1

Chem 352 - Lecture 2

Weak, Noncovalent Interactions in an Aqueous Environment

***Question of the Day**:"If non-covalent interactions are so weak, why are they so important to the creation, functioning, and maintenance of biological systems?"*

2

Introduction

Concept: *Weak, noncovalent interactions are critically important determinants of biomolecular structure, stability, and function.*

We will be focusing our attention on,

- Being able to describe and recognize the weak, noncovalent interactions.
- Being able to explain the role that water plays in influencing these interactions.
- As well as recognizing the role that *pH* plays in influencing these interactions.

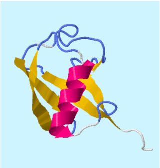
3

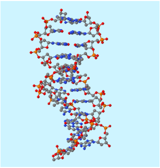
Importance of Noncovalent Interactions

4

Importance of Non-covalent Interactions

Here are a couple of examples of how weak, noncovalent interactions influence the structures of proteins and nucleic acids.


The protein ubiquitin


The nucleic acid B-DNA

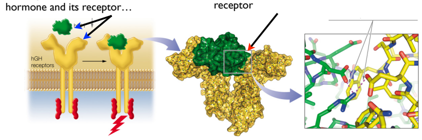
5

Importance of Non-covalent Interactions

And here is an example of how weak, noncovalent interactions influence the interactions between protein molecule.

Non-covalent interactions are involved in defining the structures of both the hormone and its receptor…

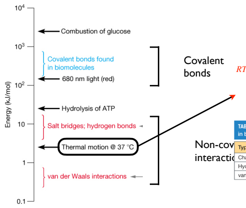
as well as the interactions that allow the hormone to bind specifically to its receptor



Human Growth Hormone (hGH) binding to its cell surface receptor and stimulating muscle growth

Importance of Non-covalent Interactions

A characteristic that distinguishes noncovalent interactions from covalent interactions (bonds) is the energy required to disrupt them.



Covalent bonds

$$RT = 8.314x10^{-3}\frac{kJ}{mol \bullet K}(37 + 273K)$$

$$= 2.5\frac{kJ}{mol}$$

Non-cov
interacti

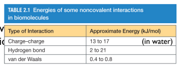


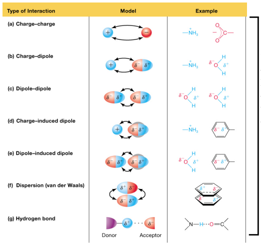
TABLE 2.1 Energies of some noncovalent interactions in biomolecules

Type of Interaction	Approximate Energy (kJ/mol)
Charge–charge	13 to 17 (in water)
Hydrogen bond	2 to 21
van der Waals	0.4 to 0.8

Types of Noncovalent Interactions

Types of Noncovalent Interactions

Types of Non-covalent Interactions



Concept: *Non-covalent interactions are fundamentally electrostatic in nature and can be described by Coulomb's law.*

δ+ = partial positive charge
δ- = partial negative charge

Types of Noncovalent Interactions

Charge-Charge Interactions

- Sometimes also called
  - An Ionic "Bond" in salts
  - or a Salt Bridge in biomolecules
- Couloumb's Law equation describes the force of interaction (*F*) between two charges, q_1 and q_2, which are separated by a distance of *r*,

$$F = k\frac{q_1 q_2}{r^2} \quad \text{(in a vacuum)}$$

- Where $k = \frac{1}{4\pi\varepsilon_0}$
  - ε_o is the *permittivity of a vacuum*, $\varepsilon_o = 8.85x10^{-12}\frac{C^2}{J \bullet m}$
  - *C* stands for coulomb and is a unit of charge.
    - The net charge on a proton or electron is equal to 1.6022×10^{-19} *C*

Odyssey:
- Charge-charge interactions

Types of Noncovalent Interactions

Charge-Charge Interactions

- When not in a vacuum, the intervening medium between the two charges can react to their presence in a way that reduces the force of interaction between the charges.
- Coulomb's Law equation can be modified to take this into consideration.

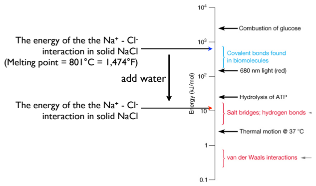
$$F = k\frac{q_1 q_2}{\varepsilon r^2}$$

- Where ε is the *relative permittivity factor* or *dielectric constant*
  - $\varepsilon = 1$ in a vacuum or in air
  - $\varepsilon = 1$ to 10 in a non-polar organic solvent
  - $\varepsilon = 74$ in water (This is one of highest.)

Types of Noncovalent Interactions

Charge-Charge Interactions

- Water's high dielectric constant, $\varepsilon = 74$, explains why it is particularly good at dissolving some salts.



