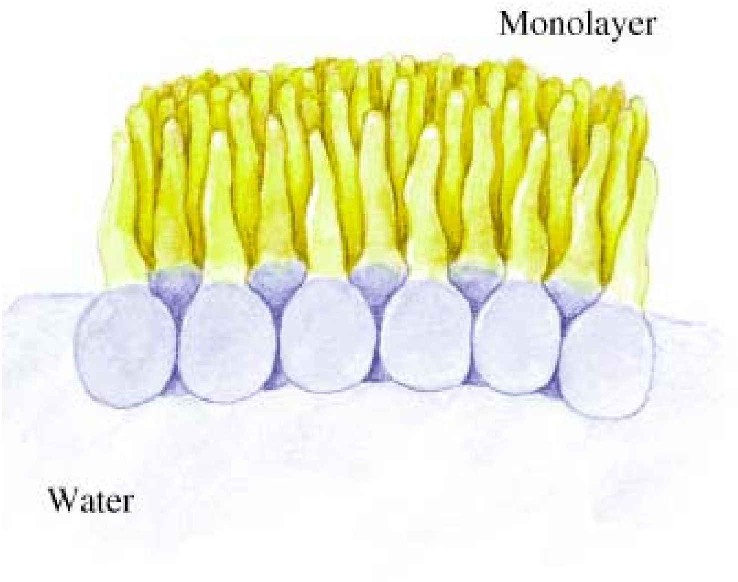
Sodium dodecyl sulfate (SDS)

- A synthetic detergent
- A 12-carbon tail
- Polar sulfate group

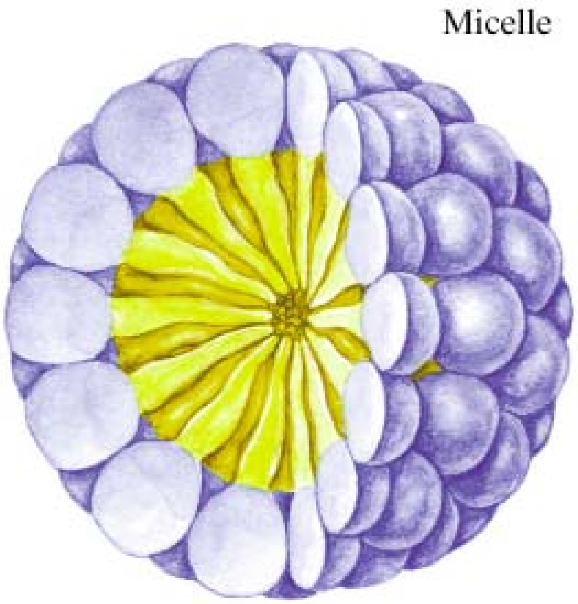


Detergents in water

- Monolayers can form on the surface



- At higher concentrations detergents can form **micelles**



Noncovalent forces

There are four major types of noncovalent forces:

1. **Charge-charge interactions**
2. **Hydrogen bonds**
3. **Van der Waals forces**
4. **Hydrophobic interactions**

A. Charge-Charge Interactions (Ion Pairing)

- Electrostatic interactions between two charged particles
- Can be the strongest type of noncovalent forces
- Can extend over greater distances than other forces
- Charge repulsion occurs between similarly charged groups

Types of attractive charged interactions

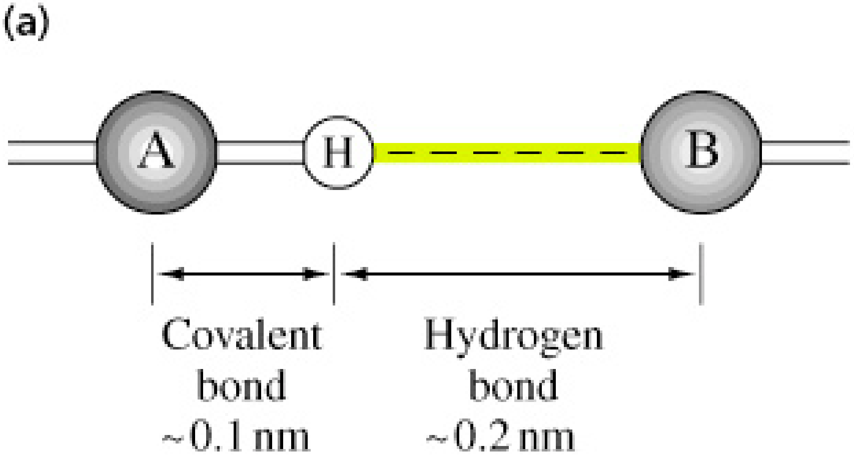
- **Salt bridges** - attractions between oppositely-charged functional groups in proteins
- **Ion pairing** - a salt bridge buried in the hydrophobic interior of a protein is stronger than one on the surface

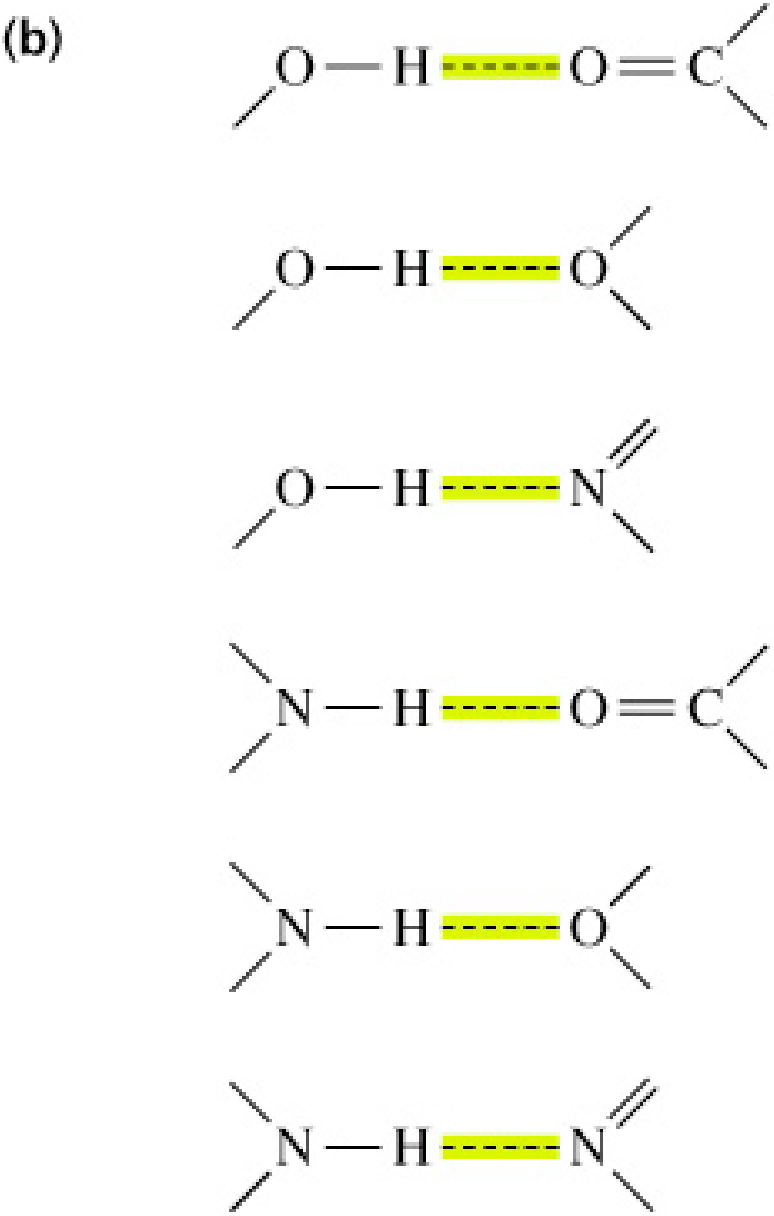
B. Hydrogen Bonds

- Among the strongest of noncovalent interactions
- H atom bonded to N, O, S can hydrogen bond to another electronegative atom (~0.2 nm distance)
- Total distance between the two electronegative atoms is ~0.27 to 0.30 nm
- In aqueous solution, water can H-bond to exposed functional groups on biological molecules

