Lecture 2 (9/9/24)

- Reading for today: Ch2, 43-53
  Ch2, 53-64
- Homework #2 & #3

NEXT

- Reading: Ch3, 70
  Ch1, 13-19
  Ch4, 106-107
- Homework #4

OUTLINE

WATER
    Properties
    The 4 S's
        Shape
        Size
        Solubility
            Hydrogen Bond
            Properties explained

Molecular Forces Important for Life
    Other Electrostatic interactions
        Salt bridges
        van der Waals Forces (Dispersion or induced dipole–induced dipole)
    Hydrophobic Effect
    – Consequences
        Stability (pH); Last of 4 S's

Quantifying Thermodynamics

For Free Energy, ΔG: **Ice** $\rightleftharpoons$ **Water**

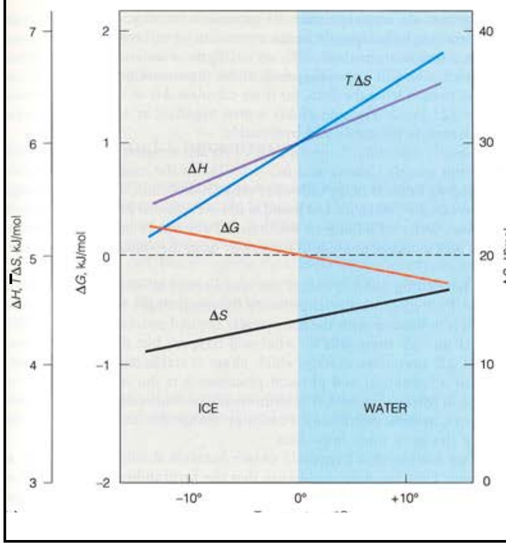
Magnitude of ΔG depends on:

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

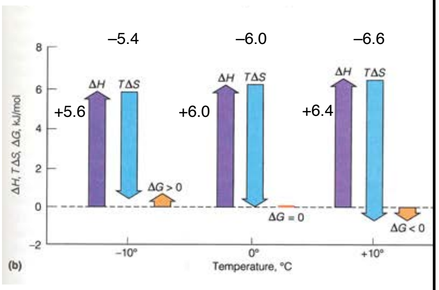
- ΔH—total energy added ($\Delta H > 0$) or released ($\Delta H < 0$); can be related to bonds
- ΔS—change in entropy, more randomness ($\Delta S > 0$) or more order ($\Delta S < 0$); Positive changes in entropy make ΔG more negative. Negative changes in entropy make ΔG more positive.

Quantifying Thermodynamics

The interplay of enthalpy and entropy in the simple ice/water reaction, as a function of the temperature:



Ice ⇌ Water



Properties of Water

1) Water has a high boiling point and relatively low melting point; its range in the liquid state is large
2) The heat of vaporization is high (more heat to change to vapor state than to raise temperature of the liquid state)
3) Liquid is more dense than the solid (e.g., most metals and other substances the solid is more dense)
4) High viscosity relative to its molecular weight (MW)
5) High surface tension

WATER

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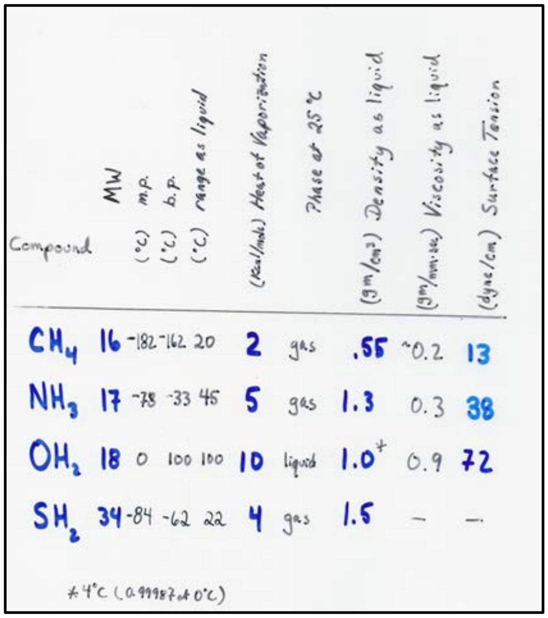
Properties of Water



Compound	MW	(°C) m.p.	(°C) b.p.	(°C) range as liquid	(Kcal/mole) Heat of Vaporization	Phase at 25 °C	(gm/cm³) Density as liquid	(gm/mm·sec) Viscosity as liquid	(dyne/cm) Surface Tension
CH_4	16	-182	-162	20	2	gas	.55	~0.2	13
NH_3	17	-78	-33	45	5	gas	1.3	0.3	38
OH_2	18	0	100	100	10	liquid	1.0*	0.9	72
SH_2	34	-84	-62	22	4	gas	1.5	–	–

* 4°C (0.99987 at 0°C)

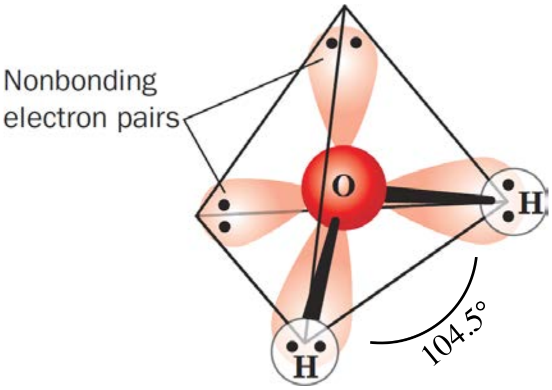
WATER

The 4 S's for Water:
  Shape
  Size
  Solubility
  Stability

Most of the properties of water are explained or due to its shape, in other words, its structure

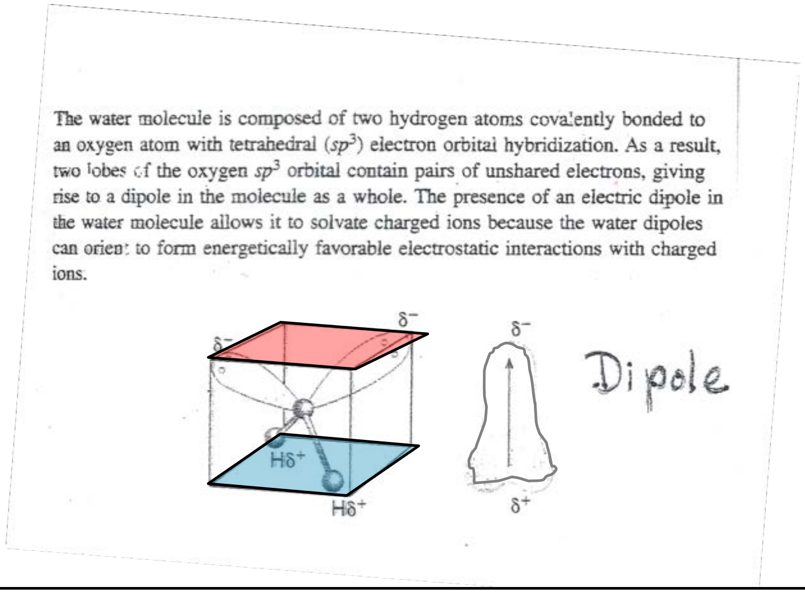
Shape of Water

- sp^3 hybridized orbitals:
  - 2 are bonding
  - 2 are filled non-bonding
- Distorted tetrahedral (equal angles of 109.5°): due to repulsion of electrons in filled orbitals



Shape of Water

Permanent DIPOLE



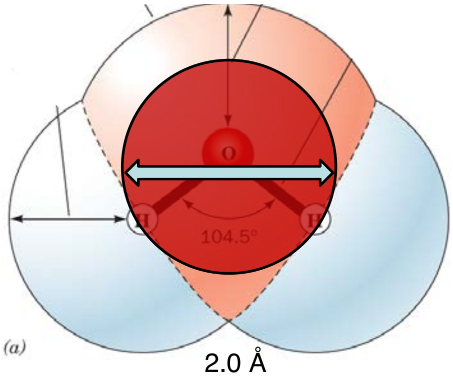
The water molecule is composed of two hydrogen atoms covalently bonded to an oxygen atom with tetrahedral (sp^3) electron orbital hybridization. As a result, two lobes of the oxygen sp^3 orbital contain pairs of unshared electrons, giving rise to a dipole in the molecule as a whole. The presence of an electric dipole in the water molecule allows it to solvate charged ions because the water dipoles can orient to form energetically favorable electrostatic interactions with charged ions.

Size of Water

Very compact structure:

2.0 Å in diameter though van der Waals diameter of oxygen atom is 2.8 Å

The O–H bond is relatively short (0.96 Å) though van der Waals diameter of hydrogen atom is 2.4 Å



What are these discrepancies due to?

