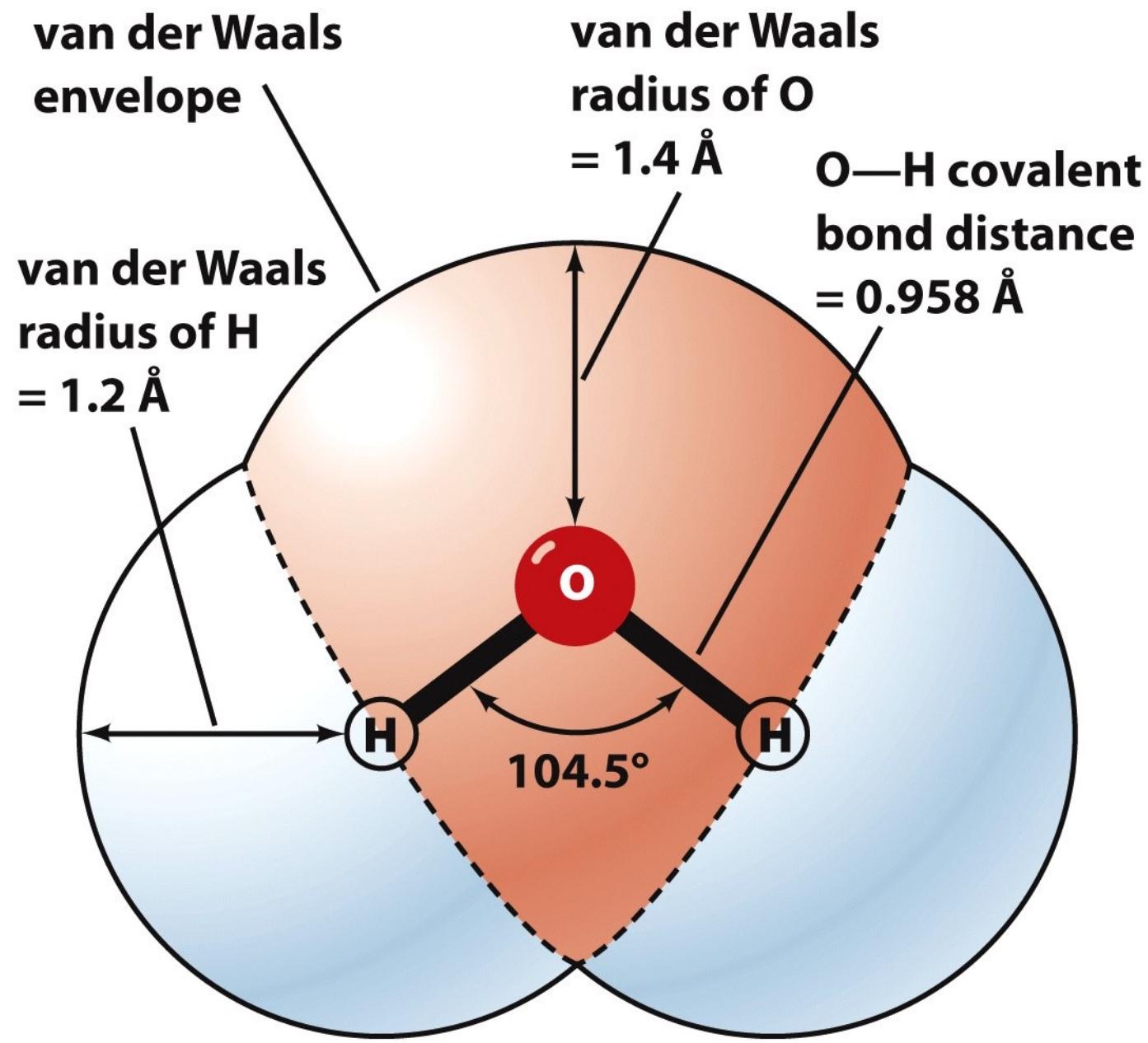
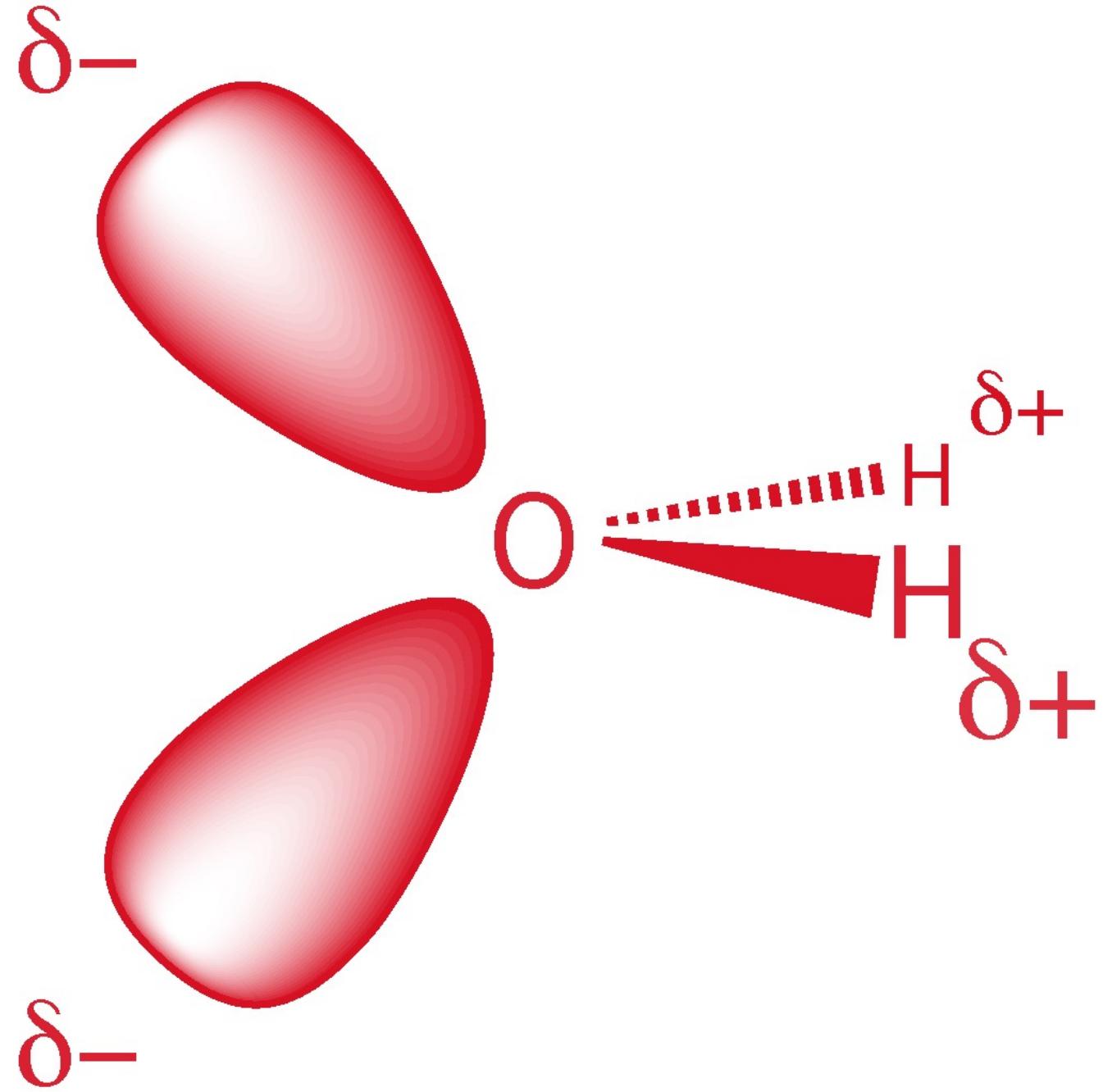
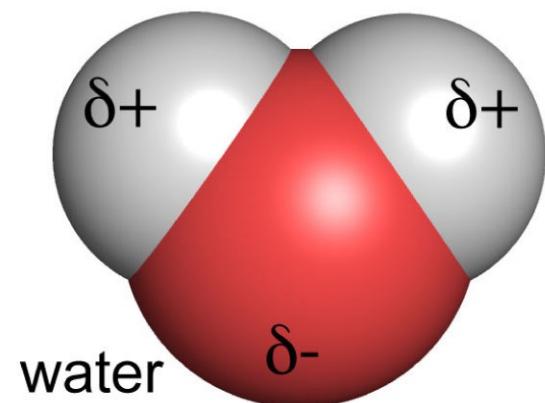


BT351
Water



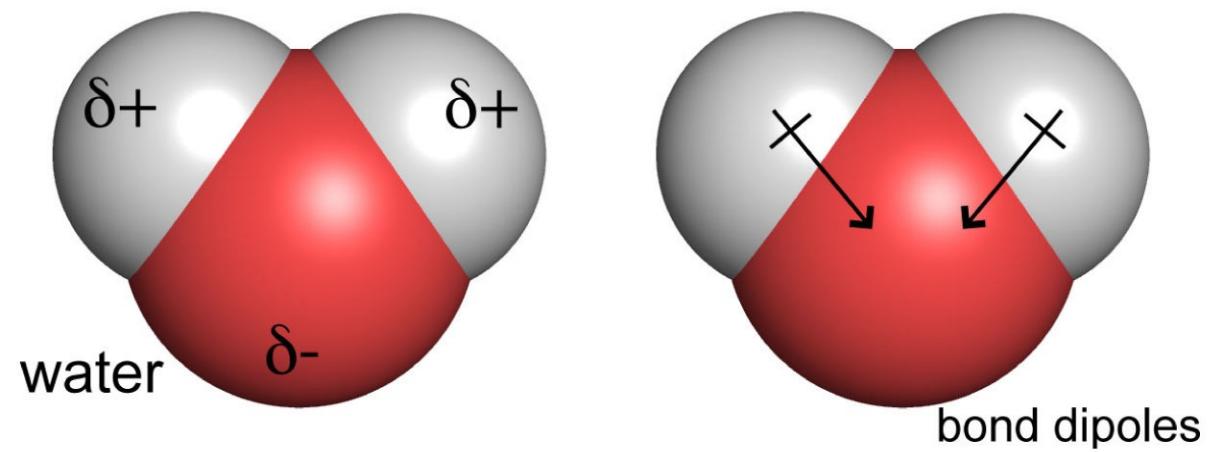


Water is a dipole



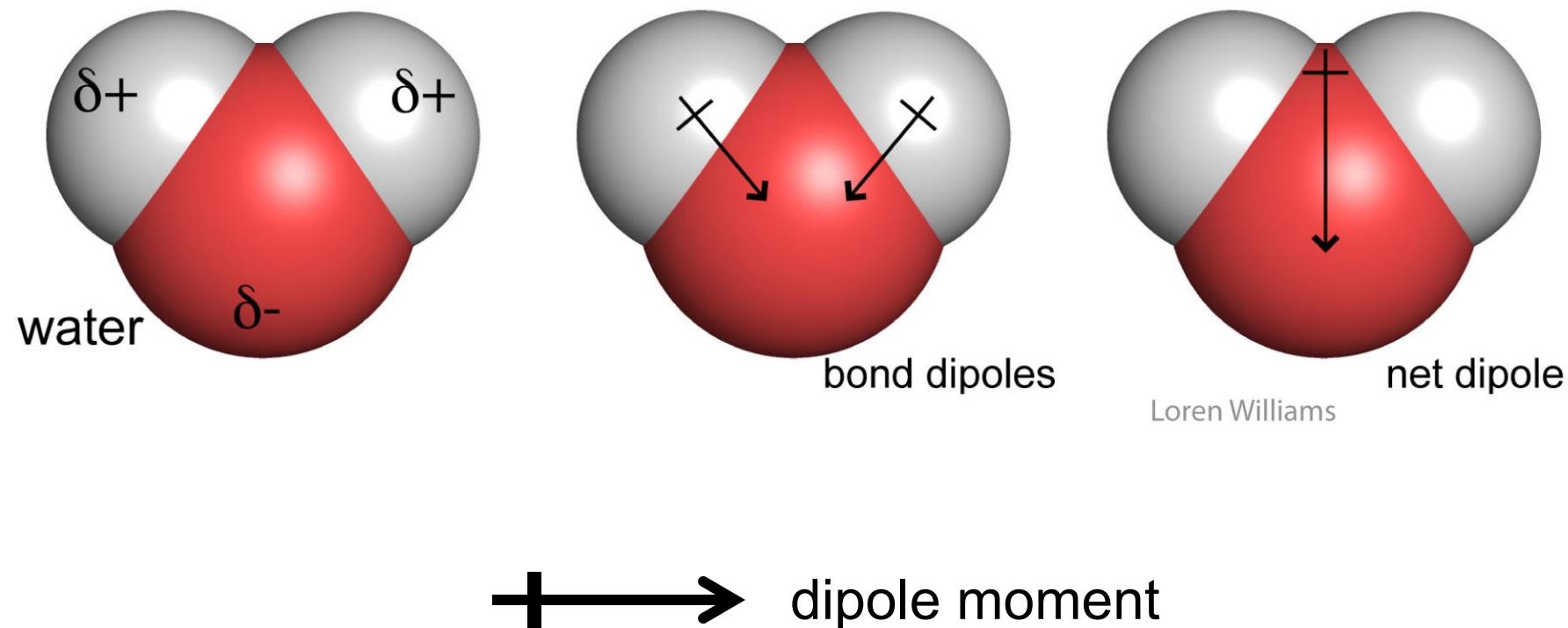
→ dipole moment

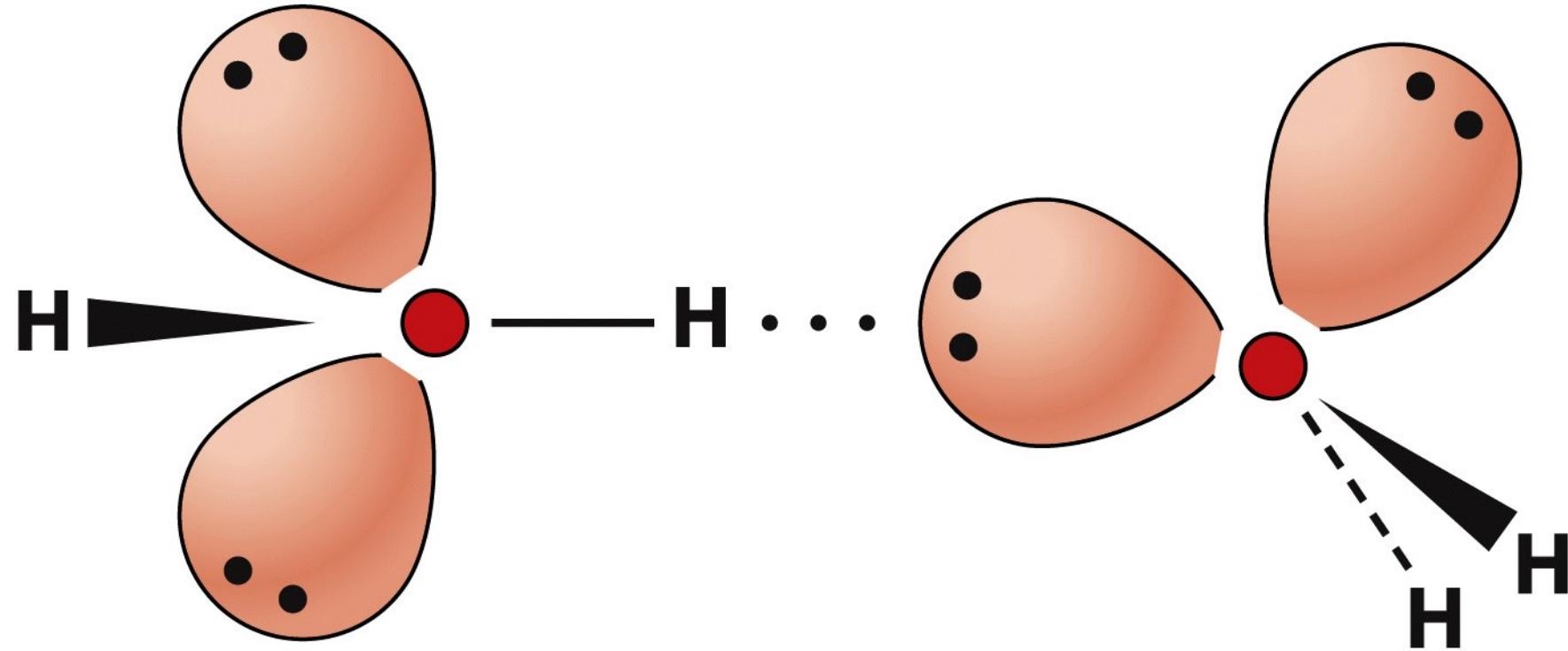
Water is a dipole



→ dipole moment

Water is a dipole





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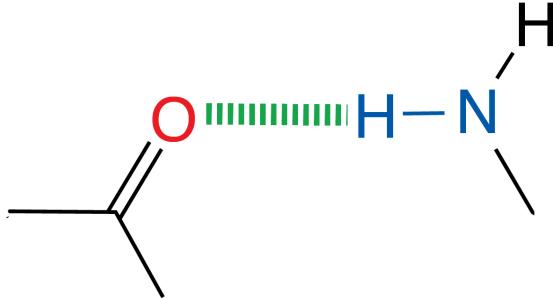
Hydrogen Bonding in Biological Systems

generic



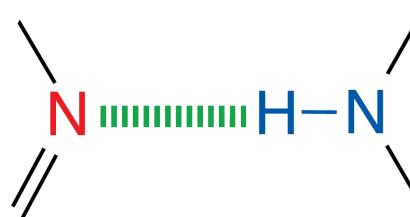
DNA

(base pairing)



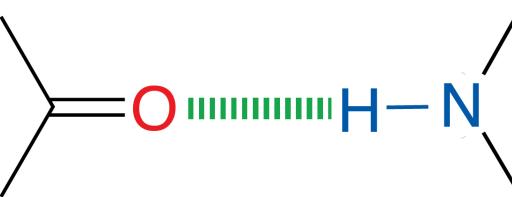
DNA

(base pairing)



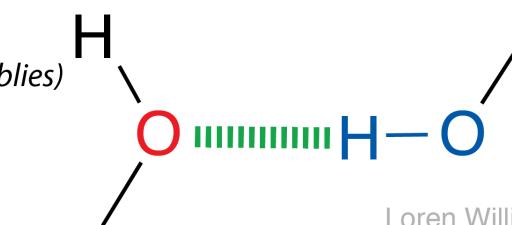
protein

(α -helix, β -sheet)

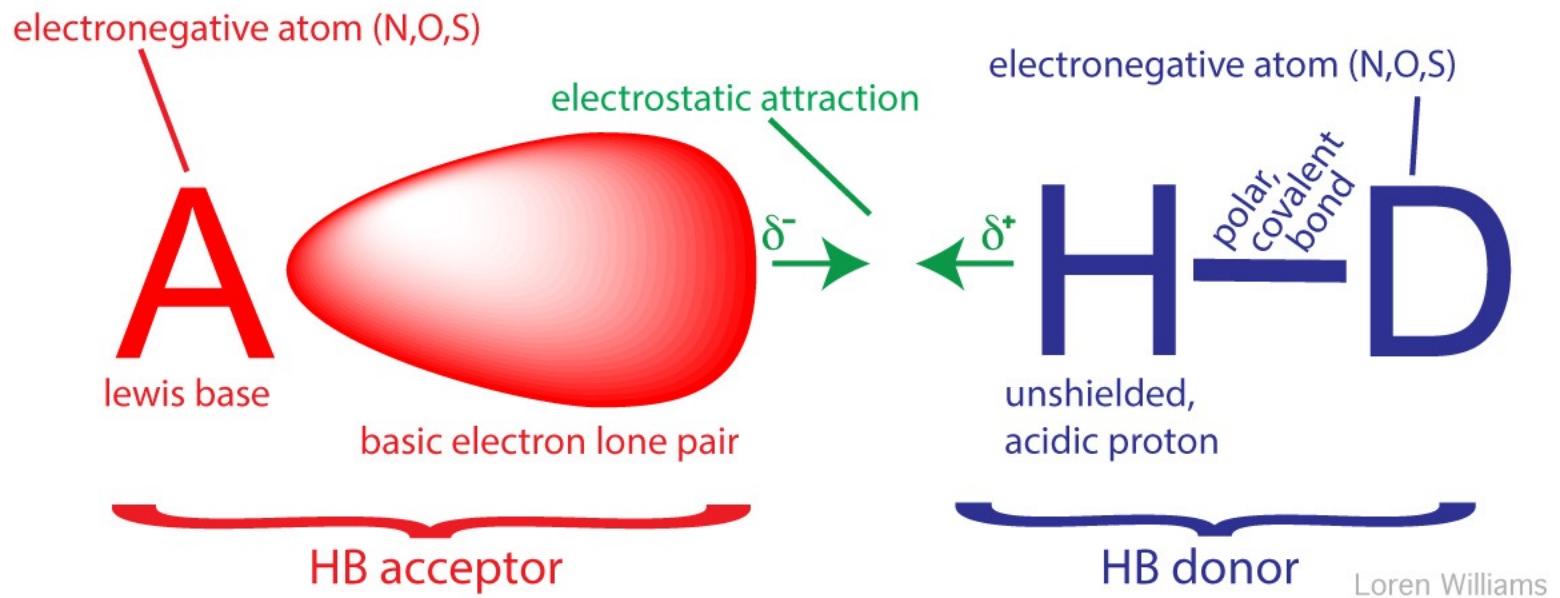


cellulose

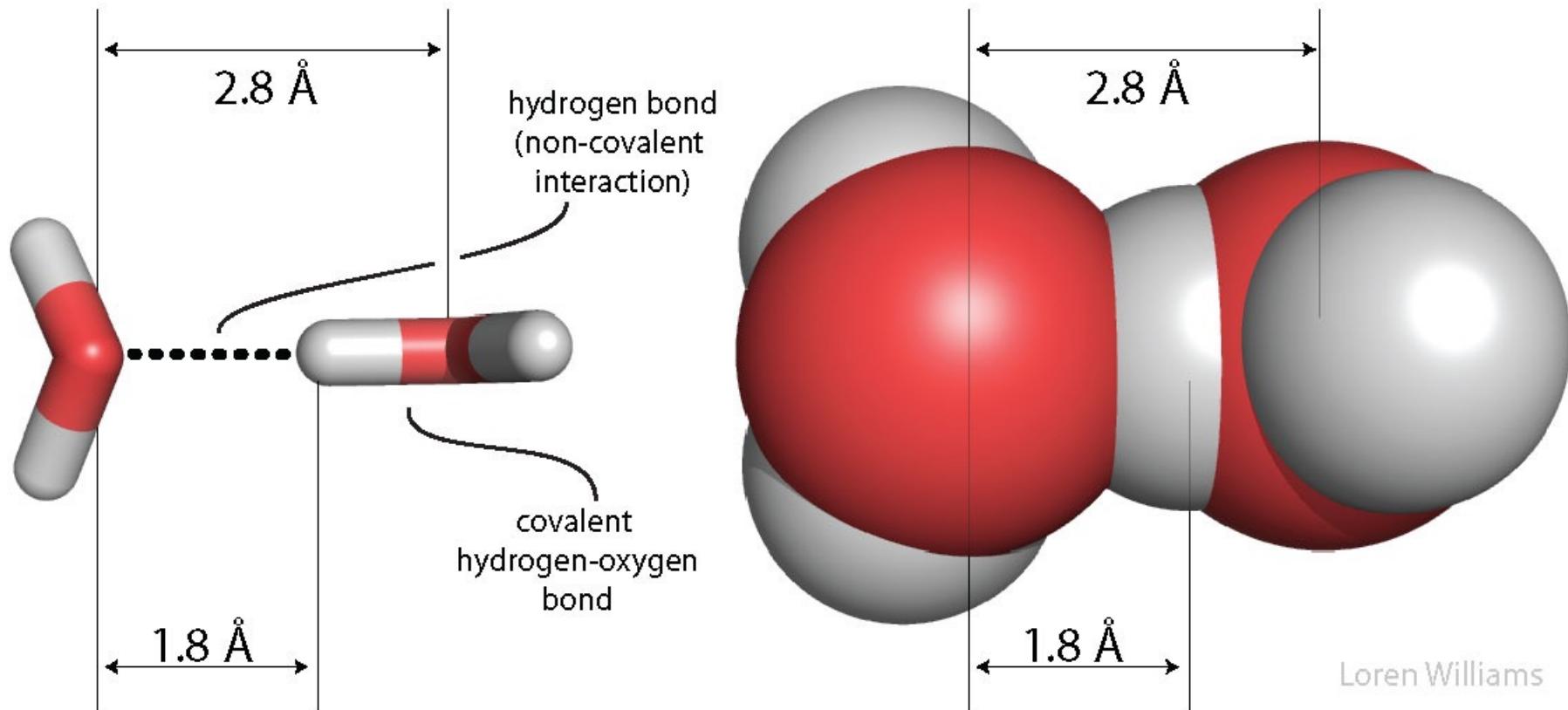
(crystalline assemblies)



