

## 1st week

- Living organisms (domains, kingdoms, definition)
- Cellular foundation: Structure and function of the cell
- Chemical foundation: Biomolecules and building blocks

## 2nd week

- Three laws of thermodynamics (1, 2)
- Is a living organism at equilibrium with surrounding?
- $\Delta G$ ?
- Equilibrium constant?
- $\Delta G^\circ$ ?
- Chemical coupling?
- Enzymes function as catalysts. How?

# Spontaneity Depends on Enthalpy (H) & Entropy (S)

***Before (H1)***

hot coffee (70 °C)



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***After (H2)***

cooled coffee (30 °C)

Where did 40 go?

$$\frac{H_2 - H_1}{> 0 ?}$$

$$\frac{H_2 - H_1}{< 0 ?}$$

$$\Delta H$$

$$\Delta H < 0$$

***Before (S1)***

clean room (10)

***After (S2)***

dirty room (100)

$$\frac{S_2 - S_1}{> 0 ?}$$

$$\frac{S_2 - S_1}{< 0 ?}$$

$$\Delta S$$

$$\Delta S > 0$$

# Spontaneity Depends on Enthalpy (H) & Entropy (S)

**TABLE 1-4 Variation of Reaction Spontaneity (Sign of  $\Delta G$ ) with the Signs of  $\Delta H$  and  $\Delta S$**

$\Delta H$	$\Delta S$	$\Delta G = \Delta H - T\Delta S$
—	+	The reaction is both enthalpically favored (exothermic) and entropically favored. It is spontaneous (exergonic) at all temperatures.
Always happens spontaneously		
—	—	The reaction is enthalpically favored but entropically opposed. It is spontaneous only at temperatures <i>below</i> $T = \Delta H/\Delta S$ .
+	+	
Temp dependent		The reaction is enthalpically opposed (endothermic) but entropically favored. It is spontaneous only at temperatures <i>above</i> $T = \Delta H/\Delta S$ .
+	—	The reaction is both enthalpically and entropically opposed. It is nonspontaneous (endergonic) at all temperatures.
Never happens spontaneously		

# Equilibrium and $\Delta G^\circ$

R = gas constant  
T = absolute Temp

Equilibrium constant: the reactants and products are at equilibrium – experimentally measurable

$$\Delta G^\circ = -RT \ln K_{eq}$$

$\Delta G^\circ$ :

- Standard free energy change
- Thermodynamic constant characteristic of each reaction

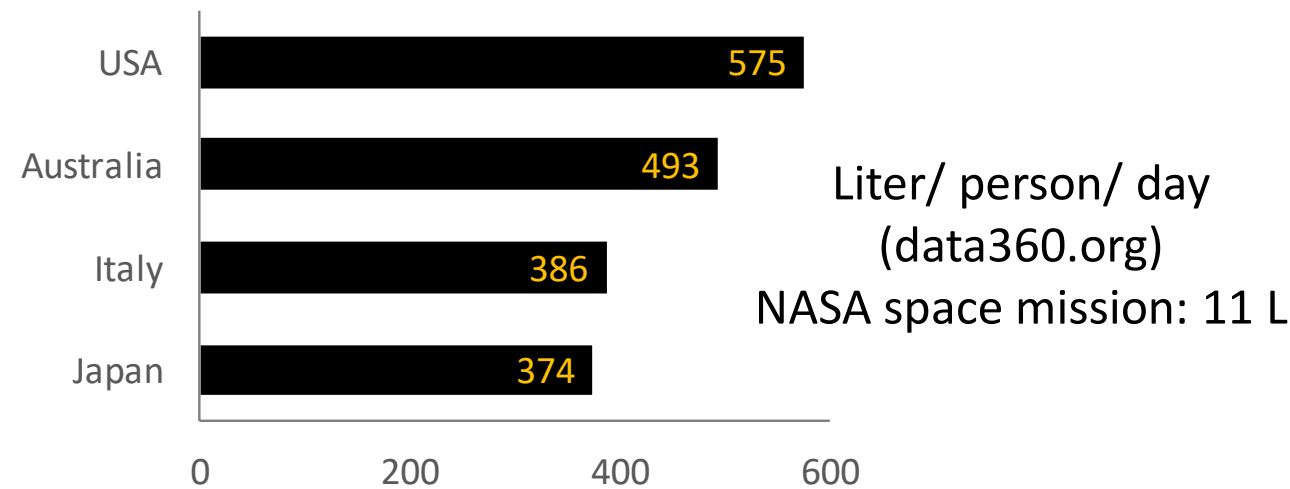
**The relationship between  $\Delta G^\circ$  and  $K_{eq}$**

When  $K_{eq} \gg 1$  ( $=\ln > 0$ ),  $\Delta G^\circ$  is large and negative.

When  $K_{eq} \ll 1$  ( $=\ln < 0$ ),  $\Delta G^\circ$  is large and positive.

# Water

Living on Mars – Making cleaning water on Mars...



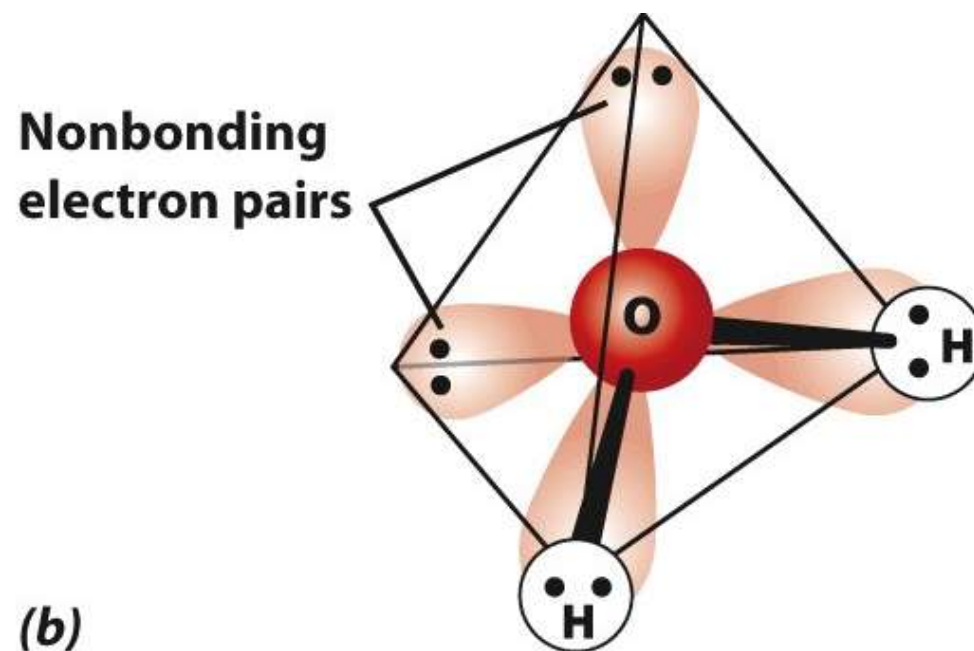
# Water Is the Medium for Life

- Organisms typically contain 70–90% water.
- Chemical reactions occur in aqueous milieu.
- Water is a critical determinant of the structure and function of proteins, nucleic acids, and membranes.

1. Hydrogen bond and dielectric force
2. Hydrophobic effect
3. osmotic effect
4. pH



# Structure of Water



- 4  $e^-$  pairs in  $sp^3$  orbitals
- 2 of 4 pairs covalently link two  $H_2$  atoms to a central O atom
- distorted tetrahedron
- net dipole moment = hydrogen donor and acceptor

# Hydrogen Bonds

- Hydrogen bonds are strong dipole-dipole or charge-dipole interactions that arise between a covalently bound hydrogen and lone pair of electrons.
- They typically involve two electronegative atoms (frequently nitrogen and oxygen).
- Hydrogen bonds are strongest when the bonded molecules allow for linear bonding patterns.
- Ideally, the three atoms involved are in a line.

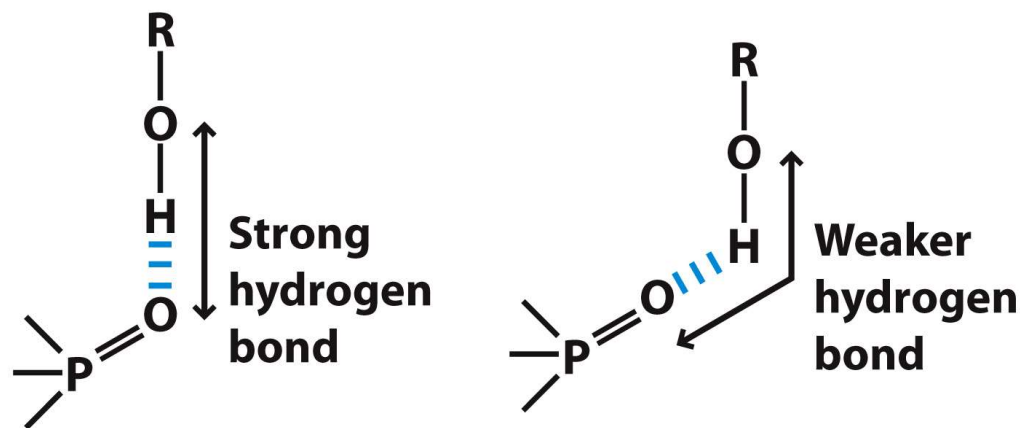


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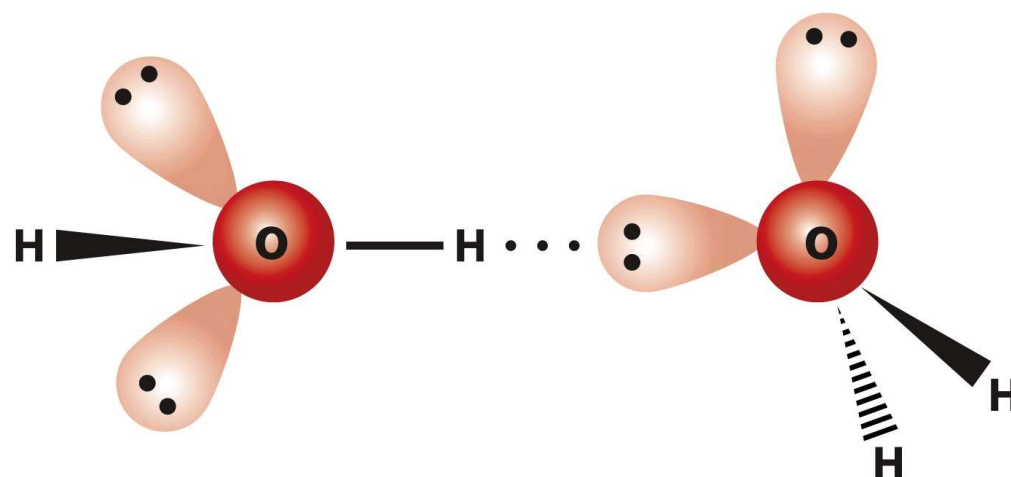


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# Hydrogen Bonding in Water

- Water can serve as both:
  - an H donor
  - an H acceptor
- Up to 4 H-bonds per water molecule gives water its:
  - anomalously high boiling point
  - anomalously high melting point
  - unusually large surface tension
- Hydrogen bonding in water is **cooperative**.
- Hydrogen bonds between neighboring molecules are weak (20 kJ/mol) relative to the H–O covalent bonds (420 kJ/mol).