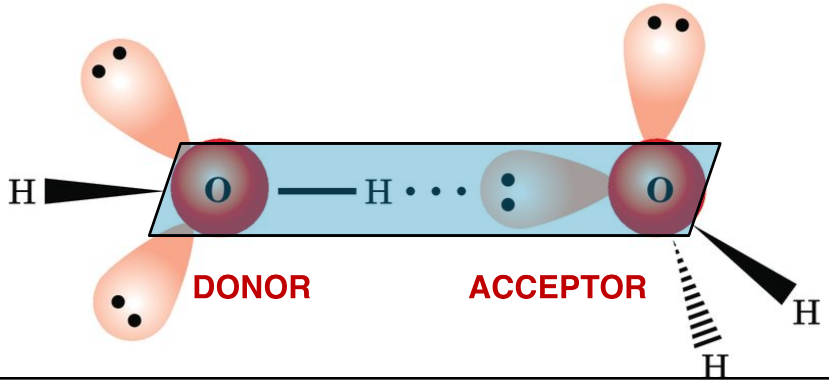
ELECTRONEGATIVITY OF OXYGEN

Solubility of Water: Hydrogen Bonding

These dipoles interact with each other in a special kind of non-covalent bond: **THE HYDROGEN BOND**.

Bit of a misnomer but named as such because it appears though two oxygen atoms of two water molecules share a hydrogen

Its not at all equal: the water with the covalent bond to hydrogen is called the DONOR. The opposite water molecule is called the ACCEPTOR



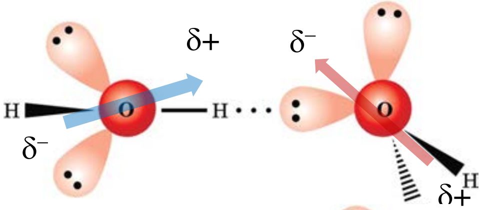
Solubility of Water: Hydrogen Bonding

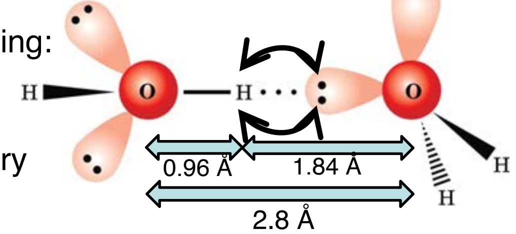
THREE important aspects that make H-bonds unique:

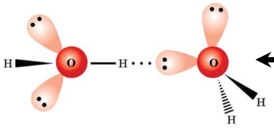
1) Electrostatic: dipole-dipole interaction

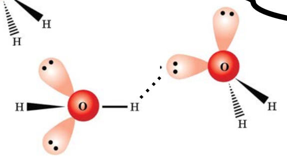
2) Partial electron sharing: partial covalency

3) Directional: geometry





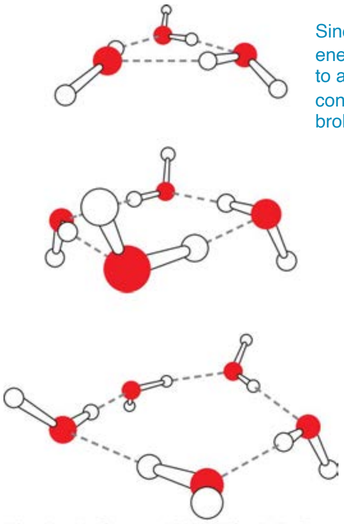




This is a stronger bond than this (due to optimizing the covalency)

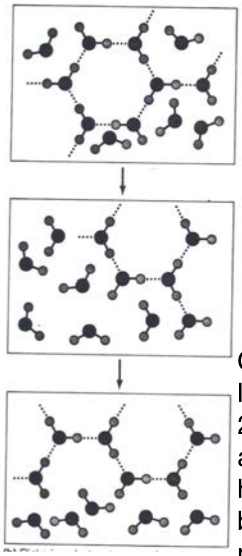
Rings of Water Molecules

“Flickering Clusters” of Water Molecules



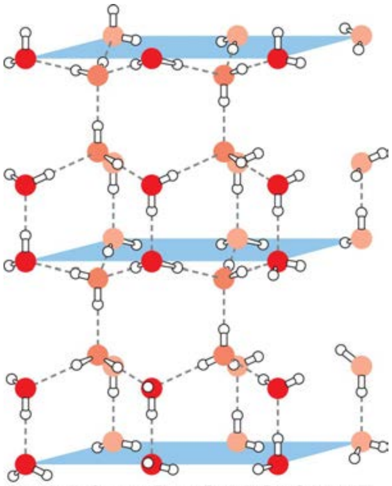
After Liu, K., Cruzan, J.D., and Saykally, R.J., Science 271, 929 (1996).

Since one H-bond is energetically equivalent to another, they are constantly being broken and made

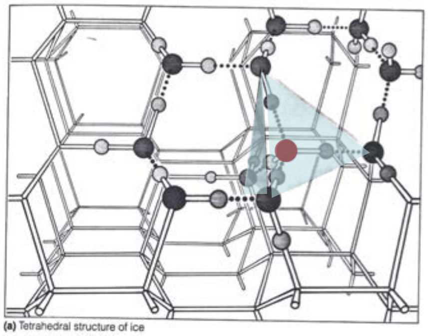


On average, liquid water at 25 °C has about 3.5 hydrogen bonds per molecule

Structure of Ice



After Liu, K., Cruzan, J.D., and Saykally, R.J., Science 271, 929 (1996).



(a) Tetrahedral structure of ice

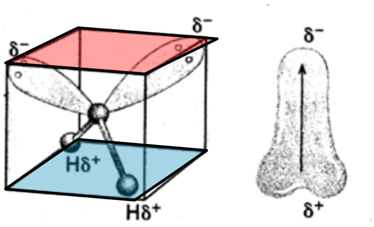
FIGURE **2.10**

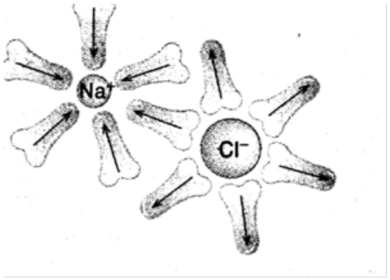
Water as a molecular lattice. **(a)** The structure of ice. Ice is a molecular lattice formed by indefinite repetition of a tetrahedral hydrogen-bonding pattern. Each molecule acts as a donor to two others and as an acceptor from two others. Because of the length of the hydrogen bonds, the structure is a relatively open one, which accounts for the low density of ice. **(b)** The structure of liquid water. When ice melts, the regular tetrahedral lattice is broken, but substantial portions of it remain, especially at low temperatures. In liquid water, flickering clusters of molecules are held together by hydrogen bonds that continually break and re-form. In this schematic "motion picture," successive frames represent changes occurring in picoseconds (10^{-12} s).

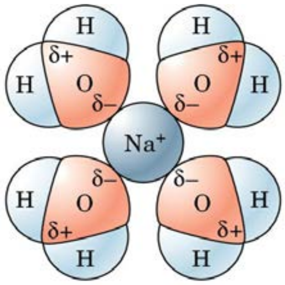
Properties of Water – explained

1) Water has a high boiling point and relatively low melting point; its range in the liquid state is large
2) The heat of vaporization is high
   - *Ave number of H-bonds in liquid water is ~3.5, but in steam ~0*
3) Liquid is more dense than the solid
   - *Ave number of H-bonds in liquid water is ~3.5, but in ice its 4, but the tetrahedral-like geometry takes over*
4) High viscosity relative to its molecular weight (MW)
   - *liquid water with ~3.5 H-bonds/molecule is sticky*
5) High surface tension
6) Water is also a great SOLVENT