Anatomy of a Hydrogen Bond

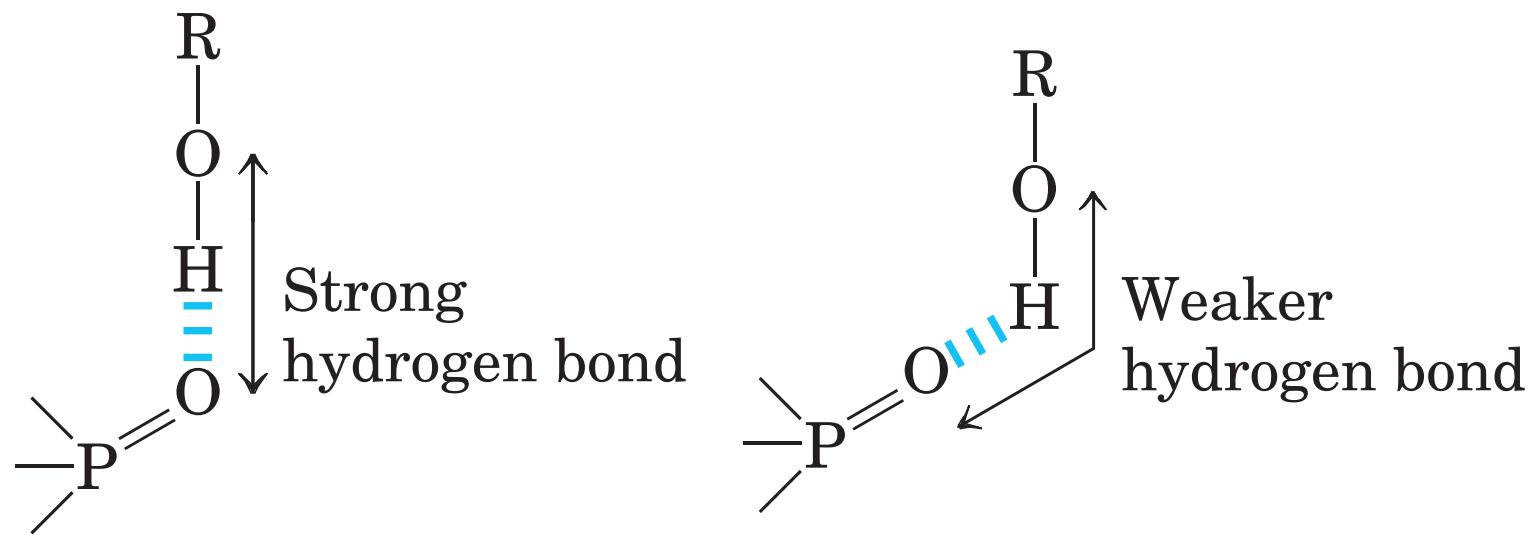


Hydrogen bonding between two water molecules

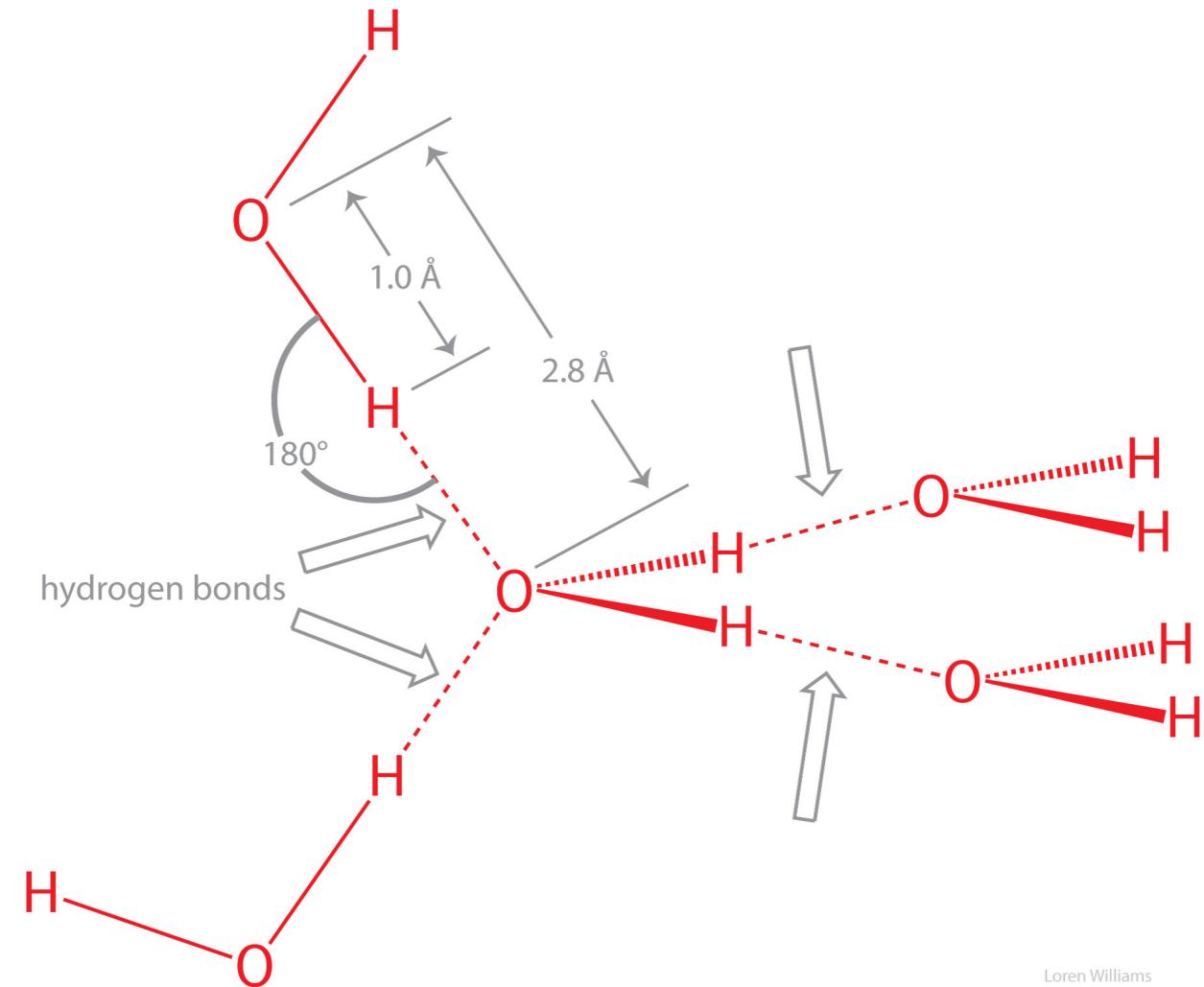
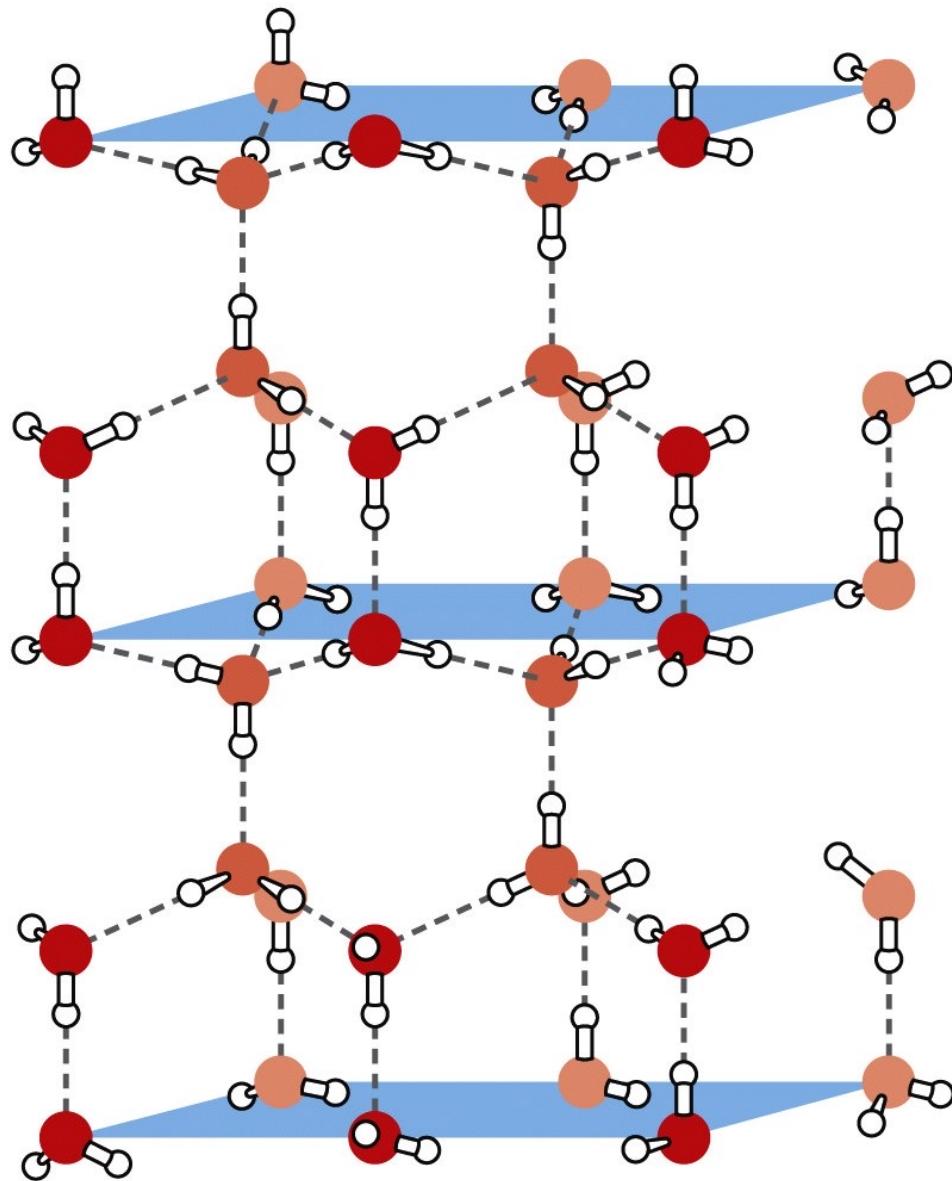


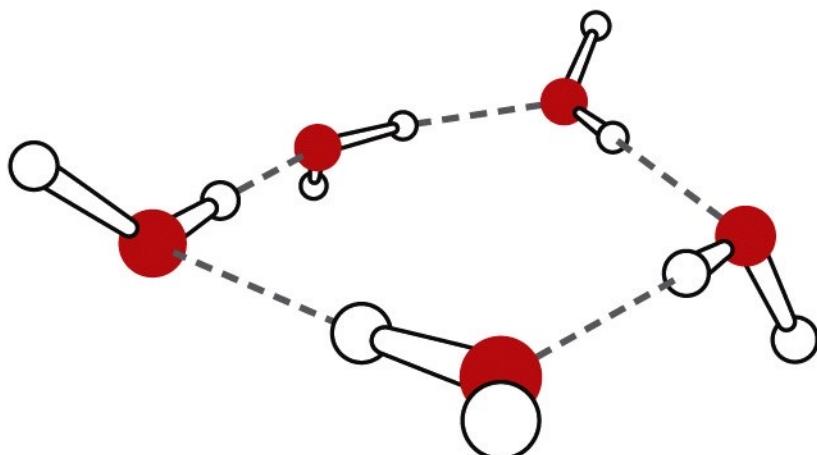
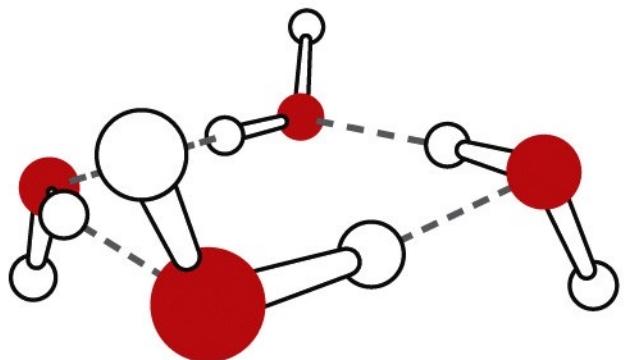
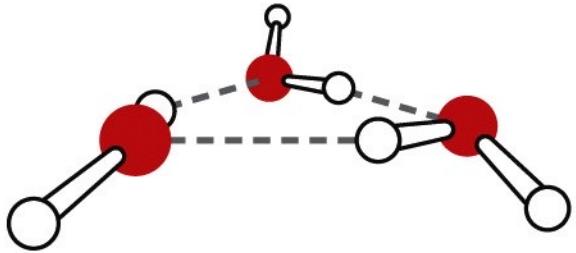
Loren Williams

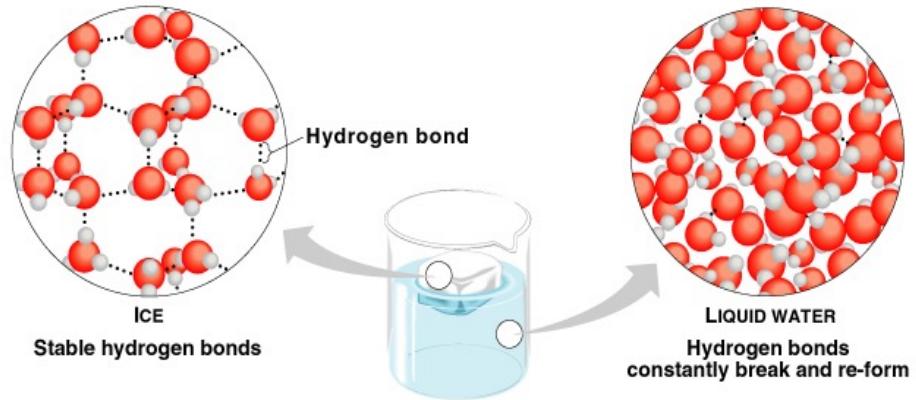
Directionality of the hydrogen bond



Water is self-complementary







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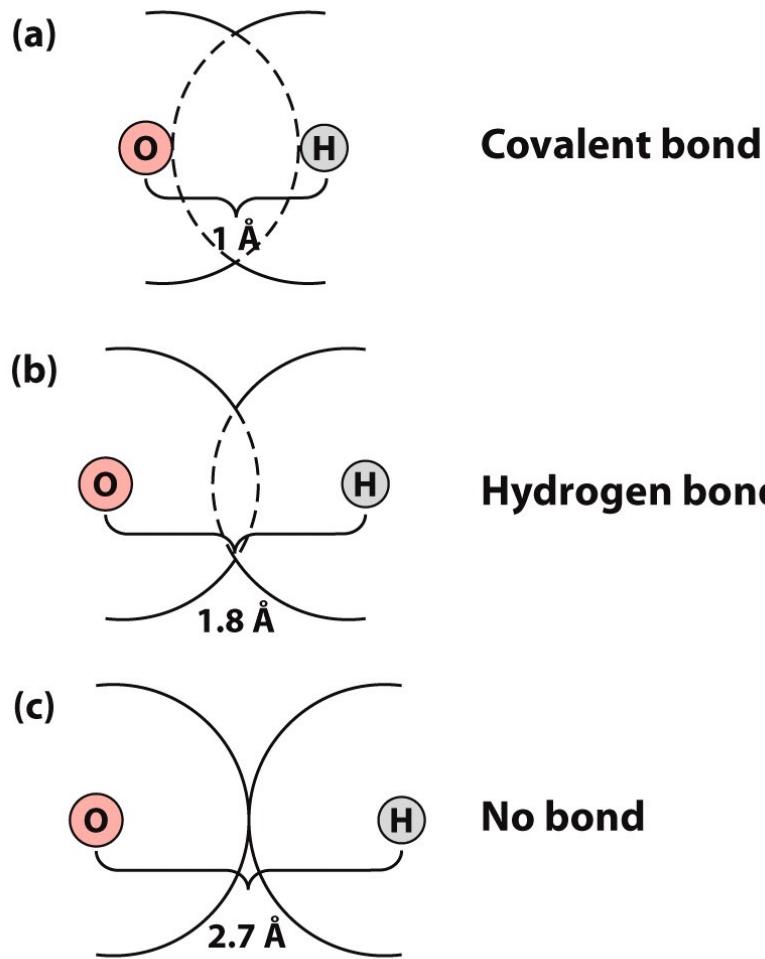
**Ice: 4 H-bonds
per water molecule**

**liquid: 2.3- 3.4 H-bonds
per water molecule.**

Table 2-1 Bond Energies in Biomolecules

Type of Bond	Example	Bond Strength (kJ · mol ⁻¹)
Covalent	O—H C—H C—C	460 414 348
Noncovalent		
Ionic interaction	—COO ⁻ ... ⁺ H ₃ N—	86
van der Waals forces	—O—H...O—	20
Hydrogen bond	—C=O...C=O	9.3
Dipole-dipole interaction		
London dispersion forces	—C—H...H—C—	0.3

Atomic distance matters



Non-covalent interaction

1) Electrostatic interactions

by coulombs law

$$U = \frac{kq_1q_2}{Dr}$$

q is the charges

r is the radius,

k equals $8.99 \times 10^9 \text{ Jm/C}^2$

D is the dielectric constant, a shielding of charge.

D = 1 in a vacuum

D = 2-3 in grease

D = 80 in water

<u>Dielectric effect</u>	D
hexane	1.9
benzene	2.3
diethyl ether	4.3
CHCl_3	5.1
acetone	21.4
Ethanol	24
methanol	33
H_2O	80
HCN	116

H_2O is an excellent solvent and dissolves a large array of polar molecules.

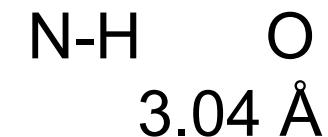
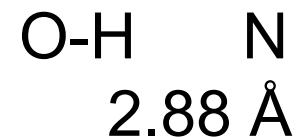
However, it also weakens ionic and hydrogen bonds

Therefore, biological systems sometimes exclude H_2O to form maximal strength bonds!!

Non-covalent interaction

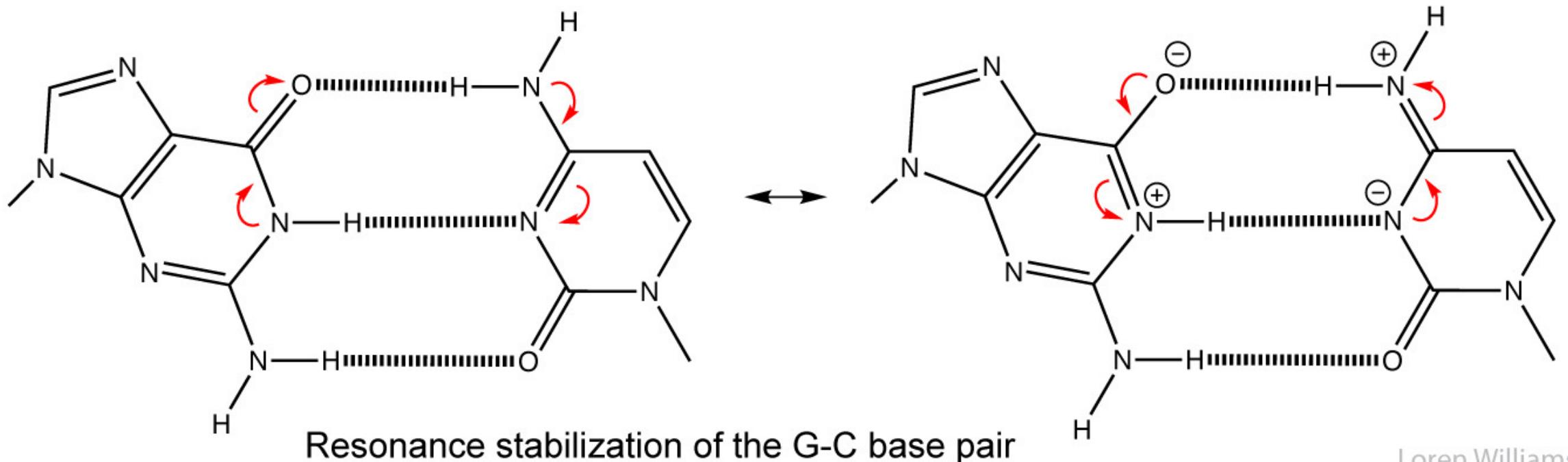
2) van der Waals attraction

- Hydrogen bonds



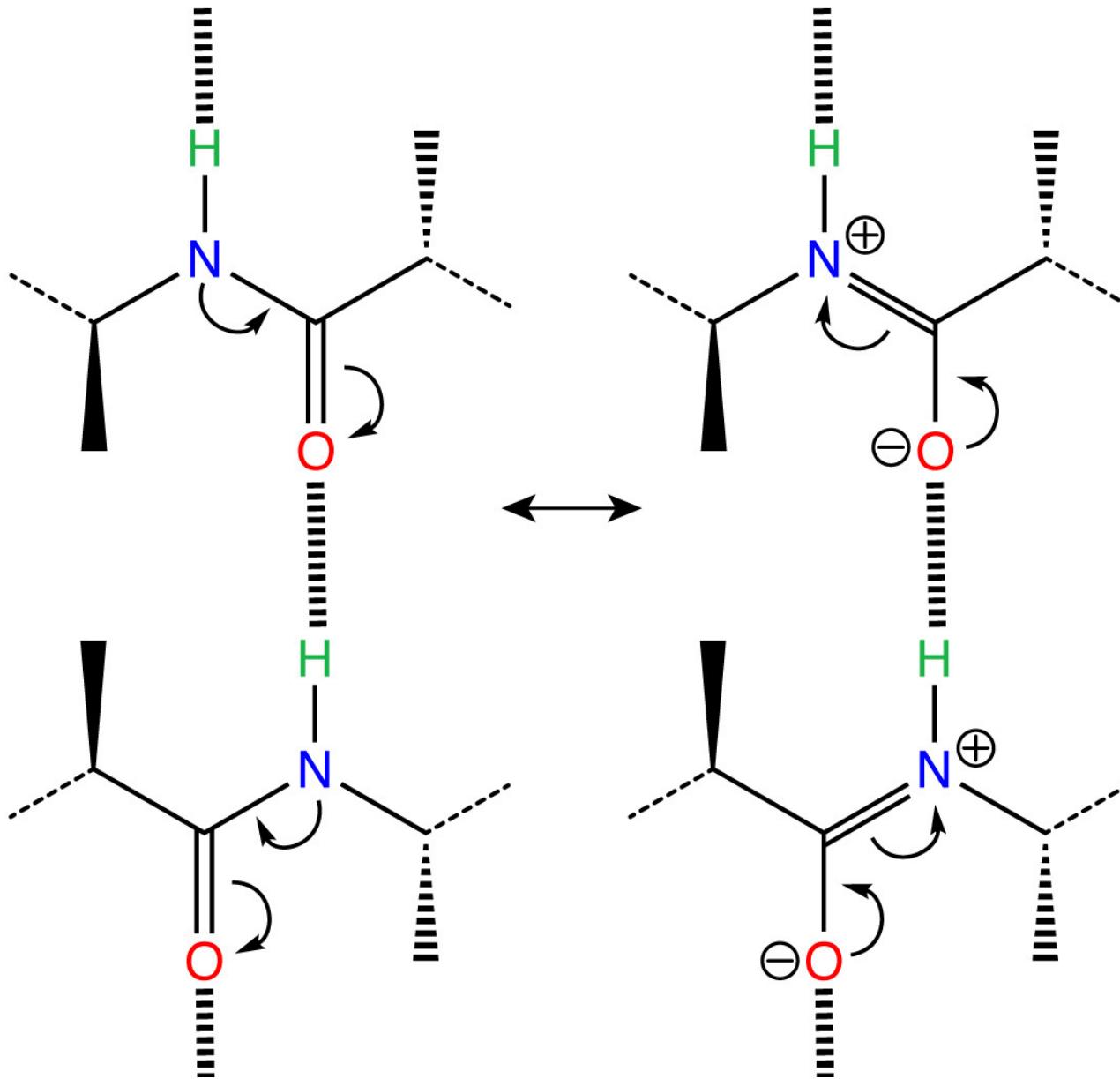
H bond donor or an H bond acceptor

In biological systems, hydrogen bonds are frequently cooperative and are stabilized by resonance involving multiple hydrogen bonds