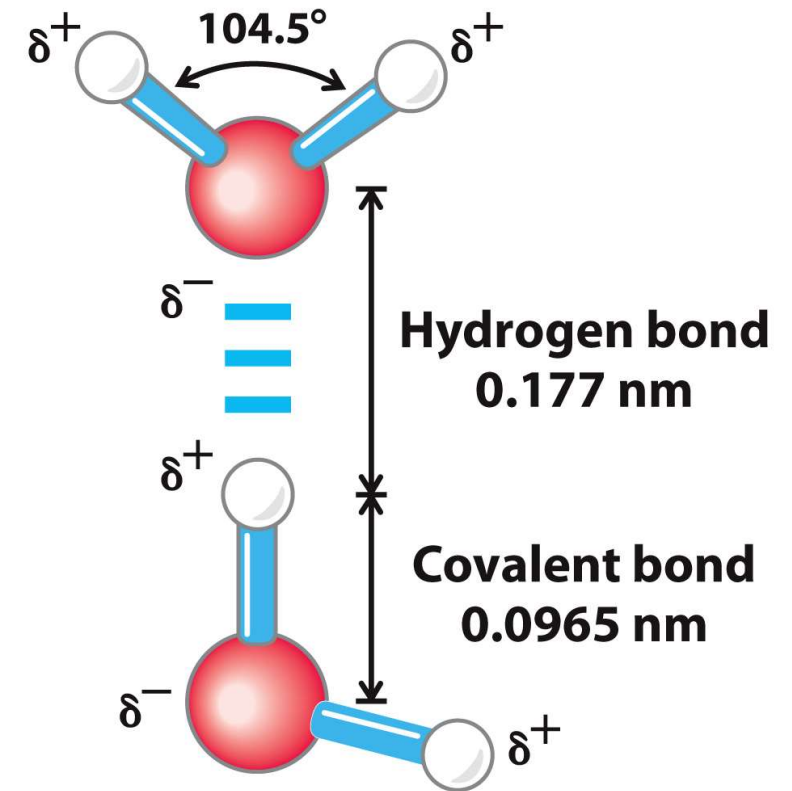


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# Importance of Hydrogen Bonds

- Source of unique properties of water
- Structure and function of proteins
- Structure and function of DNA
- Structure and function of polysaccharides
- Binding of substrates to enzymes
- Binding of hormones to receptors
- Matching of mRNA and tRNA

*“I believe that as the methods of structural chemistry are further applied to physiological problems, it will be found that the significance of the hydrogen bond for physiology is greater than that of any other single structural feature.”*

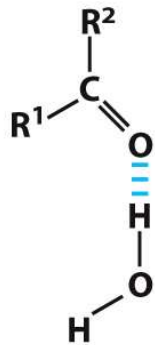
—Linus Pauling, *The Nature of the Chemical Bond*, 1939

# Biological Relevance of Hydrogen Bonds

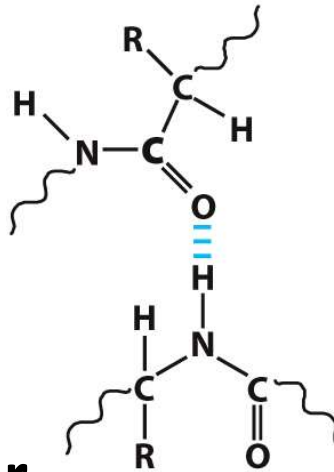
Between the hydroxyl group of an alcohol and water



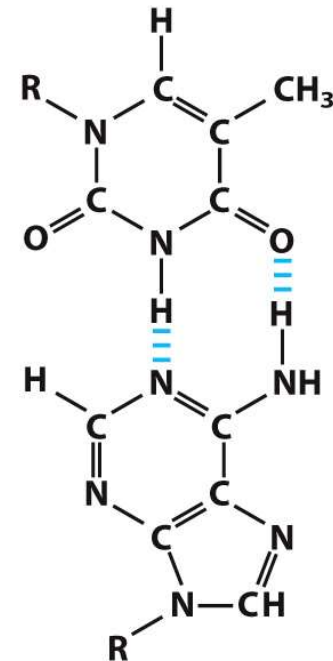
Between the carbonyl group of a ketone and water



Between peptide groups in polypeptides



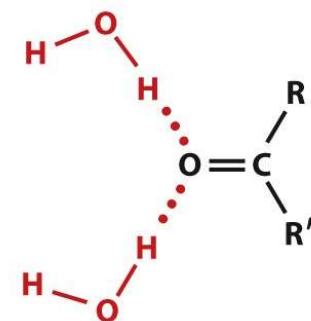
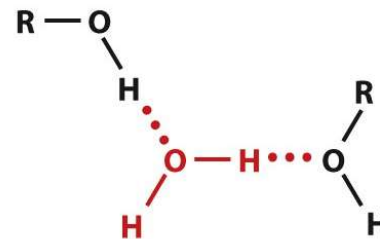
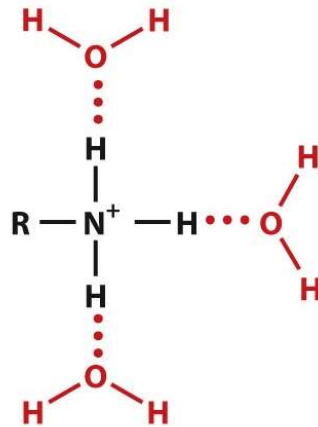
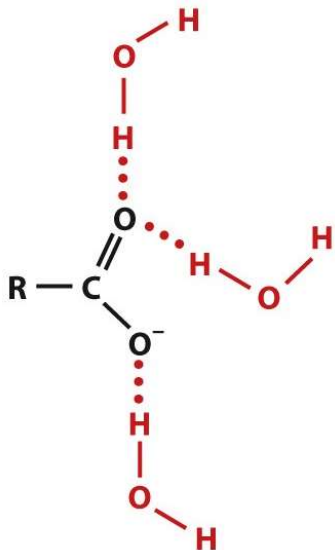
Between complementary bases of DNA



Thymine

Adenine

## Hydrogen Bonding by water



# Ice: Water in a Solid State

- Water has many different crystal forms; the hexagonal ice is the most common.
- Hexagonal ice forms an organized lattice and thus has a low entropy.
- Hexagonal ice contains maximal hydrogen bonds/ water molecules, forcing the water molecules into equidistant arrangement. Thus:
  - ice has lower density than liquid water
  - ice floats

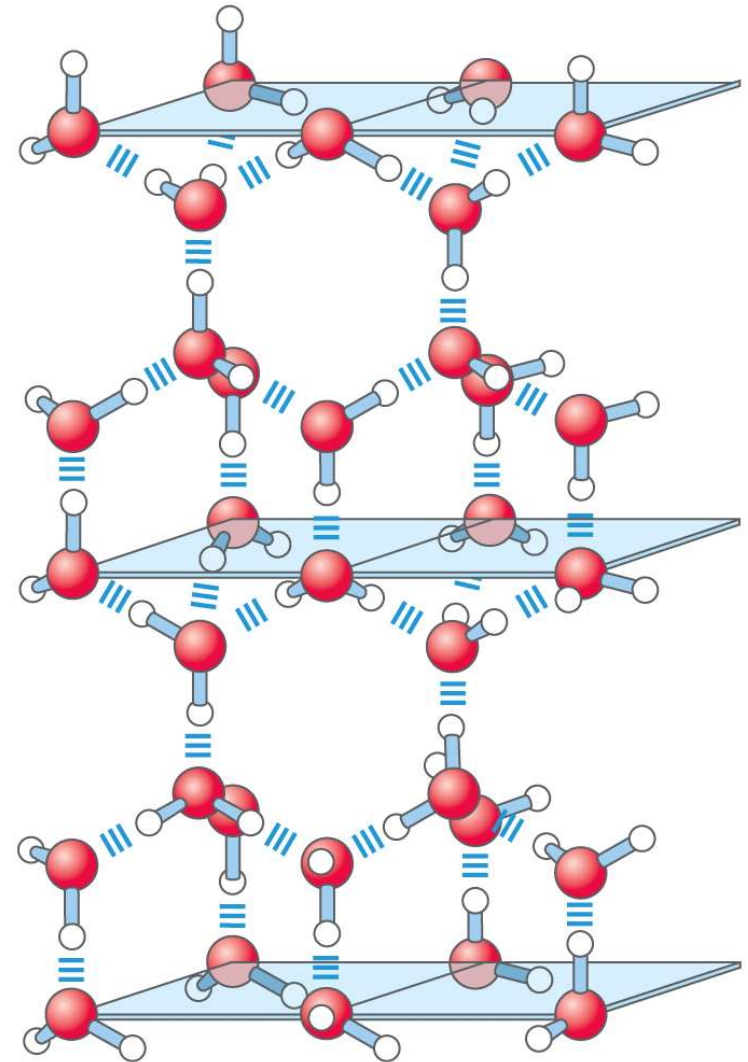


Figure 2-2

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# Water as a Solvent

amino acids, peptides  
carbohydrates  
small alcohol

**Good**

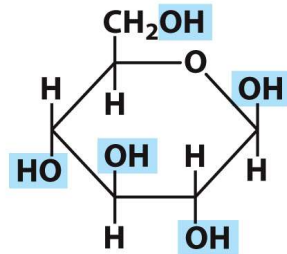
**Poor**

nonpolar gases  
aromatic moieties  
aliphatic chains

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

## Polar

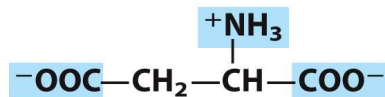
### Glucose



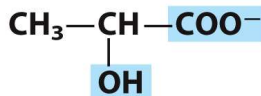
### Glycine



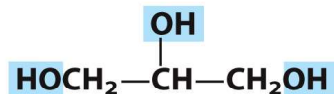
### Aspartate



### Lactate

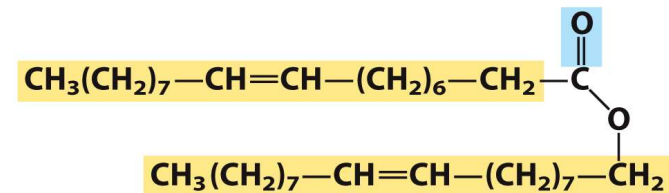


### Glycerol



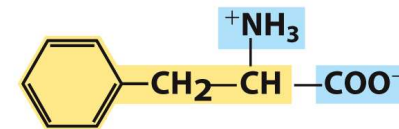
## Nonpolar

### Typical wax

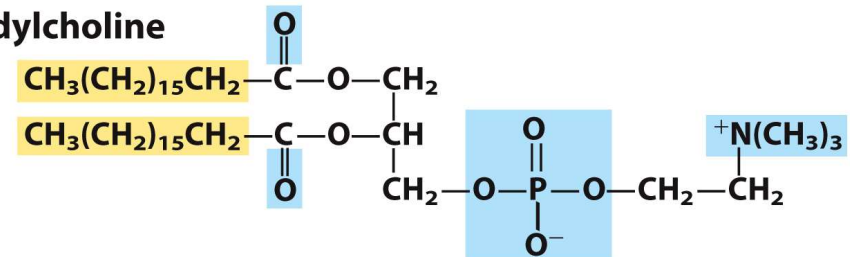


## Amphipathic

### Phenylalanine



### Phosphatidylcholine



Polar groups



Nonpolar groups

**Table 2-2**

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# Solubility of Polar and Nonpolar Solutes