(a) Hydrogen bonding between

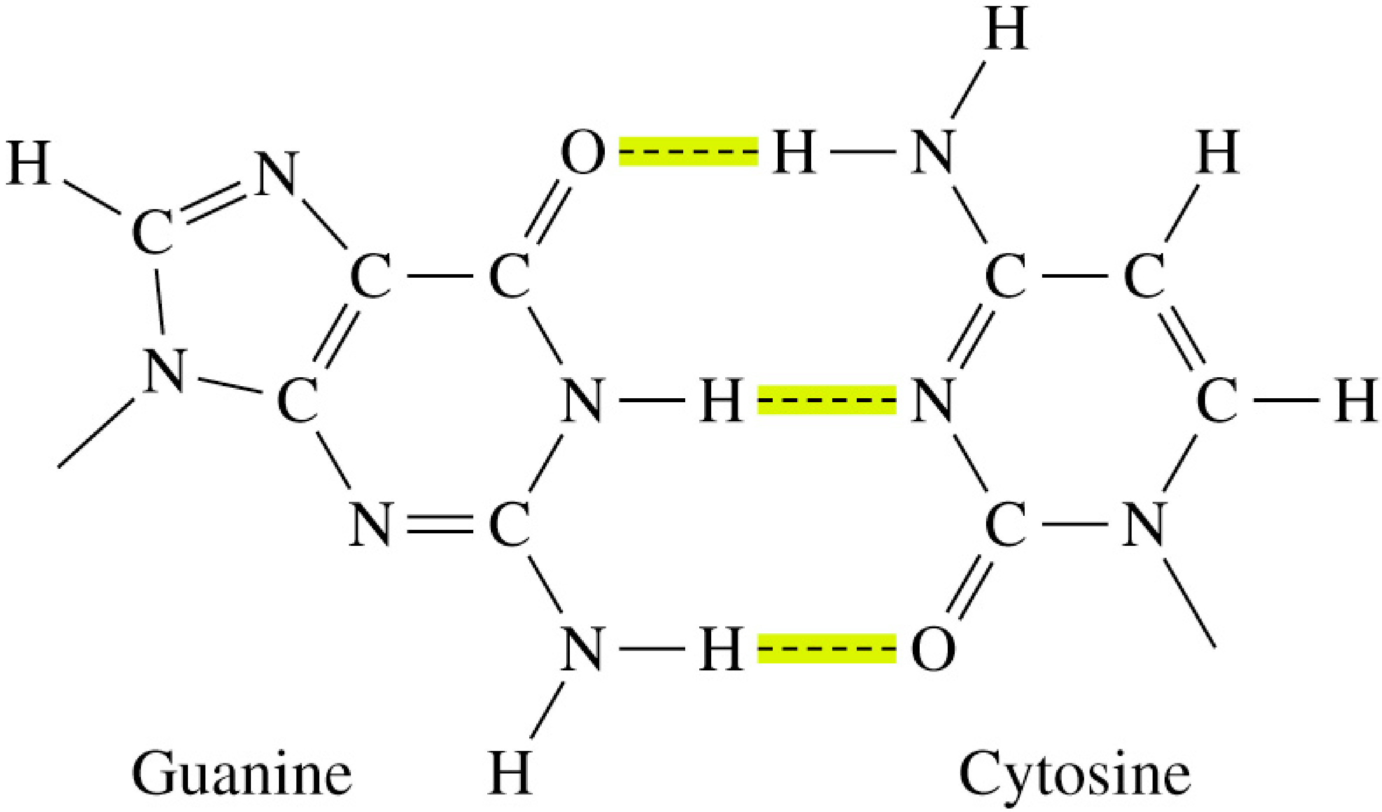
A-H and B





(b) Some biologically important H-bonds

Hydrogen bonding between complementary bases in DNA

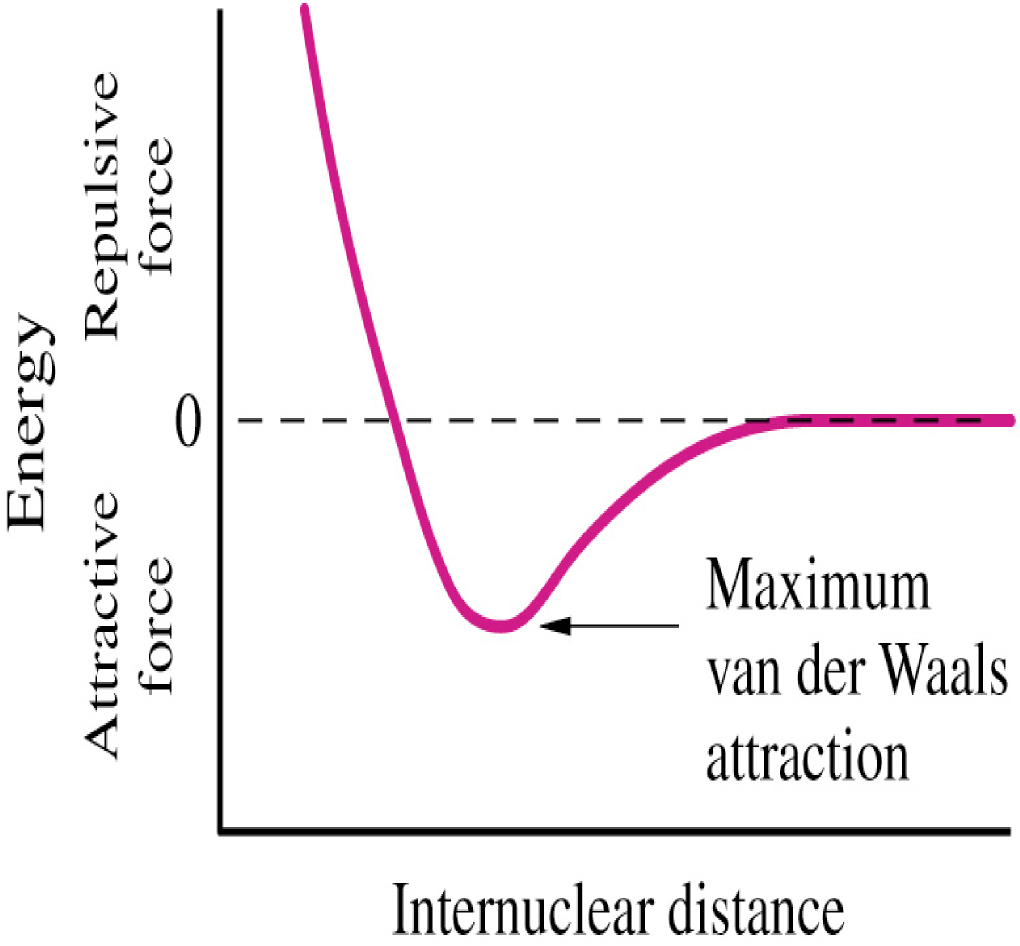


C. Van der Waals Forces

- Weak short range forces between:
  (a) Permanent dipoles of two uncharged molecules
  (b) Permanent dipole and an induced dipole in a neighboring molecule
- Although individually weak, many van der Waals interactions occur in biological macromolecules and participate in stabilizing molecular structures