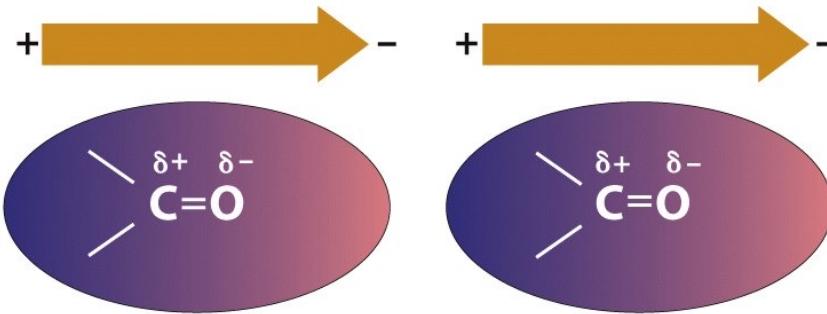
Loren Williams

Hydrogen bonding cooperativity in antiparallel β -sheets

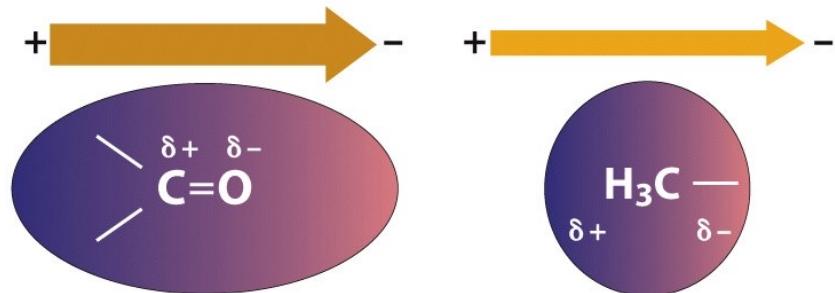


2) van der Waals attraction

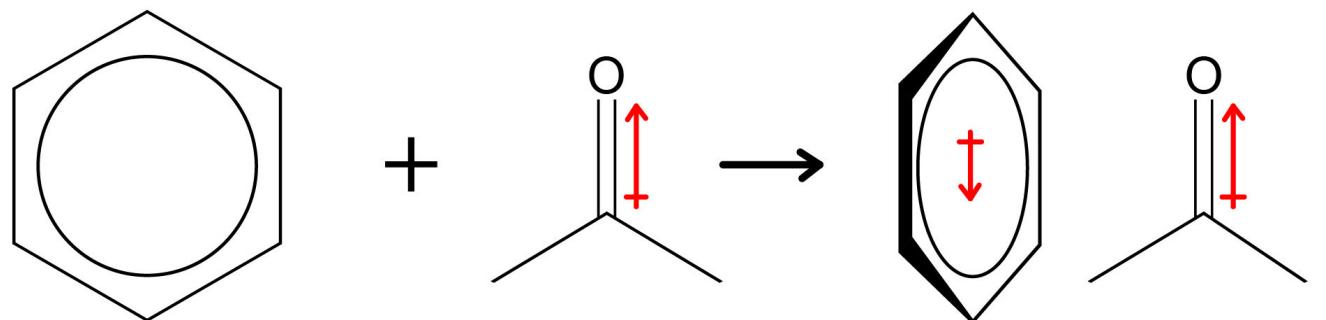
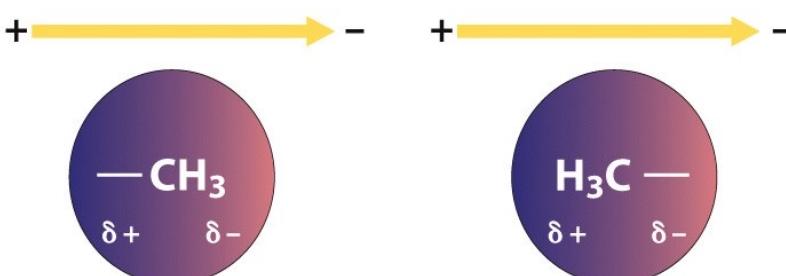
(a) Interactions between permanent dipoles



(b) Dipole-induced dipole interactions

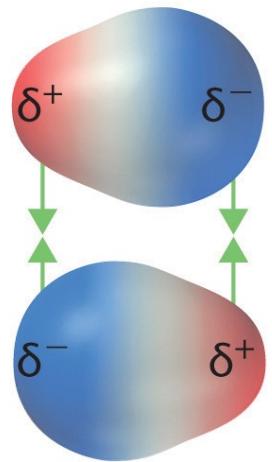


(c) London dispersion forces

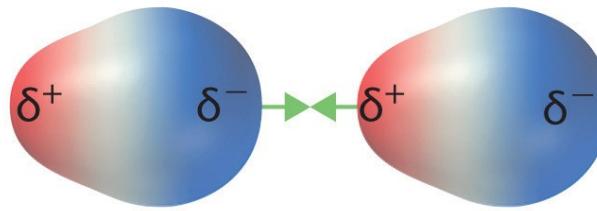


Polarization

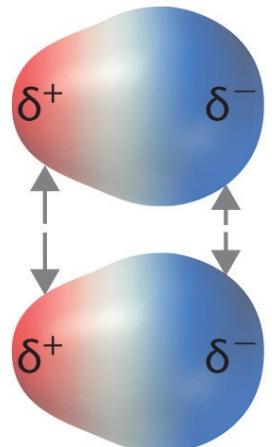
Interactions between permanent dipoles



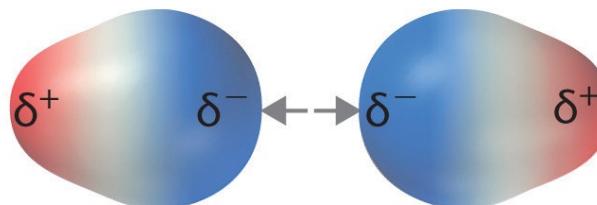
(a) Attraction



(b) Attraction

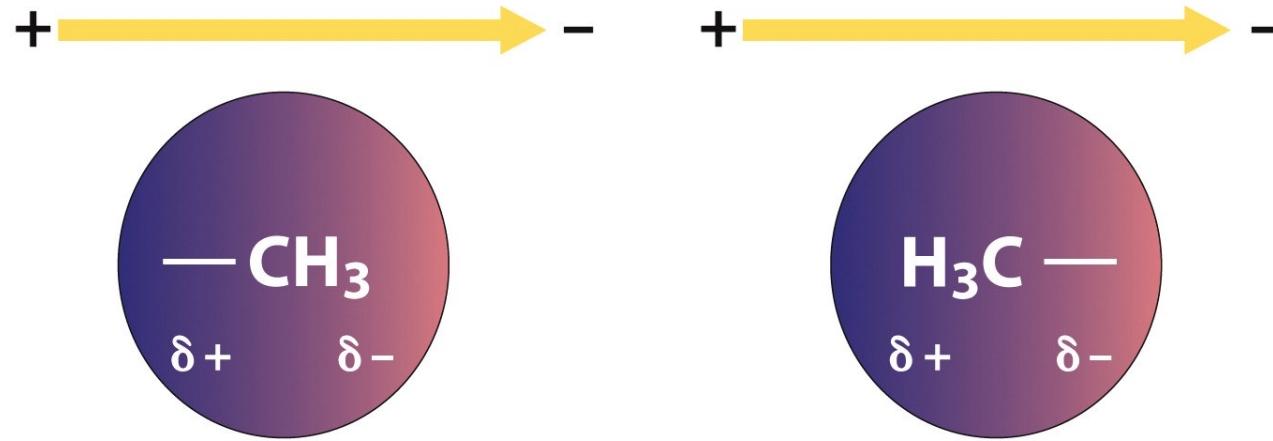


(c) Repulsion



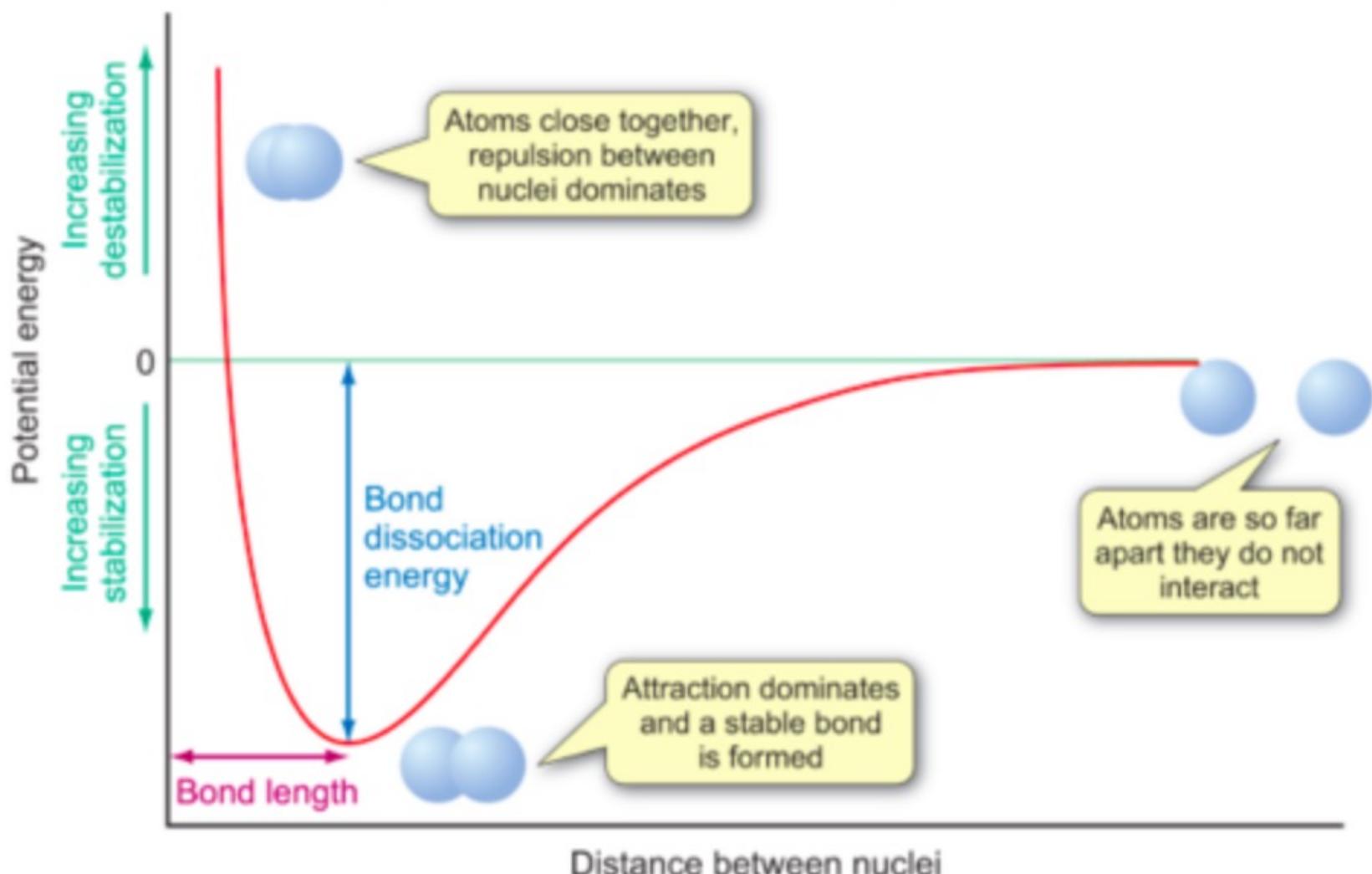
(d) Repulsion

London dispersion forces



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- Random variations in the positions of the electrons around one nucleus may create a transient electric dipole, which induces a transient, opposite electric dipole in the nearby atom.
- The two dipoles weakly attract each other, bringing the two nuclei closer.
- The total number of atom-atom dispersive interactions within a folded protein is huge, so that dispersive interactions can make large contributions to stability.
- Tryptophan, tyrosine, phenylalanine and histidine are the most polarizable amino acid sidechains and form the strongest dispersive interactions in proteins.



Water as a solvent

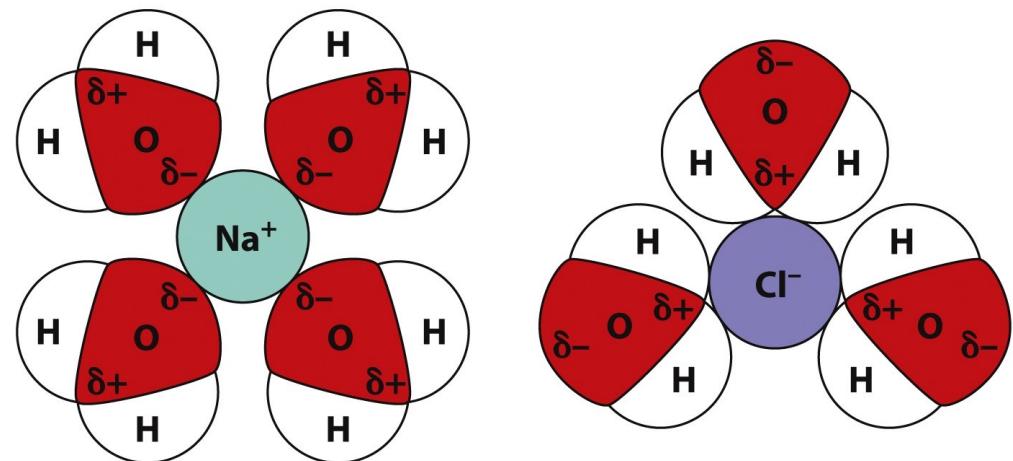
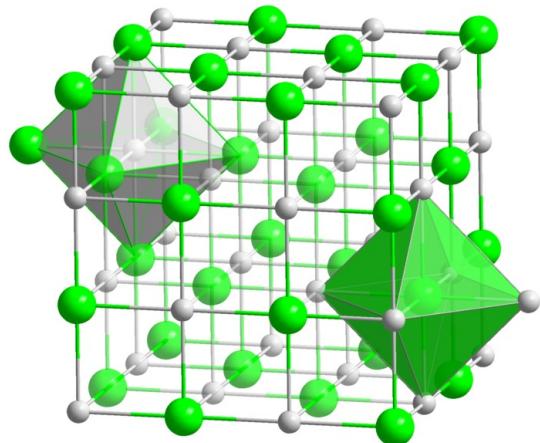
NaCl: Melting point:
Boiling point

801°C (1074 K)
1413°C (1686 K)

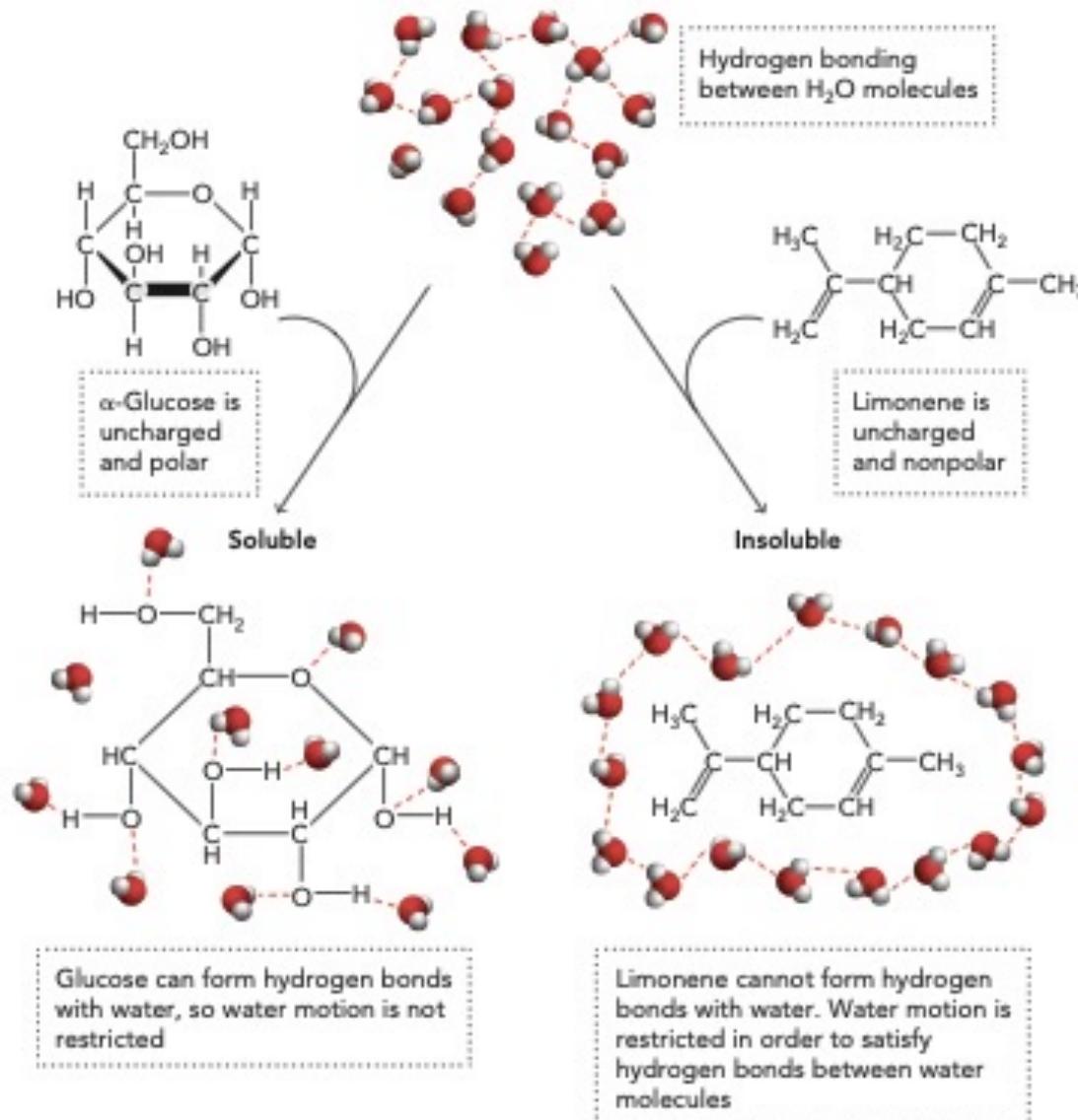
Solubility

in water
in ammonia
in methanol

359 g L⁻¹
21.5 g L⁻¹
14.9 g L⁻¹

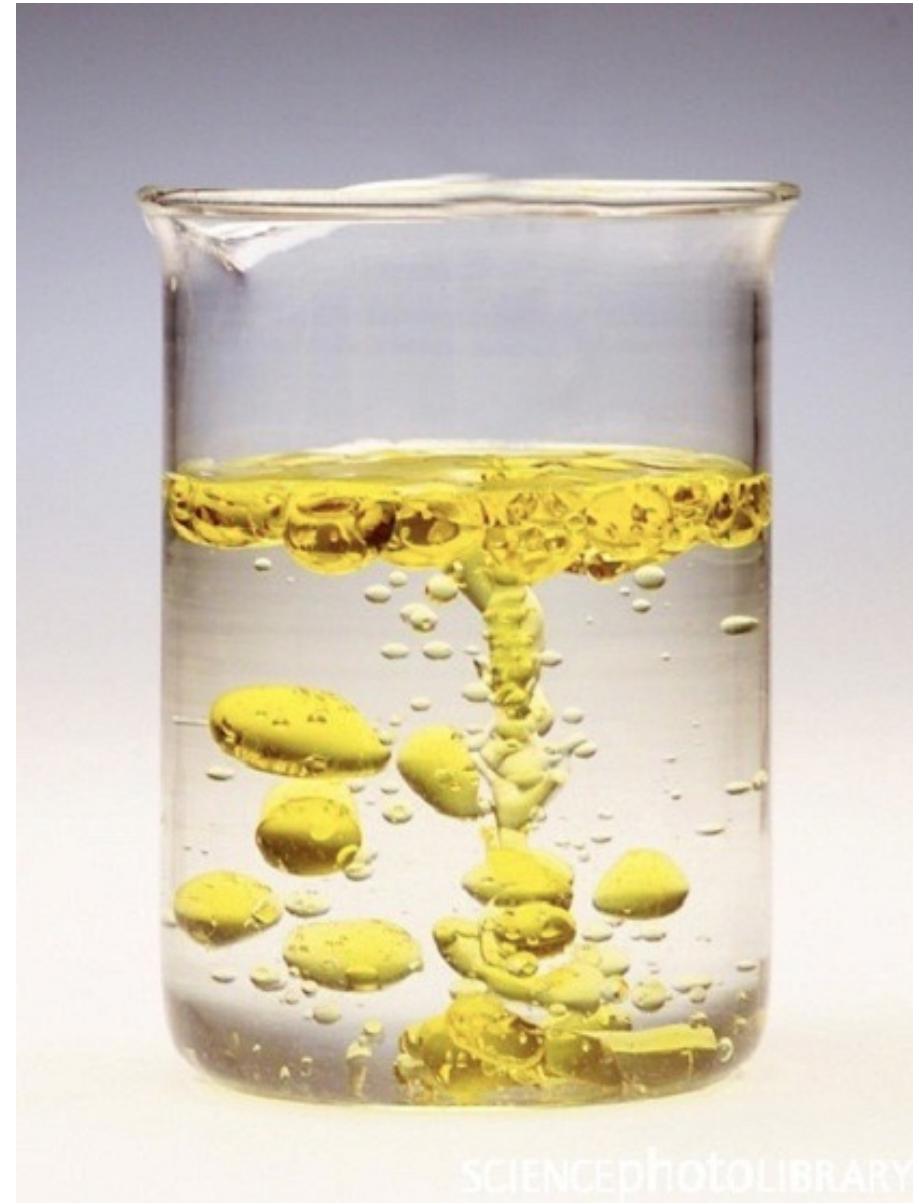


Water as a solvent



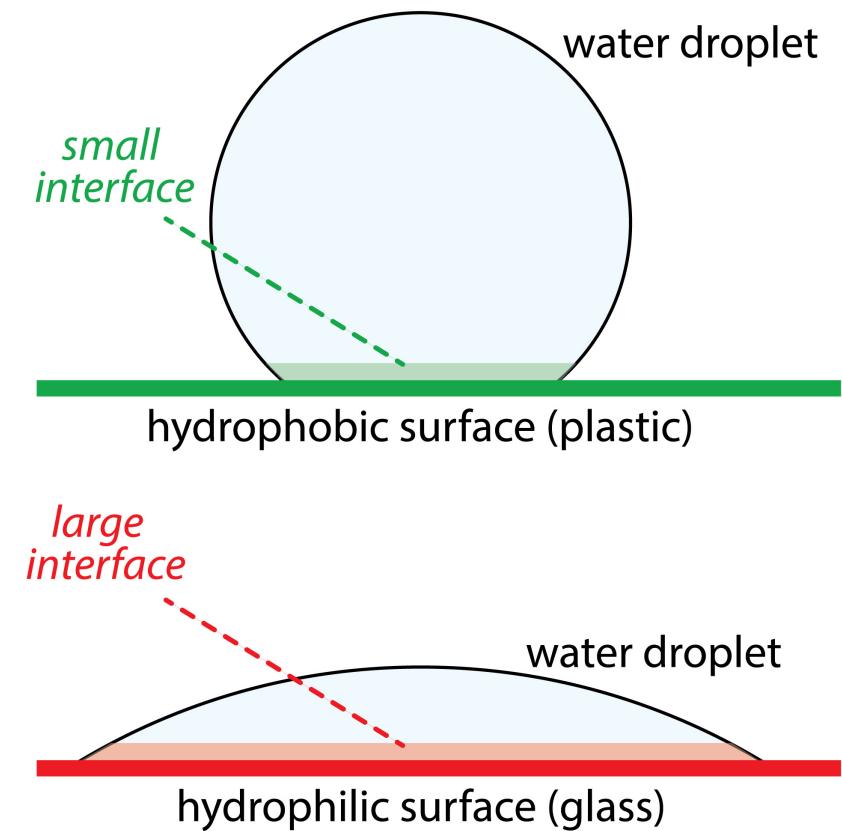
The Hydrophobic effect

- The tendency of water to minimize its contacts with hydrophobic molecules
- The hydrophobic effect is fully a property of water
- It a consequence of the distinctive molecular structure of water and the unique cohesive properties of water

