Lecture 2 (9/9/19)

• Reading for today: Ch2, 47-58
  Ch2, 58-68
• Problems for today: Ch2 (text) 1,2
  Ch2 (study guide) 3,4,5,6,7
  Ch2 (text) 5,6,9,11,14,15,17,20,22, 24,29,35

NEXT

• Reading: Ch3, 75
  Ch1, 16-20
  Ch4, 115-116
• Problems: Ch1 (text) 13,16
  Ch4 (text) 12

OUTLINE

Finish THERMO
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

Water (reprise)
  Last of 4 S’s - stability (water as a chemical reagent)
  Ionization
  Acids/Bases; pH
  Examples: Metabolic acidosis
Quantifying Thermodynamics

For Total Energy (Enthalpy), what is magnitude of $\Delta H$?

Look at each side of the reaction:

If bonds are being made, energy is there that could be released, $H$ is more

$H_{\text{product (less)}} - H_{\text{reactant (more)}} = -\Delta H$

Total energy is added

If need to add energy, b/c bonds are being broken, $H$ is less

If the other way around, with reactant having fewer bonds, more having been broken (less total energy), then $+\Delta H$ (energy is released):

$H_{\text{product (more)}} - H_{\text{reactant (less)}} = +\Delta H$

Ice $\rightleftharpoons$ Water at $T > 0^\circ$ C

More bonds  Less bonds

Protein $\rightleftharpoons$ Amino acids

Quantifying Thermodynamics

For Entropy, what is magnitude of $\Delta S$?

Look at each side of the reaction:

If more organized, $S$ is less

$S_{\text{product (more)}} - S_{\text{reactant (less)}} = +\Delta S$

If more disordered, $S$ is more.

Don’t forget that a $+\Delta S$ will contribute to a favorable reaction due to the $-T\Delta S$ term being a negative value.

Ice $\rightleftharpoons$ Water at $T > 0^\circ$ C

Less disorder, more organized

More disorder

Protein $\rightleftharpoons$ Amino acids
Quantifying Thermodynamics

For Free Energy, \( \Delta G \):

Magnitude of \( \Delta G \) depends on:

\[
\Delta G = \Delta H - T\Delta S
\]

- \( \Delta H \)—total energy added (\( \Delta H > 0 \)) or released (\( \Delta H < 0 \))
- \( \Delta S \)—change in entropy, more randomness (\( \Delta S > 0 \)) or more order (\( \Delta S < 0 \)); Positive changes in entropy make \( \Delta G \) more negative. Negative changes in entropy make \( \Delta G \) more positive.

The interplay of enthalpy and entropy in the simple ice/water reaction, as a function of the temperature:
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
Figure 2.15  Surface Tension
## Properties of Water

<table>
<thead>
<tr>
<th>Compound</th>
<th>MW</th>
<th>m.p.</th>
<th>b.p.</th>
<th>(°C) range as liquid</th>
<th>(g/cm³) density as liquid</th>
<th>(mN/m) Surface Tension</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₄</td>
<td>16</td>
<td>-82.7</td>
<td>20</td>
<td></td>
<td>0.55</td>
<td>~0.2</td>
</tr>
<tr>
<td>NH₃</td>
<td>17</td>
<td>-78</td>
<td>33</td>
<td></td>
<td>1.3</td>
<td>0.3</td>
</tr>
<tr>
<td>OH₂</td>
<td>18</td>
<td></td>
<td>100</td>
<td></td>
<td>1.0</td>
<td>0.9</td>
</tr>
<tr>
<td>SH₂</td>
<td>34</td>
<td>84</td>
<td>-2</td>
<td></td>
<td>1.5</td>
<td>~</td>
</tr>
</tbody>
</table>

Temperature at 25°C: 0.9975 g/cm³
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**

- sp³ 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 (sp³) electron orbital hybridization. As a result, two lobes of the oxygen sp³ 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. It's not at all equal: the water with the covalent bond to hydrogen is called the DONOR. The opposite water molecule is called the ACCEPTOR.

Three important aspects that make H-bonds unique:

1) Electrostatic: dipole-dipole interaction

2) Partial electron sharing: partial covalency

3) Directional: geometry
Rings of Water Molecules

"Flickering Clusters" of Water Molecules

On average, liquid water has about 3.5 hydrogen bonds per molecule.