Types of Noncovalent Interactions

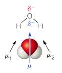
Charge-Charge Interactions

- Coulomb's Law equation allows us to calculate the force of the interaction action between two charges, how do we determine the energy of interaction?
- Energy has dimensions of *force* x *distance*.
  - To get the energy of interaction at a distance *r*, we need to integrate the force of the interaction with respect to distance from ∞ to *r*.
  - This is also the energy required to pull the two charges apart, that is say, to break the interaction

$$E = k\frac{q_1 q_2}{\varepsilon r}$$

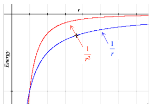
Types of Noncovalent Interactions

Charge-Dipole Interactions



- Some molecules interact because they are polar and possess a permanent dipole moment.
- Even though polar molecules have no net charge, they can still orient themselves relative to a charge to produce a net attractive interaction.
- The energy of this interaction, however, falls off more rapidly with distance than a charge-charge interaction.

$$E \propto \frac{1}{r^2}$$

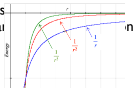


Types of Noncovalent Interactions

Dipole-Dipole Interactions

- Likewise, two molecules, each with permanent dipoles, can orient themselves in a way to produce a net attractive interaction.
- The energy of this interaction, however, falls off even more rapidly with distance than either a charge-charge or charge-dipole interaction.
  - The dipole interactions are s "short-ranged" than the char ns

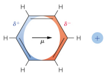
$$E \propto \frac{1}{r^3}$$



Types of Noncovalent Interactions

Induced Dipole Interactions

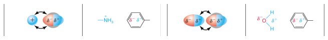
- Molecules that have no charges or permanent dipoles can, however, be induced to have a dipole.
- Such molecules are said to be *polarizable*.
- In the presence of a charge or dipole, the molecule's negatively charged electrons can be pulled or pushed relative to their positively charged nuclei to produce an *induced dipole*.



(a) Benzene has neither a net charge nor a permanent dipole moment, but a nearby charge can induce a redistribution of electrons within the benzene ring, producing an induced dipole moment (arrow).

Types of Noncovalent Interactions

Charge-Induced Dipole Interactions and
Dipole-Induced Dipole Interactions



- These interactions are always attractive.
- And the energy of these interactions fall off with distance even more rapidly than the others.

Charge-Induced Dipole

$$E \propto \frac{1}{r^4}$$

Dipole-Induced Dipole

$$E \propto \frac{1}{r^5}$$

- Therefore, these interactions are quite "short-ranged".

Types of Noncovalent Interactions

But Wait! There's More…

Induced Dipole-Induced Dipole Interactions

This one is probably the hardest one to wrap your head around, because there is no requirement that either molecule have a permanent charge (+/-) or partial charge (δ+/δ-).

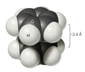
- Even for non-polar molecules in the absence of an external charge or dipole, the positions of the electrons are constantly fluctuating in time with respect to the nuclei, which leads at any moment in time, in an instantaneous dipole
- When two such molecules come very close to one another, these fluctuating dipoles will synchronize with one another to produce a net attractive interaction.
- As you probably expect by now, the energy for this interaction falls off even more rapidly with distance than any of the others.

$$E \propto \frac{1}{r^6}$$

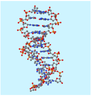
Types of Noncovalent Interactions

Induced Dipole-Induced Dipole Interactions

- This interactions is also called a *London Dispersion Force.*
- Though the weakest of all the interactions, it is always present and makes a substantial contribution to the stability of biological macromolecules.



Benzene
Boiling Point = 80.1°C



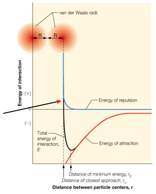
The nucleic acid B-DNA

Types of Noncovalent Interactions

Van der Waals Interactions

- **Concept**: *While molecules are attracted one another by these noncovalent interactions, they are stopped from coming any closer when their electron clouds begin to overlap.*
  - The *van der Waals interaction* combines the attractive (*London*) *dispersion interaction* with the electron repulsion interaction and is used to define the *van der Waals radius*, r_v, for an atom.
    - The electron repulsion interaction is positive and falls off very rapidly with increasing distance

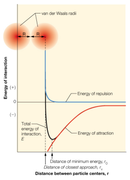
$$E \propto \frac{1}{r^{12}}$$



Types of Noncovalent Interactions

Van der Waals Interactions

- The van der Waals radii of atoms are used to produce the *spacefilling*, 3D models of molecules.