Effect of internuclear separation on van der Waals forces

- Strongly repulsive at short internuclear distances, very weak at long internuclear distances
- Van der Waals attraction is maximal when two atoms are separated by their van der Waals radii



Van der Waals radii of several atoms

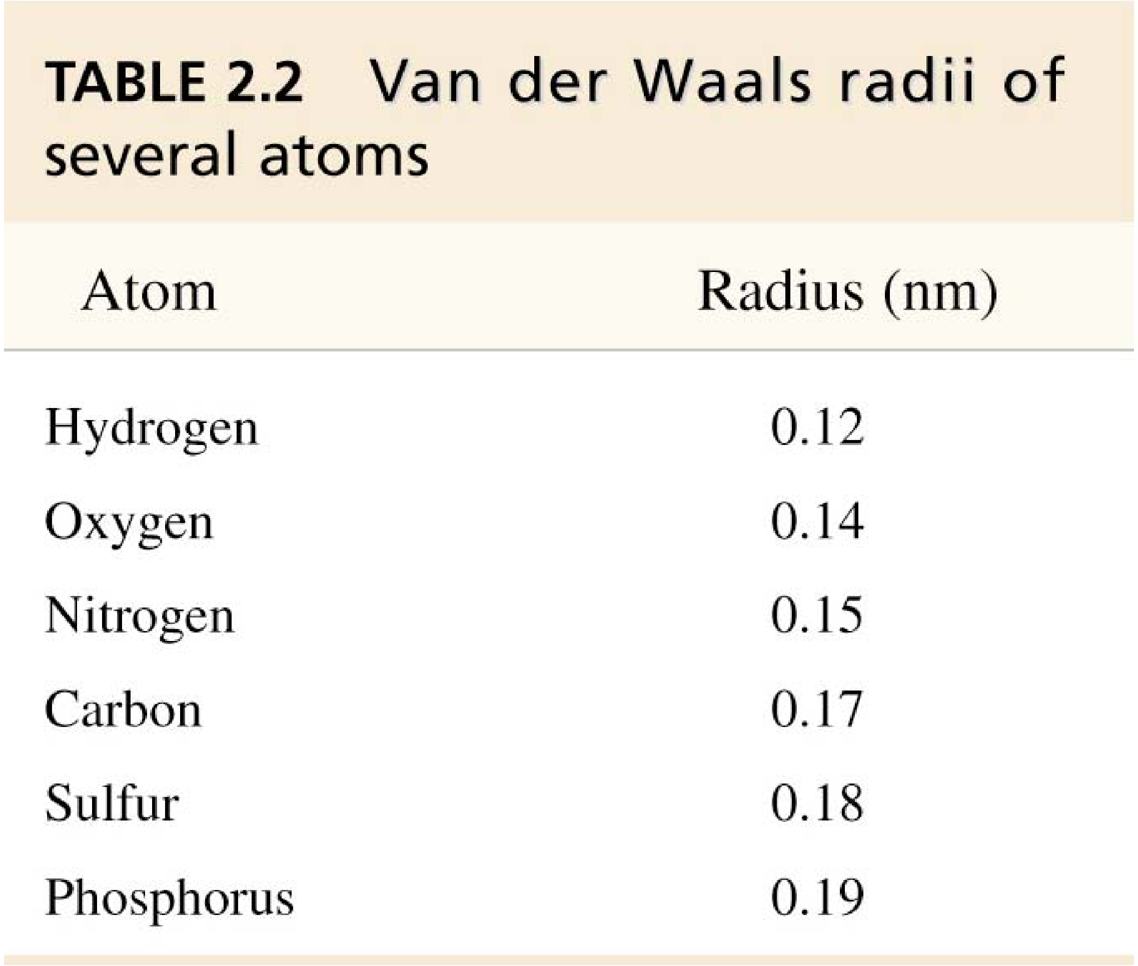


TABLE 2.2 Van der Waals radii of several atoms

Atom	Radius (nm)
Hydrogen	0.12
Oxygen	0.14
Nitrogen	0.15
Carbon	0.17
Sulfur	0.18
Phosphorus	0.19

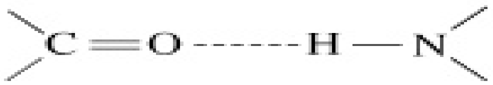
D. Hydrophobic Interactions

- Association of a relatively nonpolar molecule or group with other nonpolar molecules
- Depends upon the increased entropy (+ΔS) which occurs when water molecules surrounding a nonpolar molecule are freed to interact with each other in solution
- The cumulative effects of many hydrophobic interactions can have a significant effect on the stability of a macromolecule

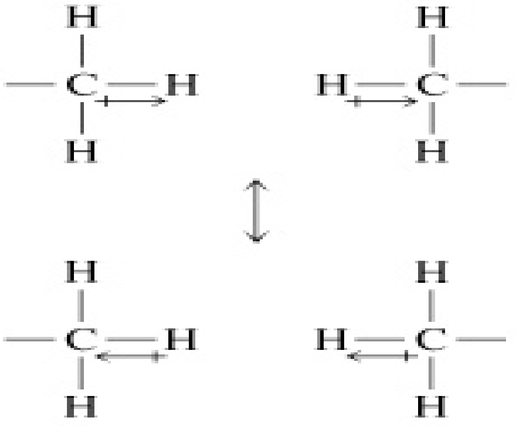
Noncovalent interactions in biomolecules

- Charge-charge interactions
- Hydrogen bonds
- Van der Waals interactions
- Hydrophobic interactions