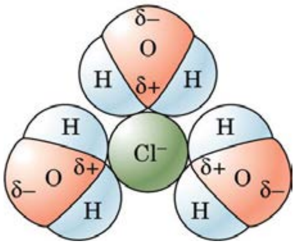
Solvation of Ions





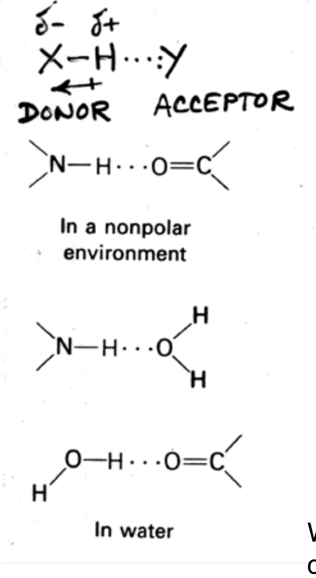


Cations



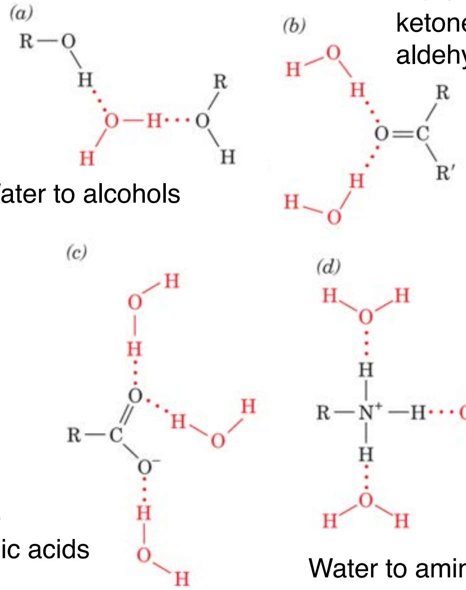
Anions

Hydrogen Bonding of Polar Molecules with and without Water



In a nonpolar environment

In water



Water to alcohols

Water to ketones/ aldehydes

Water to carboxylic acids

Water to amines

Typical Bond Energies

TABLE 2-1 Bond Energies in Biomolecules

Type of Bond	Example	Typical Bond Energy (kJ · mol^{-1})	(kcal · mol^{-1})
Covalent	O—H	460	~95
	C—H	414	
	C—C	348	
Noncovalent			
Hydrogen bond	—O—H···O<	20	4.7

WATER

The 4 S's for Water:

- ✓ Shape
- ✓ Size
- ✓ Solubility
- Stability

Before we discuss the 4th "S" of water, we need to take an important tangent and discuss the other **very important** non-covalent forces that operate constantly on macromolecules

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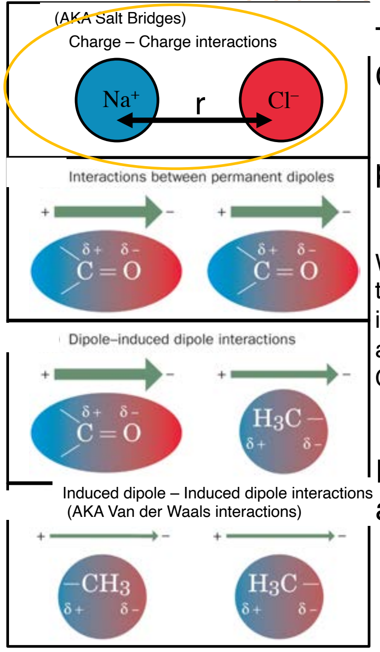
Molecular Forces Important for Life

The 4 **NON-covalent** "bonds":

- H-bonds
- Salt bridges } Electrostatic
- van der Waal's interactions
- Hydrophobic effect

Electrostatic Interactions



The strength of all these is governed by Coulomb's Law:

Force between two charged particles = $\dfrac{k\, q_1 q_2}{D\, r^2}$

Where **q** is the charge on each particle 1 and 2, **D** is the dielectric constant (unit-less; =1.0 in vacuum, ~80 in water), **r** is the distance between the two charges, and k is Coulomb's constant (9×10^9 J·m/C^2, where C=1.6×10^{-19} electron charges)

Recalling the relationship between Force and Energy (E = Force x distance (r)):

$$E = \frac{k\, q_1 q_2}{D\, r}$$

Salt Bridges

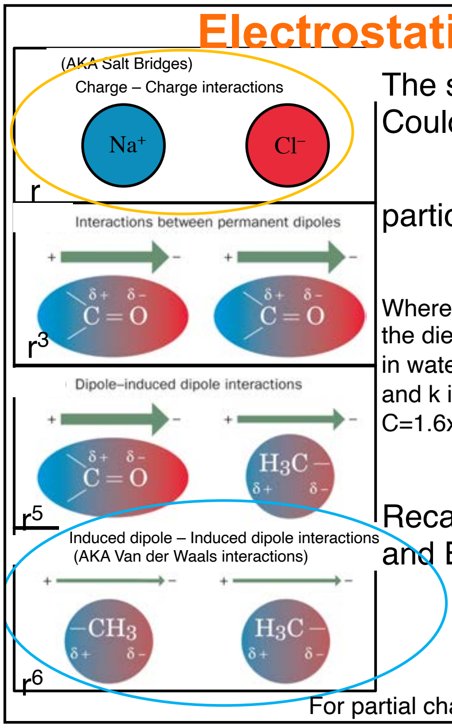
Molecular Forces Important for Life

The 4 **NON-covalent** bonds:

- ✓ H-bonds
- ✓ Salt bridges
- van der Waal's interactions
- Hydrophobic effect

} Electrostatic

Electrostatic Interactions



(AKA Salt Bridges)
Charge – Charge interactions

Interactions between permanent dipoles

Dipole–induced dipole interactions

Induced dipole – Induced dipole interactions
(AKA Van der Waals interactions)

The strength of all these is governed by Coulomb's Law:

Force between two charged particles = $\frac{k\, q_1 q_2}{D\, r^2}$

Where **q** is the charge on each particle 1 and 2, **D** is the dielectric constant (unit-less; =1.0 in vacuum, ~80 in water), **r** is the distance between the two charges, and k is Coulomb's constant ($9\text{x}10^9$ J·m/C^2, where C=$1.6\text{x}10^{-19}$ electron charges)

Recalling the relationship between Force and Energy (E = Force x distance (r)):

$$E = \frac{k\, q_1 q_2}{D\, r} \qquad E = \frac{k\, q_1 q_2}{D\, r^6}$$

For partial charges, this distance dependence is exponential

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van der Waals Interactions

Induced dipole – Induced dipole interactions
(AKA Van der Waals interactions)

$$E = \frac{k\, q_1 q_2}{D\, r^6}$$

But, as the energy is so dependent on distance, even when at r_0, its VERY weak.

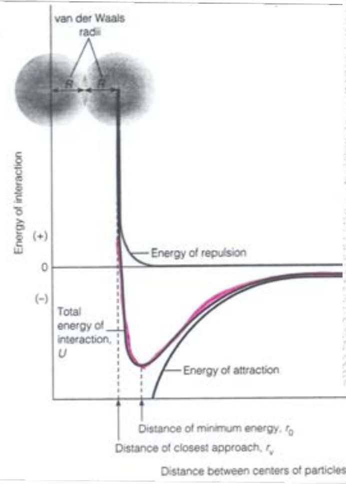


FIGURE 2.6

Noncovalent interaction energy of two approaching particles. The interaction energy of two atoms, molecules, or ions is graphed versus the distance between their centers, *r*. The total interaction energy (*U*) at any distance is the sum of the energy of attraction and the energy of repulsion. As the distance between the particles decreases (reading *right to left* along the *x*-axis), both the attractive energy (–) and the repulsive energy (+) increase, but at different rates. At first the longer-range attraction dominates, but then the repulsive energy increases so rapidly that it acts as a barrier, defining the distance of closest approach (r_v) and the van der Waals radii (*R*). The position of minimum energy (r_0) is usually very close to r_v.

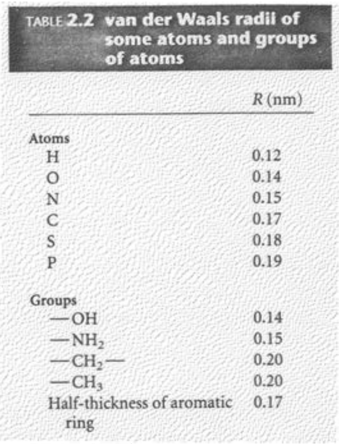


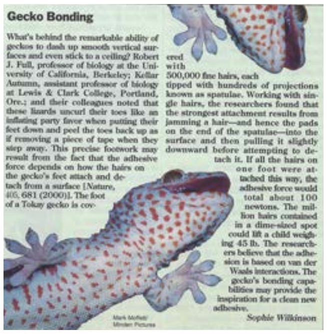
TABLE 2.2 **van der Waals radii of some atoms and groups of atoms**

	R (nm)
Atoms	
H	0.12
O	0.14
N	0.15
C	0.17
S	0.18
P	0.19
Groups	
—OH	0.14
—NH_2	0.15
—CH_2—	0.20
—CH_3	0.20
Half-thickness of aromatic ring	0.17