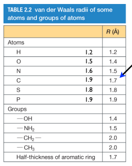
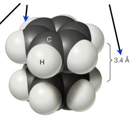


TABLE 2.2 van der Waals radii of some atoms and groups of atoms

		R (Å)
Atoms		
H	1.2	1.2
O	1.5	1.4
N	1.6	1.5
C	1.9	1.7
S	1.8	1.8
P	1.9	1.9
Groups		
—OH		1.4
—NH₂		1.5
—CH₂—		2.0
—CH₃		2.0
Half-thickness of aromatic ring		1.7

When two spheres overlap one another, its an indication that the corresponding atoms are covalently bonded

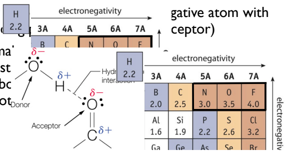
When they are merely touching one another, their distance of separation is equal to the sum of their van der Waals radii



Types of Noncovalent Interactions

Hydrogen Bonding Interactions

- This interaction is a special case of a dipole-dipole interaction.
    - It occurs when one of the dipoles involves a hydrogen atom covalently bonded to an electronegative atom (the donor).
    - The other gative atom with a non-bon ceptor)
    - Size also ma so the most hydrogen bo and F as bot acceptor.



Types of Noncovalent Interactions

Hydrogen Bonding Interactions

- **Concept:** *Hydrogen bonds are among the strongest, most specific non-covalent interactions.*
- The distances between the donor and acceptor atoms are usually less that the sum of the van der Waals radii, suggesting a partial covalent contribution to the interaction.

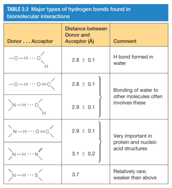


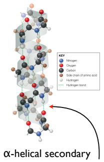
TABLE 2.3 Major types of hydrogen bonds found in biomolecular interactions

Donor . . . Acceptor	Distance between Donor and Acceptor (Å)	Comment
—O—H···O—H	2.8 ± 0.1	H bond formed in water
—O—H···O=C	2.8 ± 0.1	Bonding of water to other molecules often involves these
N—H···O—H	2.9 ± 0.1	
N—H···O=C	2.9 ± 0.1	Very important in protein and nucleic acid structures
N—H···N	3.1 ± 0.2	
N—H···S	3.7	Relatively rare; weaker than above

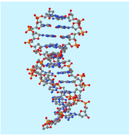
Types of Noncovalent Interactions

Hydrogen Bonding Interactions

- Hydrogen bonding interactions also play a very important role in determining biomolecular structures.



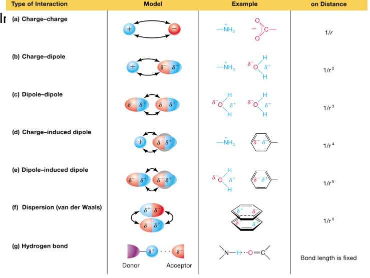
The α-helical secondary structure in a folded protein involves hydrogen-bonding between the turns



The base pairings in nucleic acids

Types of Noncovalent Interactions

Ir



Type of Interaction	Model	Example	Dependence of Energy on Distance
(a) Charge–charge		$-\overset{+}{N}H_3$ $^{-}O_2C-$	1/*r*
(b) Charge–dipole		$-\overset{+}{N}H_3$ H_2O	$1/r^2$
(c) Dipole–dipole		H_2O H_2O	$1/r^3$
(d) Charge–induced dipole		$-\overset{+}{N}H_3$	$1/r^4$
(e) Dipole–induced dipole		H_2O	$1/r^5$
(f) Dispersion (van der Waals)			$1/r^6$
(g) Hydrogen bond	Donor Acceptor	N—H···O=C	Bond length is fixed

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The Role of Water

The Role of Water

Water plays a major role in biological systems

- Water comprises approximately 70% of the mass for most living cells.
- We have also seen that with its high dielectric constant it can, when present, greatly mitigate the strength of most of the non-covalent interactions.

The Role of Water

The Structure and Properties of Water

- Water displays some very unique and unusual properties.

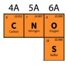

TABLE 2.4 Properties of water compared to those of some other hydrogen-containing, low-molecular-weight compounds

Compound	Molecular Weight	Melting Point (°C)	Boiling Point (°C)	Heat of Vaporization (kJ/mol)
CH_4	16.04	−182	−164	8.16
NH_3	17.03	−78	−33	23.26
H_2O	18.02	0	+100	40.71
H_2S	34.08	−86	−61	18.66

In general, the strength of the dispersion interaction scales with the molecular weight of a molecule.

Melting points and boiling points trend with the number and strengths of the non-covalent interactions

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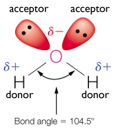
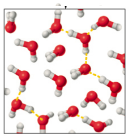
The Role of Water

The Structure and Properties of Water

- These unique properties arise from water's polarity, but also from its ability to simultaneously form 4 hydrogen bonding interactions with its neighbors.





In ice (solid water), each water molecule is hydrogen bonded to 4 neighboring water molecules

In liquid water, each water molecule is still hydrogen bonded to approximately 3.4 neighboring water molecules.

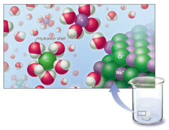
Odyssey:
- Hydrogen bonding in water

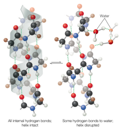
The Role of Water

Water as a Solvent

Concept: *Water is an excellent solvent for polar molecules and many salts because of its hydrogen-bonding potential and its polar nature.*

- Substances that dissolve readily in water are said to be hydrophilic.