<b>TABLE 2-3</b>		<b>Solubilities of Some Gases in Water</b>	
<b>Gas</b>	<b>Structure<sup>a</sup></b>	<b>Polarity</b>	<b>Solubility in water (g/L)<sup>b</sup></b>
<b>Nitrogen</b>	$\text{N}\equiv\text{N}$	<b>Nonpolar</b>	<b>0.018 (40 °C)</b>
<b>Oxygen</b>	$\text{O}=\text{O}$	<b>Nonpolar</b>	<b>0.035 (50 °C)</b>
<b>Carbon dioxide</b>	$\begin{array}{c} \delta- \quad \quad \delta- \\ \leftarrow \quad \rightarrow \\ \text{O}=\text{C}=\text{O} \end{array}$	<b>Nonpolar</b>	<b>0.97 (45 °C)</b>
<b>Ammonia</b>	$\begin{array}{c} \text{H} \quad \text{H} \quad \text{H} \\ \diagdown \quad   \quad / \\ \text{N} \\ \downarrow \delta- \end{array}$	<b>Polar</b>	<b>900 (10 °C)</b>
<b>Hydrogen sulfide</b>	$\begin{array}{c} \text{H} \quad \text{H} \\ \diagdown \quad / \\ \text{S} \\ \downarrow \delta- \end{array}$	<b>Polar</b>	<b>1,860 (40 °C)</b>
<p><sup>a</sup>The arrows represent electric dipoles; there is a partial negative charge (<math>\delta-</math>) at the head of the arrow, a partial positive charge (<math>\delta+</math>; not shown here) at the tail.</p> <p><sup>b</sup>Note that polar molecules dissolve far better even at low temperatures than do nonpolar molecules at relatively high temperatures.</p>			

**Table 2-3**


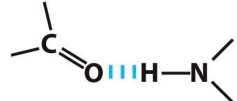


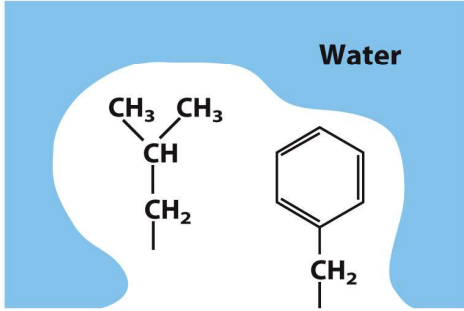
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Why are nonpolar molecules poorly soluble in water?

# Four Major Noncovalent Interactions

- **Ionic interactions**
  - electrostatic interactions between permanently charged species, or between the ion and a permanent dipole
- **Hydrogen bonds**
  - electrostatic interactions between uncharged but polar molecules
- **van der Waals interactions**
  - weak interactions between all atoms, regardless of polarity
  - attractive (dispersion) and repulsive (steric) component
- **Hydrophobic effect**
  - complex phenomenon associated with the ordering of water molecules around nonpolar substances

TABLE 2-5 Four Types of Noncovalent (“Weak”) Interactions among Biomolecules in Aqueous Solvent	
Hydrogen bonds Between neutral groups	
Between peptide bonds	
Ionic interactions Attraction	
Repulsion	
Hydrophobic interactions	
van der Waals interactions	Any two atoms in close proximity



# Dissolving Salts Involves Breaking Ionic Interactions

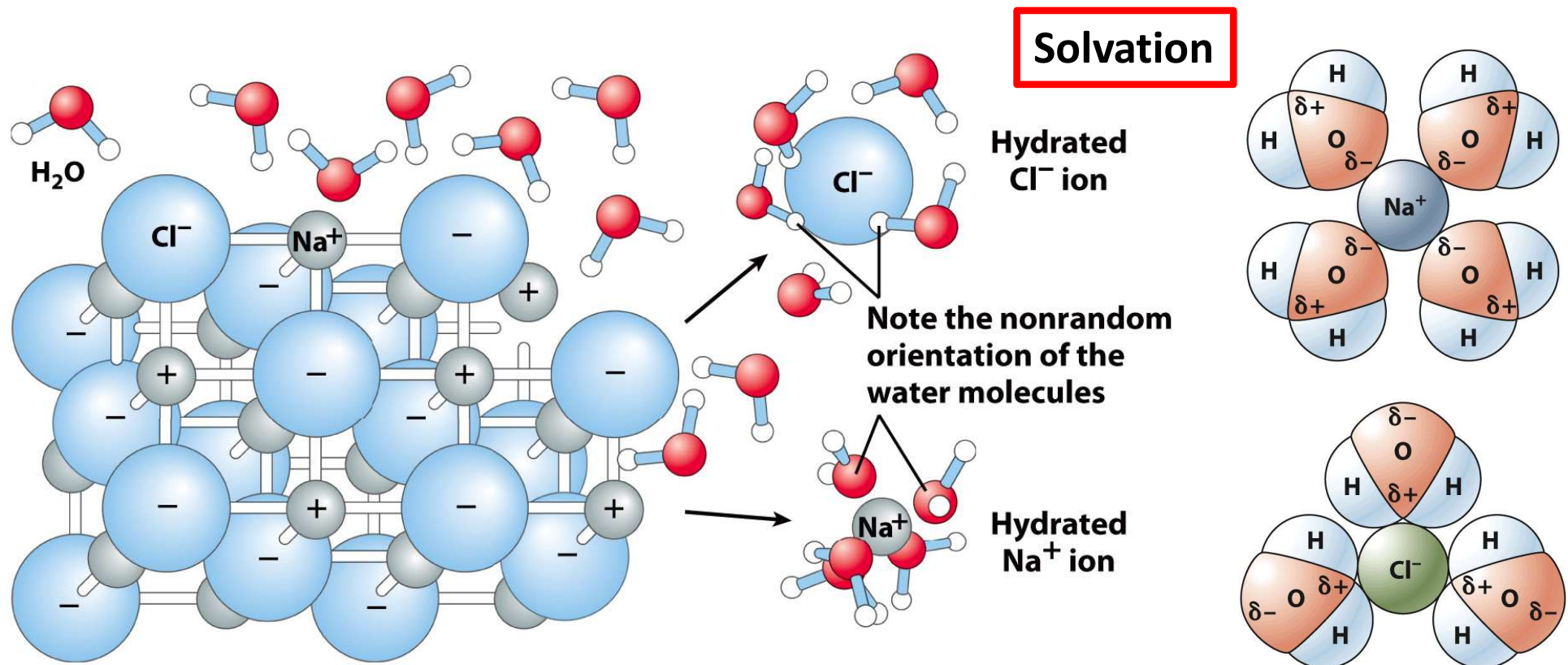


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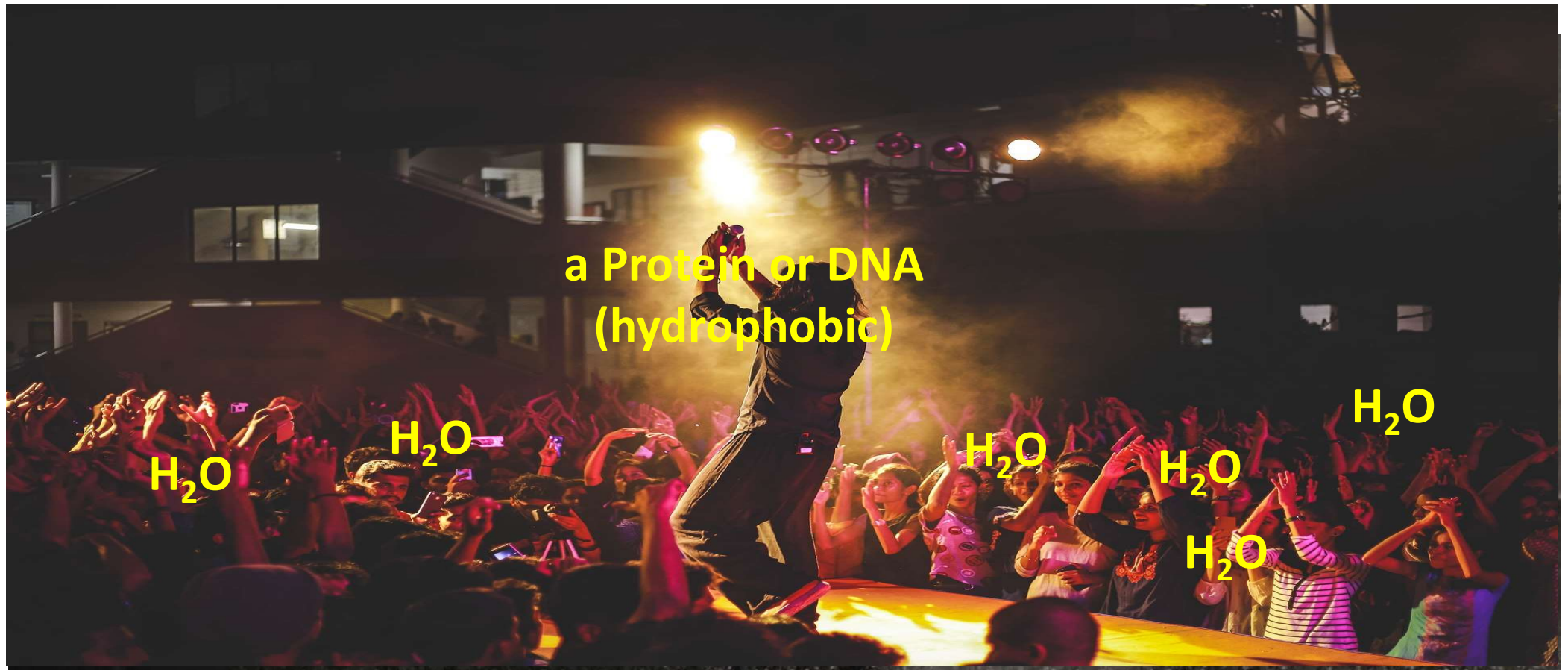
- $\Delta H$ : strong electrostatic interactions between the solvated ions and water molecules lower the total energy of the system
- $\Delta S$ : entropy increases as ordered crystal lattice is dissolved

# van der Waals Interactions

- Two components: attractive force (0.4–0.7 nm) and repulsive force (dependent on the size of atom)
- Individually weak: easily broken, reversible
- Universal: occur between any two atoms that are near each other
- Stabilizes biological macromolecules (stacking in DNA)