Structure of Ice

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
   - Ave number of H-bonds in liquid water is \( \sim 3.5 \), but in steam \( \sim 0 \)

3) Liquid is more dense than the solid
   - Ave number of H-bonds in liquid water is \( \sim 3.5 \), but in ice its 4, but the geometry takes over

4) High viscosity relative to its molecular weight (MW)
   - liquid water with \( \sim 3.5 \) H-bonds/molecule is sticky

5) High surface tension

6) Water is also a great SOLVENT

Solvation of Ions

Cations

Anions
Hydrogen Bonding to Polar Molecules by Water

- Water to alcohols
- Water to ketones/aldehydes
- Water to amines
- Water to carboxylic acids

Typical Bond Energies

<table>
<thead>
<tr>
<th>Type of Bond</th>
<th>Example</th>
<th>Typical Bond Energy (kJ·mol⁻¹)</th>
<th>Typical Bond Energy (kcal·mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covalent</td>
<td>O—H</td>
<td>460</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>C—H</td>
<td>414</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C—C</td>
<td>348</td>
<td></td>
</tr>
<tr>
<td>Noncovalent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrogen bond</td>
<td>—O—H⋯Oatings</td>
<td>20</td>
<td>4.7</td>
</tr>
</tbody>
</table>
Molecular Forces Important for Life

The 4 NON-covalent bonds:

- H-bonds
- Salt bridges
- van der Waals interactions
- Hydrophobic effect

\[
\text{Electrostatic Interactions}
\]

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

\[
\text{Force between two charged particles} = \frac{k q_1 q_2}{D r^2}
\]

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

Recalling the relationship between Force and Energy \( (E = \text{Force} \times \text{distance (r)}) \):

\[
E = \frac{k q_1 q_2}{D r}
\]

For partial charges, this distance dependence is exponential.
van der Waals Interactions

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

\[ E = \frac{k q_1 q_2}{D r^6} \]

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

<table>
<thead>
<tr>
<th>Atoms</th>
<th>( R ) (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>0.12</td>
</tr>
<tr>
<td>O</td>
<td>0.14</td>
</tr>
<tr>
<td>N</td>
<td>0.15</td>
</tr>
<tr>
<td>C</td>
<td>0.17</td>
</tr>
<tr>
<td>S</td>
<td>0.18</td>
</tr>
<tr>
<td>P</td>
<td>0.19</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Groups</th>
<th>( R ) (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>–OH</td>
<td>0.14</td>
</tr>
<tr>
<td>–NH₂</td>
<td>0.15</td>
</tr>
<tr>
<td>–CH₂</td>
<td>0.20</td>
</tr>
<tr>
<td>–CH₃</td>
<td>0.20</td>
</tr>
</tbody>
</table>

Half-thickness of aromatic ring: 0.17

10 Å / 1 nm
van der Waals Interactions

This is why the issue of COMPLEMENTARITY is so important in biology.

Typical Bond Energies

TABLE 2-1 Bond Energies in Biomolecules

<table>
<thead>
<tr>
<th>Type of Bond</th>
<th>Example</th>
<th>Typical Bond Energy (kJ·mol⁻¹)</th>
<th>(kcal·mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covalent</td>
<td>O—H</td>
<td>460</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>C—H</td>
<td>414</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C—C</td>
<td>348</td>
<td></td>
</tr>
<tr>
<td>Noncovalent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrogen bond</td>
<td>—O—H…O</td>
<td>20</td>
<td>4.7</td>
</tr>
<tr>
<td>Hydrophobic interactions</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Hydrophobic Interactions

Hydrophobic interactions: atoms “attracted” together due to water structure.

Nonpolar Solutes Aggregate in Water

Transfer of Hydrocarbons to Nonpolar Solvents is Entropically Driven

<table>
<thead>
<tr>
<th>Process</th>
<th>( \Delta H ) (kJ · mol(^{-1}))</th>
<th>(-T \Delta S) (kJ · mol(^{-1}))</th>
<th>( \Delta G ) (kJ · mol(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH(_4) in H(_2)O (\rightarrow) CH(_4) in C(_6)H(_6)</td>
<td>11.7</td>
<td>-22.6</td>
<td>-10.9</td>
</tr>
<tr>
<td>CH(_4) in H(_2)O (\rightarrow) CH(_4) in CCl(_4)</td>
<td>10.5</td>
<td>-22.6</td>
<td>-12.1</td>
</tr>
<tr>
<td>C(_2)H(_6) in H(_2)O (\rightarrow) C(_2)H(_6) in benzene</td>
<td>9.2</td>
<td>-25.1</td>
<td>-15.9</td>
</tr>
<tr>
<td>C(_2)H(_6) in H(_2)O (\rightarrow) C(_3)H(_8) in benzene</td>
<td>6.7</td>
<td>-18.8</td>
<td>-12.1</td>
</tr>
<tr>
<td>C(_3)H(_8) in H(_2)O (\rightarrow) C(_3)H(_8) in benzene</td>
<td>0.8</td>
<td>-8.8</td>
<td>-8.0</td>
</tr>
<tr>
<td>Benzene in H(_2)O (\rightarrow) liquid benzene(^a)</td>
<td>0.0</td>
<td>-17.2</td>
<td>-17.2</td>
</tr>
<tr>
<td>Toluene in H(_2)O (\rightarrow) liquid toluene(^a)</td>
<td>0.0</td>
<td>-20.0</td>
<td>-20.0</td>
</tr>
</tbody>
</table>

\(^a\)Data measured at 18°C.