All internal hydrogen bonds; helix intact

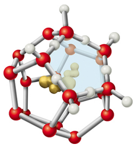
Some hydrogen bonds to water; helix disrupted

Odyssey:
- Charge-charge interactions and water

The Role of Water

Hydrophobic Molecules in Aqueous Solution

- Molecules that do not interact favorably with water and therefore do not not dissolve well in water are said to be *hydrophobic.*
  - Non-polar, organic molecules are a prime examples.
  - When water cannot interact favorable with a molecule, it will form highly organized *clathrate* structures around the molecule.
  - Because of the loss of entropy for these water molecules, dissolving non-polar molecules in water becomes thermodynamically unfavorable.



The Role of Water

Hydrophobic Molecules in Aqueous Solution

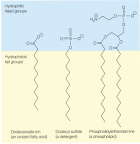
- Molecules that do not interact favorably with water and therefore do not not dissolve well in water are said to be *hydrophobic.*
  - This is why oil and water do not mix.
  - The water pushes the oil aside so as to minimize its surface contact with the oil molecules

[illegible]

The Role of Water

Amphipathic Molecules

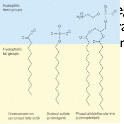
- **Concept:** *A molecule is amphipathic if some parts of its molecular surface are significantly hydrophilic while other parts are significantly hydrophobic.*
- Examples include
  - soaps
  - detergents
  - membrane phospholipids

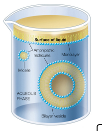


The Role of Water

Amphipathic Molecules in Aqueous Solution

- When placed in water, amphipathic molecules, such as soaps, detergents and phospholipids, will aggregate to form micelles (soaps & detergents) and bilayer vesicles (phospholipids).
- T egy to sim ir hy ater whil hy m water.



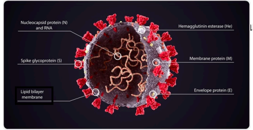


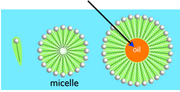
We latter see that this is how cell membranes form

The Role of Water

Amphipathic Molecules in Aqueous Solution

- When placed in water, amphipathic molecules, such as will aggregate to nd bilayer vesicles with the water.





The suspension that forms becomes cloudy because the micelles are large enough to scatter light.

Acid-Base Equilibria

Acid-Base Equilibria

Acids and Bases as Proton Donors and Acceptors

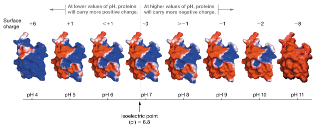
- **Concept:** *Many biological molecules are weak acids or weak bases.*
- This means that under different conditions of *pH* the charges on a molecule will change.
  - This, in turn, will influence the charge-charge-interactions they participate in.
- The *pH* of an aqueous solution is a measure of the hydrogen ion concentration.

$$pH = -\log([\mathrm{H}^+])$$

Acid-Base Equilibria

The *pH* Scale and the Physiological *pH* Range

- **Concept:** *The distribution of charges on the surface of a biomolecule affects its functional characteristics, such as receptor binding (e.g. hormones), catalysis (enzymes), and structural stability.*



(Shown is a surface model a protein at different *pH*'s that is colored to show the regions with a net positive charge (blue) and regions with a net negative charge (red))

Acid-Base Equilibria

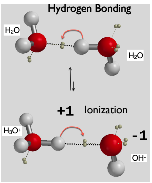
Water has a slight tendency to produce H_3O^+ and OH^- ions.

- The process is called **ionization** and can be thought of as an extension of the hydrogen bonding interactions.

$[H_2O]$ = 55 M Acceptor

At Equlibrium

$[H_3O^+]$ = 0.0000001 M Donor



Donor

$[OH^-]$ = 0.0000001 M Acceptor

Acid-Base Equilibria

Ionization of Water and the Ion Product

- The ionization reaction can be represented as either the transfer of a hydrogen ion (proton) from one water molecule to another,

$$H_2O + H_2O \rightleftharpoons H_3O^+ + OH^-$$

- or as the splitting of a water molecule into hydrogen ion plus a hydroxide ion.

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

This is just another way of representing the same reaction.