10 Å / 1 nm

van der Waals Interactions

van der Waals Interactions

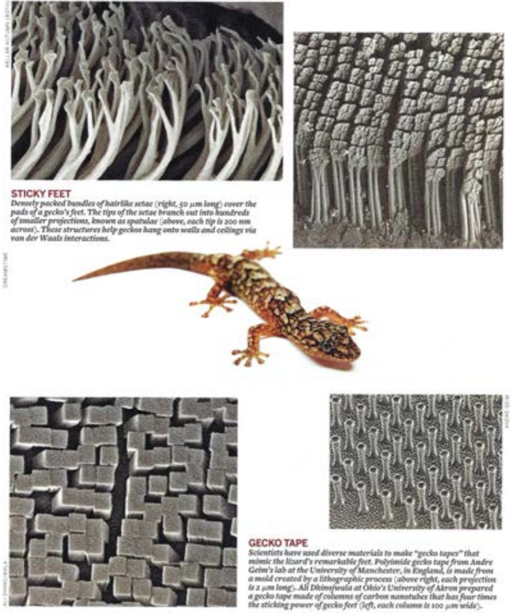


Gecko Bonding

What's behind the remarkable ability of geckos to dash up smooth vertical surfaces and even stick to a ceiling? Robert J. Full, professor of biology at the University of California, Berkeley; Kellar Autumn, assistant professor of biology at Lewis & Clark College, Portland, Ore.; and their colleagues noted that these lizards uncurl their toes like an inflating party favor when putting their feet down and peel the toes back up as if removing a piece of tape when they step away. This precise footwork may result from the fact that the adhesive force depends on how the hairs on the gecko's feet attach and detach from a surface [*Nature*, 405, 681 (2000)]. The foot of a Tokay gecko is covered with 500,000 fine hairs, each tipped with hundreds of projections known as spatulae. Working with single hairs, the researchers found that the strongest attachment results from jamming a hair—and hence the pads on the end of the spatulae—into the surface and then pulling it slightly downward before attempting to detach it. If all the hairs on one foot were attached this way, the adhesive force would total about 100 newtons. The million hairs contained in a dime-sized spot could lift a child weighing 45 lb. The researchers believe that the adhesion is based on van der Waals interactions. The gecko's bonding capabilities may provide the inspiration for a clean new adhesive.

Sophie Wilkinson

Mark Moffett/
Minden Pictures



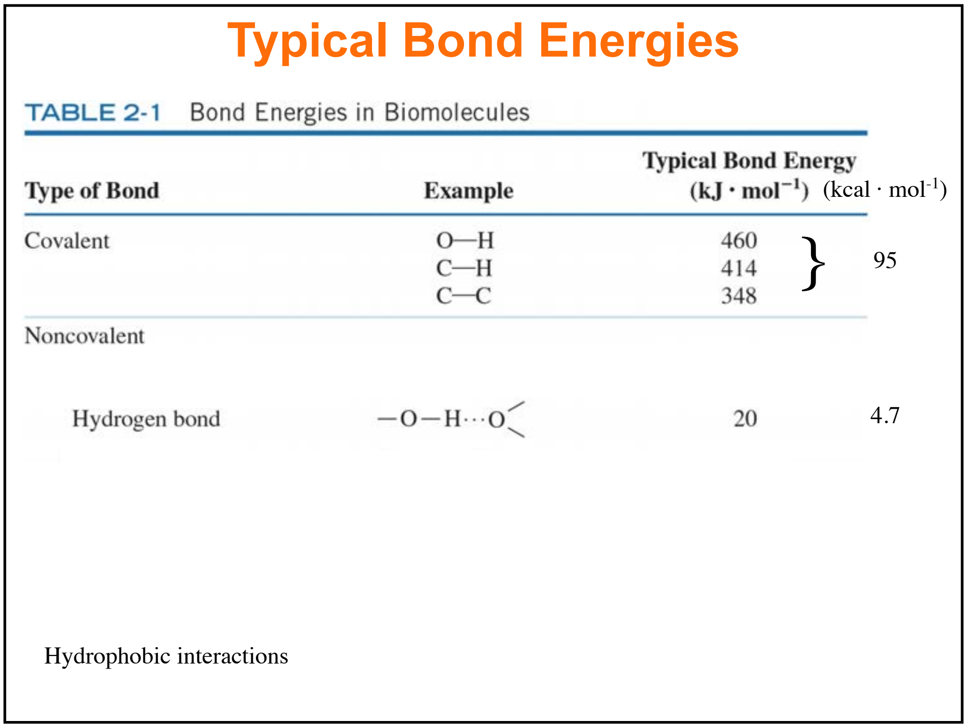
STICKY FEET

Densely packed bundles of hairlike setae (right, 50 µm long) cover the pads of a gecko's feet. The tips of the setae branch out into hundreds of smaller projections, known as spatulae (above, each tip is 200 nm across). These structures help geckos hang onto walls and ceilings via van der Waals interactions.

GECKO TAPE

Scientists have used diverse materials to make "gecko tapes" that mimic the lizard's remarkable feet. Polyimide gecko tape from Andre Geim's lab at the University of Manchester, in England, is made from a mold created by a lithographic process (above right, each projection is 2 µm long). Ali Dhinojwala at Ohio's University of Akron prepared a gecko tape made of columns of carbon nanotubes that has four times the sticking power of gecko feet (left, each column is 100 µm wide).

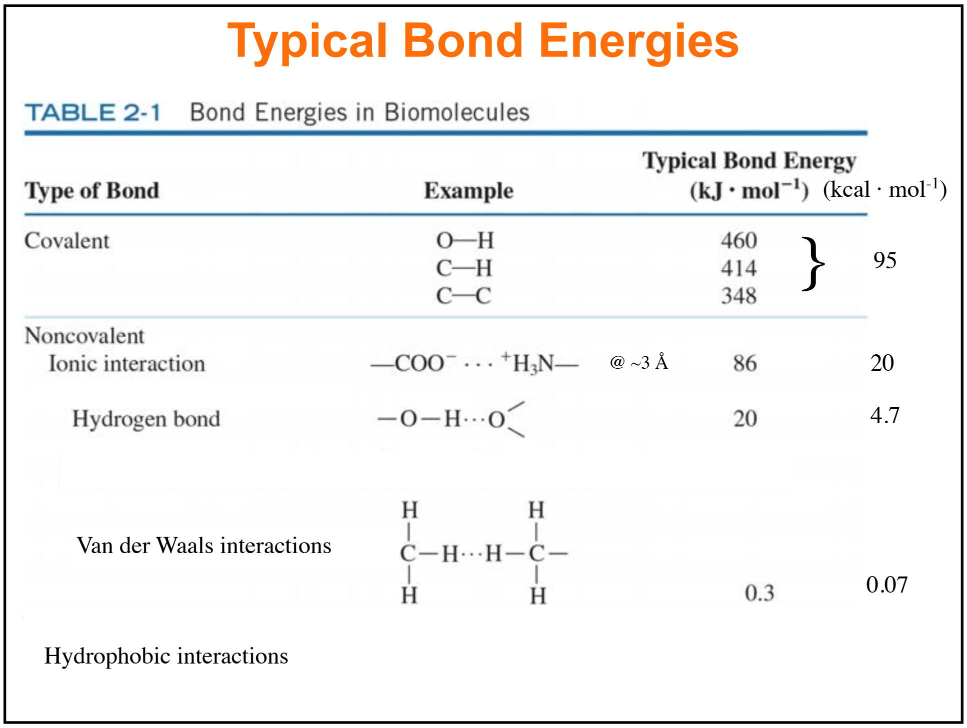
This is one example highlighting the issue of COMPLEMENTARITY, and why this is so important in biology



Typical Bond Energies

TABLE 2-1 Bond Energies in Biomolecules

Type of Bond	Example	Typical Bond Energy (kJ · mol^{-1})	(kcal · mol^{-1})
Covalent	O—H	460	95
	C—H	414	
	C—C	348	
Noncovalent			
Hydrogen bond	—O—H···O<	20	4.7
Hydrophobic interactions			



Typical Bond Energies

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	C—H	414	
	C—C	348	
Noncovalent			
Ionic interaction	—COO$^-$ · · · $^+$H$_3$N— @ ~3 Å	86	20
Hydrogen bond	—O—H···O<	20	4.7
Van der Waals interactions	$\overset{\text{H}}{\underset{\text{H}}{\text{C}}}\text{—H}\cdots\text{H—}\overset{\text{H}}{\underset{\text{H}}{\text{C}}}\text{—}$	0.3	0.07
Hydrophobic interactions			

Molecular Forces Important for Life

The 4 **NON-covalent** bonds:

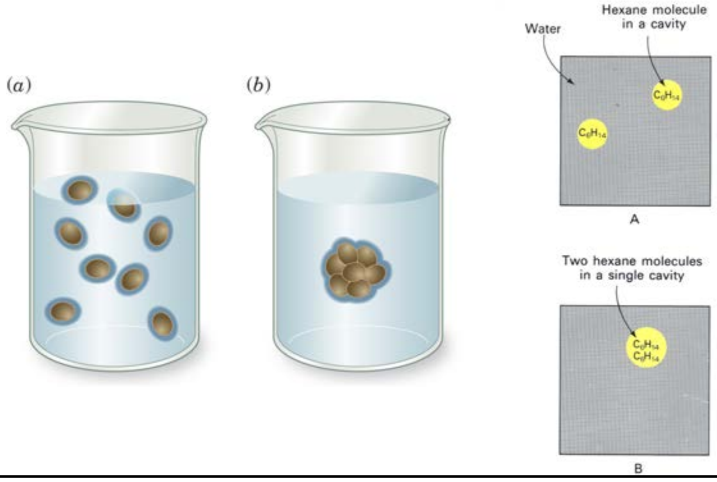
- ✓ H-bonds
- ✓ Salt bridges
- ✓ van der Waal's interactions
- Hydrophobic effect

} Electrostatic

Hydrophobic Interactions

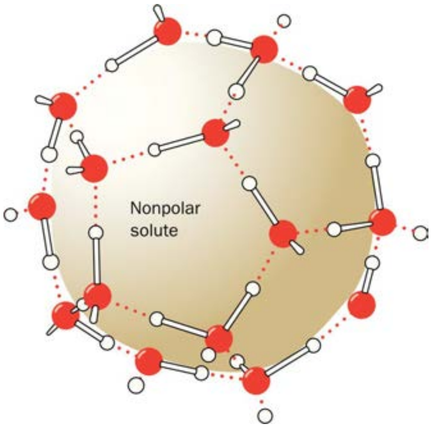
Hydrophobic interactions: atoms "attracted" together due to water structure.

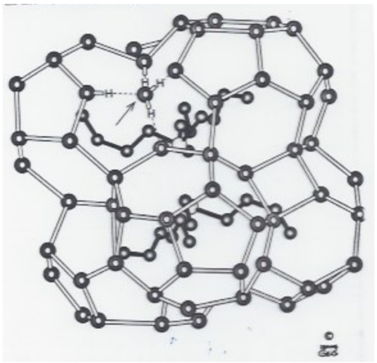
Nonpolar Solutes Aggregate in Water



Hydrophobic Interactions

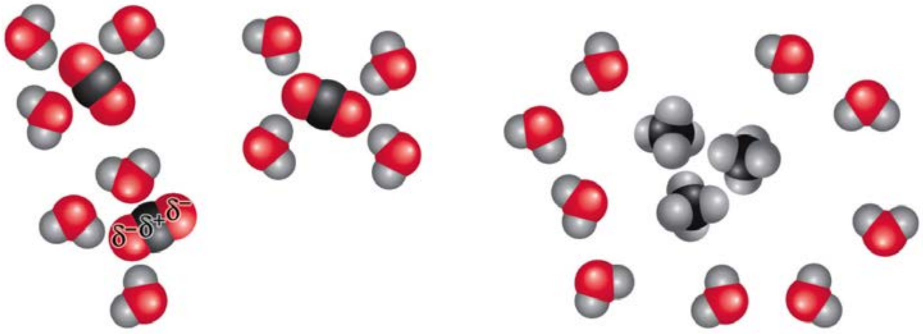
Structure: Nonpolar Solutes in Water





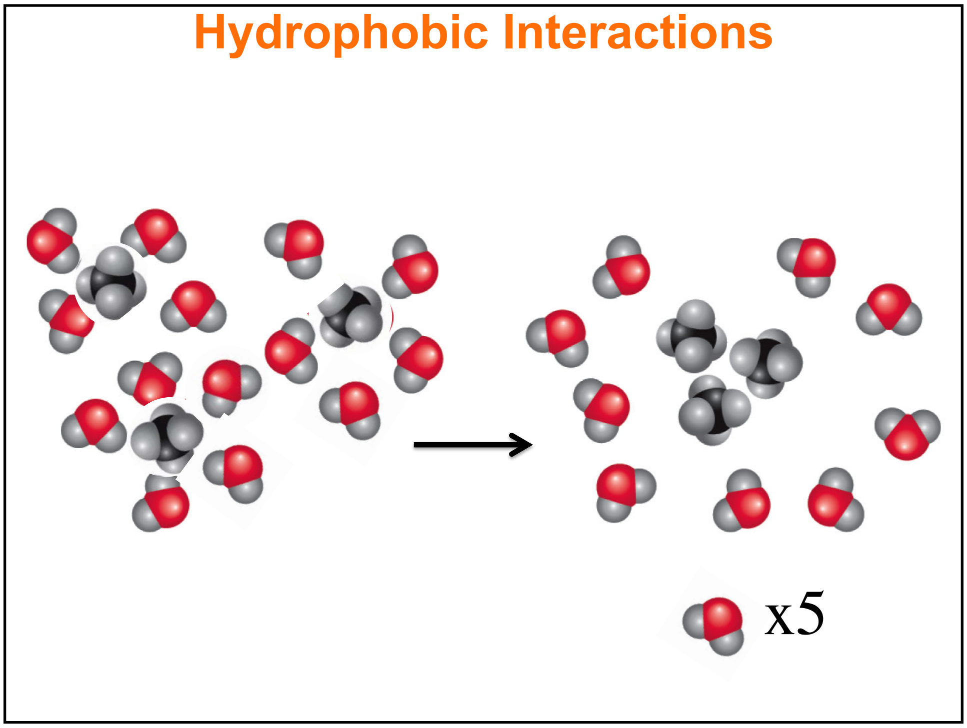
Like ICE

Hydrophilic versus Hydrophobic Interactions

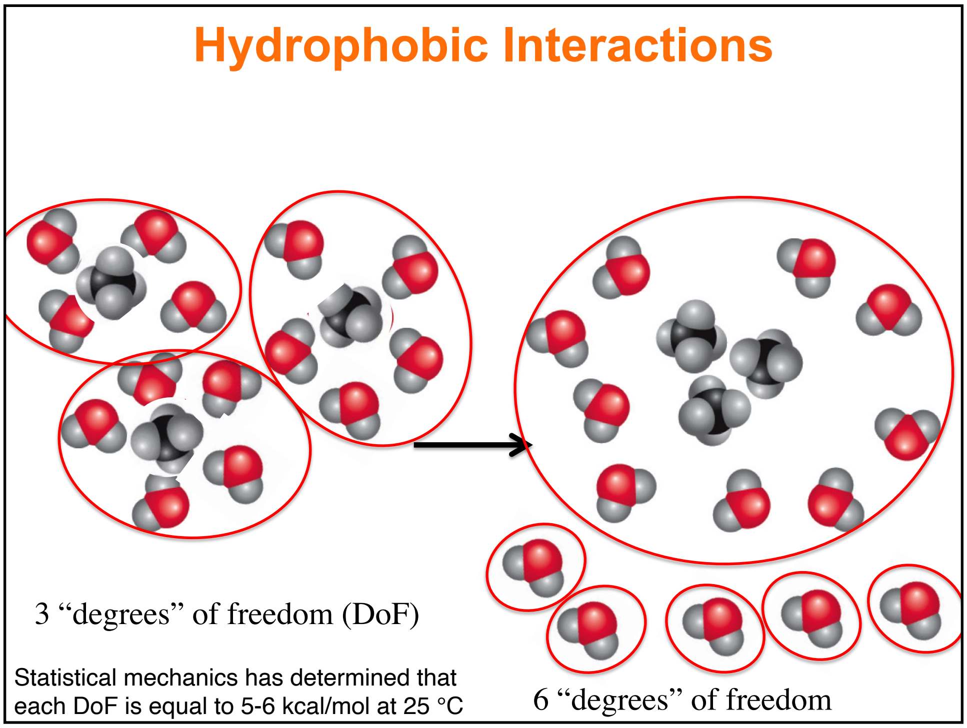


(A) Hydrophilic

(B) Hydrophobic



Hydrophobic Interactions



Hydrophobic Interactions

3 “degrees” of freedom (DoF)

Statistical mechanics has determined that each DoF is equal to 5-6 kcal/mol at 25 °C

6 “degrees” of freedom

Hydrophobic Interactions

For EXAMPLE

$$3\ [CH_4\cdot 10H_2O] \longrightarrow [(CH_4)_3\cdot 12H_2O] + 18H_2O$$

ΔG? definitely NEGATIVE: How?