Hydrophobic Interactions

Structure: Nonpolar Solutes in Water

Like ICE

Hydrophilic Interactions

(A) Hydrophilic

(B) Hydrophobic
Figure 2.12  Hydrophilic and Hydrophobic Interactions

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

For EXAMPLE

\[ 3 \text{ [CH}_4\cdot10\text{H}_2\text{O]} \rightarrow [(\text{CH}_4)_3 \cdot 12\text{H}_2\text{O}] + 18\text{H}_2\text{O} \]

\[ \Delta G \? \text{ definitely NEGATIVE: How?} \]

**Enthalpy**

- Enthalpy
  - \( 30 \text{ H}_2\text{O} \times 4 \text{ H-bonds} \) each \( \times 5 \text{ kcal/mol} = 600 \) kcal/mol to break H-bonds
  - Enthalpy
    - \( 18 \text{ H}_2\text{O} \times 3.5 \text{ H-bonds} \) each \( \times 5 \text{ kcal/mol} = 315 \text{ kcal/mol} \), plus 12\(x4\times5 = 240 \text{ kcal/mol} \); Total = 555 kcal/mol heat added in excess to break H-bonds
  - Enthalpy
    - \( 19 \text{ degrees of freedom (DoF)} \times 6 \text{ kcal/mol at 25 }^\circ\text{C per DoF} = 114 \text{ kcal/mol} \)

\[ \Delta G = \Delta H - T \Delta S \]

\[ = +45 - 96 \]

\[ = -51 \text{ kcal/mol} \]

ENTROPY DRIVEN

Bond Energies of Important Non-covalent Interactions

**TABLE 2-1** Bond Energies in Biomolecules

<table>
<thead>
<tr>
<th>Type of Bond</th>
<th>Example</th>
<th>Typical Bond Energy (\text{kJ} \cdot \text{mol}^{-1}) (\text{kcal} \cdot \text{mol}^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covalent</td>
<td>O—H</td>
<td>460</td>
</tr>
<tr>
<td></td>
<td>C—H</td>
<td>414</td>
</tr>
<tr>
<td></td>
<td>C—C</td>
<td>348</td>
</tr>
<tr>
<td></td>
<td>{</td>
<td>95</td>
</tr>
<tr>
<td>Noncovalent</td>
<td>Ionic interaction</td>
<td>—COO− ⋅ ⋅ ⋅ +H₃N— @ ~3 \AA \</td>
</tr>
<tr>
<td>Hydrogen bond</td>
<td>—O—H⋯O</td>
<td>20</td>
</tr>
<tr>
<td>Van der Waals interactions</td>
<td>[</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C—H⋯H—C—</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td>H</td>
<td></td>
</tr>
<tr>
<td>Hydrophobic interactions (per –CH₂—)</td>
<td>26</td>
<td>6</td>
</tr>
</tbody>
</table>
Amphipathic Interactions
(both hydrophobic and hydrophilic)

Example: amphiphiles like Fatty Acid Anions, detergents

\[ \text{Palmitate (C}_{15}\text{H}_{31}\text{COO}^-) \]
\[ \text{Oleate (C}_{17}\text{H}_{35}\text{COO}^-) \]

\[ \text{Sodium dodecyl sulfate (C}_{12}\text{H}_{25}\text{O}_4\text{S}) \text{ (SDS)} \]

Amphiphiles Form Micelles & Bilayers

Structure of a Micelle

Protein interiors
Disrupters of the Hydrophobic Effect

Urea

\[
\text{Urea} \quad \begin{array}{c}
\text{NH}_2 \\
\text{H}_2\text{N}--\text{C}--\text{NH}_2
\end{array}
\]

Guanidinium-HCl

\[
\text{Guanidinium-HCl} \quad \begin{array}{c}
\text{NH}_2 \\
\text{H}_3\text{N}^+=\text{C}--\text{NH}_2 \cdot \text{Cl}^-
\end{array}
\]

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 hydrogen bonded in a crystalline array, but in liquid water, hydrogen bonds rapidly break and re-form in irregular networks.
- The attractive forces acting on biological molecules include ionic interactions, hydrogen bonds, and van der Waals interactions.
- Polar and ionic substances can dissolve in water.
- 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.
The 4 S’s for Water:
Shape
Size
Solubility
Stability