- The equilibrium can be characterized by an equilibrium constant, K_w.

$$K_w = \frac{a_{H^+}\, a_{OH^-}}{a_{H_2O}}$$

where,
a_{H^+} = *activity of* H^+
a_{OH^-} = *activity of* OH^-
a_{H2O} = *activity of* H_2O

Acid-Base Equilibria

Ionization of Water and the Ion Product

- As an approximation, the activities of the hydrogen ion and the hydroxide ion can be set equal to their molar concentrations.
- And because the water is also the solvent, it is present in great excess to the water that participates in the reaction.
  - We can therefore ignore its contribution to establishing the equilibrium by setting its activity equal to 1.

$$K_w = \frac{a_{H^+}\, a_{OH^-}}{a_{H_2O}}$$

can let,
a_{H^+} = $[H^+]$
a_{OH^-} = *activity of* $[OH^-]$
a_{H2O} = *1 (because it is the solvent)*

$$K_w = \frac{[H^+]\,[OH^-]}{1}$$

$$K_w = [H^+]\,[OH^-]$$

Acid-Base Equilibria

Ionization of Water and the Ion Product

- For pure water

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

$$K_w = [H^+][OH^-]$$

$$K_w = (1.0 \times 10^{-7})(1.0 \times 10^{-7})$$

$$K_w = (1.0 \times 10^{-14})$$

- And since

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

$$pH = -\log[\mathrm{H}^+] = -\log[10^{-7}] = 7.0$$

Acid-Base Equilibria

Acids and Bases can be defined in different ways

- The **operational definitions** of an acid and a base
  - An ***acid*** is a substance, that when dissolved in water, causes the *pH* to go down from *pH* 7.
  - A ***base*** is a substance, that when dissolved in water, causes the *pH* to go up from *pH* 7.
- This is called an operational definition because you need to carry out an operation, *i.e.* measure the *pH*, in order to apply the definition.

Acid-Base Equilibria

Acids and Bases can be defined in different ways

- The **Arrhenius definitions** of acids and bases
  - An ***acid***, when dissolved in water, releases hydrogen ions, $[\mathrm{H}^+]$
  - A ***base***, when dissolved in water, releases hydroxide ions, $[\mathrm{OH}^-]$
- This definition tries to explain why the *pH* goes down when an acid is added to water
- And why the *pH* goes up when a base is added to water.

$$\text{Since,} \quad K_w = [\mathrm{H}^+][\mathrm{OH}^-]$$

$$[\mathrm{H}^+] = \frac{K_w}{[\mathrm{OH}^-]}$$

Acid-Base Equilibria

Acids and Bases can be defined in different ways

- The **Brønsted-Lowry** definitions of acids and bases
  - An ***acid*** is a proton donor
  - A ***base*** is a proton acceptor
- In every acids/base reaction
  - There are two reactants, an ***acid*** and a ***base***
  - And there are two products, also an ***acid*** and a ***base***
    - The products are referred to as the *conjugate acid* and the *conjugate base*
  - Compared to the Arrhenius definitions, the Brønsted-Lowry definitions more close reflect what is actually going on
    - They also account for some bases that are missed with the Arrhenius definitions.

Acid-Base Equilibria

Comparing the Arrhenius and Brønsted-Lowry definitions.

- The **Arrhenius** definitions
  - Acid: $HCl \longrightarrow H^+ + Cl^-$
  - Base: $NaOH \longrightarrow Na^+ + OH^-$
  - $pH = -\log([\mathrm{H}^+]) = -\log\left(\frac{K_w}{[\mathrm{OH}^-]}\right)$
- The **Brønsted-Lowry** definitions of acids and bases
  - $\underset{\text{acid}}{HBr} + \underset{\text{base}}{H_2O} \longrightarrow \underset{\text{acid}}{H_3O^+} + \underset{\text{base}}{Br^-}$
  - $H_2O + NH_3 \longrightarrow NH_4^+ + OH^-$
  - $pH = -\log([\mathrm{H_3O}^+]) = -\log\left(\frac{K_w}{[\mathrm{OH}^-]}\right)$

Note: NH_3, Br^-, and H_2O do not fit the Arrhenius definition of a base, which is a substance that releases OH^- when dissolved in water

Acid-Base Equilibria

Strong Acids

- Strong acids are those that become nearly 100% ionized

$$\underset{\sim 0\%}{HA} \longrightarrow \underset{\sim 100\%}{H^+ + A^-}$$

- There are only a handful of strong acids, including,
  - HCl
  - HBr
  - HI
  - HNO_3
  - $HClO_4$
  - H_2SO_4 and HSO_4
- For these, $[H^+]$ just equals the concentration of the acid.

Acid-Base Equilibria

Comparing the strengths of weak acids.

- Acid/Base reactions reach an equilibrium very rapidly
- The equilibrium constant for a reaction, in which an acid either releases or donates a proton, is called the ***acid dissociation constant, K_a***

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

$$HA + H_2O \rightleftharpoons H_3O^+ + A^- \qquad K_a = \frac{[H_3O^+][A^-]}{[HA]}$$

As we did when defining K_w, we set the activity of the H_2O to 1, since it is also the solvent.