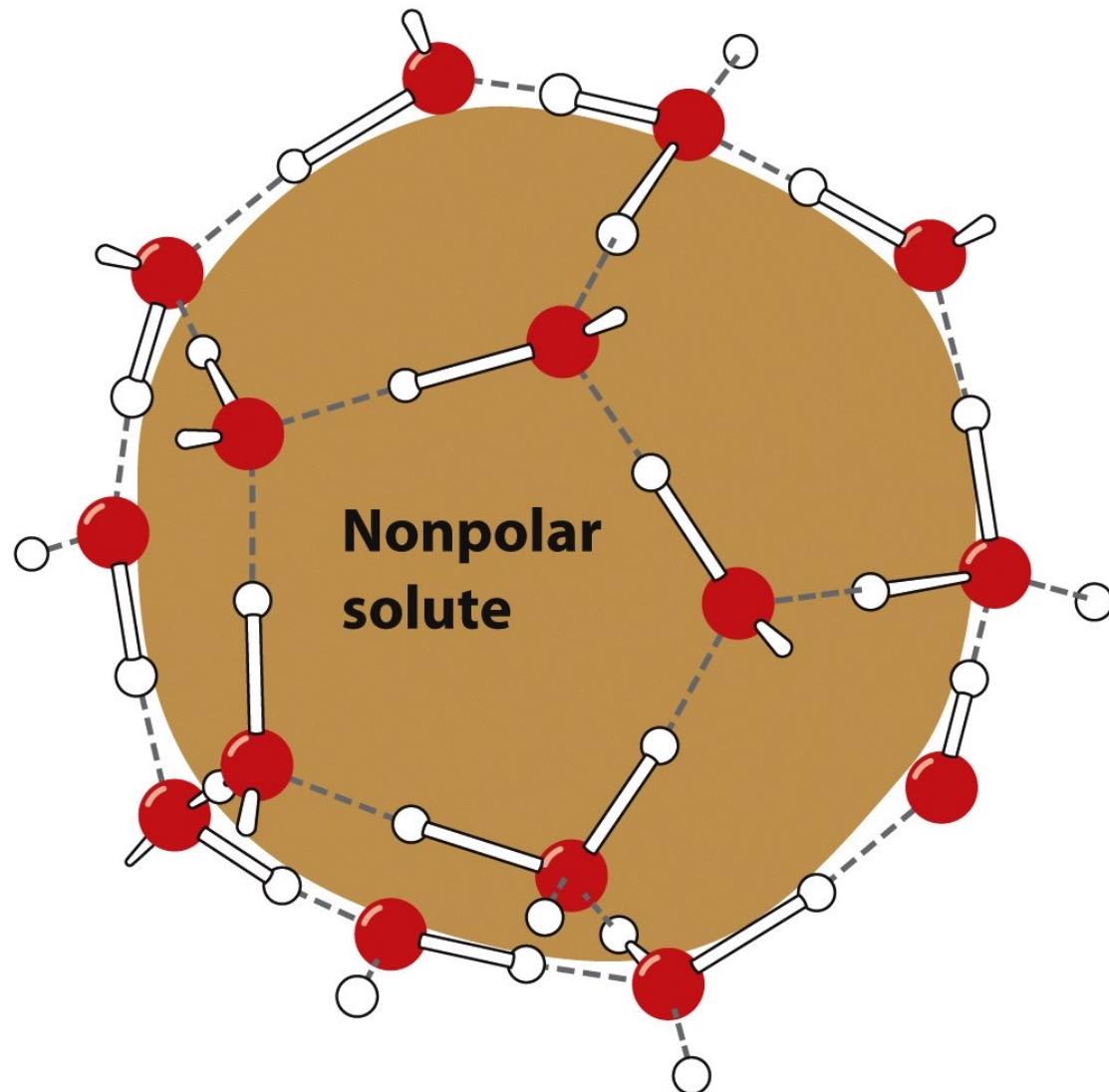


Molecular basis of the hydrophobic effect

- Water keeps hydrogen bonds intact when it is forced into contact with a non-hydrogen bonding substance like oil
- This causes strange geometry and lack of rotational and translational freedom of "interfacial water" which is unstable and has low entropy.
- In bulk water, intermolecular forces are essentially extending in all directions
- In bulk, a water molecule can rotate and still maintain hydrogen bonding interactions. At a hydrophobic interface the interactions are directional because the hydrophobic substance does not form hydrogen bonds.

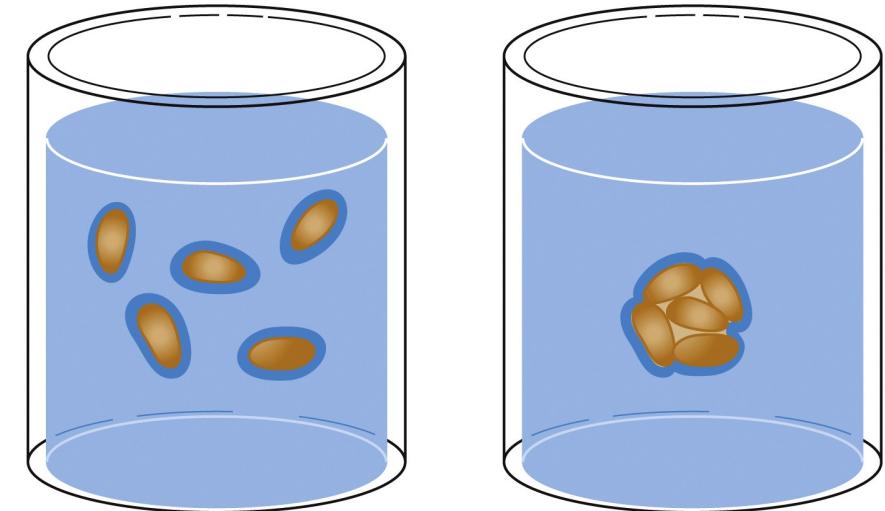


Molecular basis of the hydrophobic effect

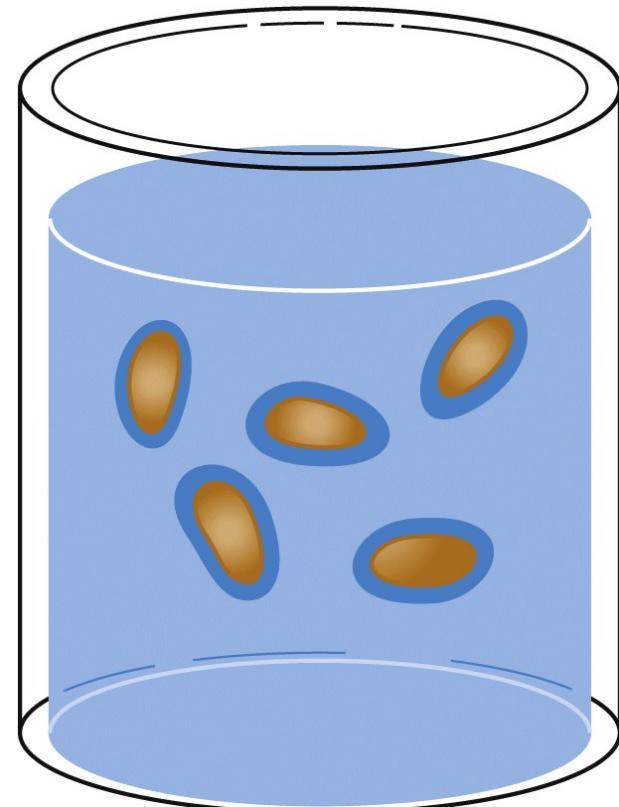


Thermodynamic basis of the hydrophobic effect

- The hydrophobic effect above can be understood by:
 1. Enthalpy (ΔH , indicates changes in molecular interactions)
 2. Entropy (ΔS , indicates changes in available rotational, translational, vibrational states).
- A hydrocarbon engages in favorable molecular interactions with water in aqueous solution.
- So why don't oil and water mix? It is the water. Water drives non-polar substances out of the aqueous phase.



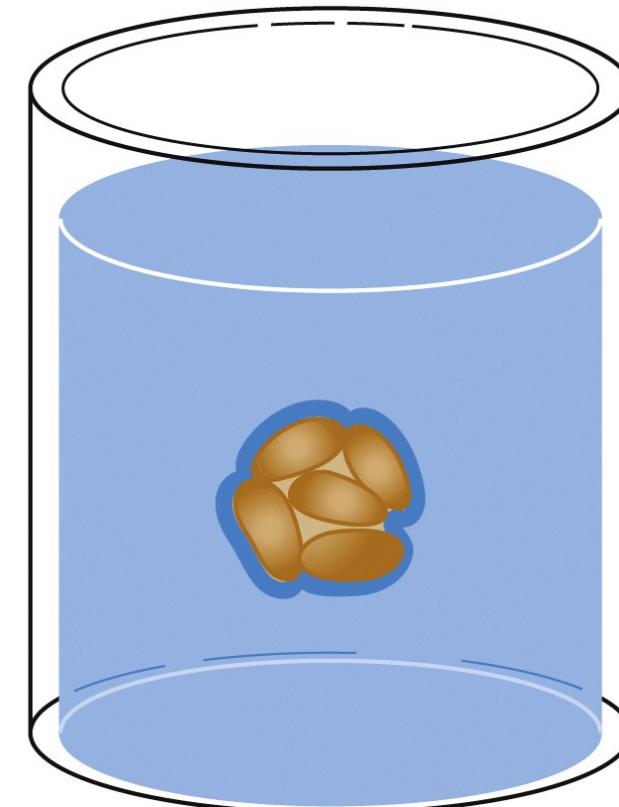
Thermodynamic basis of the hydrophobic effect



Interfacial water



When the hydrocarbon
aggregates the amount of
interfacial water decreases.



Thermodynamic basis of the hydrophobic effect

Table 2-2 Thermodynamic Changes for Transferring Hydrocarbons from Water to Nonpolar Solvents at 25°C

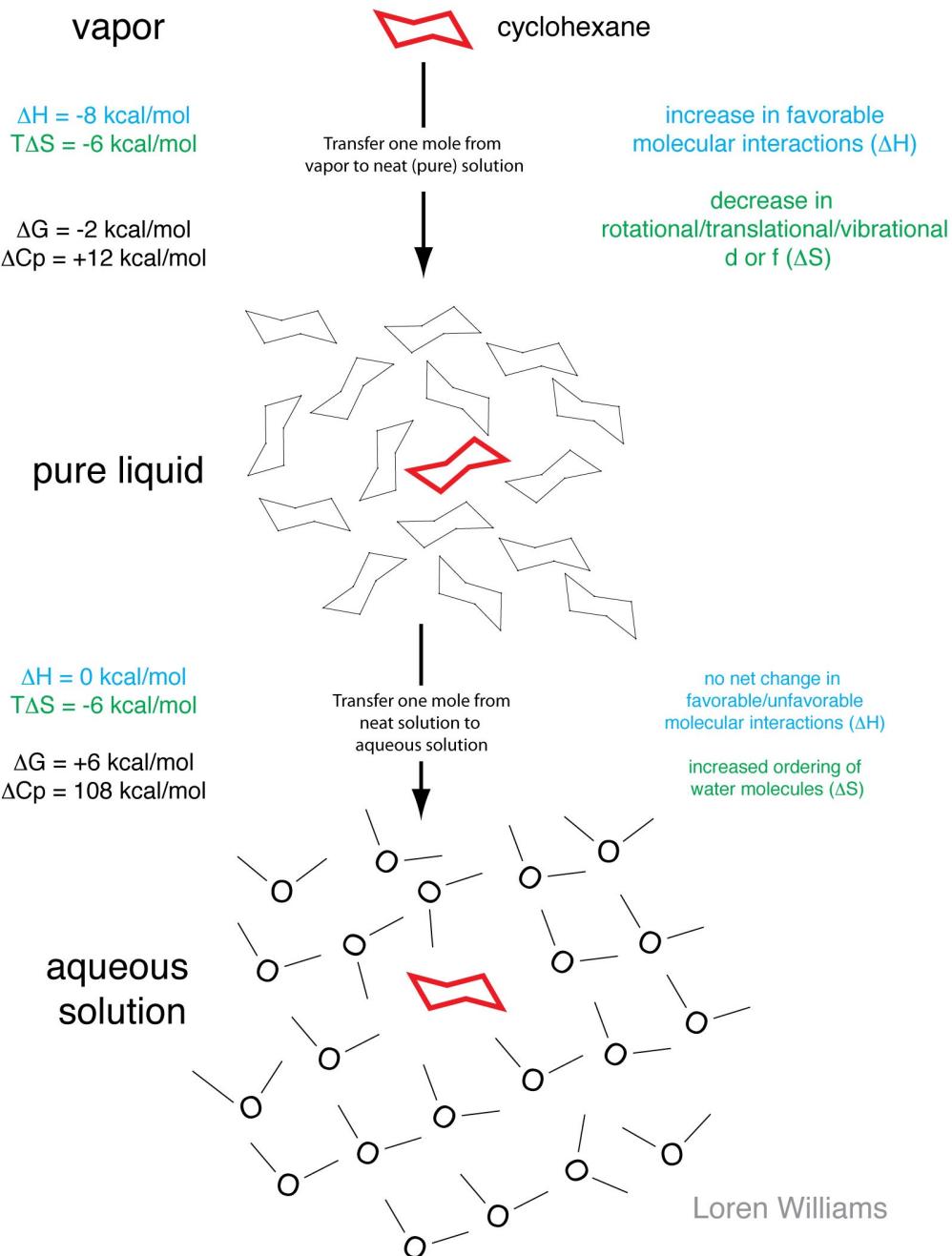
Process	ΔH (kJ · mol ⁻¹)	$-T \Delta S$ (kJ · mol ⁻¹)	ΔG (kJ · mol ⁻¹)
$\text{CH}_4 \text{ in H}_2\text{O} \rightleftharpoons \text{CH}_4 \text{ in C}_6\text{H}_6$	11.7	-22.6	-10.9
$\text{CH}_4 \text{ in H}_2\text{O} \rightleftharpoons \text{CH}_4 \text{ in CCl}_4$	10.5	-22.6	-12.1
$\text{C}_2\text{H}_6 \text{ in H}_2\text{O} \rightleftharpoons \text{C}_2\text{H}_6 \text{ in benzene}$	9.2	-25.1	-15.9
$\text{C}_2\text{H}_4 \text{ in H}_2\text{O} \rightleftharpoons \text{C}_2\text{H}_4 \text{ in benzene}$	6.7	-18.8	-12.1
$\text{C}_2\text{H}_2 \text{ in H}_2\text{O} \rightleftharpoons \text{C}_2\text{H}_2 \text{ in benzene}$	0.8	-8.8	-8.0
$\text{Benzene in H}_2\text{O} \rightleftharpoons \text{liquid benzene}^a$	0.0	-17.2	-17.2
$\text{Toluene in H}_2\text{O} \rightleftharpoons \text{liquid toluene}^a$	0.0	-20.0	-20.0

^aData measured at 18°C.

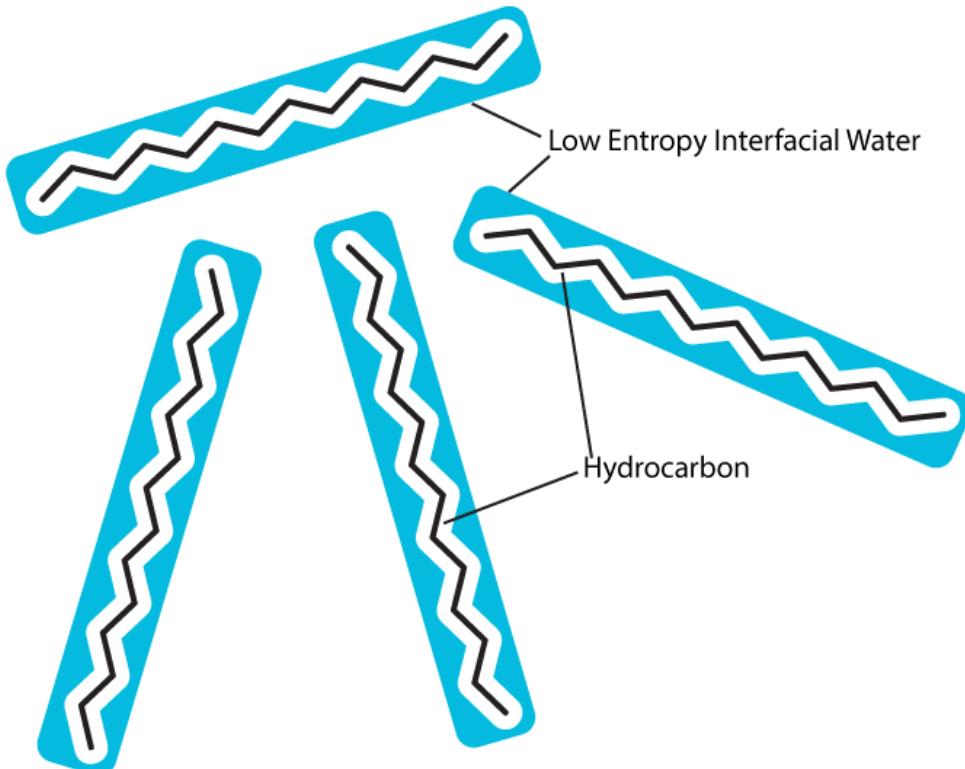
Source: Kauzmann, W., *Adv. Protein Chem.* 14, 39 (1959).