Enthalpy
30 H_2O x 4 H-bonds each x 5 kcal/mol = 600 kcal/mol heat release to make H-bonds

Enthalpy
18 H_2O x 3.5 H-bonds each x 5 kcal/mol = 315 kcal/mol, **plus** 12 H_2O x 4 H-bonds x 5 = 240 kcal/mol; Total = 555 kcal/mol heat released to make bonds

ΔH = +45 kcal/mol added in excess to break H-bonds

$\Delta H = -555 - (-600)$
$= +45$

Entropy
3 degrees of freedom (DoF) x 6 kcal/mol at 25 °C per DoF = 18 kcal/mol

Entropy
19 degrees of freedom (DoF) x 6 kcal/mol at 25 °C per DoF = 114 kcal/mol

$T\Delta S = 114 - 18$
$= 96$

TΔS = +96 kcal/mol in entropic energy gained

$\Delta G = \Delta H - T\Delta S$
$= +45 - 96$
$= -51$ kcal/mol

ENTROPY DRIVEN

Hydrophobic Interactions

Transfer of Hydrocarbons to Nonpolar Solvents is Entropically Driven

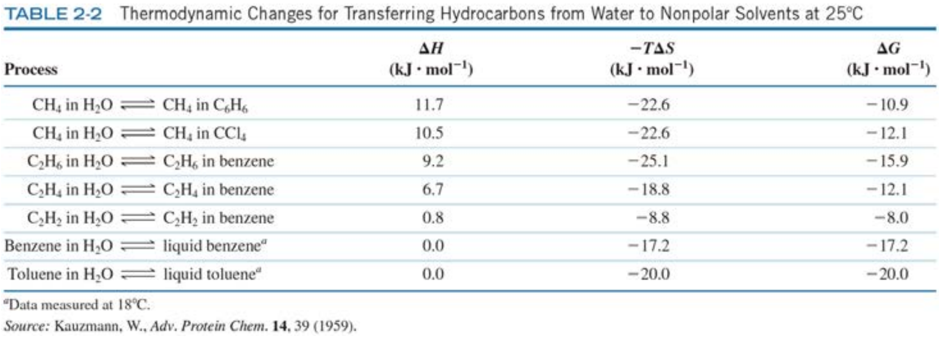


TABLE 2-2 Thermodynamic Changes for Transferring Hydrocarbons from Water to Nonpolar Solvents at 25°C

Process	ΔH (kJ · mol^{-1})	$-T\Delta S$ (kJ · mol^{-1})	ΔG (kJ · mol^{-1})
CH_4 in $H_2O \rightleftharpoons CH_4$ in C_6H_6	11.7	−22.6	−10.9
CH_4 in $H_2O \rightleftharpoons CH_4$ in CCl_4	10.5	−22.6	−12.1
C_2H_6 in $H_2O \rightleftharpoons C_2H_6$ in benzene	9.2	−25.1	−15.9
C_2H_4 in $H_2O \rightleftharpoons C_2H_4$ in benzene	6.7	−18.8	−12.1
C_2H_2 in $H_2O \rightleftharpoons C_2H_2$ in benzene	0.8	−8.8	−8.0
Benzene in $H_2O \rightleftharpoons$ liquid benzene[a]	0.0	−17.2	−17.2
Toluene in $H_2O \rightleftharpoons$ liquid toluene[a]	0.0	−20.0	−20.0

[a] Data measured at 18°C.

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

Note the bottom two: Reaction in reverse is the completely entropic positive values of +17-20 kJ/mol for putting benzene or toluene into water

Bond Energies of Important Non-covalent Interactions

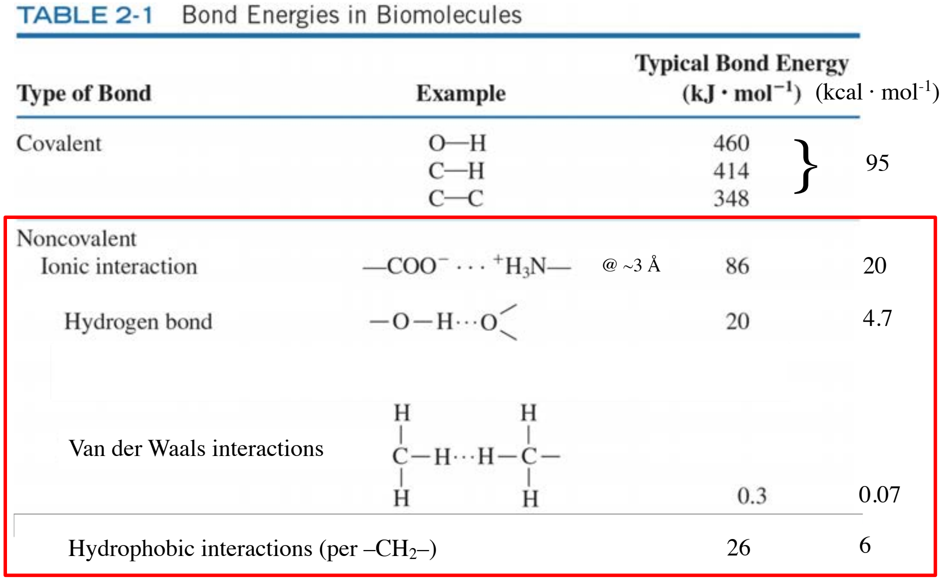


TABLE 2-1 Bond Energies in Biomolecules

Type of Bond	Example		Typical Bond Energy (kJ · mol^{-1})	(kcal · mol^{-1})
Covalent	O—H		460	95
	C—H		414	
	C—C		348	
Noncovalent				
Ionic interaction	$—COO^{-} \cdots {}^{+}H_3N—$	@ ~3 Å	86	20
Hydrogen bond	$-O-H\cdots O<$		20	4.7
Van der Waals interactions	$\overset{H}{\underset{H}{C}}-H\cdots H-\overset{H}{\underset{H}{C}}-$		0.3	0.07
Hydrophobic interactions (per $–CH_2–$)			26	6

Molecular Forces Important for Life

The 4 **NON-covalent** bonds:

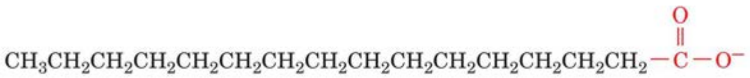
- ✓ H-bonds
- ✓ Salt bridges
- ✓ van der Waal's interactions
- ✓ Hydrophobic effect

} Electrostatic

Amphipathic Interactions

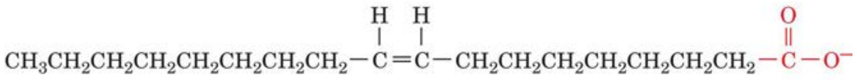
(both hydrophobic and hydrophilic)

Example: amphiphiles like Fatty Acid Anions, detergents



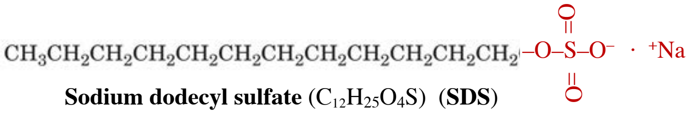
$$\mathrm{CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2}-\overset{\overset{\displaystyle O}{\|}}{C}-O^-$$

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



$$\mathrm{CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2}-\overset{\overset{\displaystyle H}{|}}{C}=\overset{\overset{\displaystyle H}{|}}{C}-\mathrm{CH_2CH_2CH_2CH_2CH_2CH_2CH_2}-\overset{\overset{\displaystyle O}{\|}}{C}-O^-$$

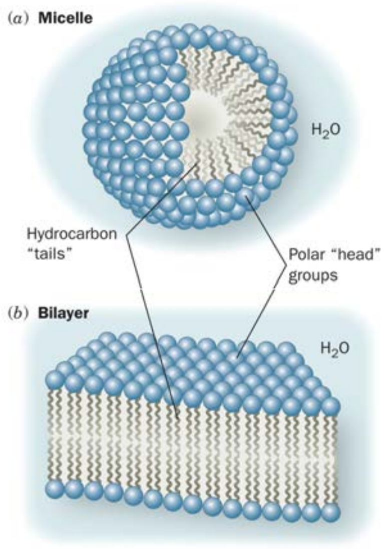
Oleate ($C_{17}H_{33}COO^-$)



$$\mathrm{CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2}-O-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle O}{\|}}{S}}-O^-\ \cdot\ {}^+Na$$

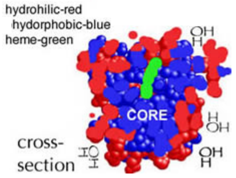
Sodium dodecyl sulfate ($C_{12}H_{25}O_4S$) (**SDS**)

Amphiphiles Form Micelles & Bilayers



Courtesy of Michael Garavito and Shelagh Ferguson-Miller, Michigan State University.