Acid-Base Equilibria

K_a and pK_a

- **Concept:** *A convenient way to express the strength of an acid is by its pK_a; the lower the value of pK_a, the stronger the acid.*
  - $pK_a = -\log(K_a)$

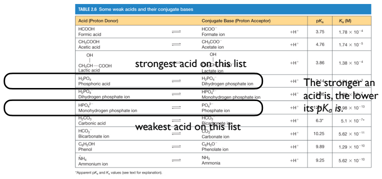


TABLE 2.6 Some weak acids and their conjugate bases

Acid (Proton Donor)		Conjugate Base (Proton Acceptor)		pK_a	K_a (M)
HCOOH Formic acid	$\rightleftharpoons$	$HCOO^-$ Formate ion	$+H^+$	3.75	1.78×10^{-4}
CH_3COOH Acetic acid	$\rightleftharpoons$	CH_3COO^- Acetate ion	$+H^+$	4.76	1.74×10^{-5}
OH $CH_3CH—COOH$ Lactic acid	$\rightleftharpoons$	OH [illegible] Lactate ion	$+H^+$	3.86	1.38×10^{-4}
H_3PO_4 Phosphoric acid	$\rightleftharpoons$	$H_2PO_4^-$ Dihydrogen phosphate ion	$+H^+$	2.14	[illegible]
$H_2PO_4^-$ Dihydrogen phosphate ion	$\rightleftharpoons$	HPO_4^{2-} Monohydrogen phosphate ion	$+H^+$	6.86	[illegible]
HPO_4^{2-} Monohydrogen phosphate ion	$\rightleftharpoons$	PO_4^{3-} Phosphate ion	$+H^+$	[illegible]	[illegible] $.98 \times 10^{-13}$
H_2CO_3 Carbonic acid	$\rightleftharpoons$	HCO_3^- Bicarbonate ion	$+H^+$	6.3*	5.1×10^{-7}*
HCO_3^- Bicarbonate ion	$\rightleftharpoons$	CO_3^{2-} Carbonate ion	$+H^+$	10.25	5.62×10^{-11}
C_6H_5OH Phenol	$\rightleftharpoons$	$C_6H_5O^-$ Phenolate ion	$+H^+$	9.89	1.29×10^{-10}
NH_4^+ Ammonium ion	$\rightleftharpoons$	NH_3 Ammonia	$+H^+$	9.25	5.62×10^{-10}

*Apparent pK_a and K_a values (see text for explanation).

strongest acid on this list

weakest acid on this list

The stronger an acid is, the lower its pK_a is.

Acid-Base Equilibria

Weak Acid and Base Equilibria: K_a and pK_a

- Determining the *pH* of a strong acid
- Determining the *pH of* a strong base
- Determining the *pH* of a weak acid
- Determining the *pH of* a weak base

Problem:

What is the *pH* of a 0.35 M hydrochloric acid solution (C_a = 0.35 M)? (Hint: HCl is a strong acid, so when HCl dissolves in water it completely dissociate to form H^+ and Cl^- ions.

For Strong Acids

$$[H^+] = C_a \qquad \text{(except } H_2SO_4\text{)}$$

$$pH = -\log[C_a]$$

Acid-Base Equilibria

Weak Acid and Base Equilibria: K_a and pK_a

- Determining the *pH* of a strong acid
- Determining the *pH of* a strong base
- Determining the *pH* of a weak acid
- Determining the *pH of* a weak base

Problem:

What is the *pH* of a 0.35 M sodium hydroxide solution?

For Strong Bases MOH_x

$$[OH^-] = xC_b$$

$$[H^+] = \frac{K_w}{[OH^-]} = \frac{K_w}{xC_b}$$

$$pH = pK_w + \log[xC_b]$$

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Acid-Base Equilibria

Weak Acid and Base Equilibria: K_a and pK_a

- Determining the *pH* of a strong acid
- Determining the *pH* of a strong base
- Determining the *pH* of a weak acid
- Determining the *pH of* a weak base

To derive this equation, start with the equilibrium expression,

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

We want to solve for [H+], but we still have two additional unknowns, [A-] and [HA].

We therefore need two more equations that relate these variables.

$$[\mathrm{A^-}] = [\mathrm{H^+}]$$

We can use this one to eliminate [A-]

$$C_a = [\mathrm{HA}] + [\mathrm{A^-}] \quad \text{or} \quad [\mathrm{HA}] = C_a - [\mathrm{H^+}]$$

And we can use this one to eliminate [HA]

Combining these three equations and you get,

$$K_a = \frac{[\mathrm{H^+}]^2}{C_a - [\mathrm{H^+}]} \quad \text{or} \quad [\mathrm{H^+}]^2 + K_a[\mathrm{H^+}] - K_aC_a = 0$$

This is a quadratic equation, so you will need to use the quadratic formula to solve for [H+].

$$x = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a}$$

Where,

- $x = [\mathrm{H^+}]$
- $a = 1$
- $b = K_a$
- $c = -K_aC_a$

$$[\mathrm{H^+}] = \frac{-K_a + \sqrt{K_a^2 + 4K_aC_a}}{2} \quad \text{or} \quad [\mathrm{H^+}] = \sqrt{K_a(C_a - [\mathrm{H^+}])}$$

$$[\mathrm{H^+}] \approx \sqrt{K_a(C_a)}$$

For weak acids, $C_a >> [\mathrm{H^+}]$

$$pH \approx \frac{1}{2}(pK_a - \log[C_a])$$

The approximation allows you to solve for [H+] without needing to use the quadratic formula.