Charge-charge interaction
~40 to 200 kJ mol^{-1}



Hydrogen bond
~2 to 20 kJ mol^{-1}



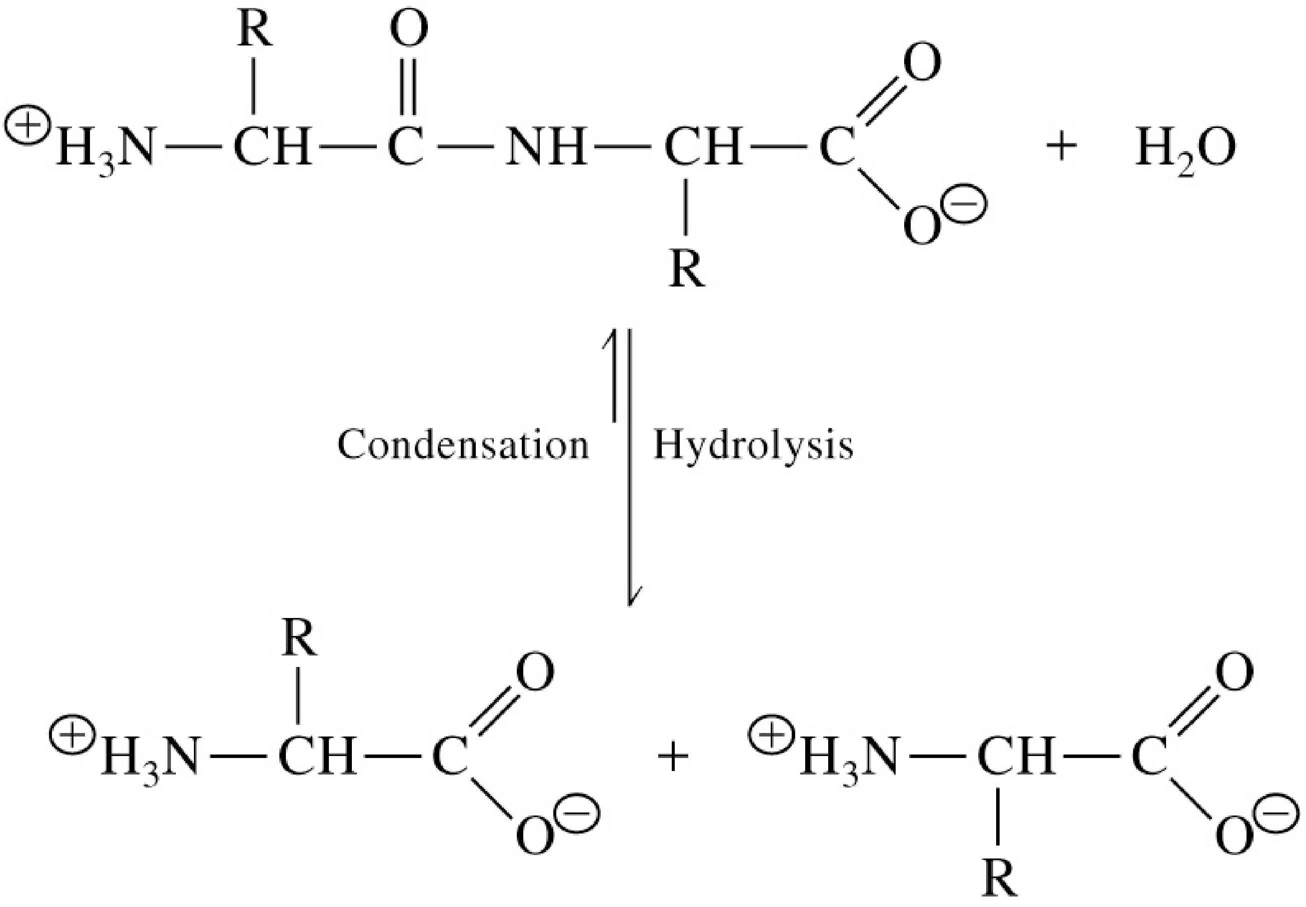
van der Waals interaction
~0.4 to 4 kJ mol^{-1}

Hydrophobic interaction
~3 to 10 kJ mol^{-1}

Water Is Nucleophilic

- **Nucleophiles** - electron-rich atoms or groups
- **Electrophiles** - electron-deficient atoms or groups
- Water is a relatively weak nucleophile
- Due to its high cellular concentration, hydrolysis reactions in water are thermodynamically favored

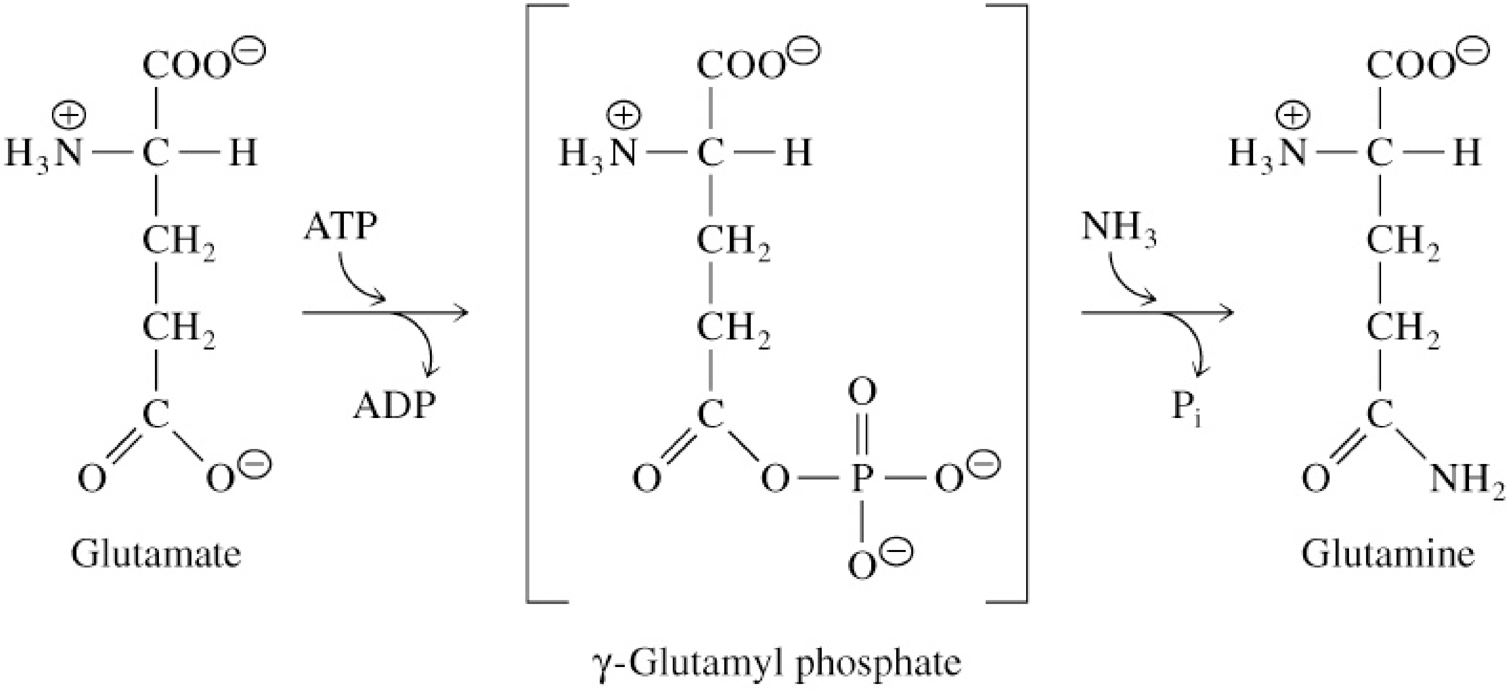
Hydrolysis of a peptide



$$^{\oplus}H_3N-\underset{}{\overset{R}{CH}}-\overset{O}{\overset{\|}{C}}-NH-\underset{R}{CH}-COO^{\ominus} + H_2O \rightleftharpoons {}^{\oplus}H_3N-\overset{R}{CH}-COO^{\ominus} + {}^{\oplus}H_3N-\underset{R}{CH}-COO^{\ominus}$$

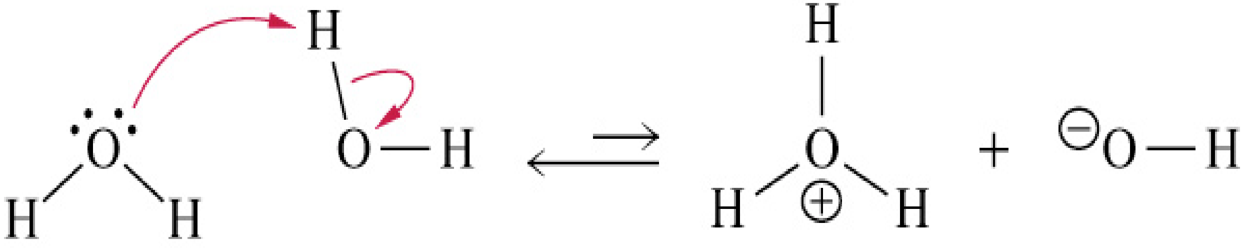
Condensation reactions can be favorable in cells

- ATP chemical energy can be used to drive reactions
- Glutamine synthetase catalyzes a condensation reaction