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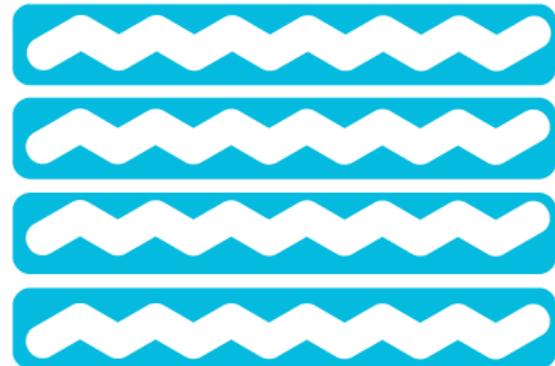
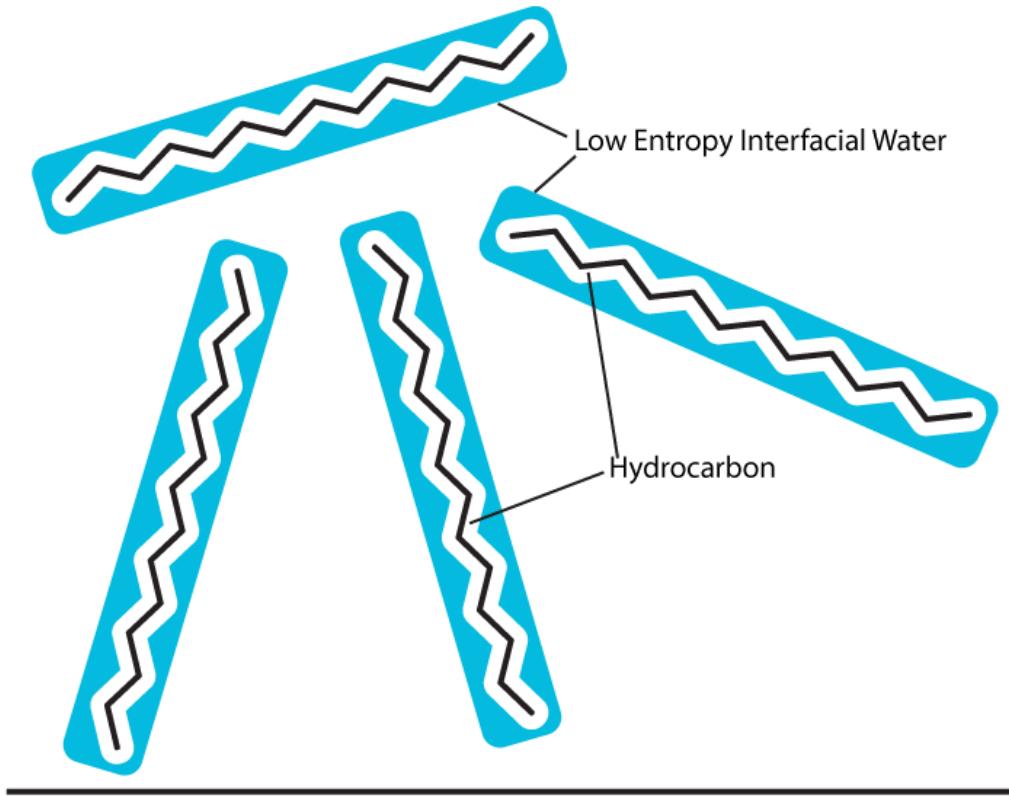
Transfer of Cyclohexane from Vapor Phase to Pure Liquid to Aqueous Phase



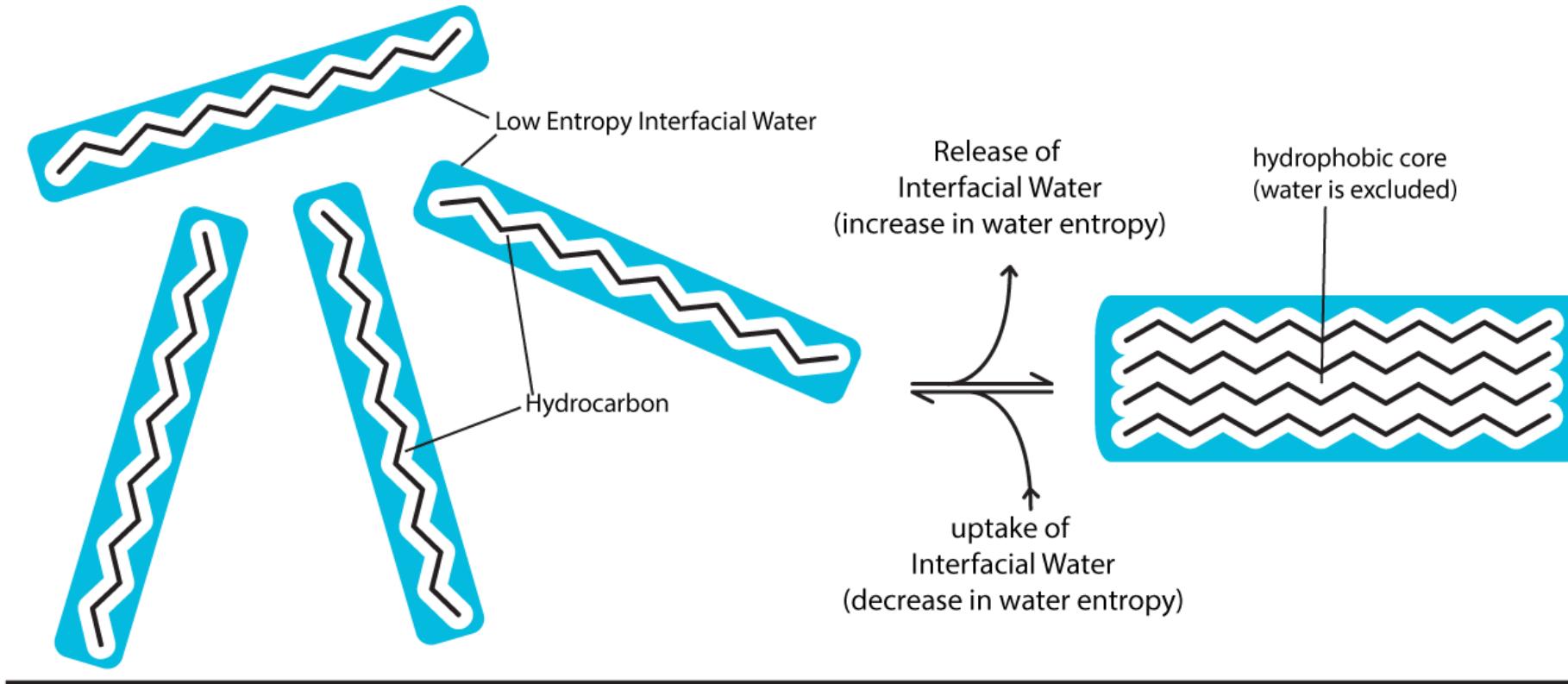
Thermodynamic basis of the hydrophobic effect



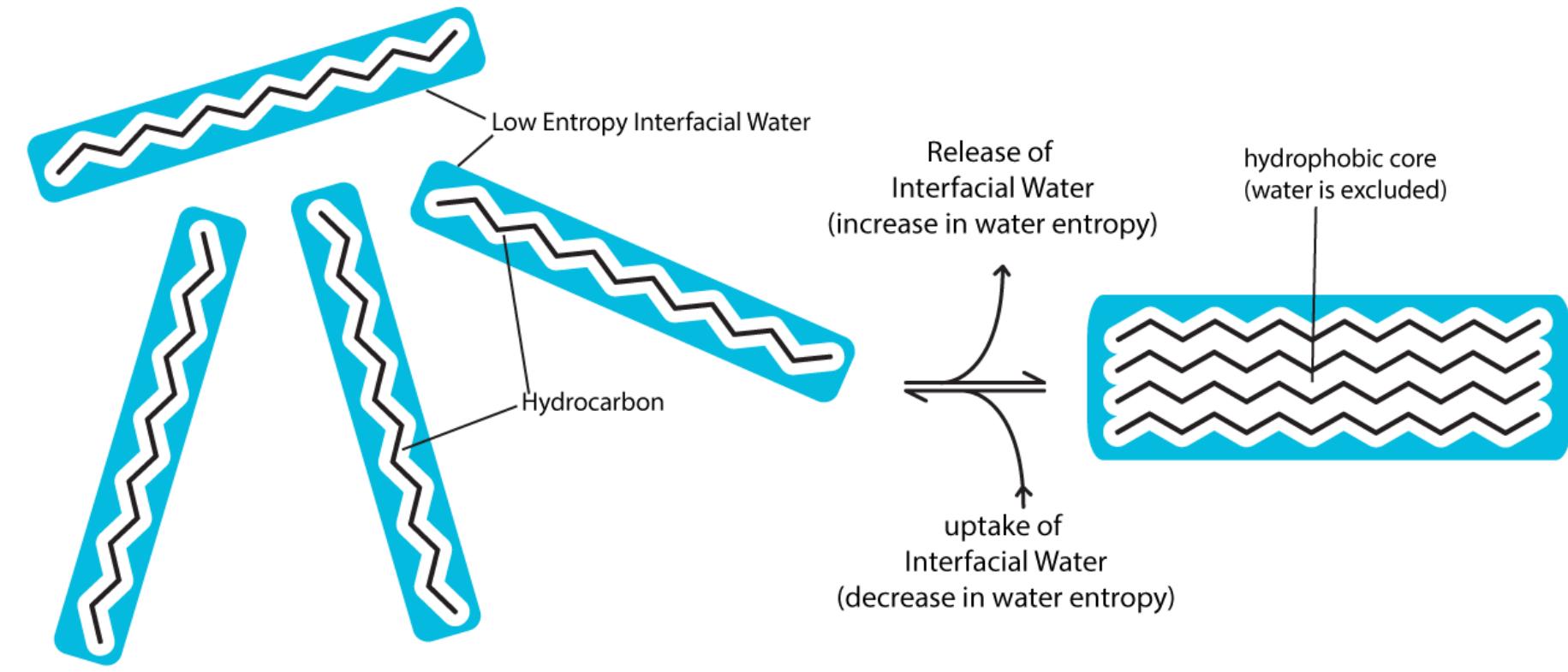
Thermodynamic basis of the hydrophobic effect



Thermodynamic basis of the hydrophobic effect



Thermodynamic basis of the hydrophobic effect

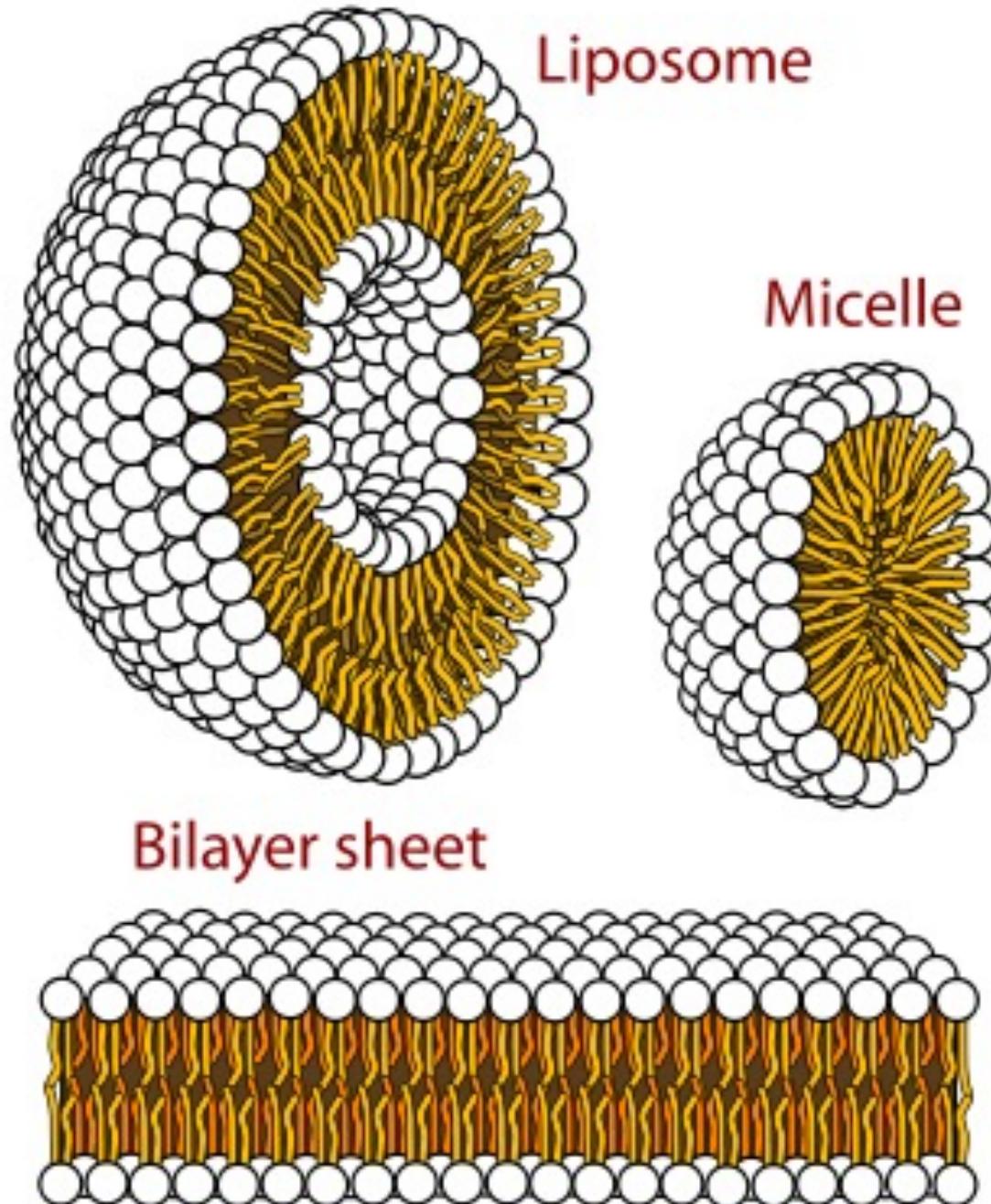


When the hydrocarbon aggregates the amount of interfacial water decreases.

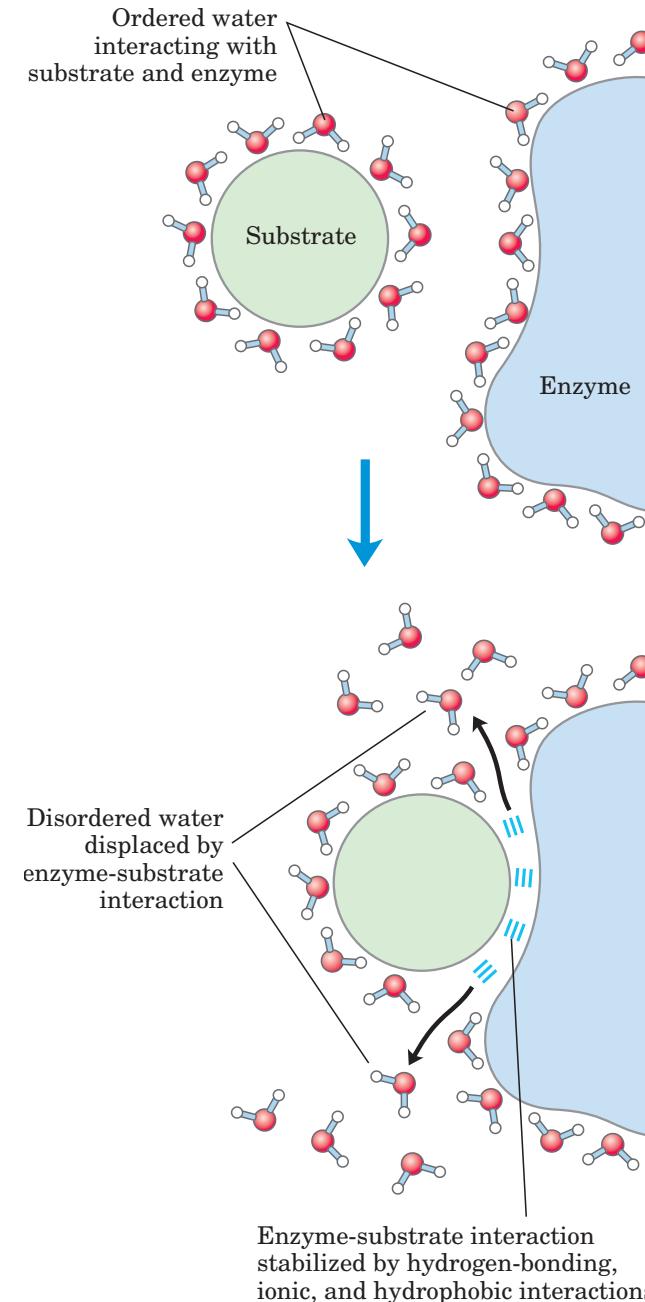


Thermodynamic basis of the hydrophobic effect

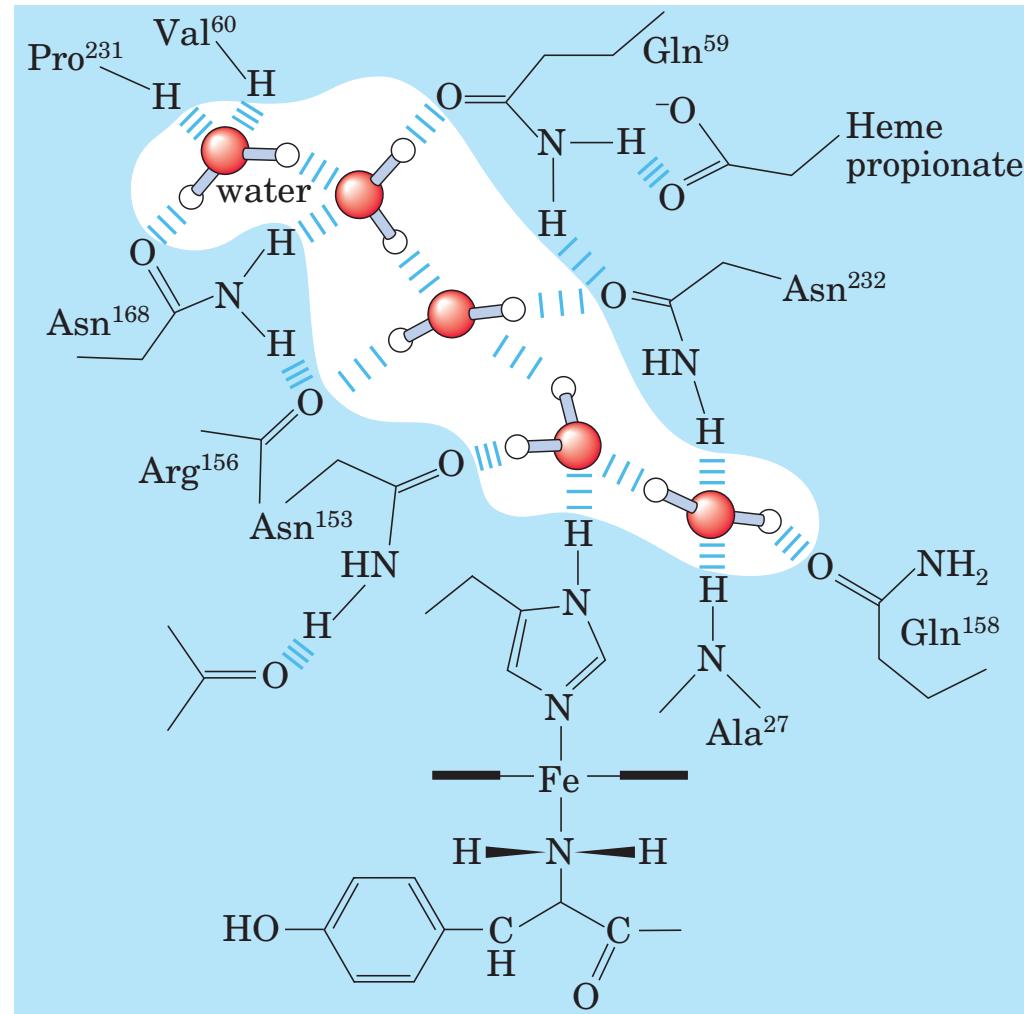
- When hydrocarbon molecules aggregate in aqueous solution, the total volume of interfacial water decreases.
- The driving force for aggregation of hydrophobic substances arises from an increase in entropy of the water.
- The driving force for aggregation does not arise from intrinsic attraction between hydrophobic solute molecules.



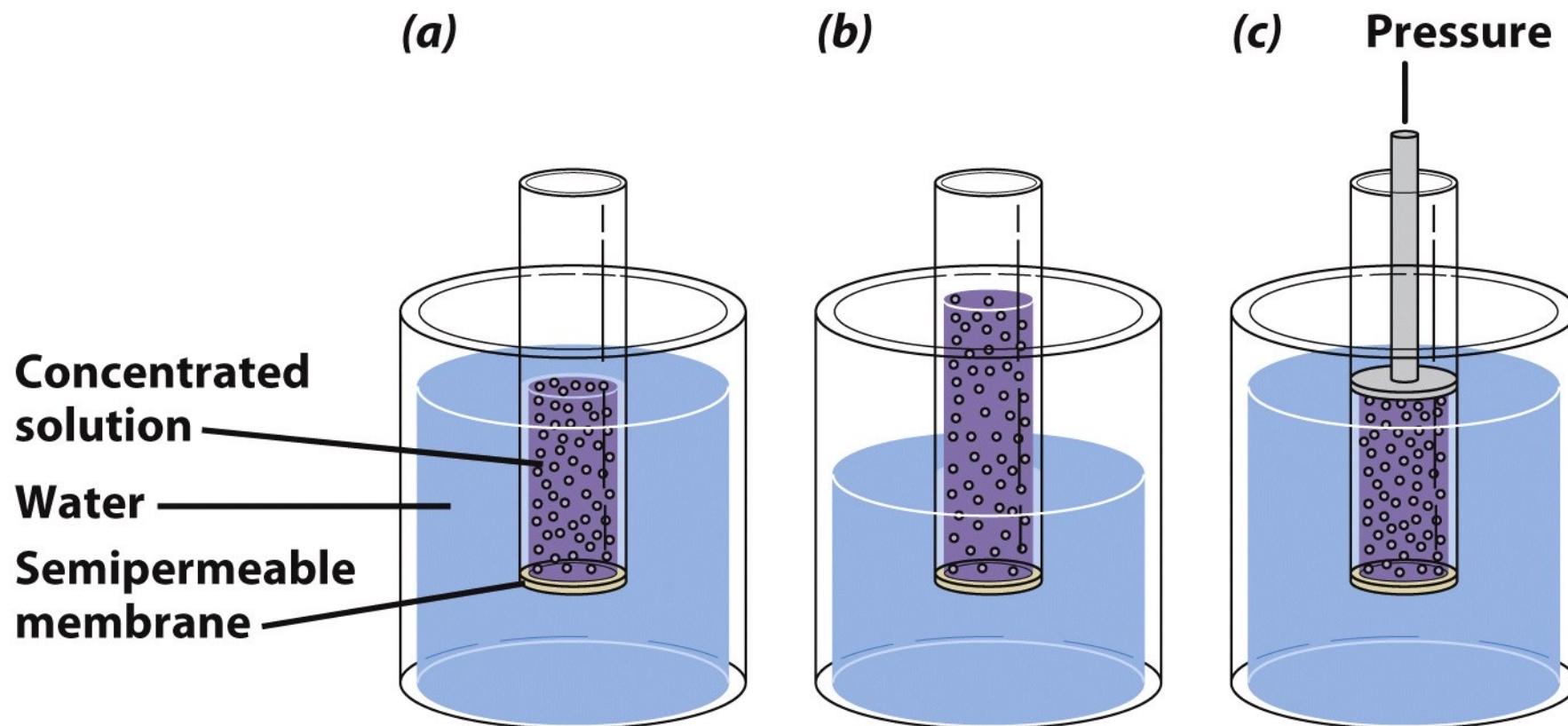
**Release of ordered water
favors formation of an
enzyme-substrate complex**



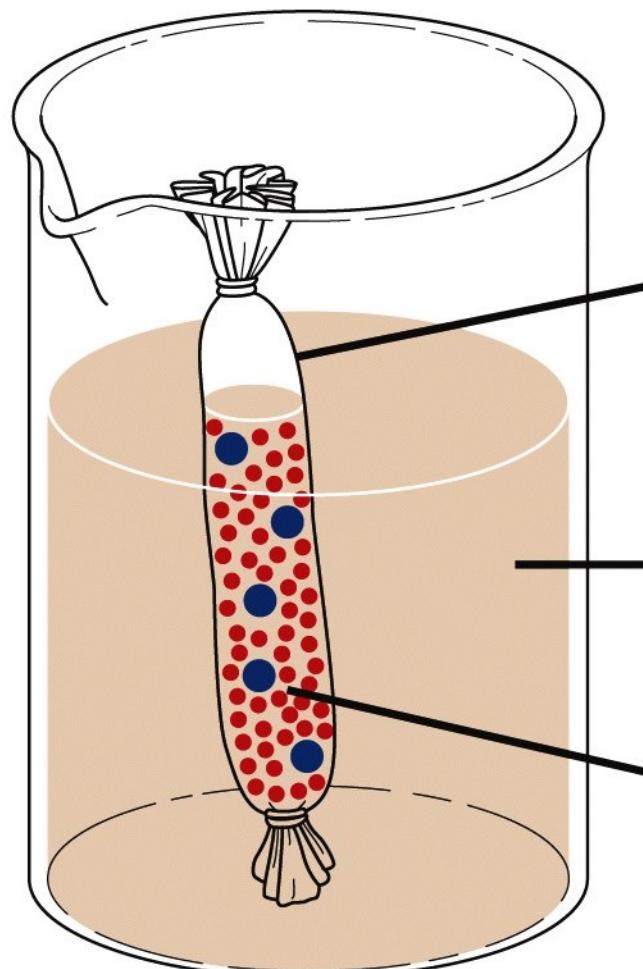
For many proteins, tightly bound water molecules are essential to their function