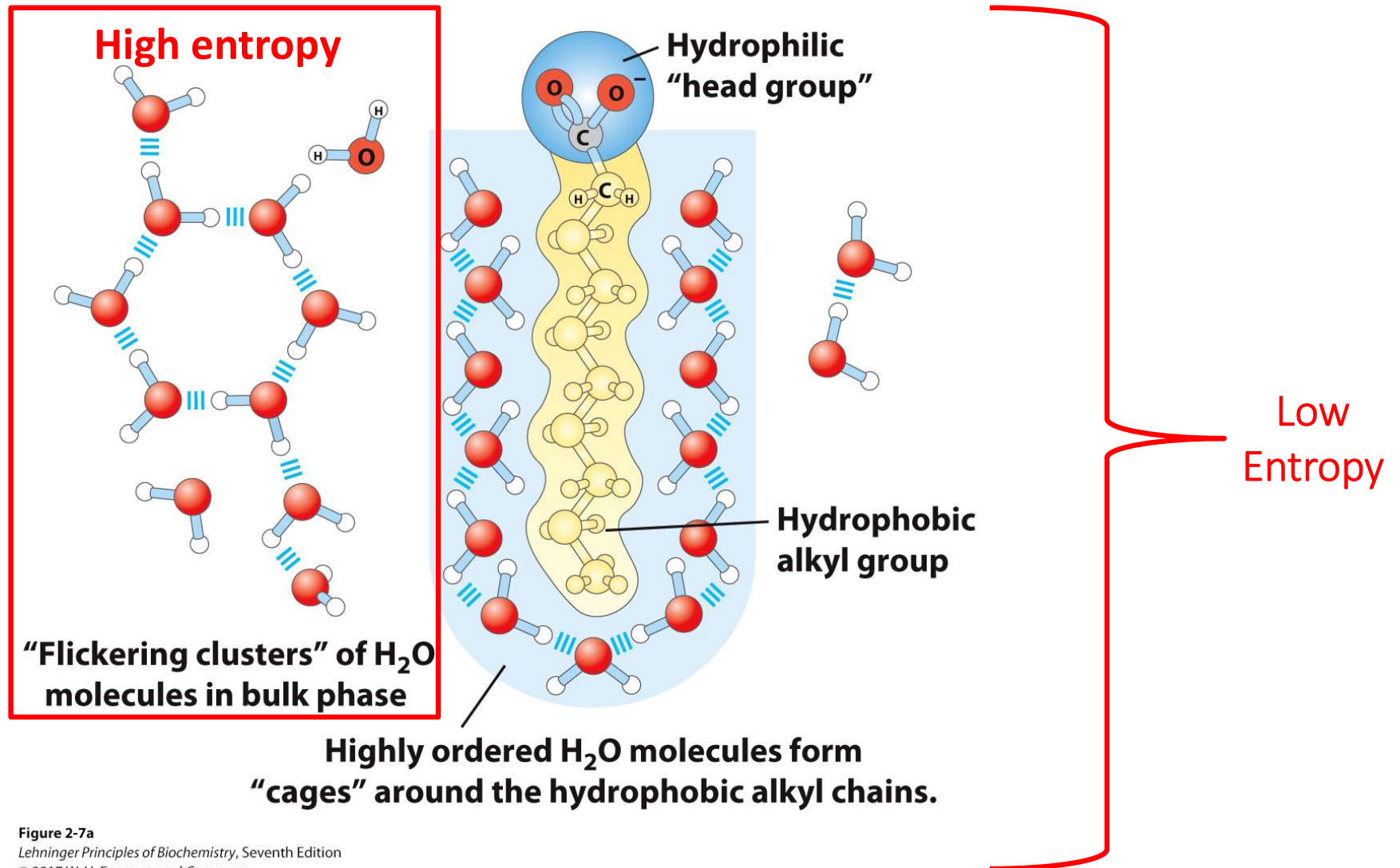
# The Hydrophobic Effect

- Refers to the association or interaction of nonpolar molecules or components of molecules in the aqueous solution
- Is one of the main factors behind:
  - protein folding
  - protein-protein association
  - formation of lipid micelles
  - binding of steroid hormones to their receptors
- Does **not** arise because of some attractive direct force between two nonpolar molecules



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# Water Surrounding Nonpolar Solutes Has Lower Entropy

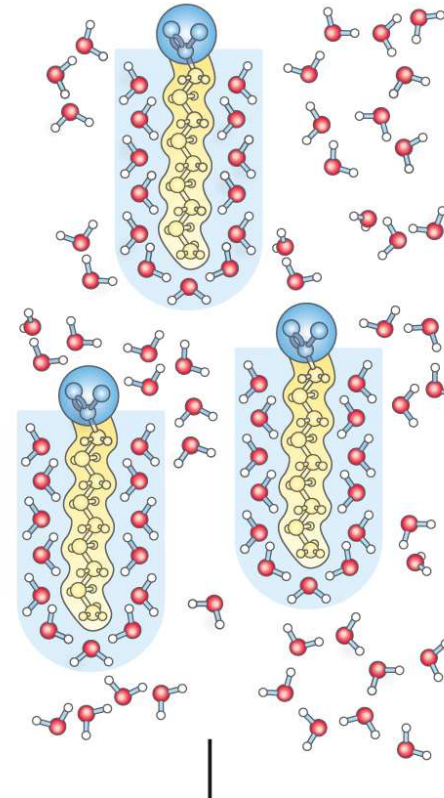


Low entropy is thermodynamically unfavorable, thus hydrophobic solutes have low solubility.



# Origin of the Hydrophobic Effect

- Consider **amphipathic** lipids in water.
- Lipid molecules disperse in the solution; nonpolar tails of lipid molecules are surrounded by ordered water molecules.
- Entropy of the system decreases.
- The system is now in an unfavorable state.

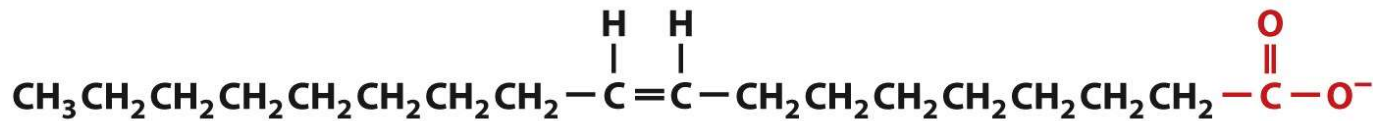


**Dispersion of lipids in H<sub>2</sub>O**

**Each lipid molecule forces surrounding H<sub>2</sub>O molecules to become highly ordered.**



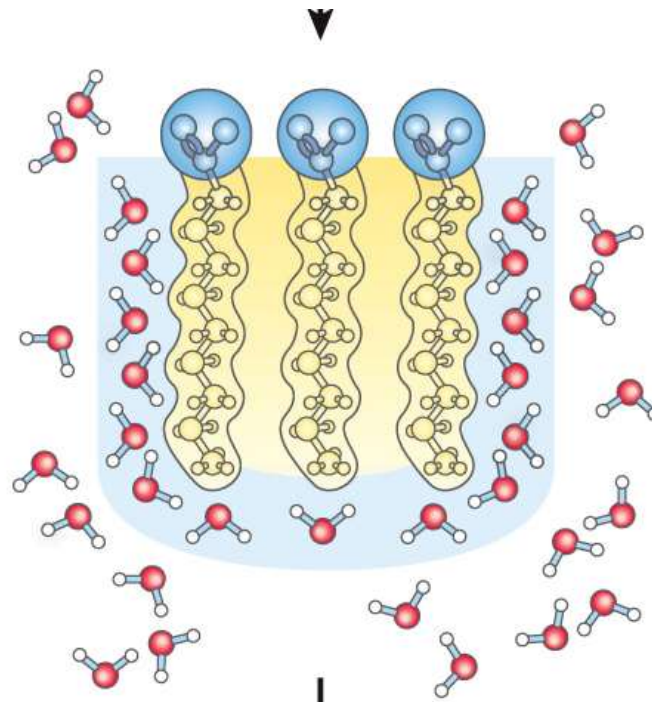
### Palmitate ( $C_{15}H_{31}COO^-$ )



**Oleate ( $C_{17}H_{33}COO^-$ )**

# Origin of the Hydrophobic Effect

- Nonpolar portions of the amphipathic molecule aggregate so that fewer water molecules are ordered and entropy increases.
- All nonpolar groups are sequestered from water, and the released water molecules increase the entropy further.
- Only polar “head groups” are exposed.

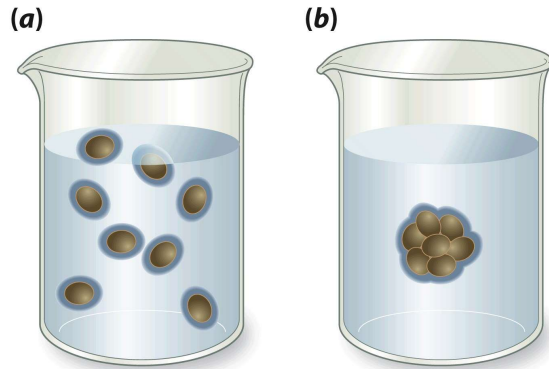


**Clusters of lipid molecules**

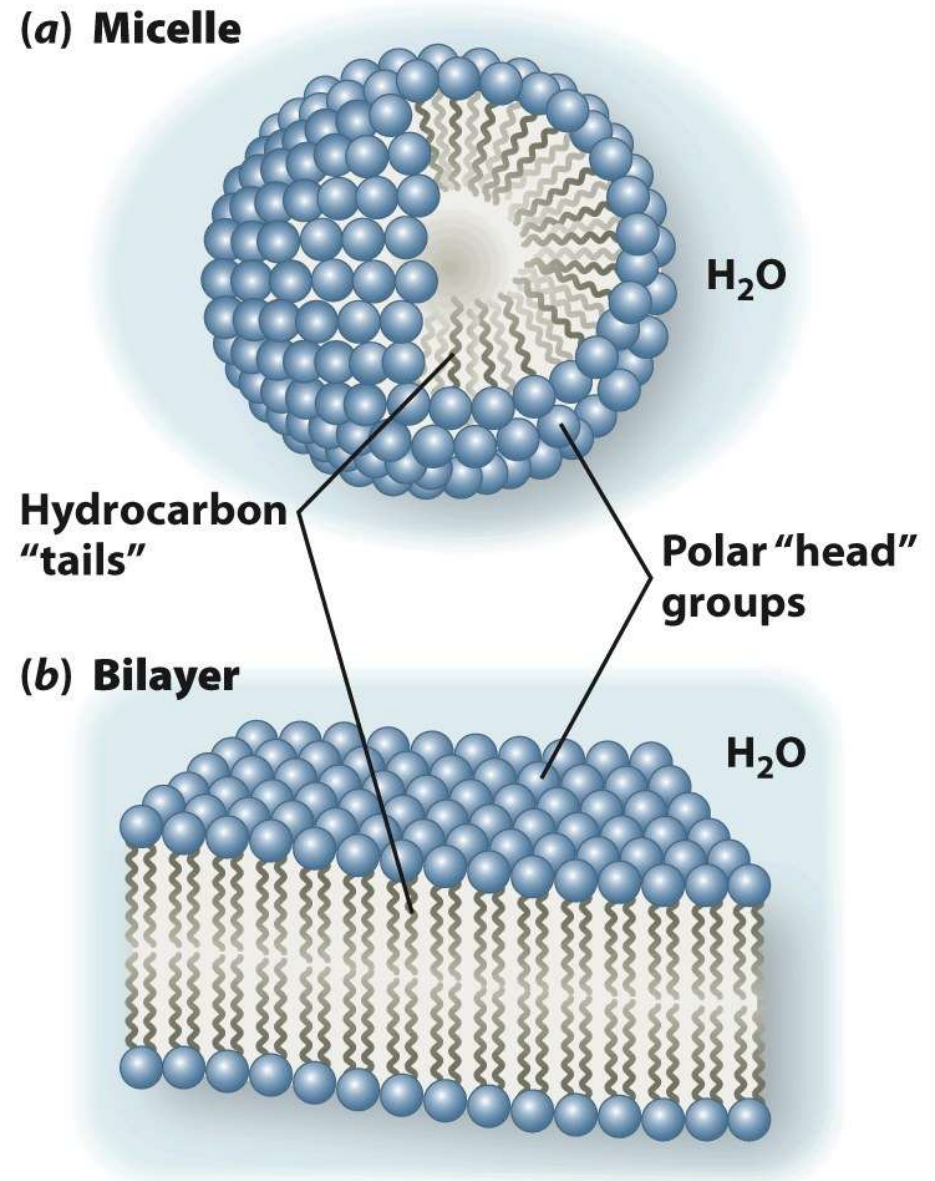
**Only lipid portions at the edge of the cluster force the ordering of water. Fewer H<sub>2</sub>O molecules are ordered, and entropy is increased.**