Problem:

What is the *pH* of a 0.35 M acetic acid solution?

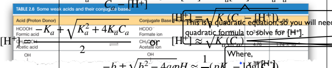

TABLE 2.6 Some weak acids and their conjugate bases

Acid (Proton Donor)		Conjugate Base (Proton Acceptor)
HCOOH Formic acid		HCOO⁻ Formate ion
CH₃COOH Acetic acid	⇌	CH₃COO⁻ Acetate ion
OH		OH

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Acid-Base Equilibria

Titration of Weak Acids and the The Henderson-Hasselbalch Equation

- When describing titration curves and analyzing buffers, it is helpful to rearrange the equilibrium expression for the acid dissociation constant to produce what is called the Henderson-Hasselbalch Equation.

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

$$[\mathrm{H^+}] = K_a\left(\frac{[\mathrm{HA}]}{[\mathrm{A^-}]}\right)$$

$$pH = pK_a + \log\left(\frac{[\mathrm{A^-}]}{[\mathrm{HA}]}\right)$$

Henderson-Hasselbalch Equation

When [A-] = [HA], *pH* = *pK*a

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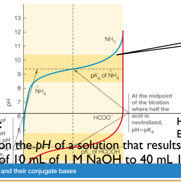
Acid-Base Equilibria

Titration of Weak Acids: The Henderson-Hasselbalch Equation

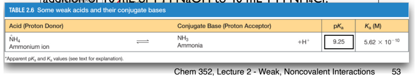


The Henderson-Hasselbalch equation describes an acid/base titration curve

Henderson-Hasselbalch Equation

Problem:

Calculation the *pH* of a solution that results following the addition of 10 mL of 1 M NaOH to 40 mL 1 M NH₄Cl?



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NH_4^+ Ammonium ion	⇌	NH_3 Ammonia	+H⁺	9.25	5.62 × 10^{-10}

*Apparent pK_a and K_a values (see text for explanation).

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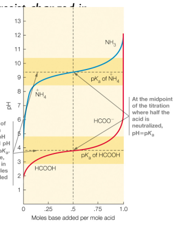
Acid-Base Equilibria

Buffer Solutions

- **Concept:** *Buffer solutions functic… pH be… solutic… of a w… conjug… least s… acid o… near t… acid. T… acid a… of the… in nea…*



ammonia buffer

formate buffer

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Acid-Base Equilibria

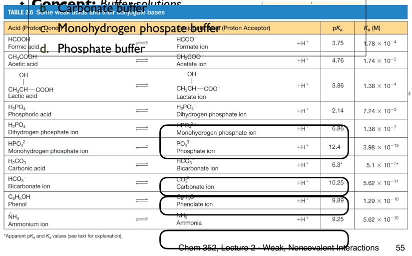
Buffer Solutions

- **Concept:** *Buffer solutions*

Clicker Question:

Which buffer system would be your best choice to use if you wished to maintain the *pH* of a solution at *pH* 7?

a. Lactate buffer
b. Carbonate buffer
c. Monohydrogen phospate buffer
d. Phosphate buffer



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H_3PO_4 Phosphoric acid	⇌	$H_2PO_4^-$ Dihydrogen phosphate ion	+H⁺	2.14	7.24 × 10^{-3}
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HPO_4^{2-} Monohydrogen phosphate ion	⇌	PO_4^{3-} Phosphate ion	+H⁺	12.4	3.98 × 10^{-13}
H_2CO_3 Carbonic acid	⇌	HCO_3^- Bicarbonate ion	+H⁺	6.3*	5.1 × 10^{-7}*
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*Apparent pK_a and K_a values (see text for explanation).

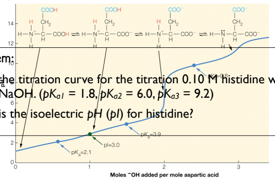
Acid-Base Equilibria

Titrations Curves

- For molecules with multiple ionizable groups, each is treated independently.

pI = Isoelectric *pH*

Net Charge = +1 0 -1 -2



Problem:

Draw the titration curve for the titration 0.10 M histidine with 1.0 M NaOH. (pK_{a1} = 1.8, pK_{a2} = 6.0, pK_{a3} = 9.2)

What is the isoelectric *pH* (*pI*) for histidine?