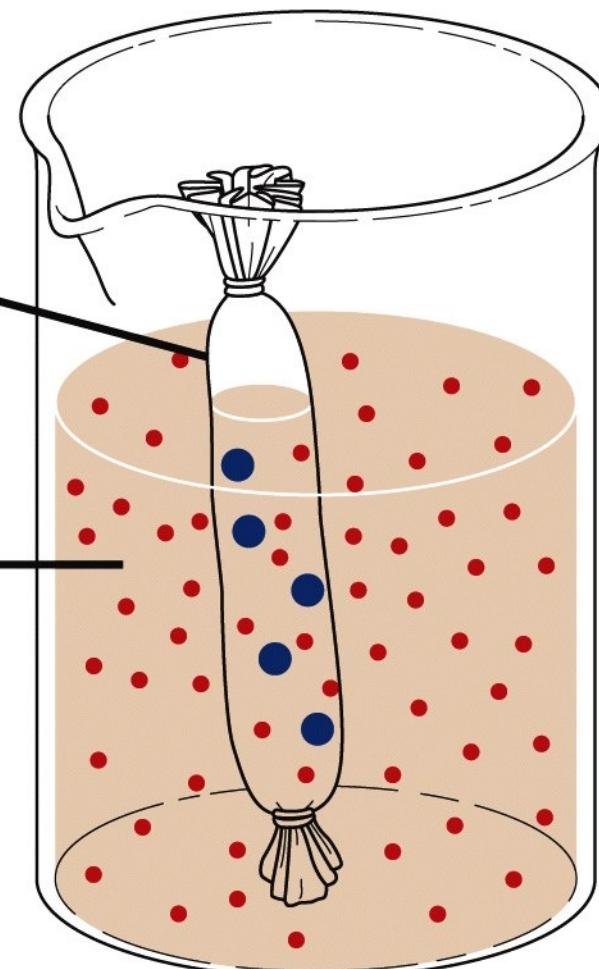
Osmosis



(a) At start of dialysis



(b) At equilibrium



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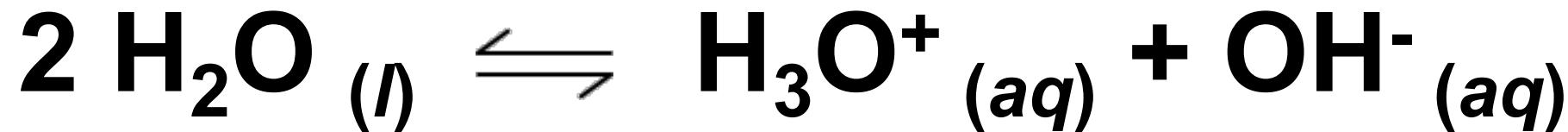
Acids and Bases



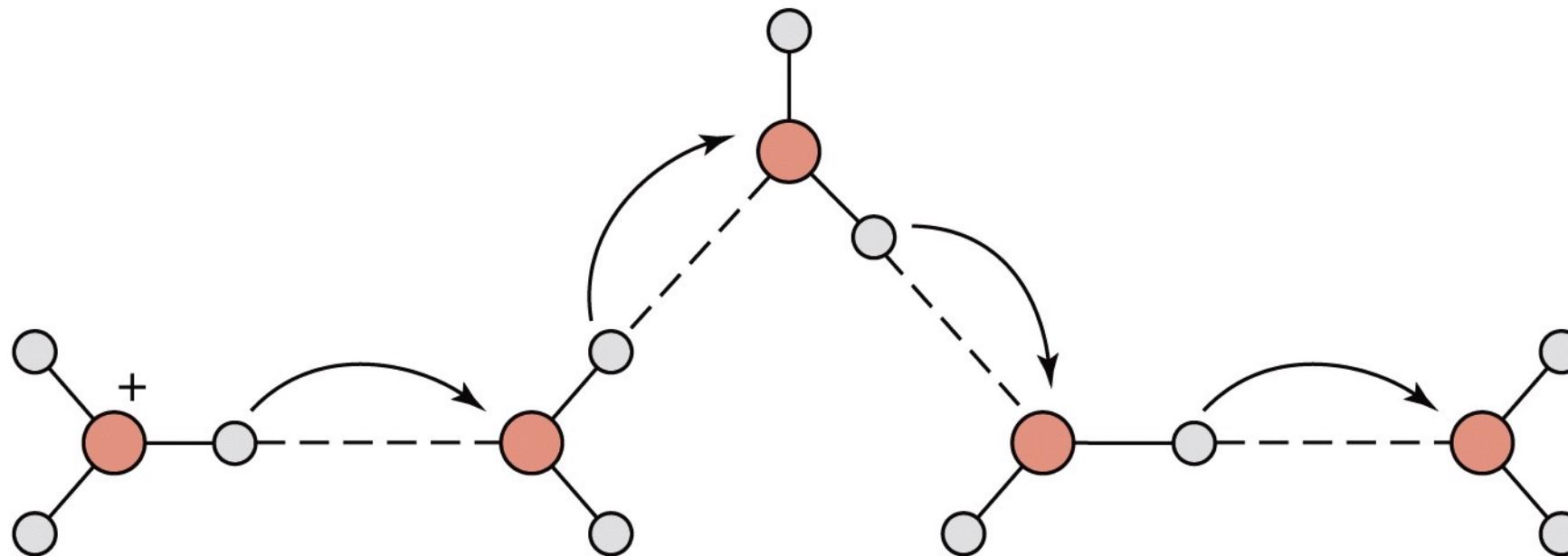
HA = generic acid

Water as an Acid and a Base

Autoionization of water



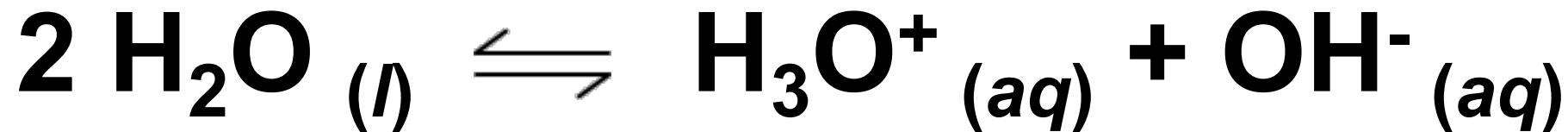
Proton jumping



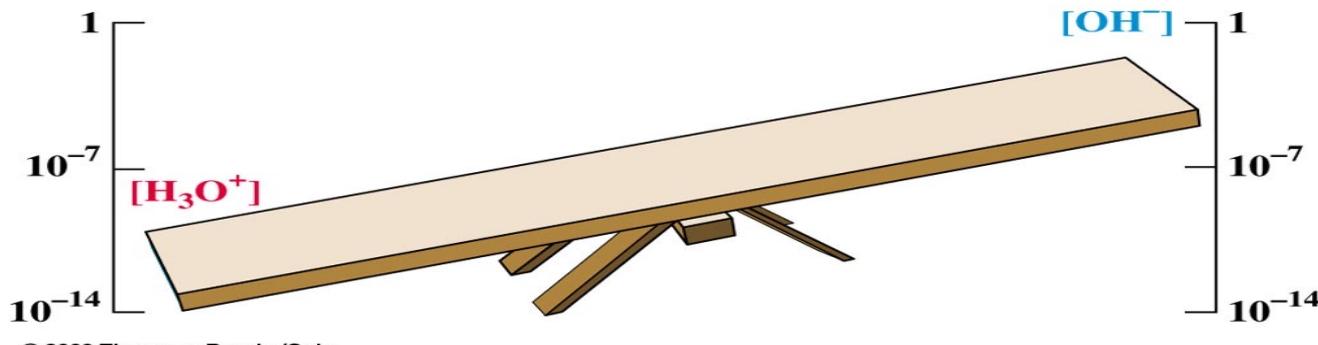
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Water as an Acid and a Base

Autoionization of water



$$K_w = 1.0 \times 10^{-14} \text{ (at } 25^\circ\text{C})$$



pH scale

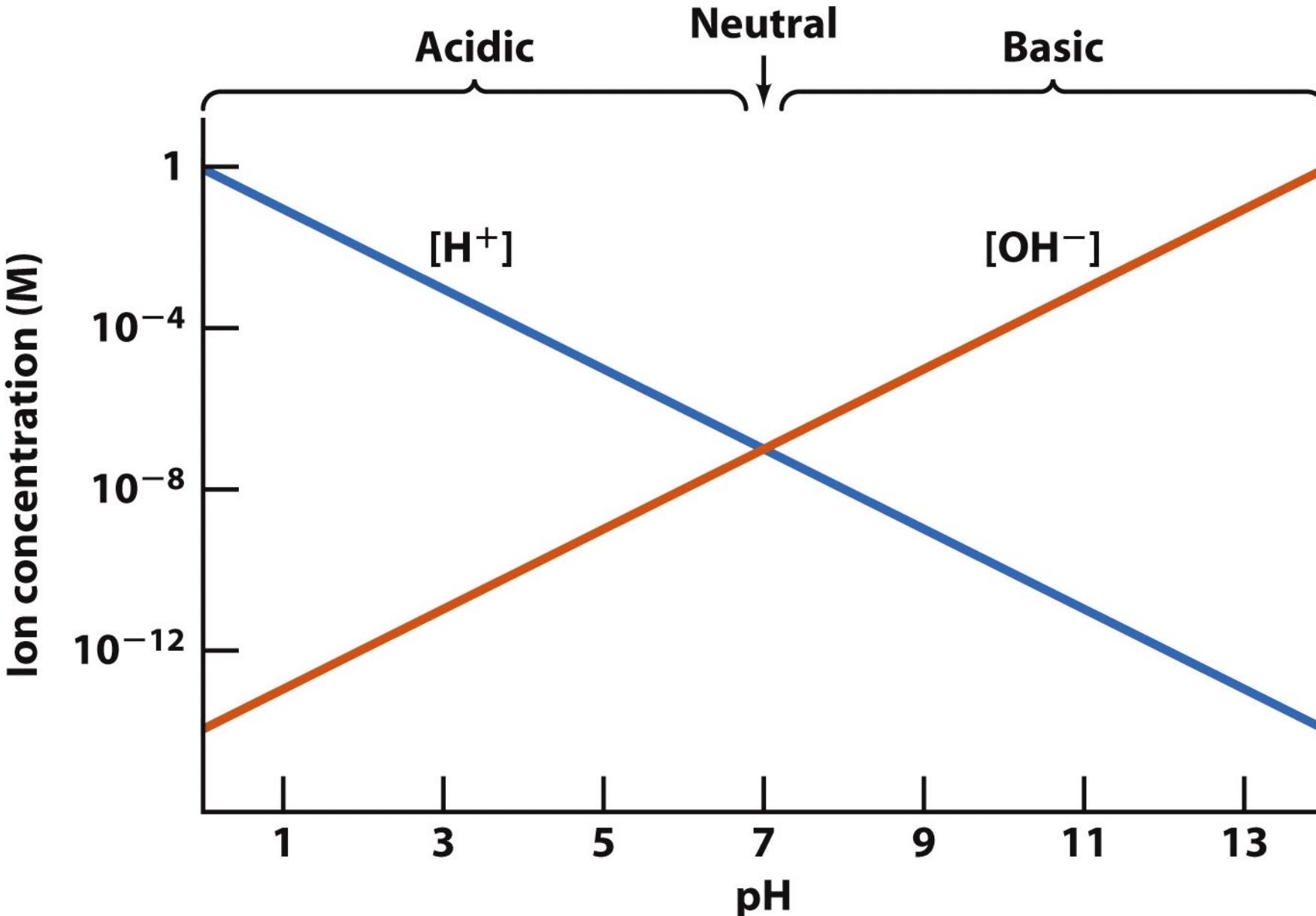
TABLE 2.2 pH Scale

The hydrogen ion and hydroxyl ion concentrations are given in moles per liter at 25°C.

pH	[H ⁺]	[OH ⁻]
0	(10 ⁰)	1.0
1	(10 ⁻¹)	0.1
2	(10 ⁻²)	0.01
3	(10 ⁻³)	0.001
4	(10 ⁻⁴)	0.0001
5	(10 ⁻⁵)	0.00001
6	(10 ⁻⁶)	0.000001
7	(10⁻⁷)	0.000001
8	(10 ⁻⁸)	0.0000001
9	(10 ⁻⁹)	0.00000001
10	(10 ⁻¹⁰)	0.000000001
11	(10 ⁻¹¹)	0.0000000001
12	(10 ⁻¹²)	0.00000000001
13	(10 ⁻¹³)	0.000000000001
14	(10 ⁻¹⁴)	0.0000000000001

TABLE 2.3 The pH of Various Common Fluids

Fluid	pH
Household lye	13.6
Bleach	12.6
Household ammonia	11.4
Milk of magnesia	10.3
Baking soda	8.4
Seawater	7.5–8.4
Pancreatic fluid	7.8–8.0
Blood plasma	7.4
Intracellular fluids	
Liver	6.9
Muscle	6.1
Saliva	6.6
Urine	5–8
Boric acid	5.0
Beer	4.5
Orange juice	4.3
Grapefruit juice	3.2
Vinegar	2.9
Soft drinks	2.8
Lemon juice	2.3
Gastric juice	1.2–3.0
Battery acid	0.35



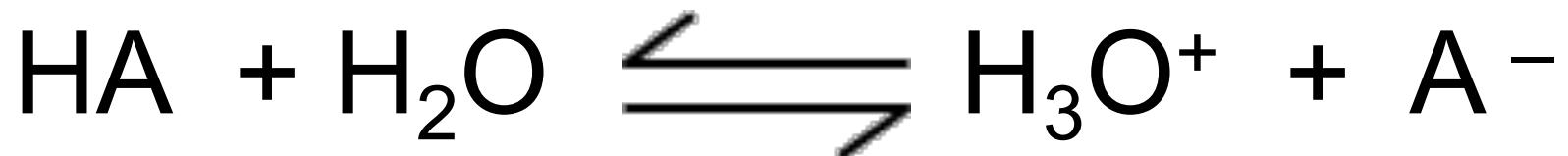
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Figure 2-16

Acids and Bases



Acids and Bases



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

Henderson-Hasselbalch

- Henderson-Hasselbalch equation

$$\text{pH} = \text{pK}_a + \log \frac{[\text{Conjugate base}]}{[\text{Weak acid}]}$$

- From this equation, we see that
 - when the concentrations of **weak acid** and its **conjugate base** are equal, the **pH** of the solution equals the **pK_a** of the weak acid

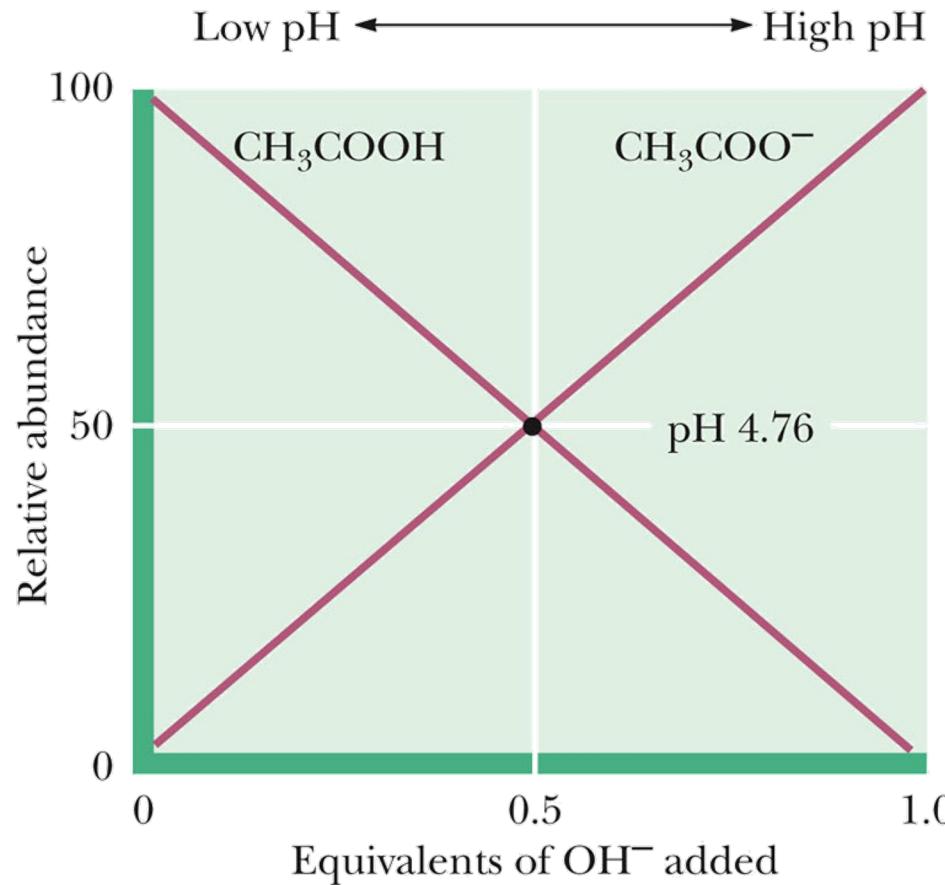
$$\text{pH} = \text{pK}_a$$

- when $\text{pH} < \text{pK}_a$, the weak acid predominates (**Protonated**)
- when $\text{pH} > \text{pK}_a$, the conjugate base predominates (**deprotonated**)

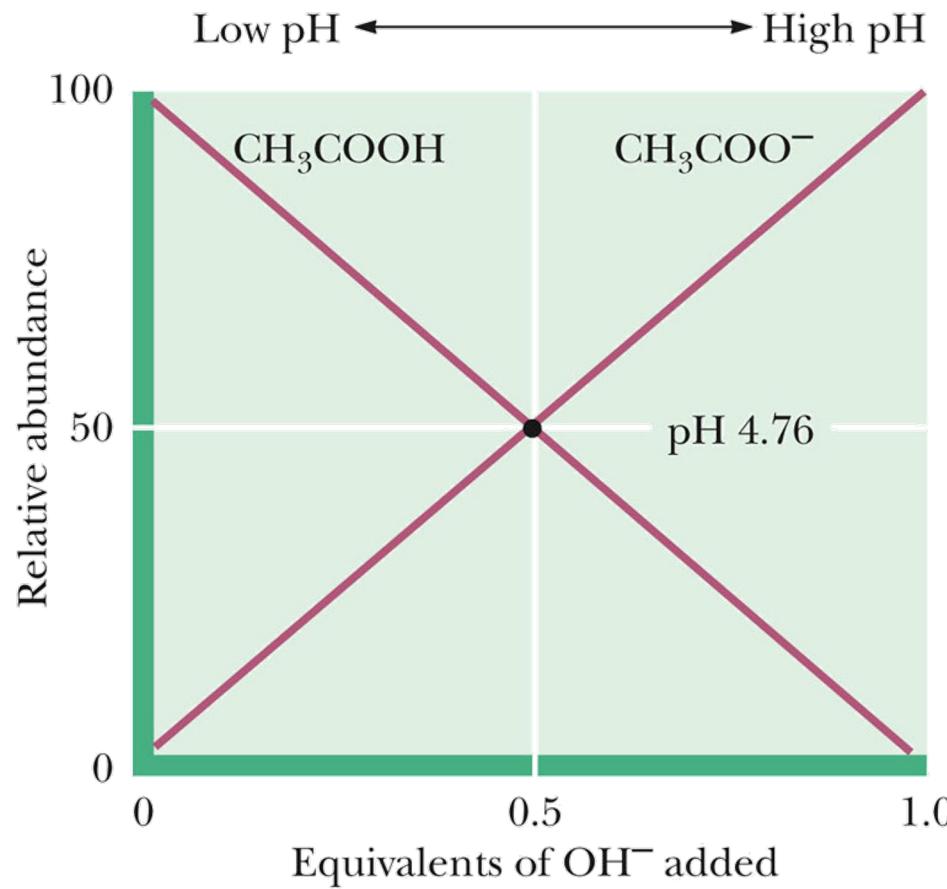
Titration Curves

- An experiment in which measured amounts of acid (or base) are added to measured amounts of base (or acid)
- You can follow the course of reaction with pH meter
 - monoprotic acid releases one H^+ and has 1 pK_a
 - diprotic acid releases two H^+ and has 2 pK_a 's
 - triprotic acid releases three H^+ and has 3 pK_a 's