# Amphiphiles Form Micelles & Bilayers

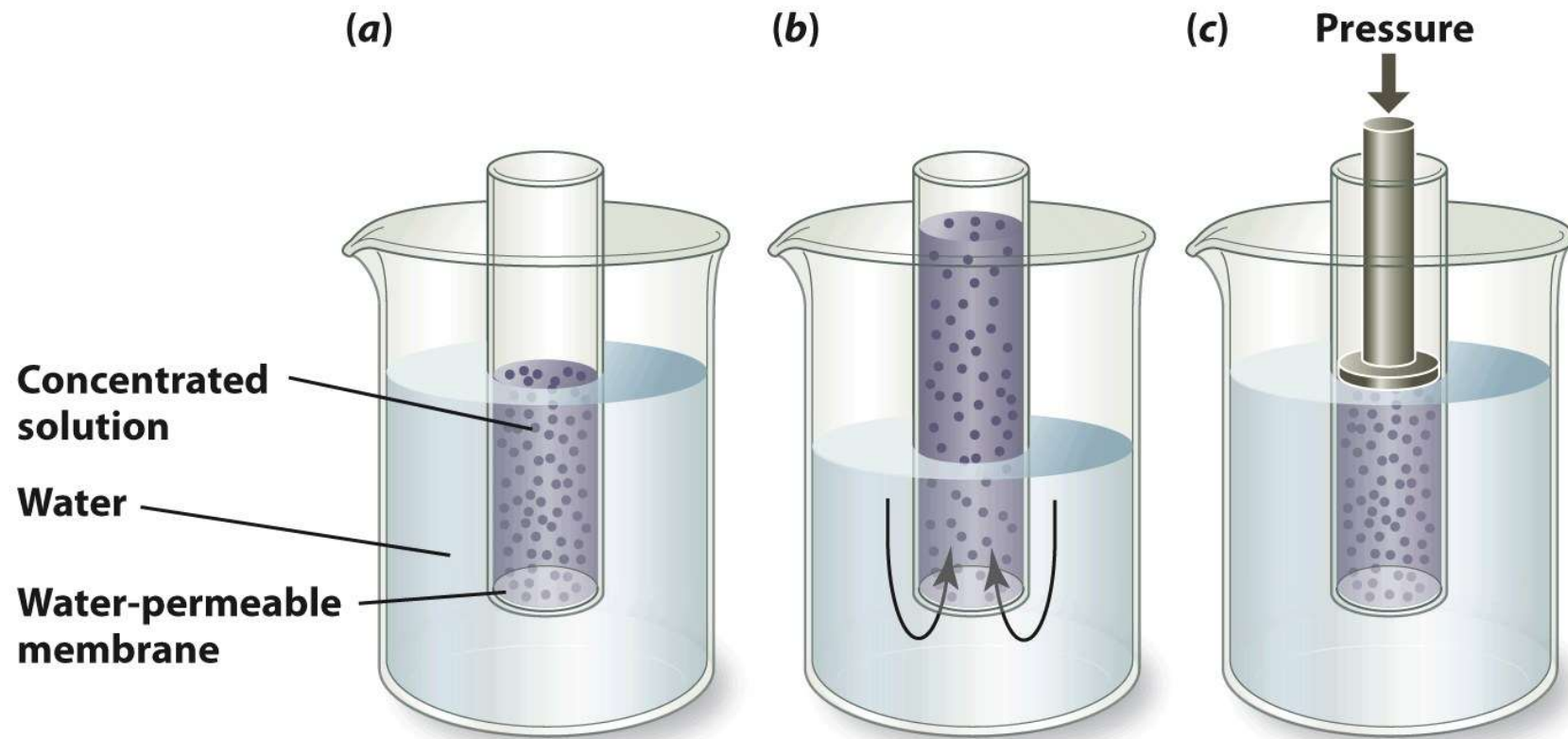


- With high enough concentration of amphipathic molecules, complete aggregation into micelles is possible.
- All hydrophobic groups are sequestered from water; ordered shell of  $\text{H}_2\text{O}$  molecules is minimized, and entropy is further increased.

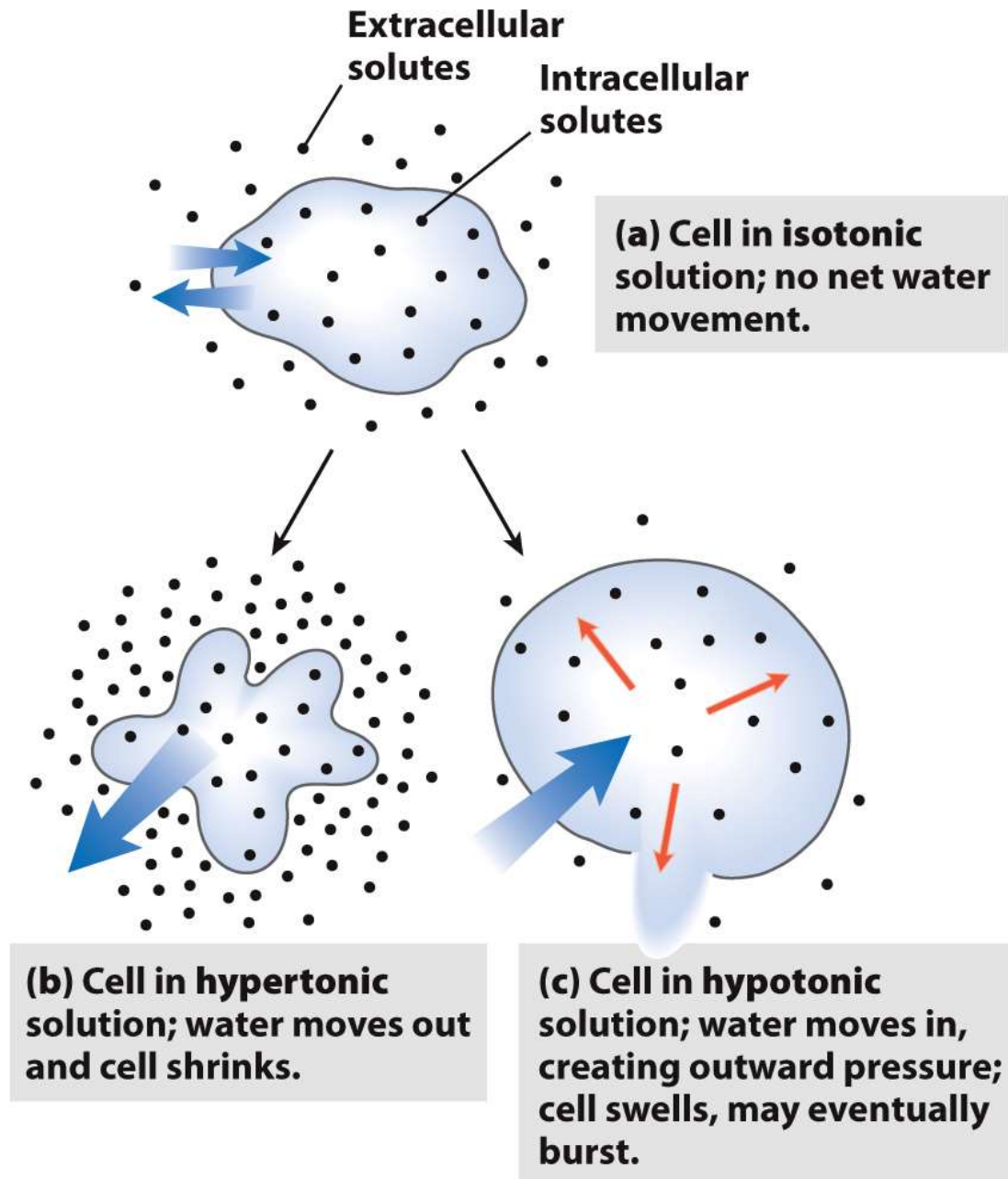


# Osmotic Pressure

- Water moves from areas of high water concentration (low solute concentration) to areas of low water concentration (high solute concentration).
- Osmotic pressure ( $\pi$ ) is the force necessary to resist the movement.
- Dissociated components of a solute individually influence the osmotic pressure.



# Effect of Osmotic Pressure on Cells



# Ionization of Water



- O-H bonds are polar and can dissociate heterolytically.
- Products are a **proton** ( $\text{H}^+$ ) and a **hydroxide ion** ( $\text{OH}^-$ ).
- Dissociation of water is a rapid reversible process.
- Most water molecules remain un-ionized, thus pure water has very low electrical conductivity (resistance:  $18 \text{ M}\Omega\cdot\text{cm}$ ).
- The equilibrium is strongly to the left (low  $K_{\text{eq}}$ ).
- The extent of dissociation depends on the temperature.