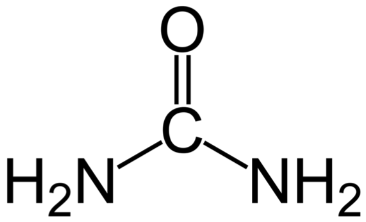
Structure of a Micelle



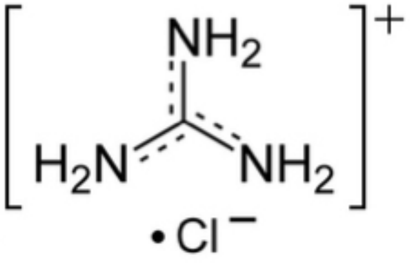
Protein interiors

Disrupters of the Hydrophobic Effect

Urea



Guanidinium-HCl



Physical Properties of Water

Learning Goals: Concepts about water

- Water molecules, which are polar, can form hydrogen bonds with other molecules.
- In ice, water molecules are maximally hydrogen bonded in a crystalline array, but in liquid water, still with many hydrogen bonds, they rapidly break and re-form in irregular networks.
- Polar and ionic substances can dissolve in water.
- The attractive forces acting on biological molecules include ionic interactions, hydrogen bonds, and van der Waals interactions.
- The hydrophobic effect explains the exclusion of nonpolar groups as a way to maximize the entropy of water molecules.
- Amphiphilic substances form micelles or bilayers that hide their hydrophobic groups while exposing their hydrophilic groups to water.

WATER

The 4 S's for Water:

- Shape ✓
- Size ✓
- Solubility ✓
- Stability

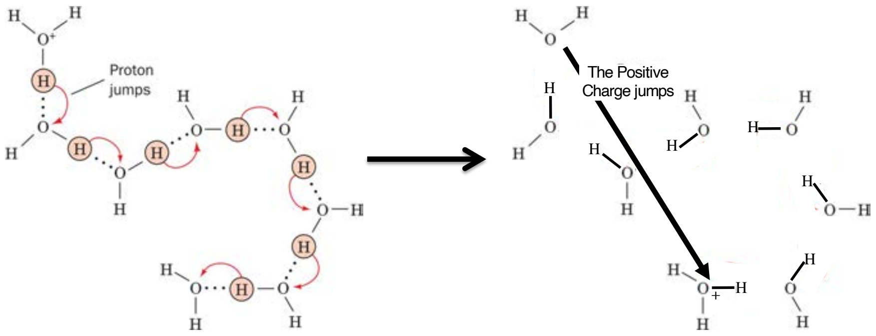
The discussion of water's stability is a discussion of its ionization.

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

$$2H_2O \leftrightarrows H_3O^+ + OH^-$$

Ionization of Water

Proton "Transfers" Occurs Rapidly



Proton "transfers" are very rapid!

$$2H_2O \leftrightarrows H_3O^+ + OH^-$$

What is the concentration of OH^- and H_3O^+ (protons)?

Ionization of Water

What is the concentration of OH^-?

$$2H_2O \leftrightarrows H_3O^+ + OH^-$$

Equilibrium constant for this acid dissociation (aka deprotonation) reaction

K_{eq} is 1.8×10^{-16} M

$$K_{eq} = 1.8 \times 10^{-16}\ \mathrm{M} = \frac{[H^+][OH^-]}{[H_2O]}$$

$[H_2O]1.8 \times 10^{-16}\ \mathrm{M} = [H^+][OH^-]$ $\quad [H_2O] = 55.5$ M*

$55.5\ \mathrm{M} \times 1.8 \times 10^{-16}\ \mathrm{M} = [H^+][OH^-]$ $\quad$ since $[H^+] = [OH^-]$

$55.5\ \mathrm{M} \times 1.8 \times 10^{-16}\ \mathrm{M} = [H^+]^2$

$1.0 \times 10^{-14}\ \mathrm{M}^2 = [H^+]^2$

$1.0 \times 10^{-7}\ \mathrm{M} = [H^+]$

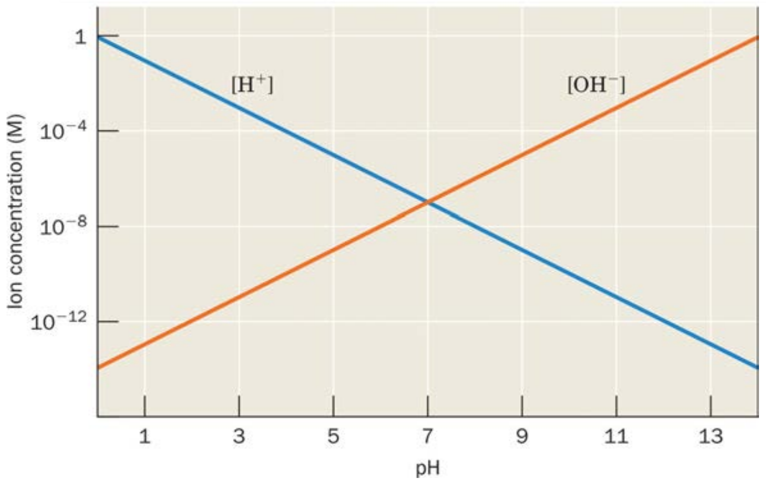
Take the **–log** of both sides:

$7 = \mathrm{pH}$ $\quad$ call the $-\log[H^+] = \mathrm{pH}$

*1 L water = 1000 g/L ÷ 18 g/mol = 55.5 M

Ionization of Water

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



$$2H_2O \leftrightarrows H_3O^+ + OH^-$$

Ionization of Water

pH Values of Common Substances

Substance	pH
1 M NaOH	14
Household ammonia	12
Seawater	8
Blood	7.4
Milk	7
Saliva	6.6
Tomato juice	4.4
Vinegar	3
Gastric juice	1.5
1 M HCl	0

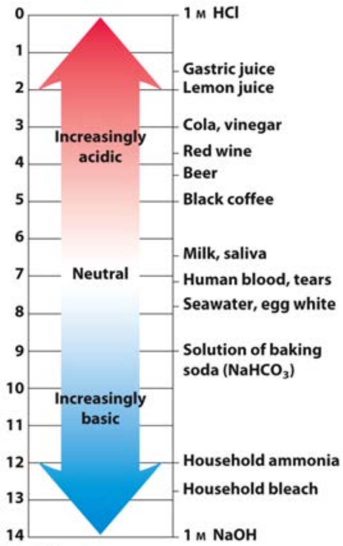


Figure 2-15
Lehninger Principles of Biochemistry, Seventh Edition
© 2017 W. H. Freeman and Company

Ionization of Water

Definitions of Acids and Bases:

$HA \leftrightarrows H^+ + A^-$ If dissociation is >water: ACID →

$HB \leftrightarrows H^+ + B^-$ If dissociation is <water: BASE ←

When B^- associates with protons, it leaves a net difference in $[OH^-]$

$$2H_2O \leftrightarrows H_3O^+ + OH^-$$

In other words: A proton donor is an Acid (HA)
A proton acceptor is a Base (B^-)

Likewise: The resulting anion from acid dissociation is called the conjugate base (A^-)
The resulting protonated base is called a conjugate acid (HB)

These are Bronsted/Lowry definitions used in Biochemistry

Ionization of Water

Definitions of Acids and Bases:

And the [HA] added is the [H+] in solution.

Strong Acid $HA \rightarrow H^+ + A^-$

Strong Base $H^+ + B^- \rightarrow HB$

Protons come from pulling the water dissociation equilibrium

$$2H_2O \rightleftarrows H_3O^+ + OH^-$$

And the [B–] added is the [OH–] in solution.

Weak Acid $HA \rightleftarrows H^+ + A^-$

Weak Base $HB \rightleftarrows H^+ + B^-$

For weak acids/bases, all 3 species are in measurable concentrations.

How do you calculate these concentrations and how are they related to the pH?

Ionization of Water

How do you calculate these concentrations and how are they related to the pH?

Use the Equilibrium Constant (K_{eq}) for the dissociation reaction

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

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

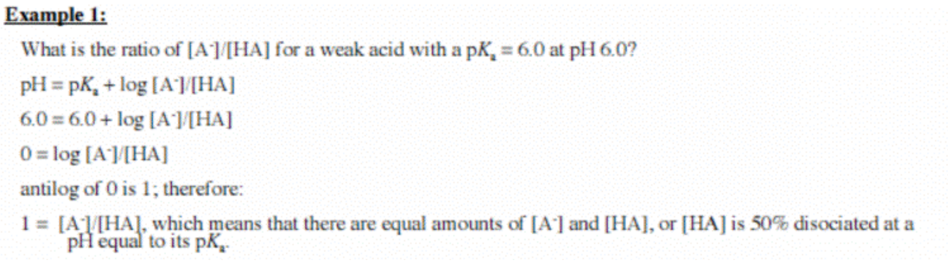
since [H+] is best expressed as pH, can take –log of each side:

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

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

This is called the **Henderson-Hasselbalch** equation

Ionization of Water



Example 1:

What is the ratio of $[A^-]/[HA]$ for a weak acid with a $pK_a = 6.0$ at pH 6.0?