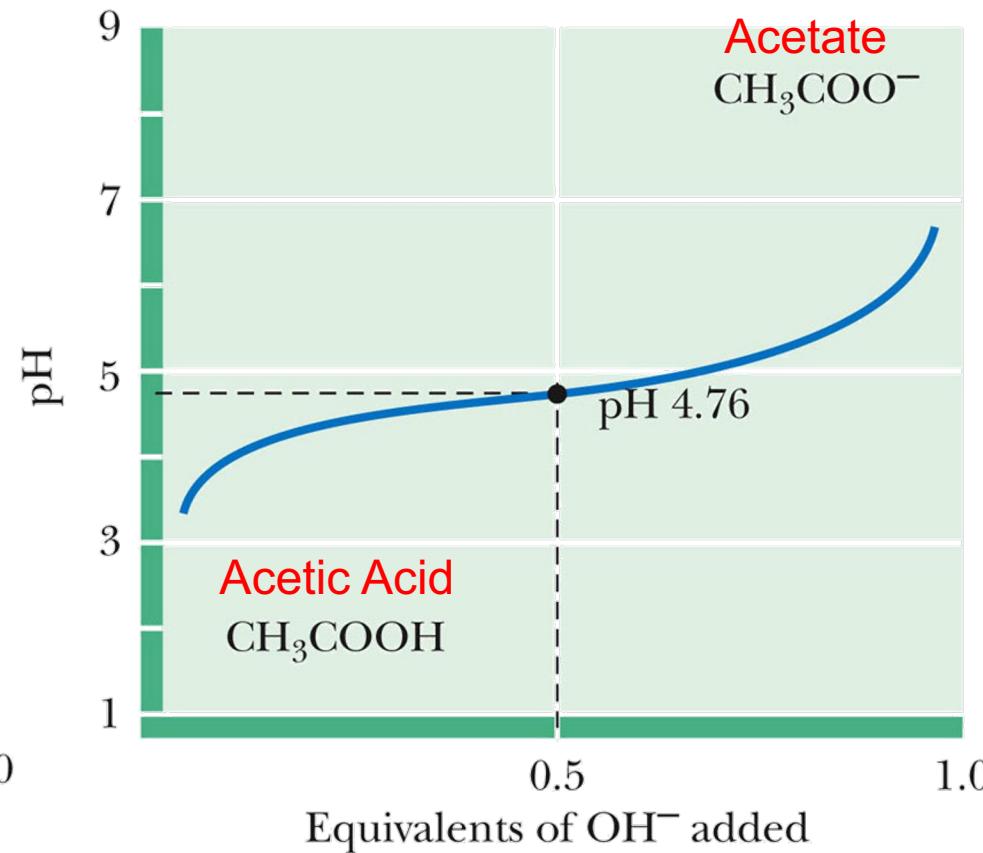
Titration Curves



Titration Curves



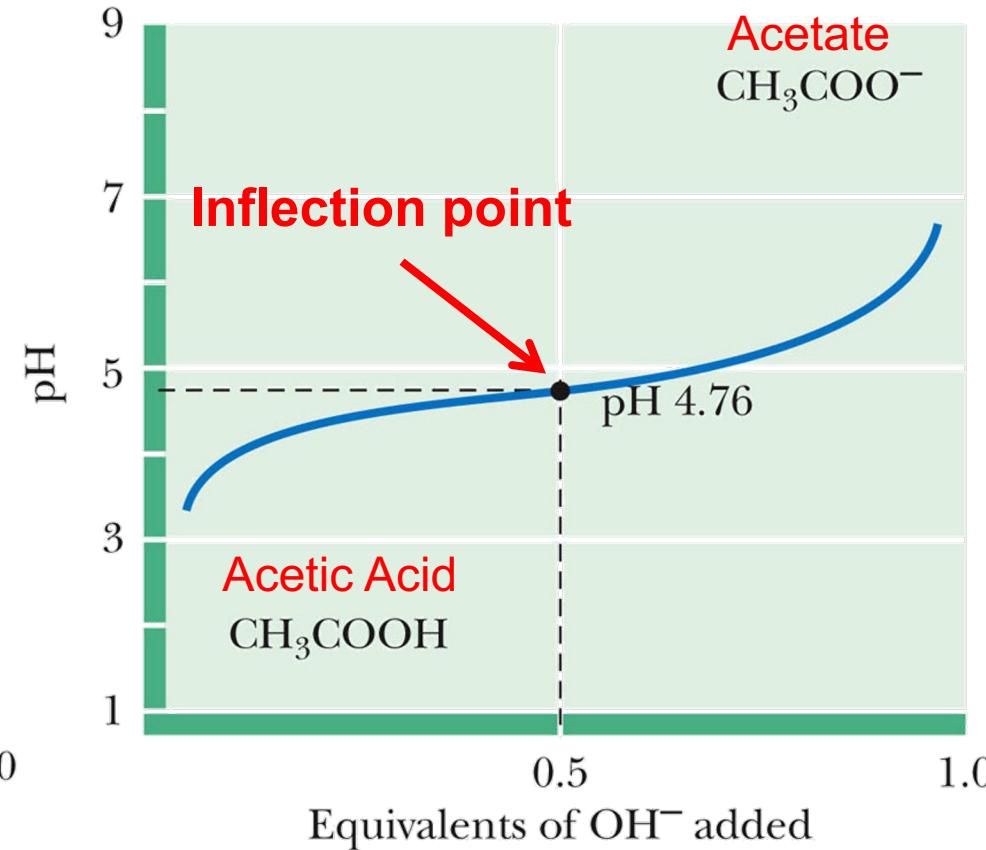
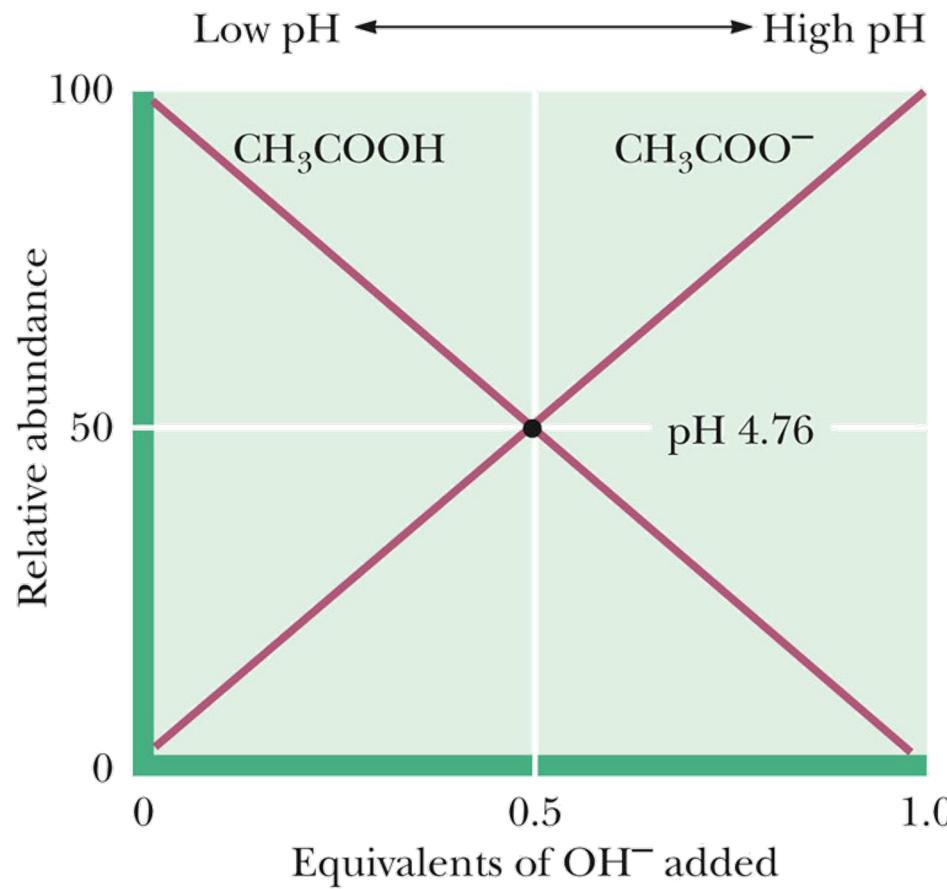
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pka of acetic acid is 4.76

Titration Curves



pka of acetic acid is 4.76

Polyprotic Acids

TABLE 7.4 Stepwise Dissociation Constants for Several Common Polyprotic Acids

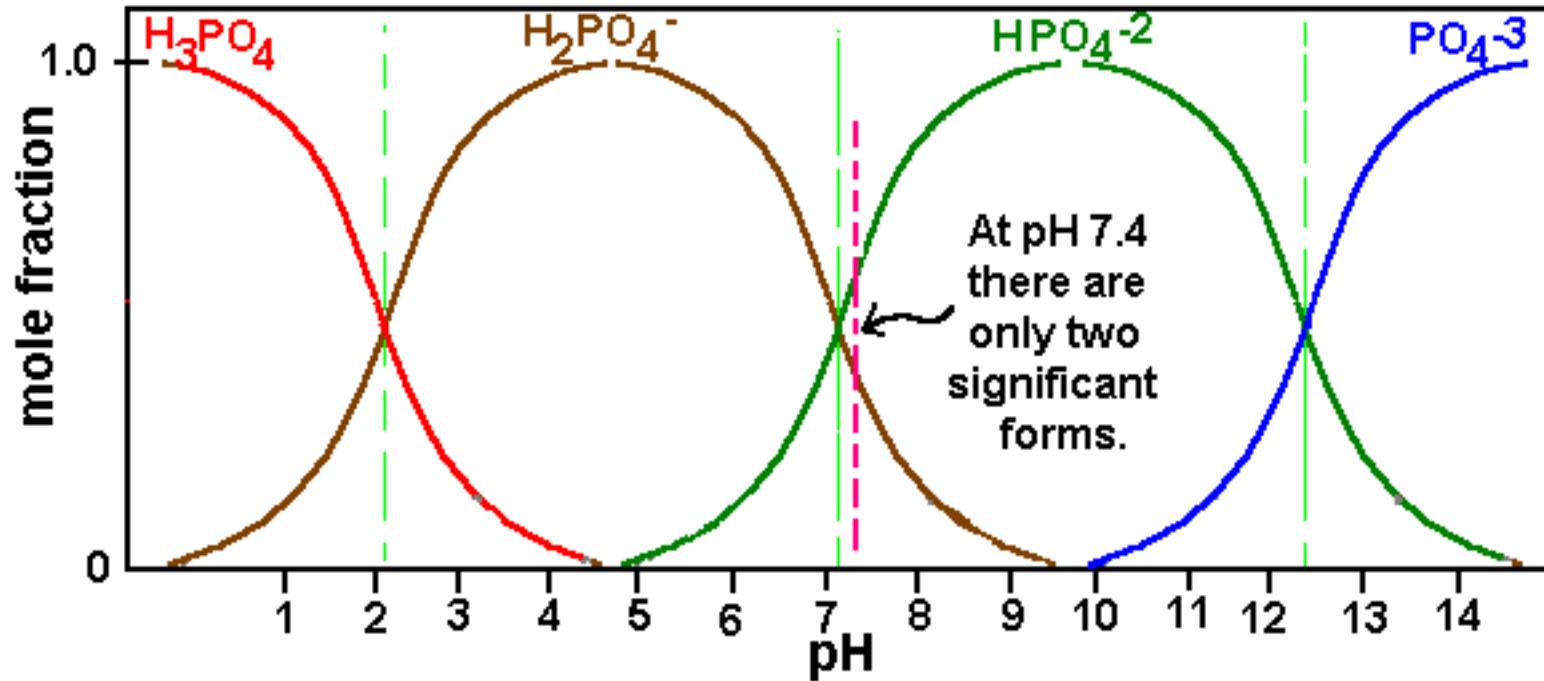
Name	Formula	K_{a_1}	K_{a_2}	K_{a_3}
Phosphoric acid	H_3PO_4	7.5×10^{-3}	6.2×10^{-8}	4.8×10^{-13}
Arsenic acid	H_3AsO_4	5×10^{-3}	8×10^{-8}	6×10^{-10}
Carbonic acid*	H_2CO_3	4.3×10^{-7}	4.8×10^{-11}	
Sulfuric acid	H_2SO_4	Large	1.2×10^{-2}	
Sulfurous acid	H_2SO_3	1.5×10^{-2}	1.0×10^{-7}	
Hydrosulfuric acid†	H_2S	1.0×10^{-7}	$\approx 10^{-19}$	
Oxalic acid	$H_2C_2O_4$	6.5×10^{-2}	6.1×10^{-5}	
Ascorbic acid (vitamin C)	$H_2C_6H_6O_6$	7.9×10^{-5}	1.6×10^{-12}	

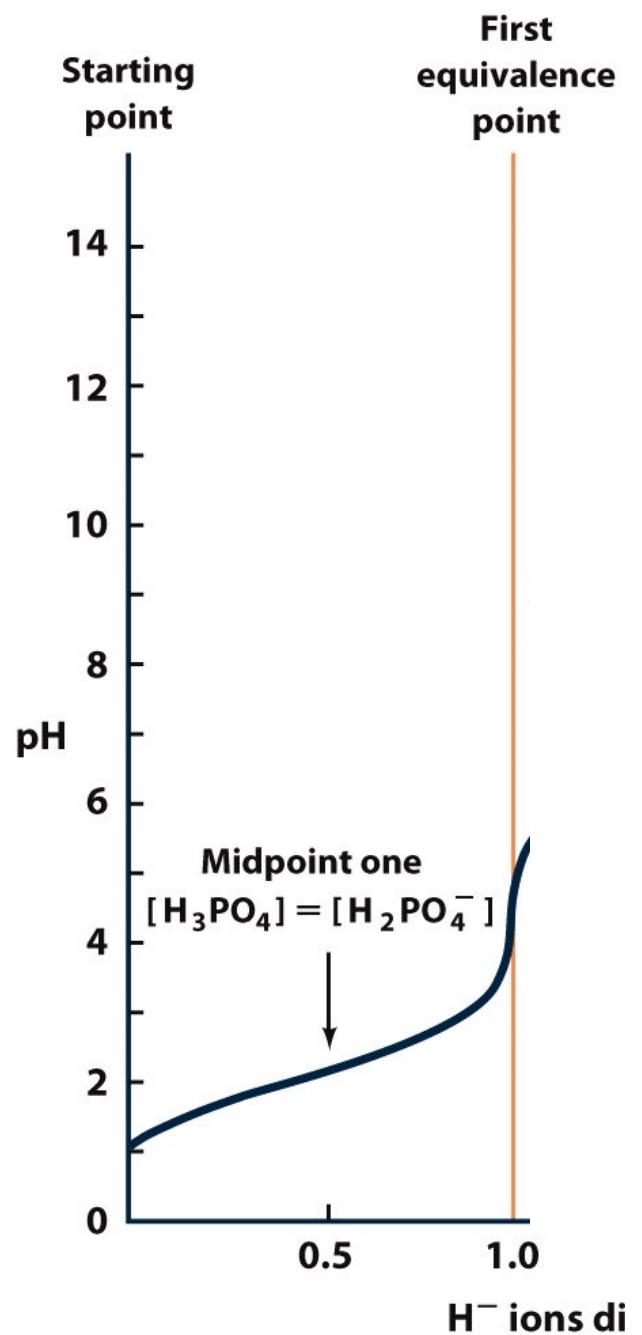
*This is really $CO_2(aq)$.

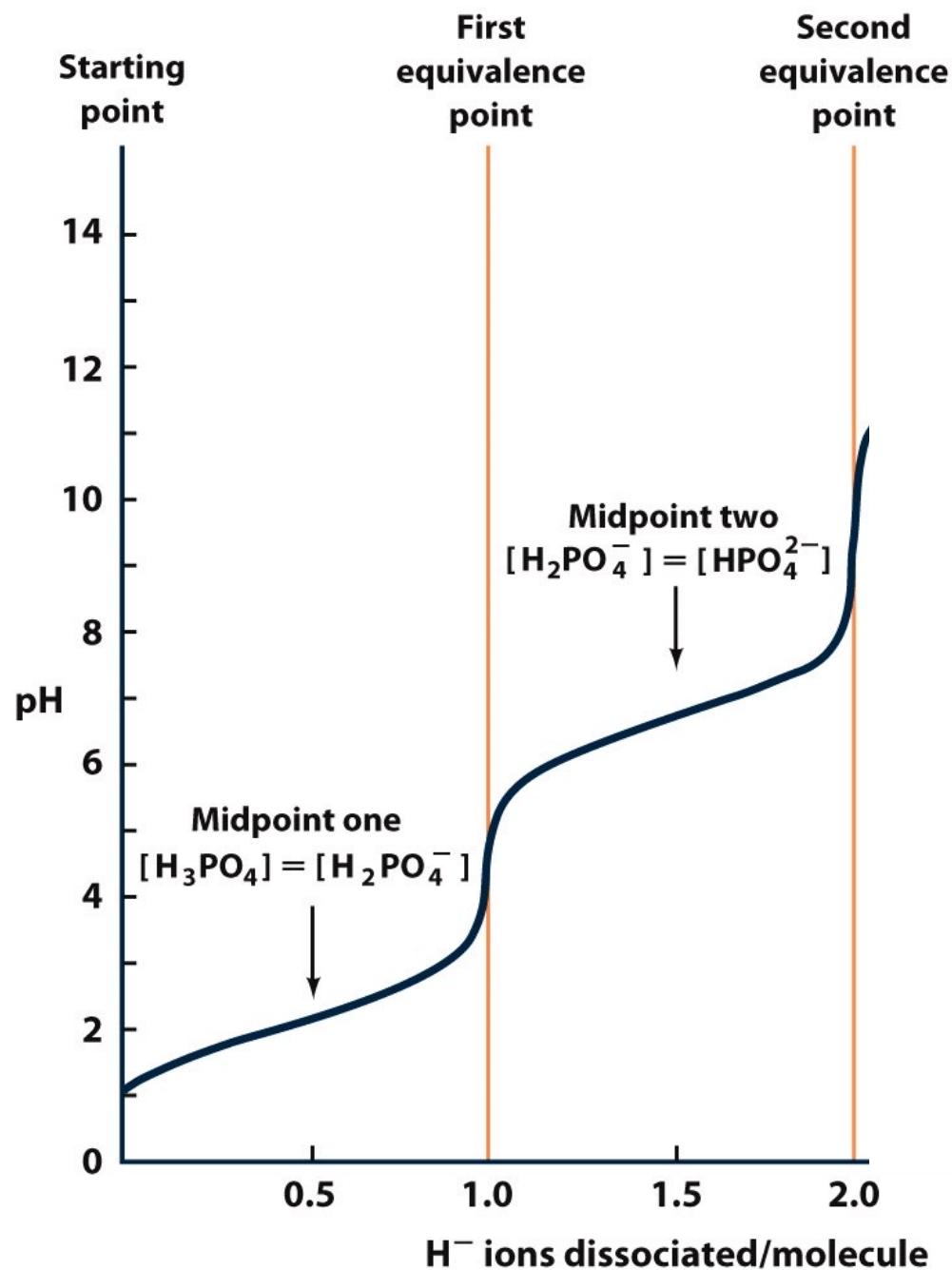
†The K_{a_2} value for H_2S is quite uncertain. Its small size makes it very difficult to measure.

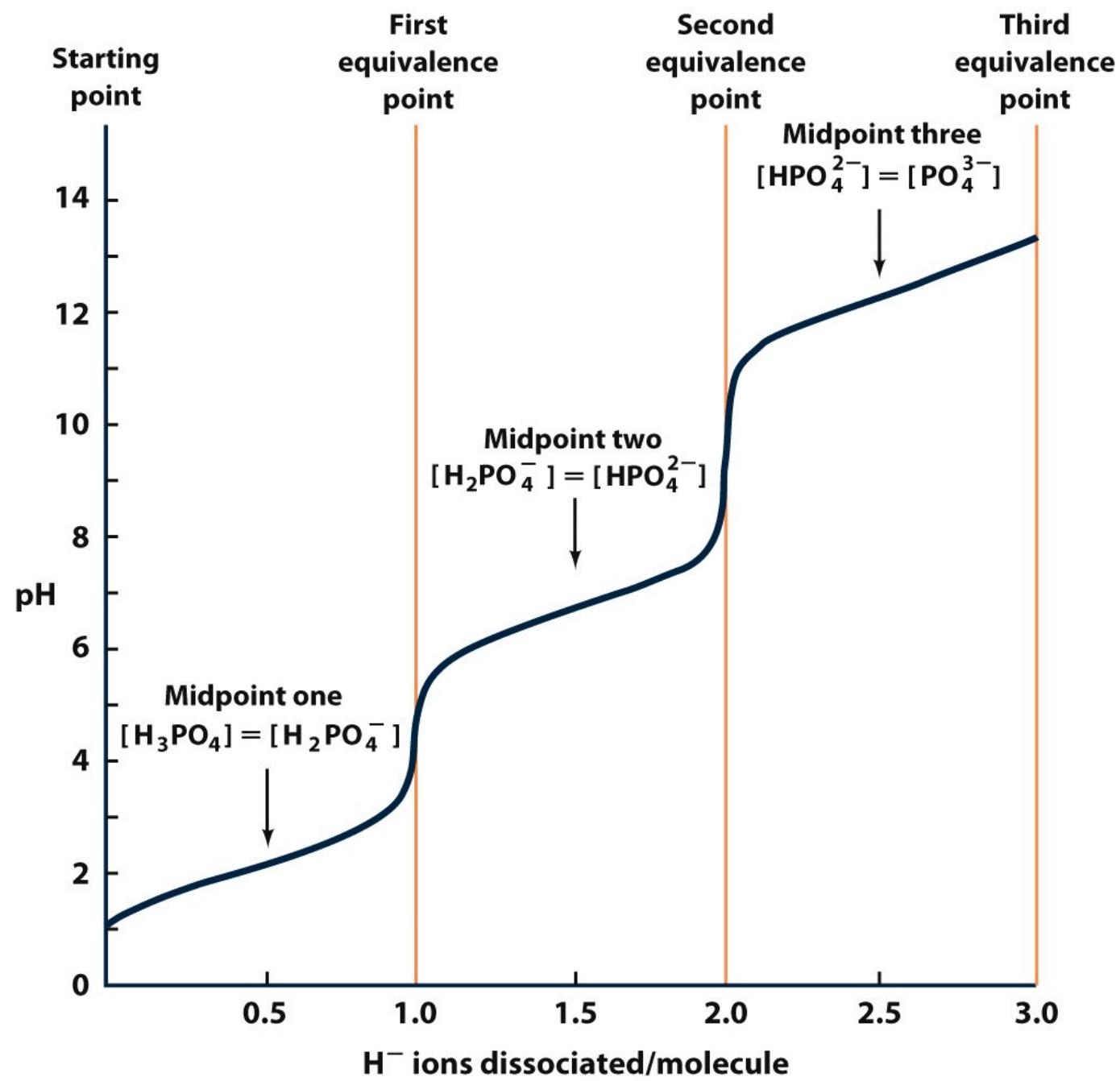


H_3PO_4 : phosphoric acid



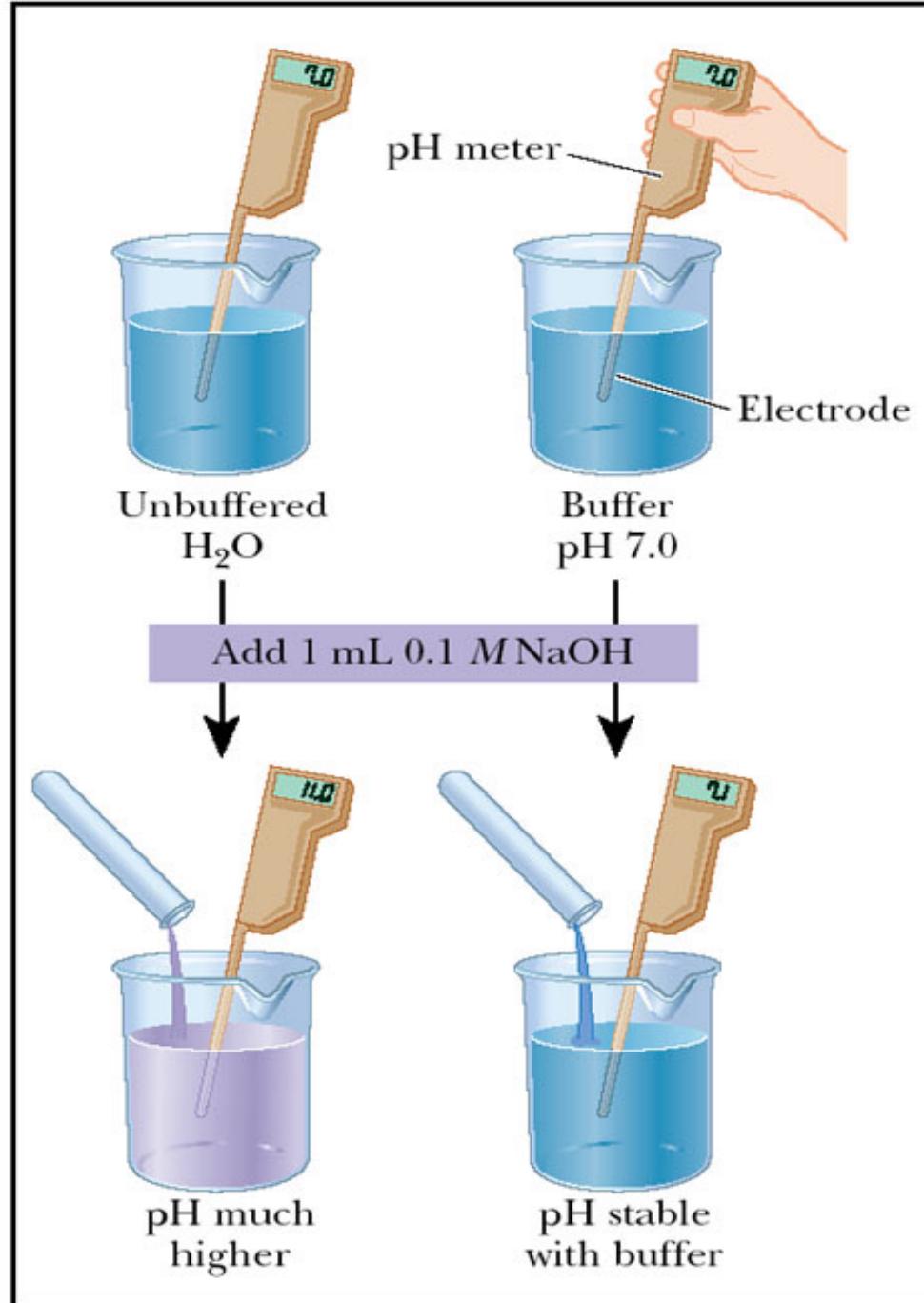
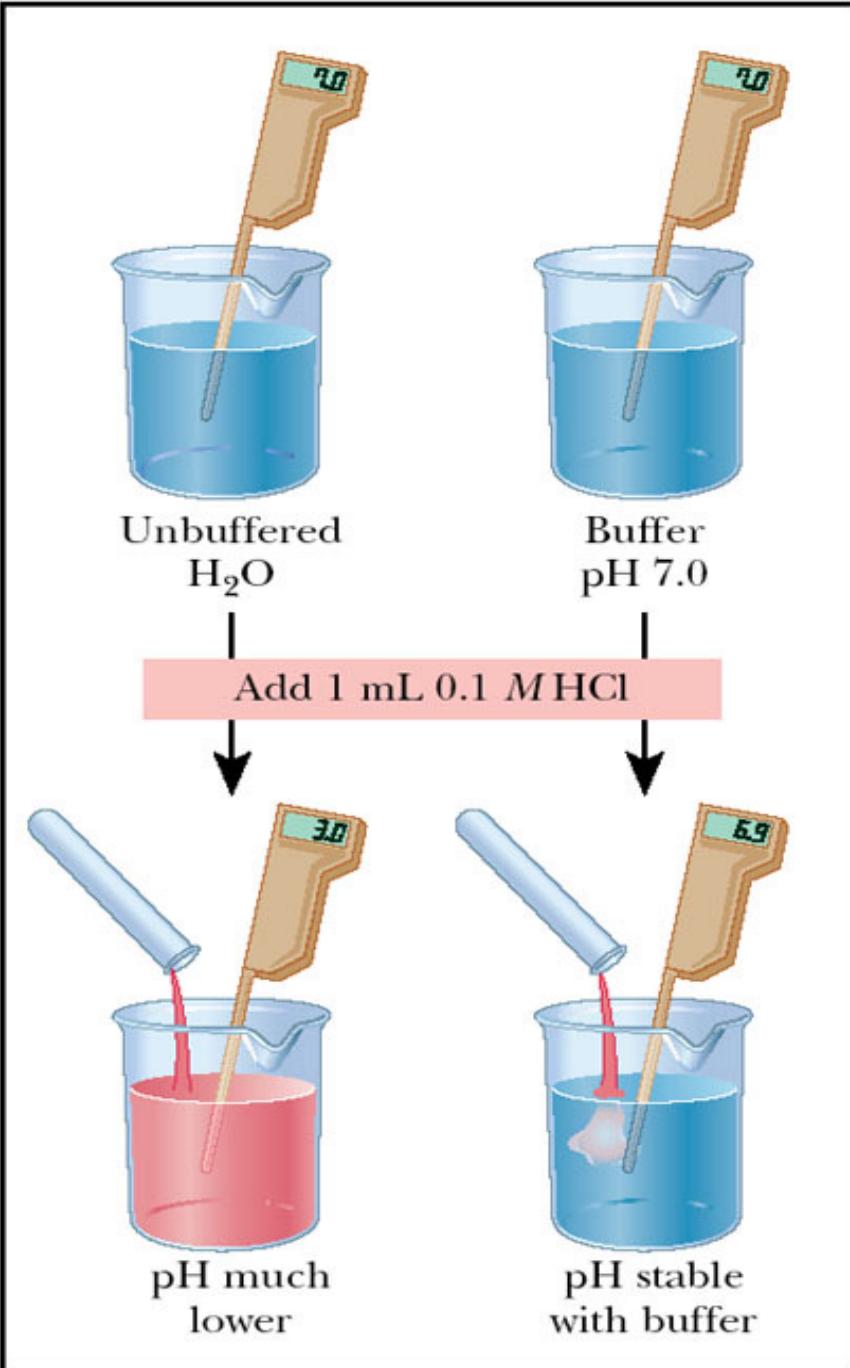