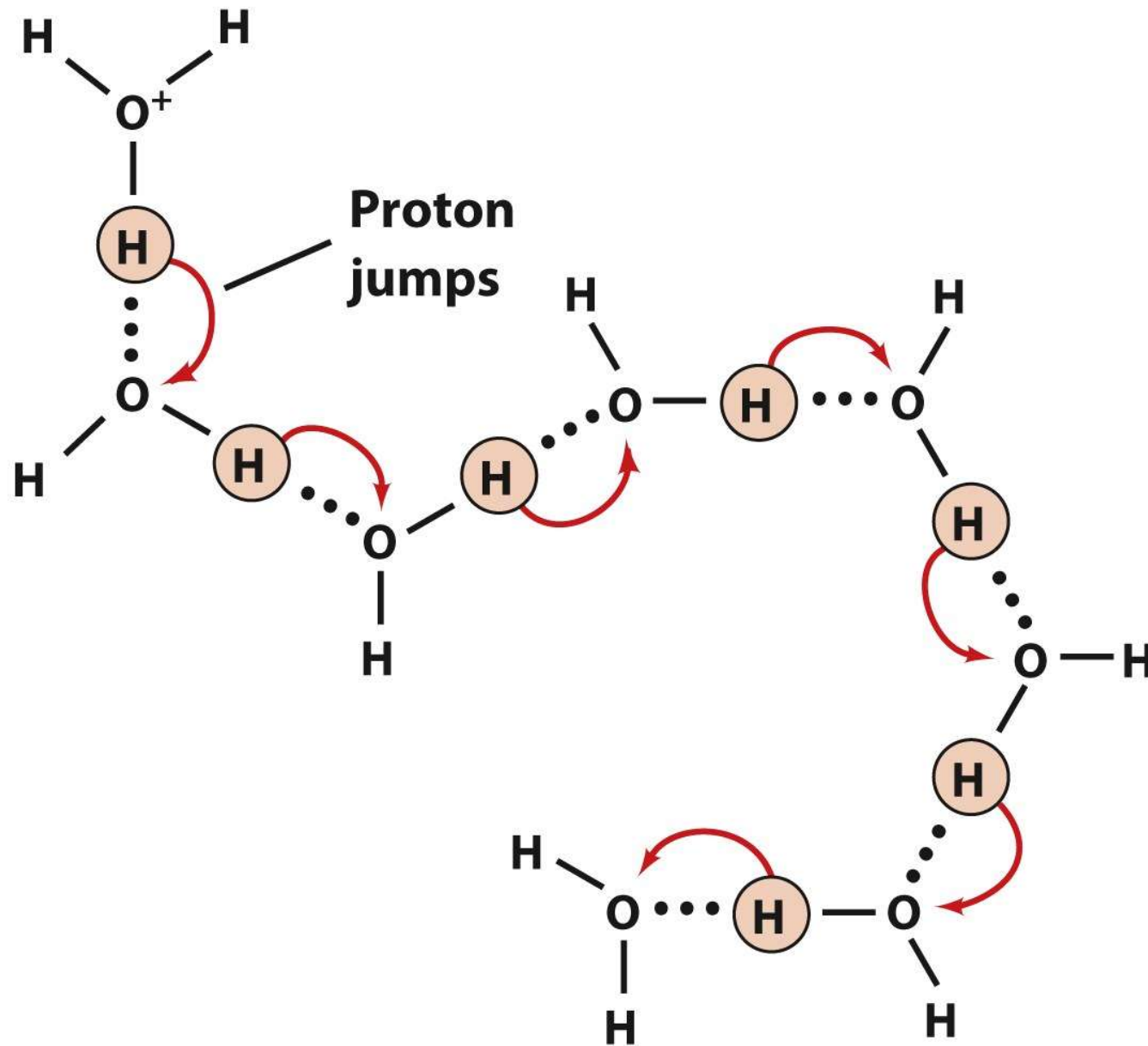
# Proton Hydration

- Protons do not exist free in solution.
- They are immediately hydrated to form **hydronium ions** ( $\text{H}_3\text{O}^+$ ).

$$K_{\text{eq}} = \frac{[\text{H}^+][\text{OH}^-]}{[\text{H}_2\text{O}]}$$

- A hydronium ion is a water molecule with a proton associated with one of the nonbonding electron pairs.
- **Hydronium ions are solvated** by nearby water molecules.
- The covalent and hydrogen bonds are interchangeable. This allows for an extremely fast mobility of protons in water via “proton hopping.”

# Proton hopping



# Ionization of Water: Quantitative Treatment

Concentrations of participating species in an equilibrium process are not independent but are related via the **equilibrium constant**:



$$K_{\text{eq}} = \frac{[\text{H}^+] \cdot [\text{OH}^-]}{[\text{H}_2\text{O}]}$$

$K_{\text{eq}}$  can be determined experimentally, it is  $1.8 \cdot 10^{-16} \text{ M}$  at  $25^\circ\text{C}$ .  
Concentration of  $\text{H}_2\text{O}$   $[\text{H}_2\text{O}]$  can be determined from water density, 55.5 M.

Density: 1000 g/L  
M.W.: 18.015 g/mol

- Ionic product (dissociation constant) of water:

$$K_w = K_{\text{eq}} \cdot [\text{H}_2\text{O}] = [\text{H}^+][\text{OH}^-] = 1 \cdot 10^{-14} \text{ M}^2$$

- In pure water,  $[\text{H}^+] = [\text{OH}^-] = 10^{-7} \text{ M}$ .



# pH


$$\text{pH} = -\log[\text{H}^+]$$

$$K_w = [\text{H}^+][\text{OH}^-] = 1 \cdot 10^{-14} \text{ M}^2$$

$$-\log[\text{H}^+] - \log[\text{OH}^-] = +14$$

$$\text{pH} + \text{pOH} = 14$$

- pH is defined as the negative logarithm of the hydrogen ion concentration.
- The pH and pOH must always add up to 14.
- In neutral solution,  $[\text{H}^+] = [\text{OH}^-]$  and the pH is 7.
- pH can be negative ( $[\text{H}^+] = 6 \text{ M}$ ).

## calculation of $[H^+]$

What is the concentration of  $H^+$  in a solution of 0.1 M NaOH?

answer:  $10^{-13}$  M

## calculation of $[OH^-]$

What is the concentration of  $OH^+$  in a solution with an  $H^+$  concentration of  $1.3 \times 10^{-4}$  M?

answer:  $7.7 \times 10^{-11}$  M

# Relationship of pH, $[H^+]$ , and $[OH^-]$

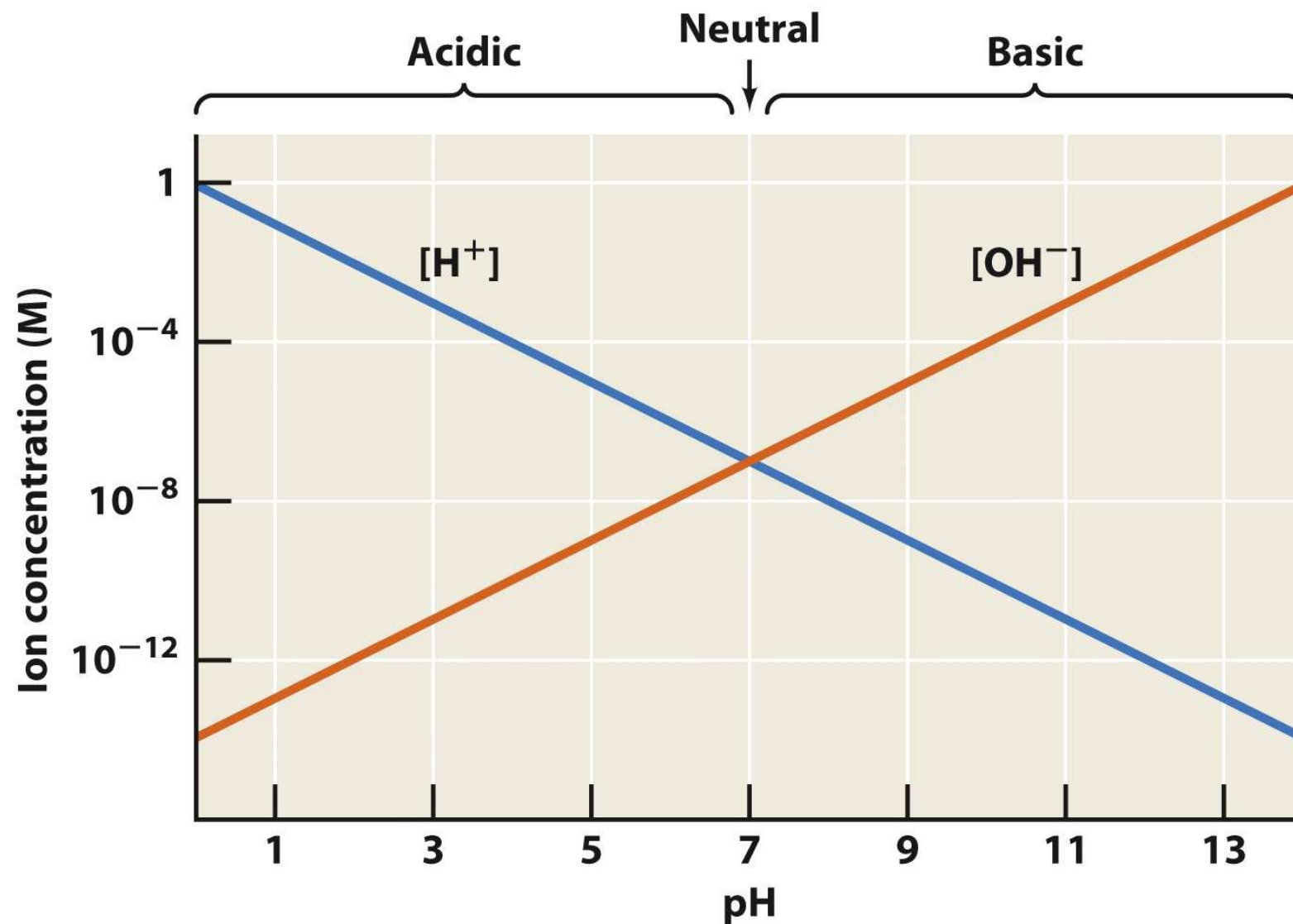


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# pH of Some Common Liquids

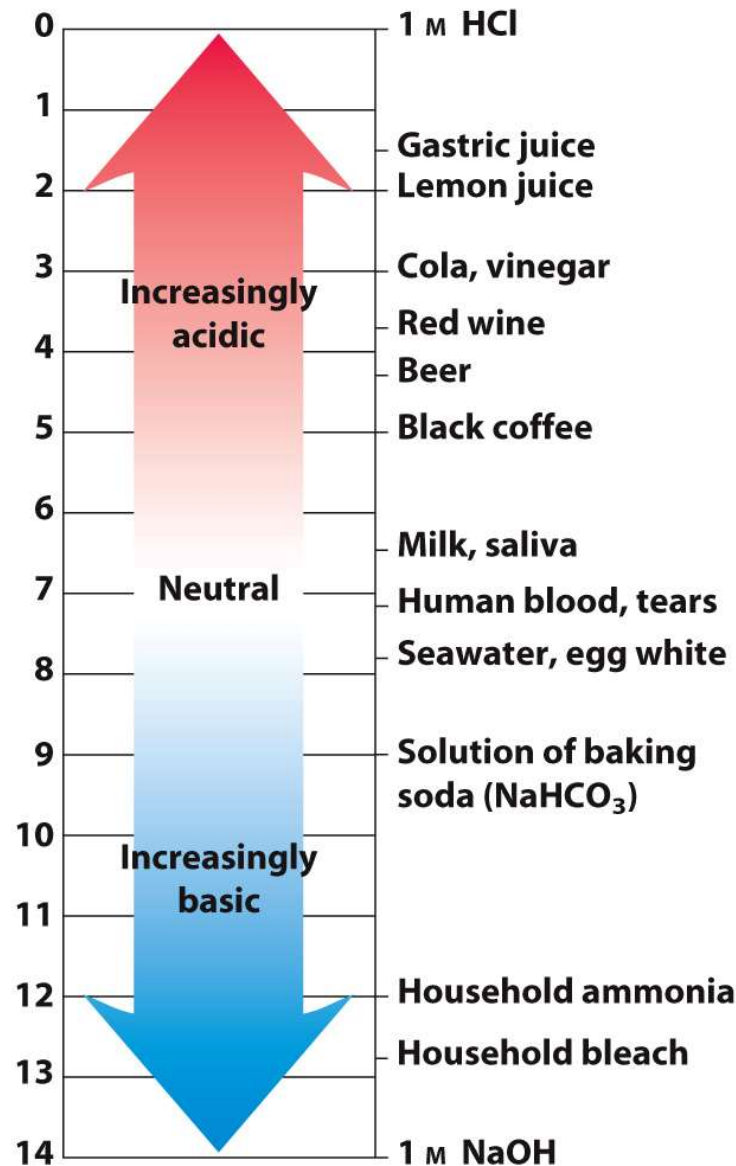
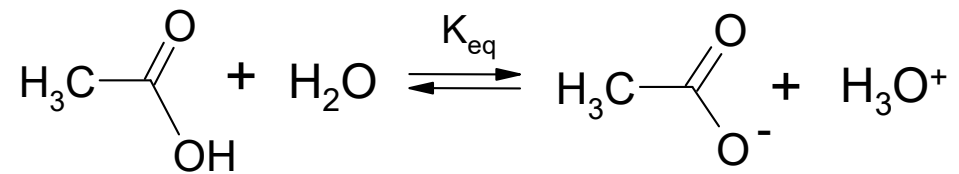