Ionization of Water

- Pure water consists of a low concentration of **hydronium ions** (**H_3O^+**) and an equal concentration of **hydroxide ions** (**OH^-**)
- **Acids** are proton donors (e.g. H_3O^+) and **bases** are proton acceptors (e.g. OH^-)



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$$H_2O + H_2O \rightleftharpoons H_3O^{\oplus} + OH^{\ominus}$$

The pH Scale

- **pH** is defined as the negative logarithm of the concentration of H^+

$$\mathrm{pH} = -\log[\mathrm{H}^{\oplus}] = \log \frac{1}{[\mathrm{H}^{\oplus}]}$$

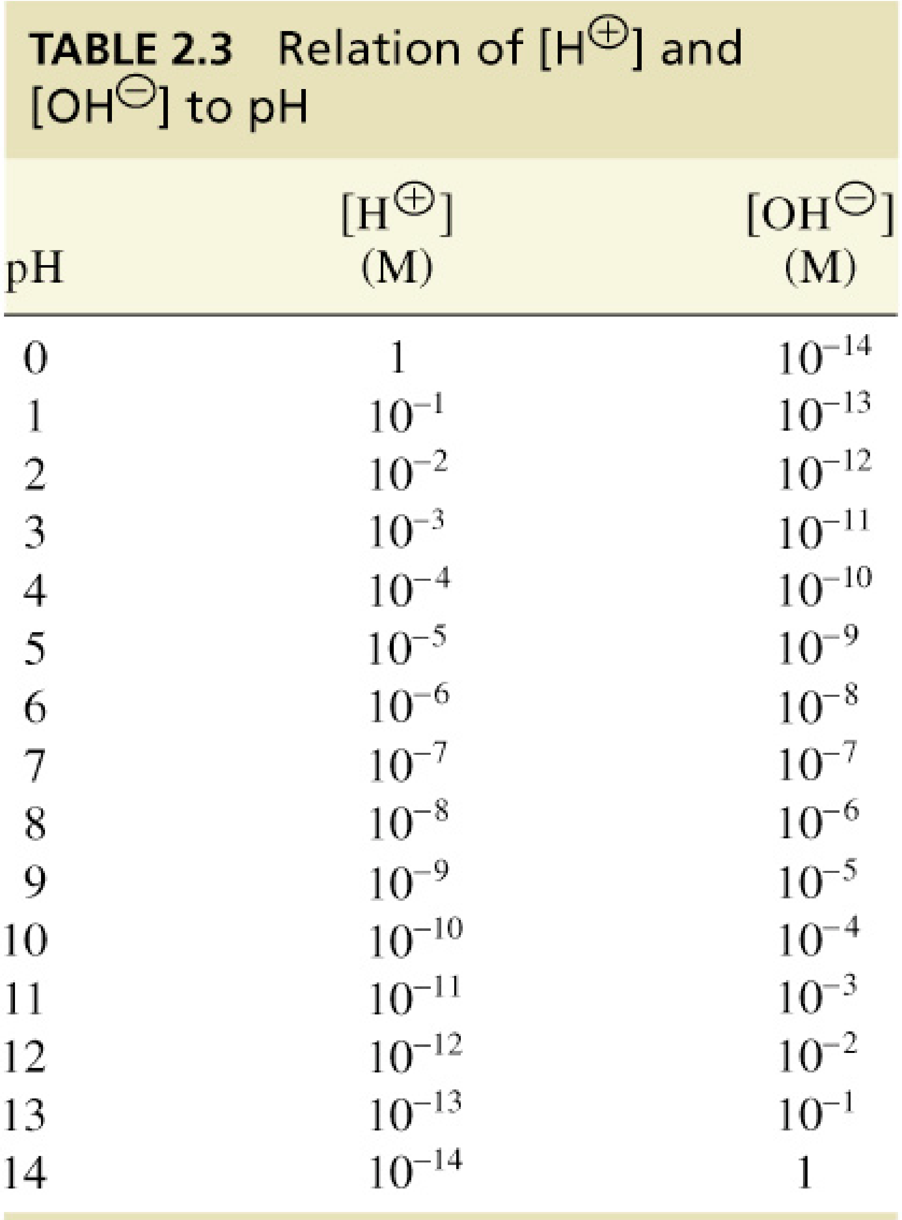
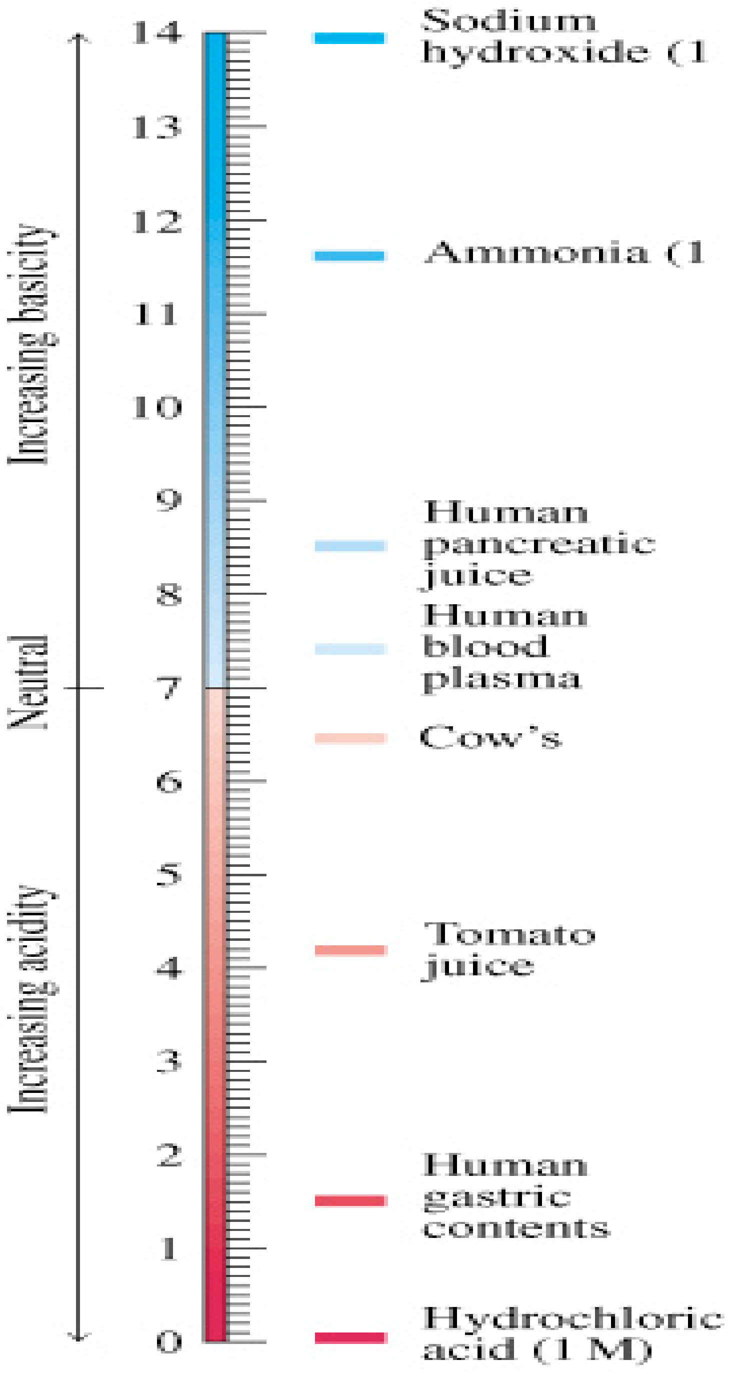