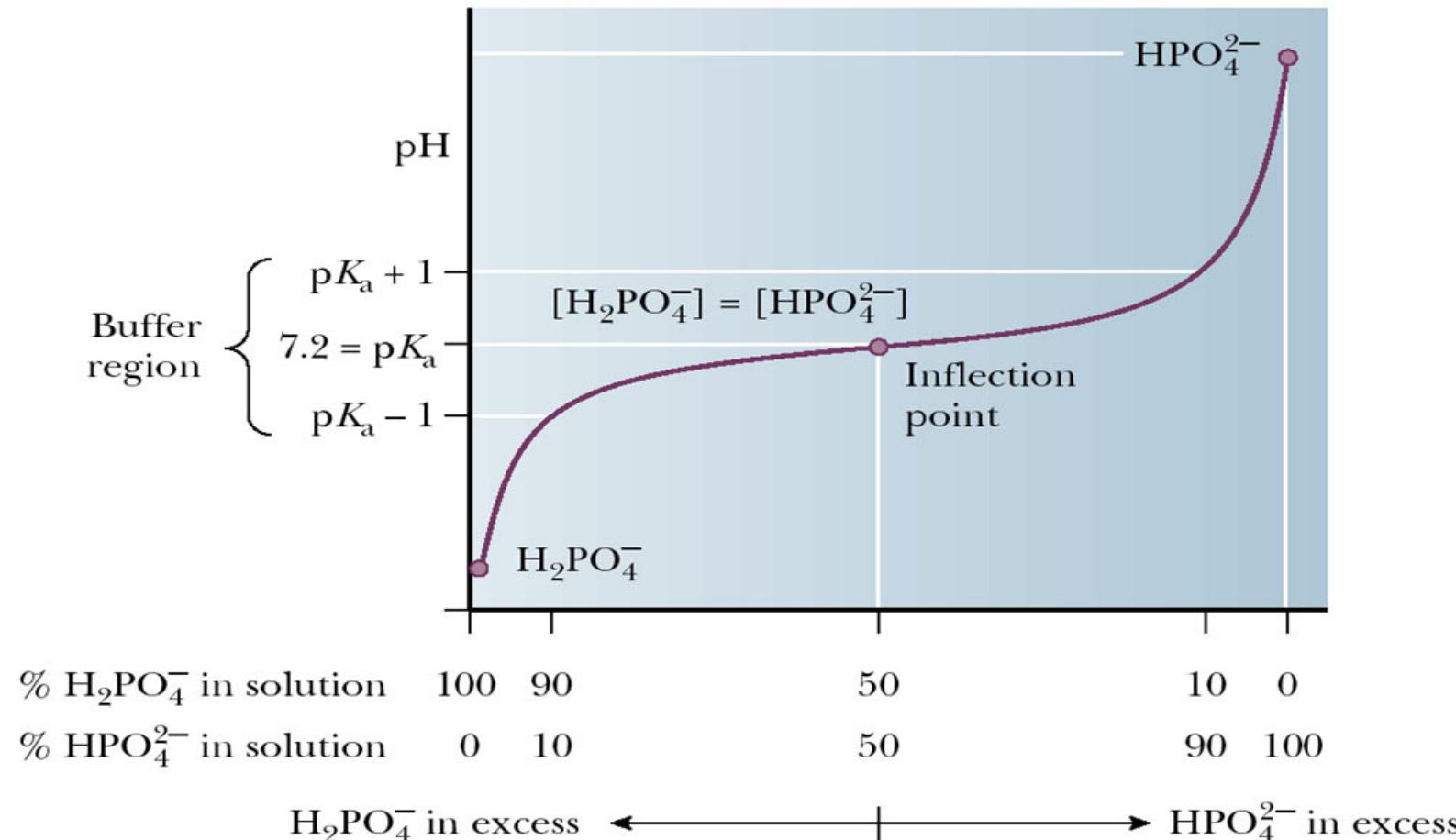
Buffers

- Buffer solutions is characterized by their tendency to resist a change in pH on the addition of relatively small amounts of acid or base
- The control of pH by buffers depends on the fact that their compositions reflect the acid/base concentration ratio in the region of the titration curve in which there is little change in pH.
- **Consists of a weak acid and its conjugate base**
- **Buffers can only be used effectively within one pH unit of their pKa.**



The relationship between the titration curve and buffering action in H_2PO_4^- :

The titration curve of H_2PO_4^- , showing the buffer region for the $\text{H}_2\text{PO}_4^-/\text{HPO}_4^{2-}$ pair.



The relationship between the titration curve and buffering action in H_2PO_4^-

Relative abundance of H_2PO_4^- and HPO_4^{2-} :

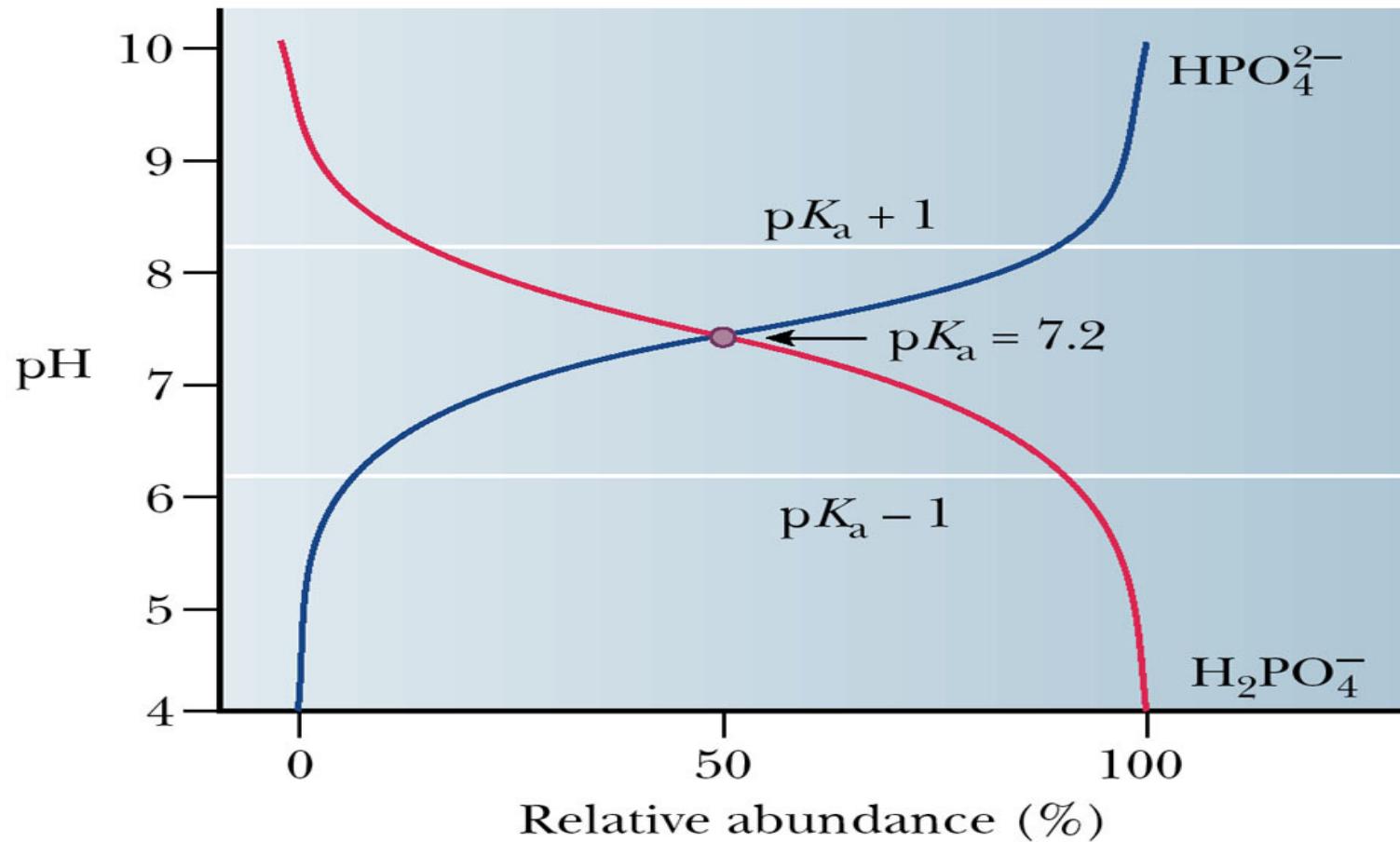
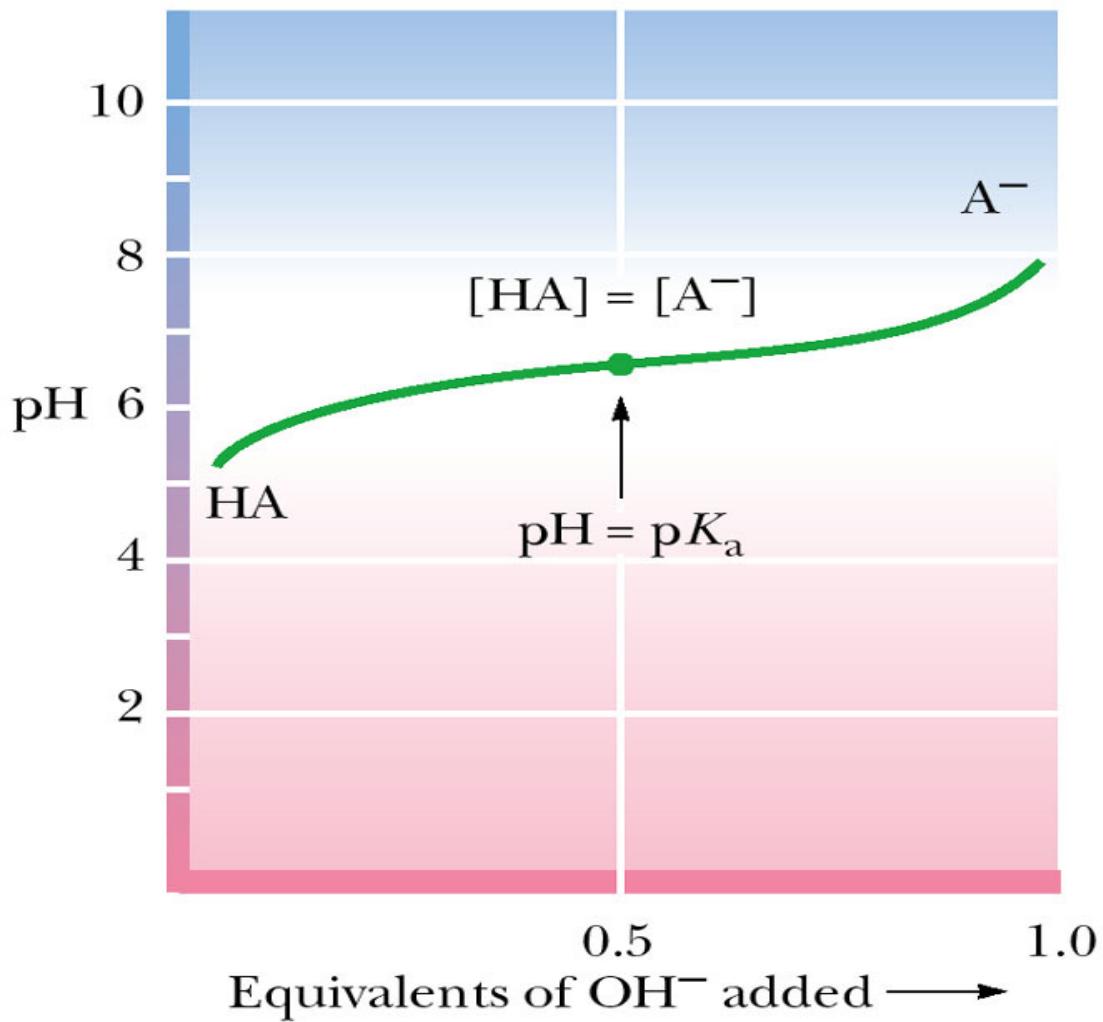


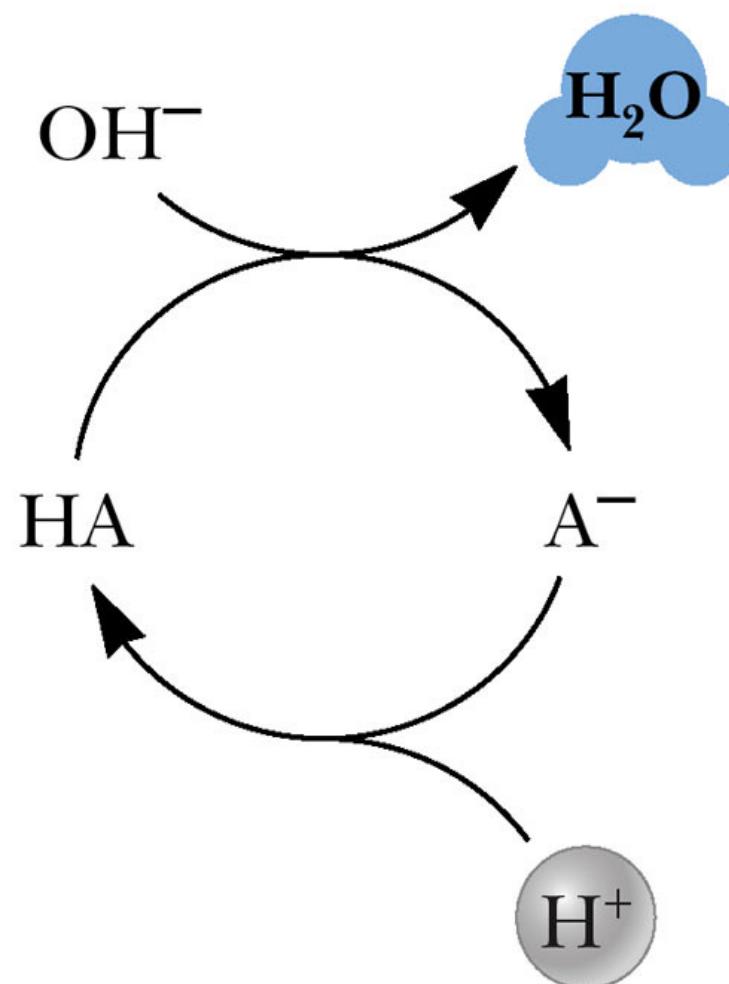
Table 2.7**pH Values and Base/Acid Ratios for Buffers**

If the pH equals	The ratio of base form/acid form equals
$pK_a - 3$	1/1000
$pK_a - 2$	1/100
$pK_a - 1$	1/10
pK_a	1/1
$pK_a + 1$	10/1
$pK_a + 2$	100/1
$pK_a + 3$	1000/1

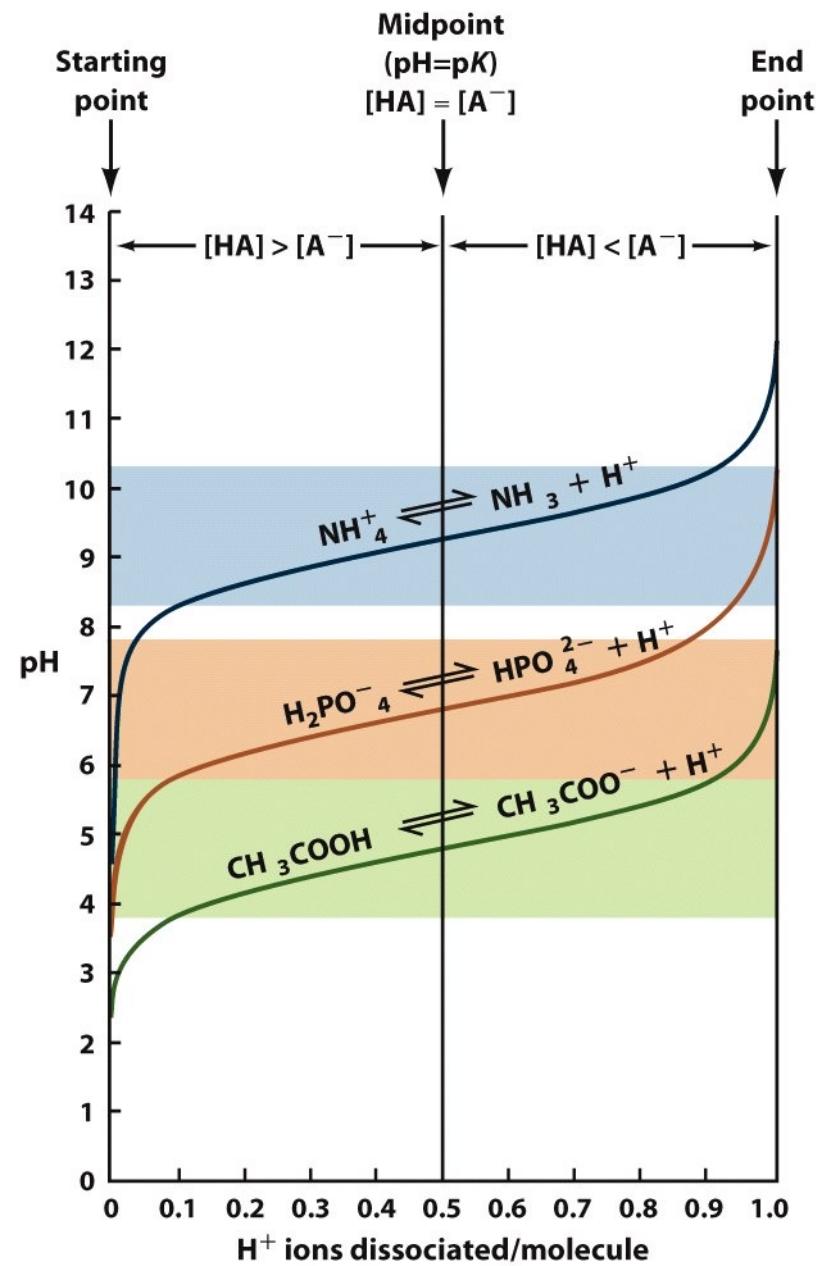


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Buffer action:



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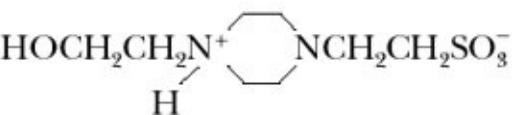
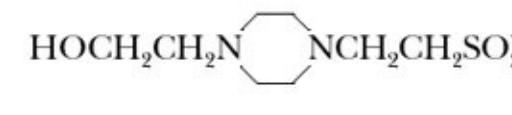
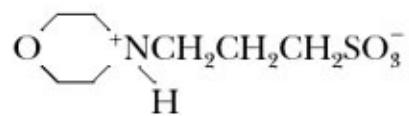
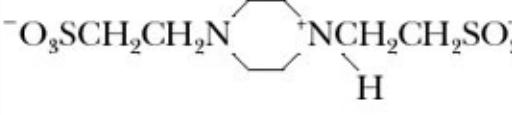
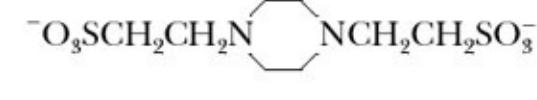


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Figure 2-17

Table 2.8

Acid and Base Forms of Some Useful Biochemical Buffers

Acid Form		Base Form	pK_a
TRIS—H ⁺ (protonated form) (HOCH ₂) ₃ CNH ₃ ⁺	N— <i>tris</i> [hydroxymethyl]aminomethane (TRIS)	TRIS (free amine) (HOCH ₂) ₃ CNH ₂	8.3
^-TES—H ⁺ (zwitterionic form) (HOCH ₂) ₃ CNH ₂ CH ₂ CH ₂ SO ₃ ⁻	N— <i>tris</i> [hydroxymethyl]methyl-2-aminoethane sulfonate (TES)	^-TES (anionic form) (HOCH ₂) ₃ CNHCH ₂ CH ₂ SO ₃ ⁻	7.55
^-HEPES—H ⁺ (zwitterionic form) 	N—2—hydroxyethylpiperazine-N'-2-ethane sulfonate (HEPES)	^-HEPES (anionic form) 	7.55
^-MOPS—H ⁺ (zwitterionic form) 	3—[N—morpholino]propane-sulfonic acid (MOPS)	^-MOPS (anionic form) 	7.2
²⁻ PIPERES—H ⁺ (protonated dianion) 	Piperazine—N,N'-bis[2-ethanesulfonic acid] (PIPERES)	²⁻ PIPERES (dianion) 	6.8