Figure 2-15

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# Dissociation of Weak Electrolytes: Principle



- Weak electrolytes dissociate only partially in water.

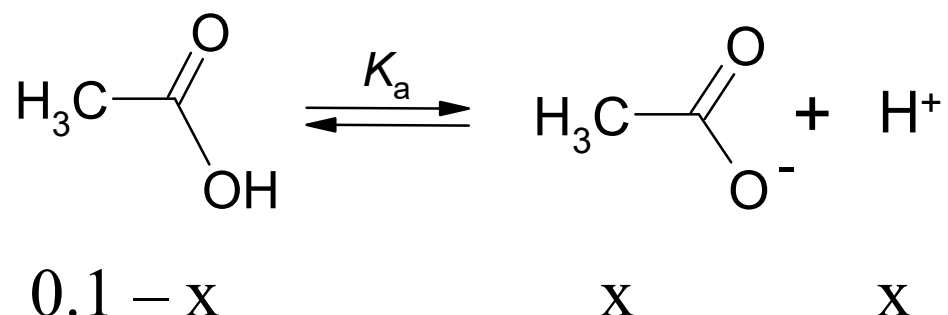
- The extent of dissociation is determined by the **acid dissociation constant  $K_a$** .

$$K_a = \frac{[\text{H}^+][\text{CH}_3\text{COO}^-]}{[\text{CH}_3\text{COOH}]} = 1.74 \cdot 10^{-5} \text{ M}$$

- We can calculate the pH if the  $K_a$  is known. But some algebra is needed!

## Dissociation of Weak Electrolytes: Example

What is the final pH of a solution when 0.1 moles of acetic acid is added to water to a final volume of 1L?



$$K_a = \frac{[x][x]}{[0.1 - x]} = 1.74 \cdot 10^{-5} \text{ M}$$

$$x^2 = 1.74 \cdot 10^{-6} - 1.74 \cdot 10^{-5} x$$

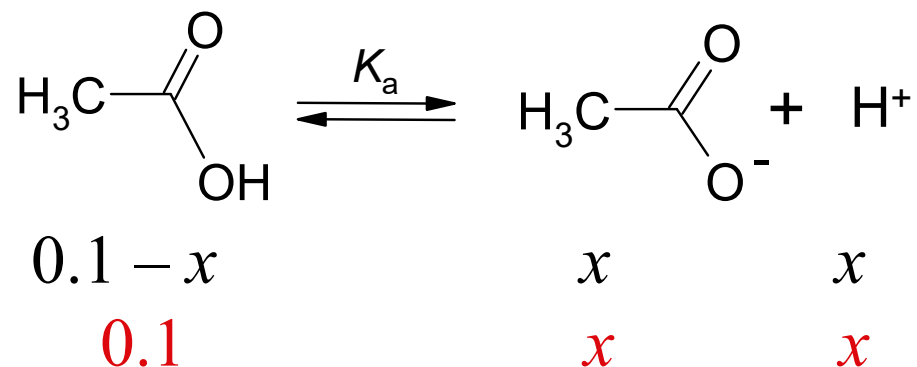
$$x^2 + 1.74 \cdot 10^{-5} x - 1.74 \cdot 10^{-6} = 0$$

$$x = 0.001310, \quad \text{pH} = 2.883 \quad (= -\log_{10} 0.001310)$$

- We assume that the only source of  $\text{H}^+$  is the weak acid.

- To find the  $[\text{H}^+]$ , a quadratic equation must be solved.

## Dissociation of Weak Electrolytes: Simplification



$$K_a = \frac{[x][x]}{[0.1]} = 1.74 \cdot 10^{-5} \text{ M}$$

$$x^2 = 1.74 \cdot 10^{-6}$$

$$x = 0.00132, \quad \text{pH} = 2.880$$

- The equation can be **simplified** if the amount of dissociated species is much less than the amount of undissociated acid.
- Approximation works for sufficiently **weak** acids and bases.
- Check that  $x < [\text{total acid}]$ .



# pK<sub>a</sub> Measures Acidity

$$pK_a = -\log K_a$$

## Monoprotic acids

Acetic acid  
( $K_a = 1.74 \times 10^{-5} \text{ M}$ )

Ammonium ion  
( $K_a = 5.62 \times 10^{-10} \text{ M}$ )

## Diprotic acids

Carbonic acid  
( $K_a = 1.70 \times 10^{-4} \text{ M}$ );  
Bicarbonate  
( $K_a = 6.31 \times 10^{-11} \text{ M}$ )

Glycine, carboxyl  
( $K_a = 4.57 \times 10^{-3} \text{ M}$ );  
Glycine, amino  
( $K_a = 2.51 \times 10^{-10} \text{ M}$ )

## Triprotic acids

Phosphoric acid  
( $K_a = 7.25 \times 10^{-3} \text{ M}$ );  
Dihydrogen phosphate  
( $K_a = 1.38 \times 10^{-7} \text{ M}$ );  
Monohydrogen phosphate  
( $K_a = 3.98 \times 10^{-13} \text{ M}$ )

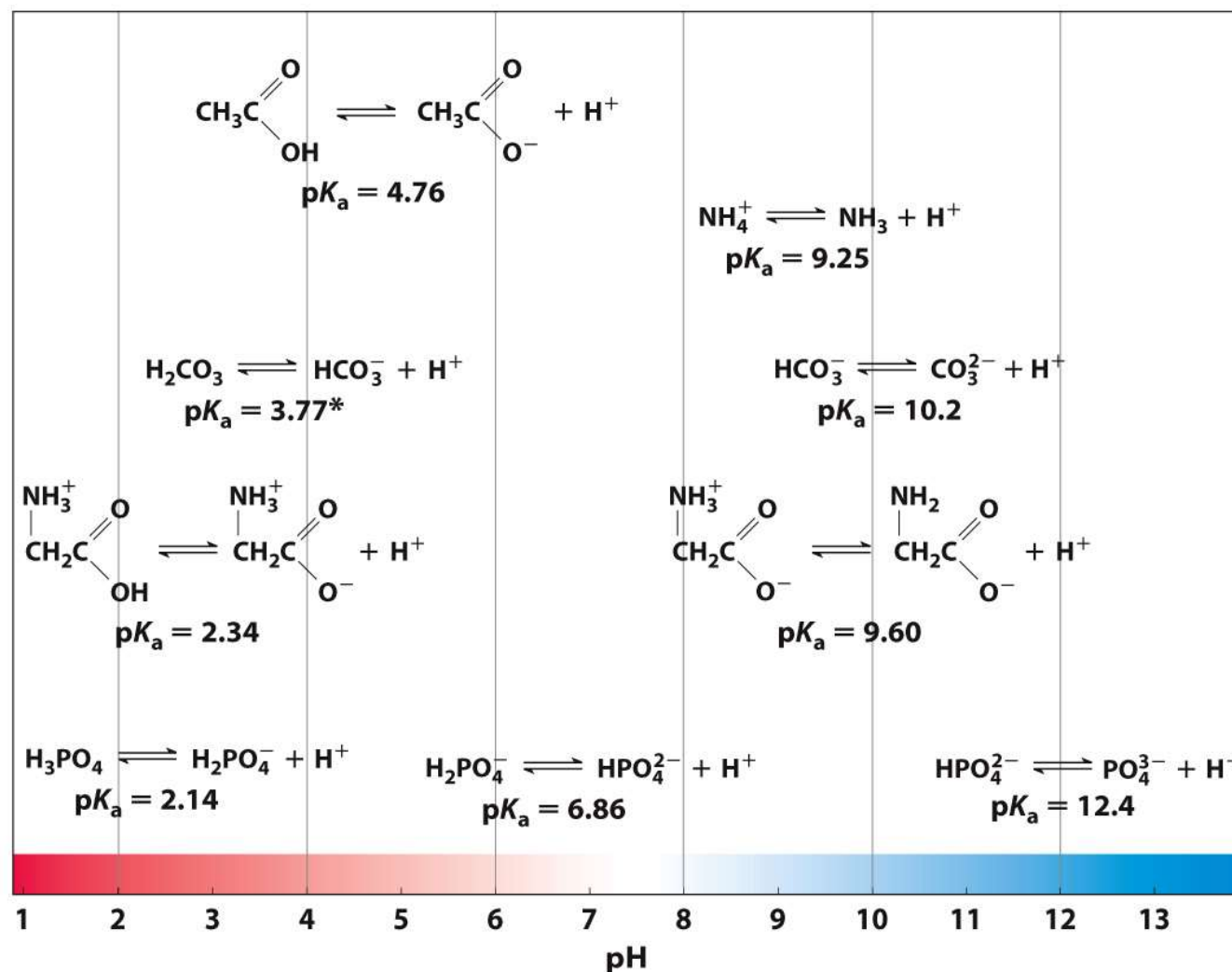
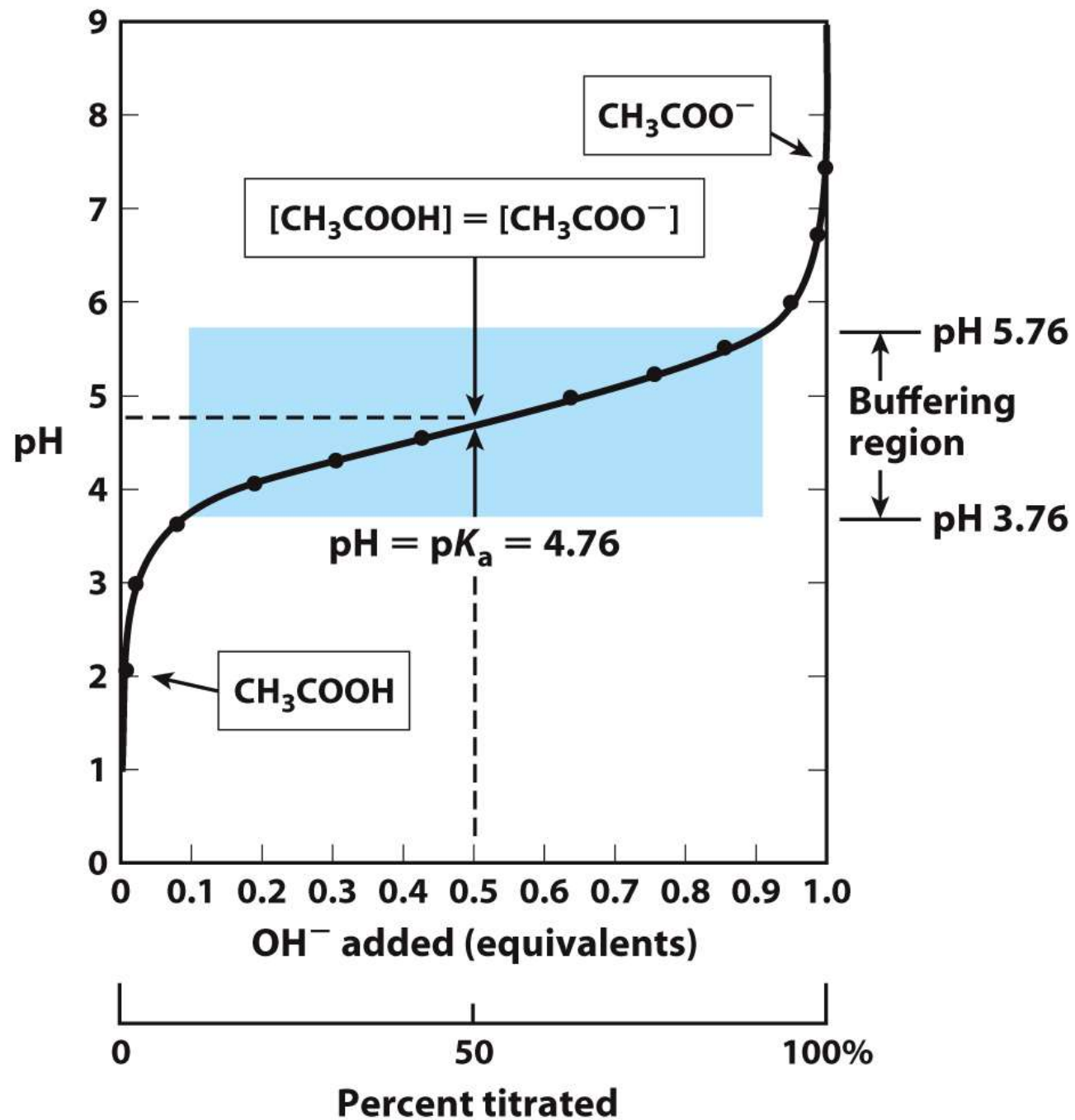