TABLE 2.3 Relation of $[H^{\oplus}]$ and $[OH^{\ominus}]$ to pH

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

pH values for some fluids

- Lower values are acidic fluids
- Higher values are basic fluids



Acid Dissociation Constants of Weak Acids

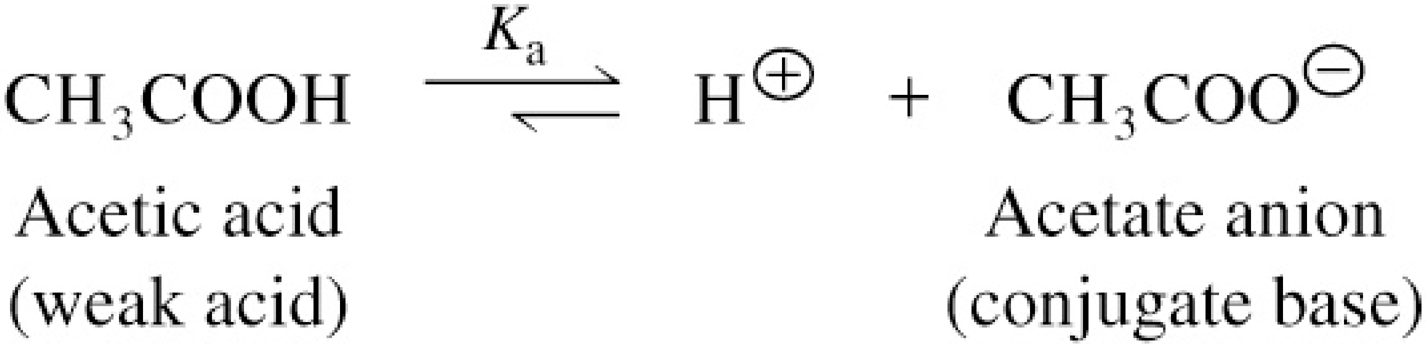
- Strong acids and bases dissociate completely in water

$$HCl + H_2O \rightleftharpoons Cl^- + H_3O^+$$

- Cl^- is the **conjugate base** of HCl
- H_3O^+ is the **conjugate acid** of H_2O

Acetic acid is a weak acid

- Weak acids and bases do not dissociate completely in H_2O



$$CH_3COOH \underset{}{\overset{K_a}{\rightleftharpoons}} H^{\oplus} + CH_3COO^{\ominus}$$

The Henderson-Hasselbalch Equation

- Defines the pH of a solution in terms of:

  (1) The pK_a of the weak acid

  (2) Concentrations of the weak acid (HA) and conjugate base (A^-)

$$\mathrm{pH} = \mathrm{p}K_\mathrm{a} + \log \frac{[\mathrm{A}^{\ominus}]}{[\mathrm{HA}]}$$

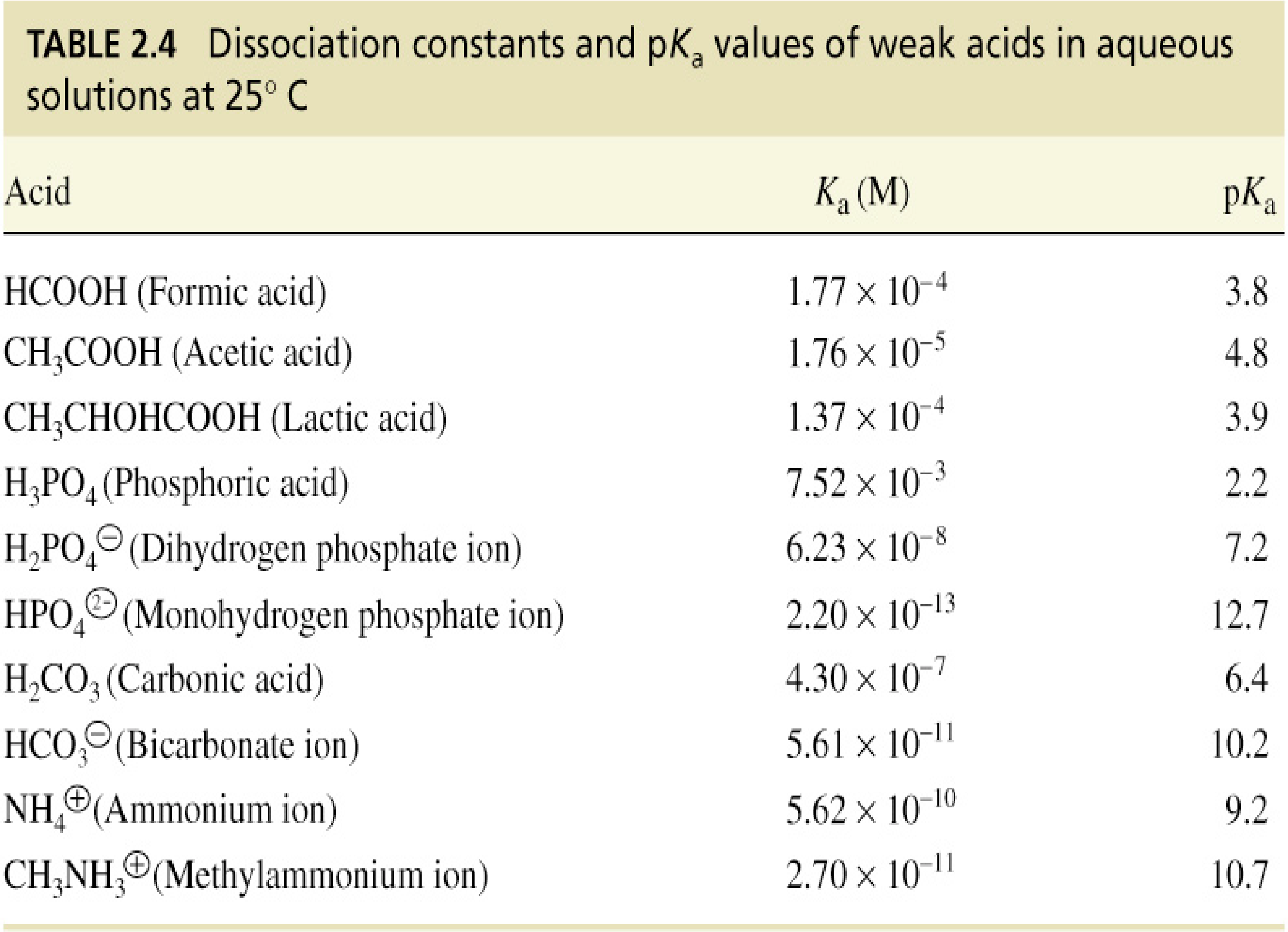
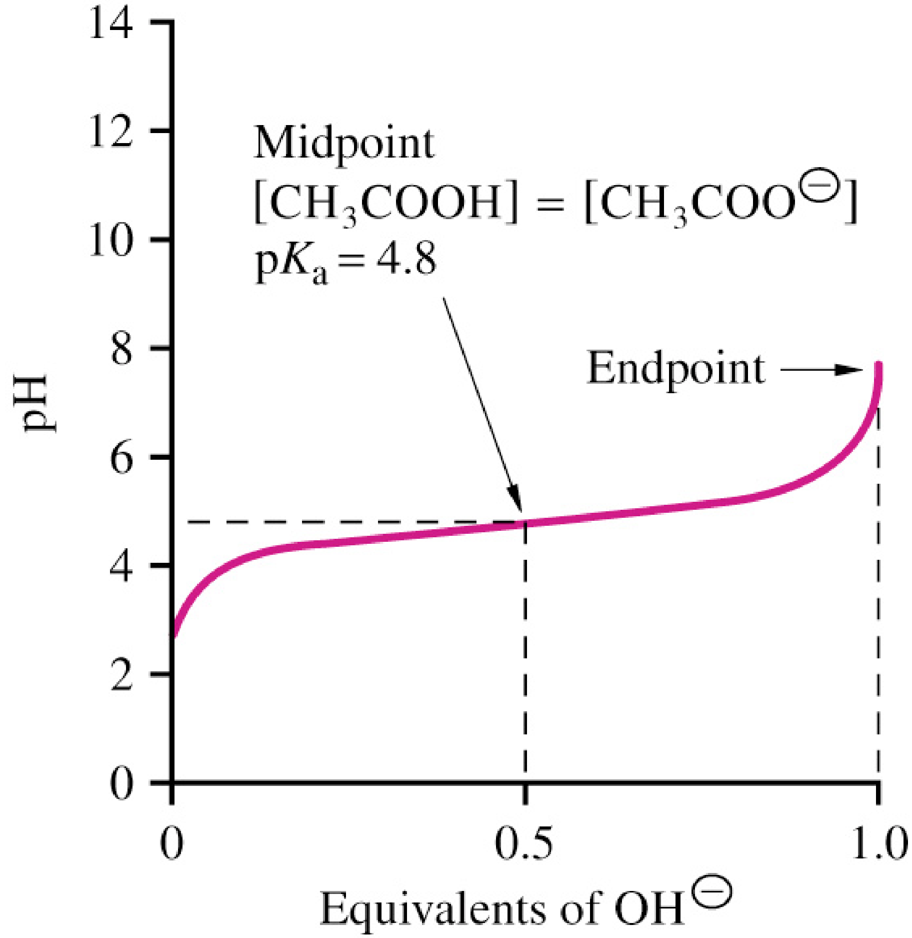