$pH = pK_a + \log [A^-]/[HA]$

$6.0 = 6.0 + \log [A^-]/[HA]$

$0 = \log [A^-]/[HA]$

antilog of 0 is 1; therefore:

$1 = [A^-]/[HA]$, which means that there are equal amounts of $[A^-]$ and [HA], or [HA] is 50% disociated at a pH equal to its pK_a.

Ionization of Water

Dissociation Constants and pK_a Values of Some Acids

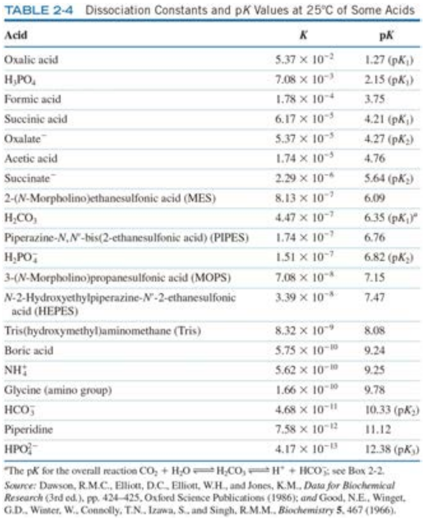


TABLE 2-4 Dissociation Constants and p*K* Values at 25°C of Some Acids

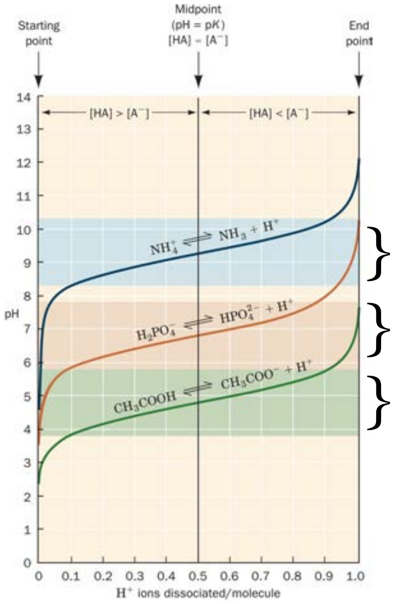
Acid	*K*	p*K*
Oxalic acid	5.37×10^{-2}	1.27 (pK_1)
H_3PO_4	7.08×10^{-3}	2.15 (pK_1)
Formic acid	1.78×10^{-4}	3.75
Succinic acid	6.17×10^{-5}	4.21 (pK_1)
Oxalate$^-$	5.37×10^{-5}	4.27 (pK_2)
⇨ Acetic acid	1.74×10^{-5}	4.76
Succinate$^-$	2.29×10^{-6}	5.64 (pK_2)
2-(*N*-Morpholino)ethanesulfonic acid (MES)	8.13×10^{-7}	6.09
H_2CO_3	4.47×10^{-7}	6.35 (pK_1)^a
Piperazine-*N*,*N*′-bis(2-ethanesulfonic acid) (PIPES)	1.74×10^{-7}	6.76
⇨ $H_2PO_4^-$	1.51×10^{-7}	6.82 (pK_2)
3-(*N*-Morpholino)propanesulfonic acid (MOPS)	7.08×10^{-8}	7.15
N-2-Hydroxyethylpiperazine-*N*′-2-ethanesulfonic acid (HEPES)	3.39×10^{-8}	7.47
Tris(hydroxymethyl)aminomethane (Tris)	8.32×10^{-9}	8.08
Boric acid	5.75×10^{-10}	9.24
⇨ NH_4^+	5.62×10^{-10}	9.25
Glycine (amino group)	1.66×10^{-10}	9.78
HCO_3^-	4.68×10^{-11}	10.33 (pK_2)
Piperidine	7.58×10^{-12}	11.12
HPO_4^{2-}	4.17×10^{-13}	12.38 (pK_3)

^{a}The p*K* for the overall reaction $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$; see Box 2-2.

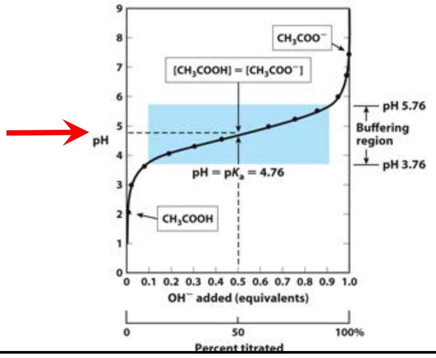
Source: Dawson, R.M.C., Elliott, D.C., Elliott, W.H., and Jones, K.M., *Data for Biochemical Research* (3rd ed.), pp. 424–425, Oxford Science Publications (1986); *and* Good, N.E., Winget, G.D., Winter, W., Connolly, T.N., Izawa, S., and Singh, R.M.M., *Biochemistry* **5**, 467 (1966).

Ionization of Water

Buffers: Titration Curves of Weak Acids



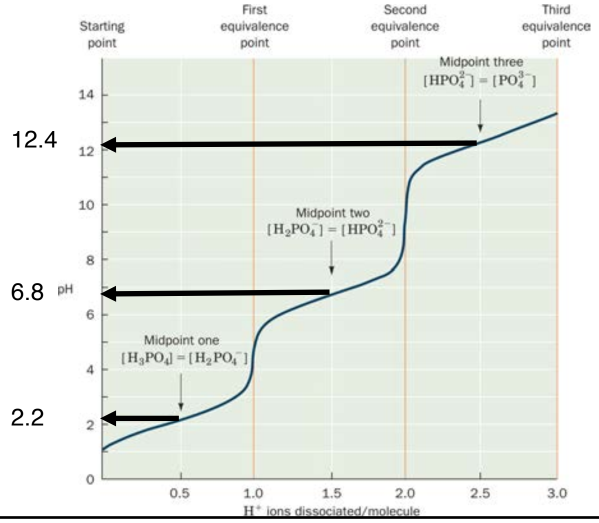
NOTICE: Adding protons, but pH not changing very much = BUFFER



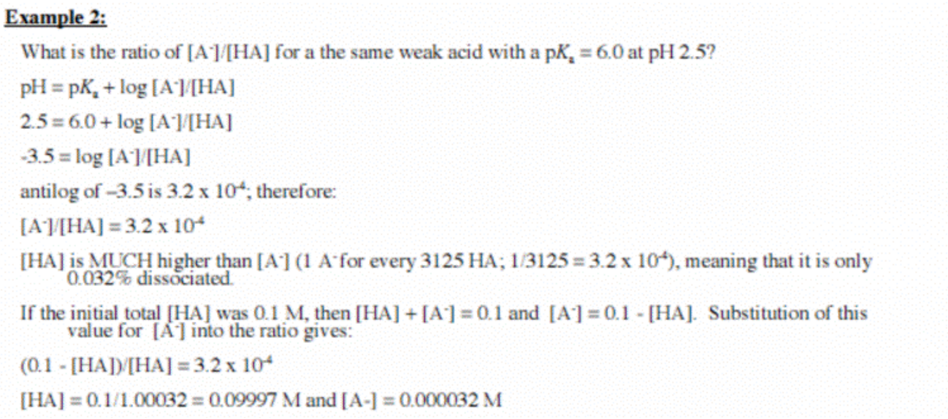
Ionization of Water

Buffers: Titration of a Polyprotic Acid

$$H_3PO_4 \underset{pK_1}{\leftrightarrows} H^+ + H_2PO_4^- \underset{pK_2}{\leftrightarrows} H^+ + HPO_4^{2-} \underset{pK_3}{\leftrightarrows} H^+ + PO_4^{3-}$$



Ionization of Water



Example 2:

What is the ratio of $[A^-]/[HA]$ for a the same weak acid with a $pK_a = 6.0$ at pH 2.5?

$pH = pK_a + \log [A^-]/[HA]$

$2.5 = 6.0 + \log [A^-]/[HA]$

$-3.5 = \log [A^-]/[HA]$

antilog of -3.5 is 3.2×10^{-4}; therefore:

$[A^-]/[HA] = 3.2 \times 10^{-4}$

$[HA]$ is MUCH higher than $[A^-]$ (1 A^- for every 3125 HA; $1/3125 = 3.2 \times 10^{-4}$), meaning that it is only 0.032% dissociated.

If the initial total $[HA]$ was 0.1 M, then $[HA] + [A^-] = 0.1$ and $[A^-] = 0.1 - [HA]$. Substitution of this value for $[A^-]$ into the ratio gives:

$(0.1 - [HA])/[HA] = 3.2 \times 10^{-4}$

$[HA] = 0.1/1.00032 = 0.09997$ M and $[A-] = 0.000032$ M

Does this make sense? …. Go back to the reaction:

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

At low pH, $[H^+]$ is high, forcing the equilibrium to the left = more HA, less A^-