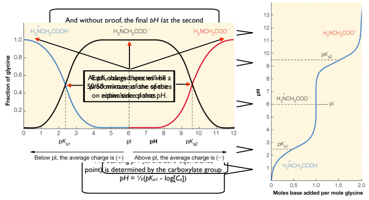
Video Tutorial
Sketching a Titration Curve

Acid-Base Equilibria

Titrations Curve for the Amino acid Glycine

- Glycine has two titratable groups
  - a carboxylic acid group (*pK_{a1}=2.5)*
  - an ammonium group (*pK_{a2}=9.5*)

And without proof, the final *pH* (at the second



At *pKa* charged species will a 50/50 mixture of the species on either side of that *pH*.

point) is determined by the carboxylate group

pH = ½(*pK_{a1}* - log[*C_a*])

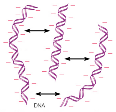
Resource
MarvinSketch

Interactions Between Macroions

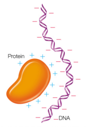
Interactions Between Macroions

Large molecules with multiple ionizable groups are called ***polyelectrolytes***

- Examples include nucleic acids and proteins.
- These molecules are also referred to as ***macroions***
- Macroions with a net negative or positive charge, will tend to repel other copies of themselves.
- Whereas mixtures of positively and negatively charged macroions will tend to attract each other



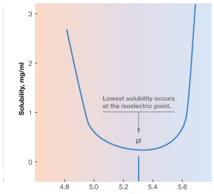
(a) Repulsion. DNA molecules, with many negative charges, strongly repel one another in solution.



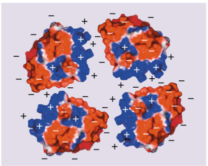
(b) Attraction. If DNA is mixed with a positively charged protein, these molecules have a strong tendency to associate.

Interactions Between Macroions

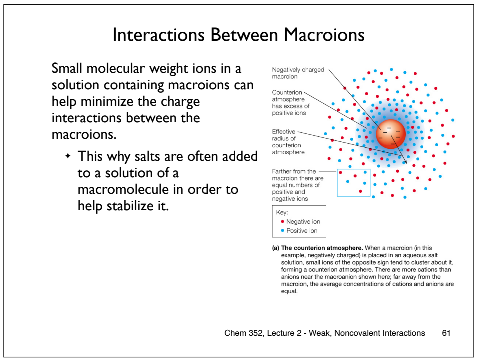
Dependence of protein solubility on pH



(d) Solubility of β-lactoglobulin with varying pH.



(b) Isoelectric point: protein aggregates. At the isoelectric point, where a protein has no net charge, the molecules retain regions of positive and negative charge on their surfaces, resulting in an increased tendency to aggregate and precipitate.



Interactions Between Macroions

Small molecular weight ions in a solution containing macroions can help minimize the charge interactions between the macroions.

- This why salts are often added to a solution of a macromolecule in order to help stabilize it.

(a) The counterion atmosphere. When a macroion (in this example, negatively charged) is placed in an aqueous salt solution, small ions of the opposite sign tend to cluster about it, forming a counterion atmosphere. There are more cations than anions near the macroanion shown here; far away from the macroion, the average concentrations of cations and anions are equal.

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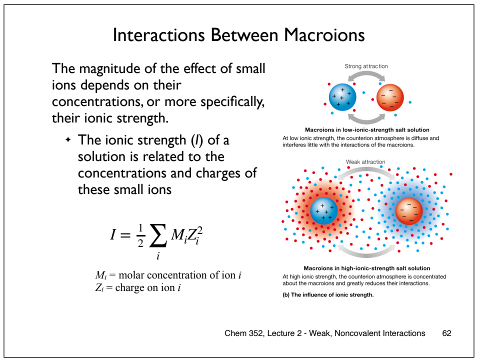

Interactions Between Macroions

The magnitude of the effect of small ions depends on their concentrations, or more specifically, their ionic strength.

- The ionic strength (I) of a solution is related to the concentrations and charges of these small ions

$$I = \frac{1}{2}\sum_i M_i Z_i^2$$

M_i = molar concentration of ion i
Z_i = charge on ion i

Macroions in low-ionic-strength salt solution
At low ionic strength, the counterion atmosphere is diffuse and interferes little with the interactions of the macroions.

Macroions in high-ionic-strength salt solution
At high ionic strength, the counterion atmosphere is concentrated about the macroions and greatly reduces their interactions.

(b) The influence of ionic strength.

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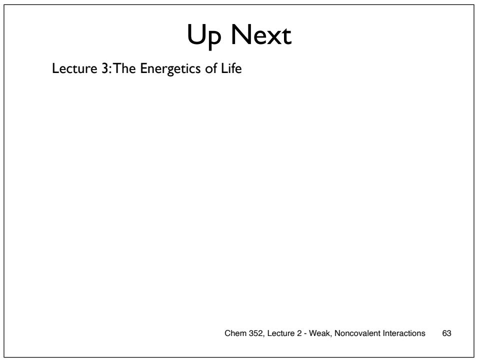

Up Next

Lecture 3:The Energetics of Life

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