TABLE 2.4 Dissociation constants and pK_a values of weak acids in aqueous solutions at 25° C

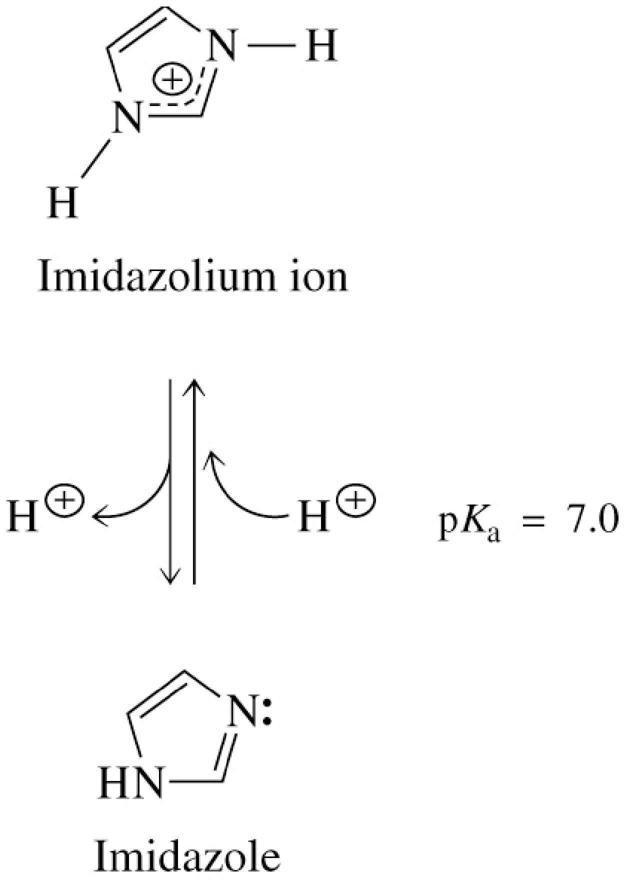
Acid	K_a (M)	pK_a
HCOOH (Formic acid)	1.77×10^{-4}	3.8
CH_3COOH (Acetic acid)	1.76×10^{-5}	4.8
$CH_3CHOHCOOH$ (Lactic acid)	1.37×10^{-4}	3.9
H_3PO_4 (Phosphoric acid)	7.52×10^{-3}	2.2
$H_2PO_4^{\ominus}$ (Dihydrogen phosphate ion)	6.23×10^{-8}	7.2
HPO_4^{2-} (Monohydrogen phosphate ion)	2.20×10^{-13}	12.7
H_2CO_3 (Carbonic acid)	4.30×10^{-7}	6.4
$HCO_3^{\ominus}$ (Bicarbonate ion)	5.61×10^{-11}	10.2
$NH_4^{\oplus}$ (Ammonium ion)	5.62×10^{-10}	9.2
$CH_3NH_3^{\oplus}$ (Methylammonium ion)	2.70×10^{-11}	10.7

Titration curve of acetic acid (CH_3COOH)

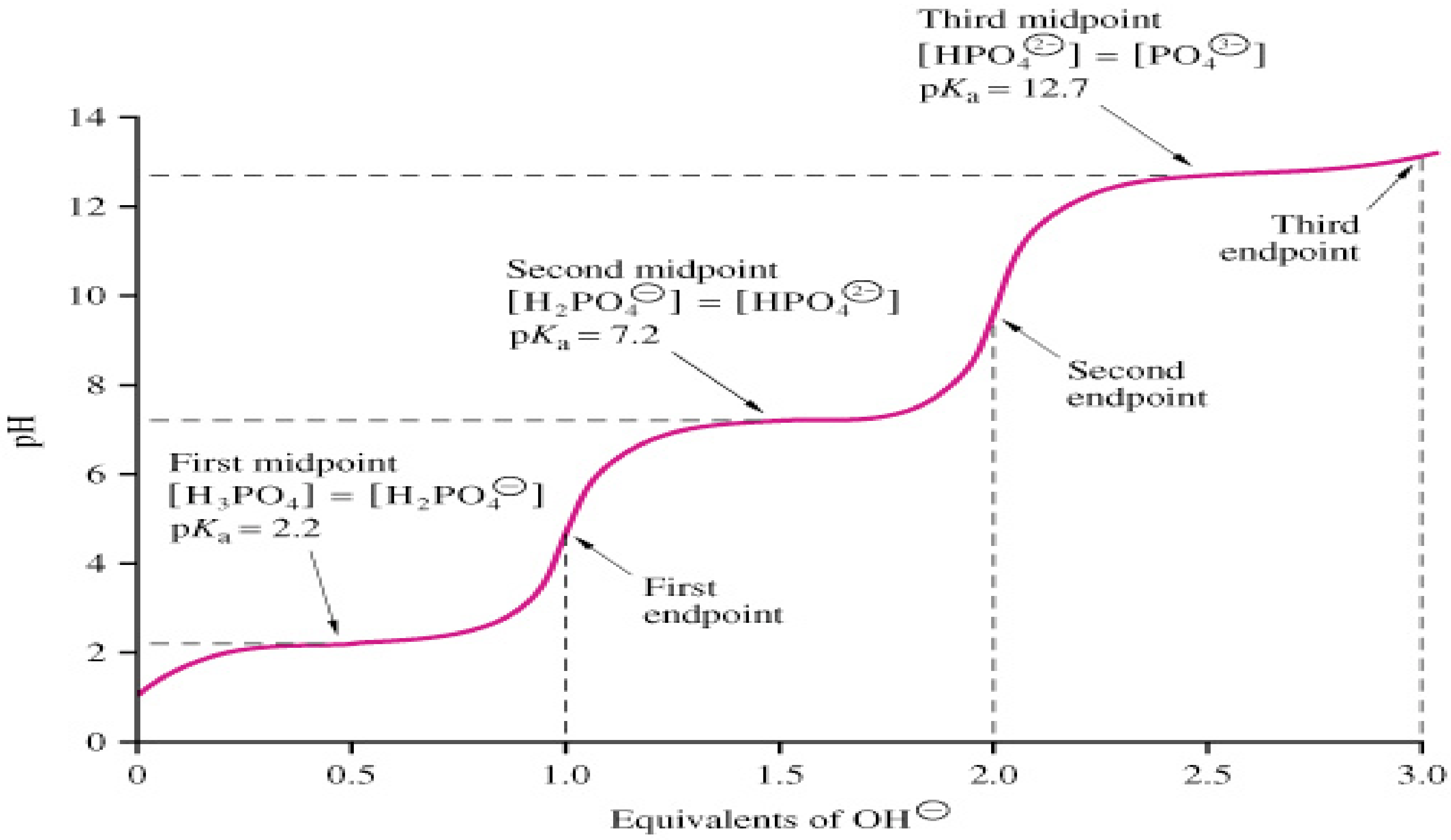
- Titration curves are used to determine pK_a values