Figure 2-16

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# Buffers Are Mixtures of Weak Acids and Their Anions (Conjugate Base)

- Buffers resist change in pH.
- At  $\text{pH} = \text{p}K_a$ , there is a 50:50 mixture of acid and anion forms of the compound.
- **Buffering capacity** of acid/anion system **is greatest at  $\text{pH} = \text{p}K_a$ .**
- Buffering capacity is lost when the pH differs from  $\text{p}K_a$  by more than 1 pH unit.

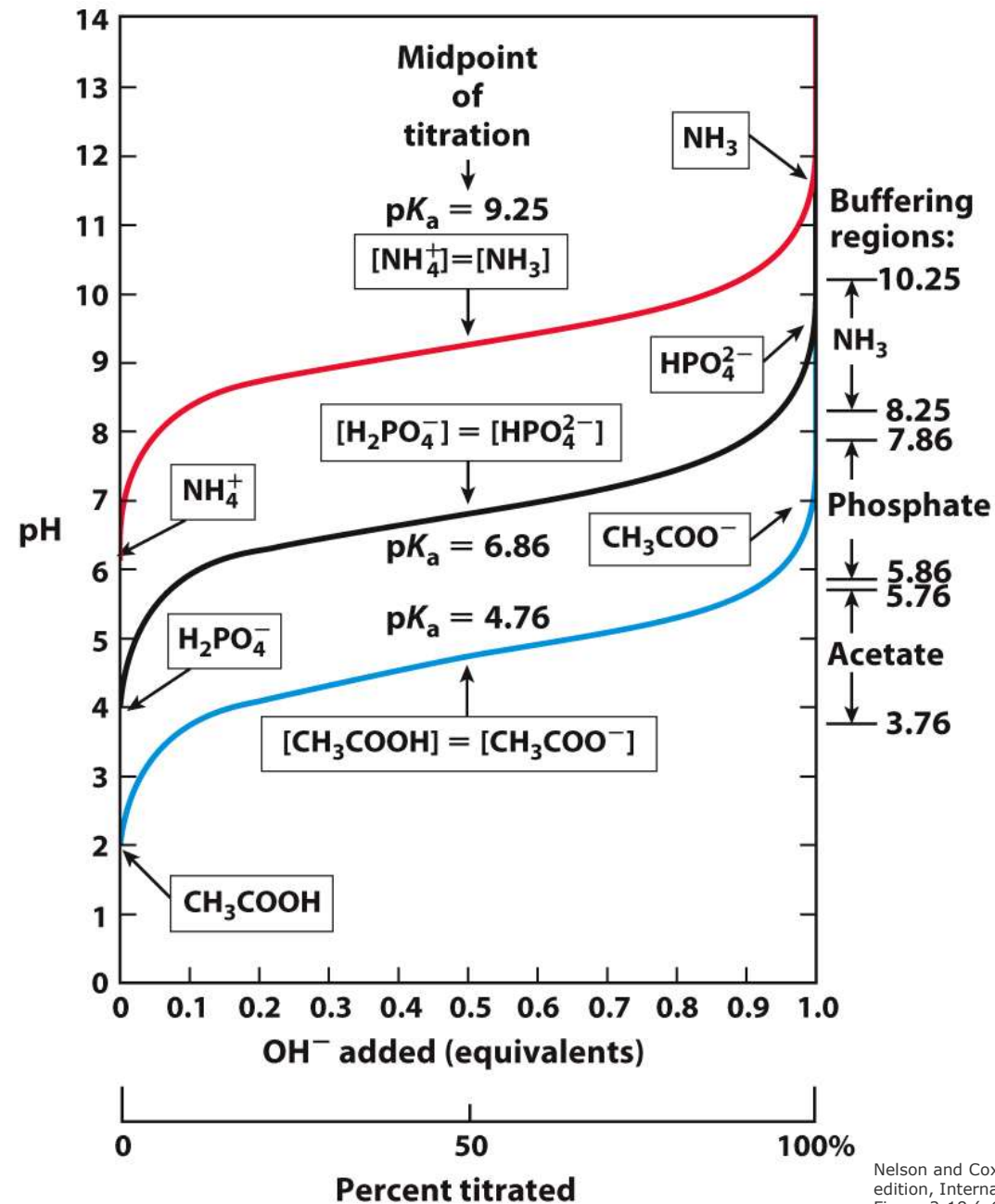


**Figure 2-17**

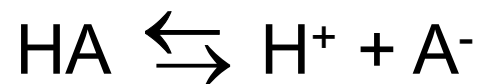
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# Weak Acids Have Different $pK_a$ s



# Henderson–Hasselbalch Equation: Derivation



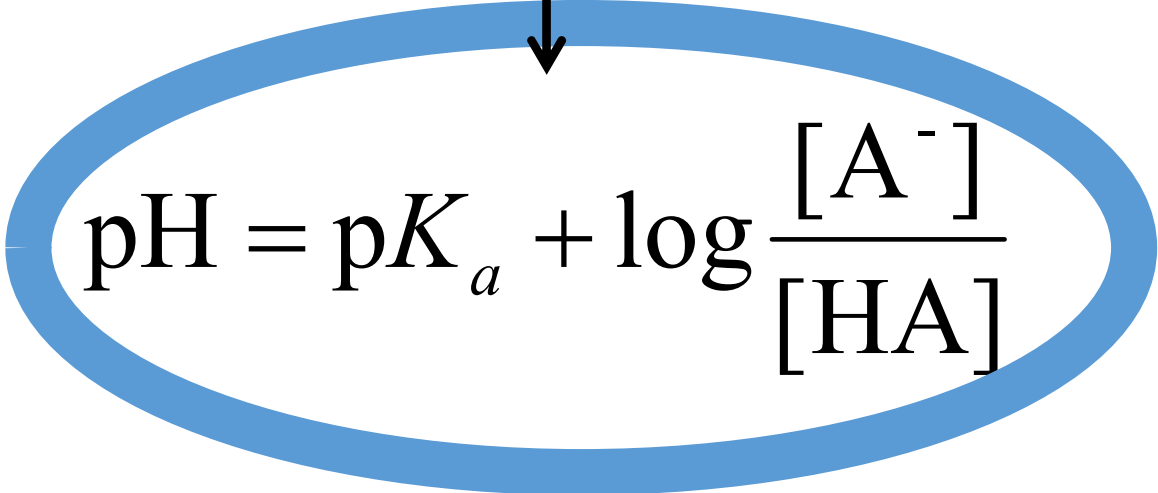
$$K_a = \frac{[\text{H}^+][\text{A}^-]}{[\text{HA}]}$$

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



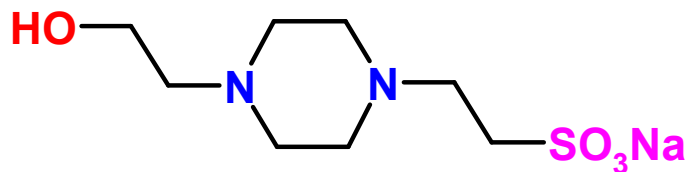
$$-\log[\text{H}^+] = -\log K_a - \log \frac{[\text{HA}]}{[\text{A}^-]}$$




$$\text{pH} = \text{p}K_a + \log \frac{[\text{A}^-]}{[\text{HA}]}$$

# Biological Buffer Systems

- Maintenance of intracellular pH is vital to all cells.
  - Enzyme-catalyzed reactions have optimal pH.
  - Solubility of polar molecules depends on H-bond donors and acceptors.
  - Equilibrium between CO<sub>2</sub> gas and dissolved HCO<sub>3</sub><sup>-</sup> depends on pH.
- Buffer systems *in vivo* are mainly based on:
  - phosphate, concentration in millimolar range
  - bicarbonate, important for blood plasma
  - histidine, efficient buffer at neutral pH
- Buffer systems *in vitro* are often based on sulfonic acids of cyclic amines.
  - HEPES
  - PIPES
  - CHES



## Chapter 2: Summary

- nature of intermolecular forces
- properties and structure of liquid water
- behavior of weak acids and bases in water
- way water can participate in biochemical reactions

H.W: What are acidosis and alkalosis?