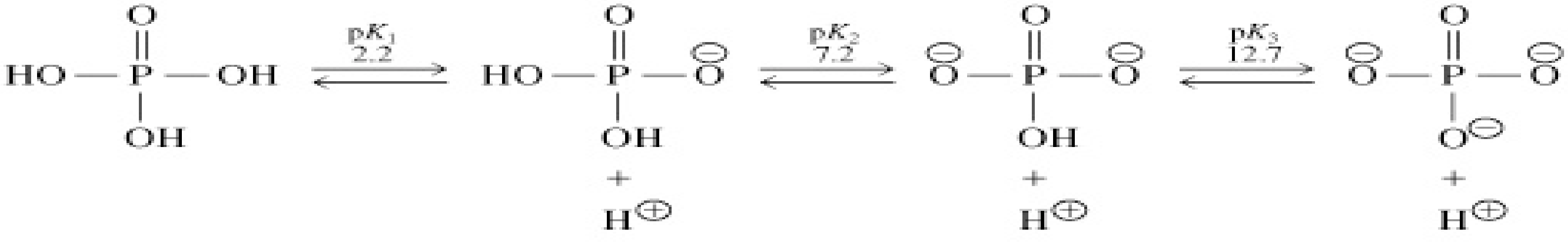


Titration of the imidazolium ion



Titration curve for phosphoric acid (H_3PO_4)





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Buffered Solutions Resist Changes in pH

- Buffer capacity is the ability of a solution to resist changes in pH
- Most effective buffering occurs where:

  solution pH = buffer pK_a
- At this point: [weak acid] = [conjugate base]
- Effective buffering range is usually at pH values equal to the pKa ± 1 pH unit

Regulation of pH in the blood of animals

- Blood plasma of mammals has a constant pH which is regulated by a buffer system of:
  carbon dioxide /carbonic acid /bicarbonate
- Buffer capacity depends upon equilibria between:
  (1) Gaseous CO_2 (air spaces of the lungs)
  (2) Aqueous CO_2 (dissolved in the blood)
  (3) Carbonic acid
  (4) Bicarbonate

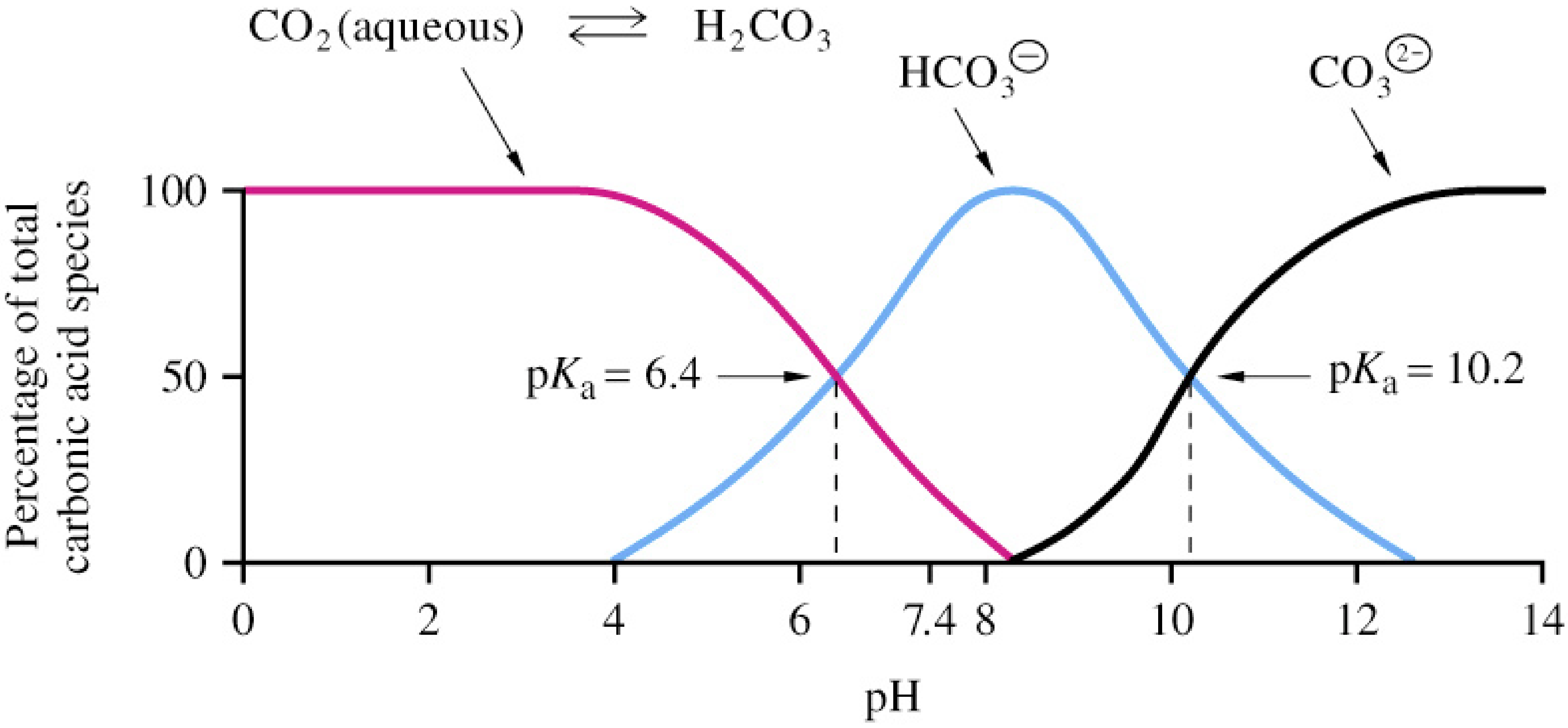
Carbonate buffering equilibria

$$H_2CO_3 \rightleftharpoons H^{\oplus} + HCO_3^{\ominus}$$

$$CO_2\text{(aqueous)} + H_2O \rightleftharpoons H_2CO_3$$

$$CO_2\text{(gaseous)} \rightleftharpoons CO_2\text{(aqueous)}$$

Percentages of carbonic acid and its conjugate bases as a function of pH



Regulation of the pH of blood in mammals