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

\[ \text{H}_2\text{O} \rightleftharpoons \text{H}^+ + \text{OH}^- \]

\[ 2\text{H}_2\text{O} \rightleftharpoons \text{H}_3\text{O}^+ + \text{OH}^- \]

**Ionization of Water**

**Proton Jumping Occurs Rapidly**

Proton transfers are very rapid!

\[ 2\text{H}_2\text{O} \rightleftharpoons \text{H}_3\text{O}^+ + \text{OH}^- \]

What is the concentration of \( \text{OH}^- \) and \( \text{H}_3\text{O}^+ \) (protons)?
Ionization of Water

What is the concentration of OH⁻?

\[2H_2O \rightleftharpoons H_3O^+ + OH^-\]

Equilibrium constant \((K_{eq})\) is \(1.8 \times 10^{-16} \text{ M}\)

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

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

\(55.5 \text{ M} \times 1.8 \times 10^{-16} \text{ M} = [H^+] [OH^-] \quad \text{since} \ [H^+] = [OH^-]\)

\(55.5 \text{ M} \times 1.8 \times 10^{-16} \text{ M} = [H^+]^2\)

\(1.0 \times 10^{-14} \text{ M}^2 = [H^+]^2\)

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

Take the \(-\log\) of both sides: \(7 = \text{pH}\)

\(*1 \text{ L water} = 1000 \text{ g} \div 18 \text{ g/mol} = 55.5 \text{ M}\)

---

Ionization of Water

**Relationship of pH, [H⁺], and [OH⁻]**

\[2H_2O \rightleftharpoons H_3O^+ + OH^-\]
**Ionization of Water**

**pH Values of Common Substances**

<table>
<thead>
<tr>
<th>Substance</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 M NaOH</td>
<td>14</td>
</tr>
<tr>
<td>Household ammonia</td>
<td>12</td>
</tr>
<tr>
<td>Seawater</td>
<td>8</td>
</tr>
<tr>
<td>Blood</td>
<td>7.4</td>
</tr>
<tr>
<td>Milk</td>
<td>7</td>
</tr>
<tr>
<td>Saliva</td>
<td>6.6</td>
</tr>
<tr>
<td>Tomato juice</td>
<td>4.4</td>
</tr>
<tr>
<td>Vinegar</td>
<td>3</td>
</tr>
<tr>
<td>Gastric juice</td>
<td>1.5</td>
</tr>
<tr>
<td>1 M HCl</td>
<td>0</td>
</tr>
</tbody>
</table>

**Definitions of Acids and Bases:**

- **HA**: \( \text{H}^+ + \text{A}^- \) 
  - If dissociation is >water: **ACID**

- **HB**: \( \text{H}^+ + \text{B}^- \) 
  - If dissociation is <water: **BASE**

When \( \text{B}^- \) associates with protons, it leaves a net difference in \([\text{OH}^-]\):

\[
2\text{H}_2\text{O} \rightleftharpoons \text{H}_3\text{O}^+ + \text{OH}^- 
\]

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.
**Ionization of Water**

**Definitions of Acids and Bases:**

![Image](image-url)

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

Protons come from pulling the water dissociation equilibrium.

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

**Strong Acid**

\[
\text{HA} \rightarrow \text{H}^+ + \text{A}^-
\]

**Strong Base**

\[
\text{H}^+ + \text{B}^- \rightarrow \text{HB}
\]

**Weak Acid**

\[
\text{HA} \rightleftharpoons \text{H}^+ + \text{A}^-
\]

**Weak Base**

\[
\text{HB} \rightleftharpoons \text{H}^+ + \text{B}^-
\]

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?

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

\[
\text{HA} \rightleftharpoons \text{H}^+ + \text{A}^-
\]

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

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

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

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

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?

\[
pH = pK_a + \log \frac{[A^-]}{[HA]}
\]
Ionization of Water

Dissociation Constants and pK<sub>a</sub> Values of Some Acids

### TABLE 2-4 Dissociation Constants and pH Values at 25°C of Some Acids

<table>
<thead>
<tr>
<th>Acid</th>
<th>k</th>
<th>pK&lt;sub&gt;a&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ornithic acid</td>
<td>5.37 × 10⁻⁷</td>
<td>7.27 (pK&lt;sub&gt;a&lt;/sub&gt;)</td>
</tr>
<tr>
<td>H&lt;sub&gt;2&lt;/sub&gt;PO&lt;sub&gt;4&lt;/sub&gt;</td>
<td>7.06 × 10⁻³</td>
<td>2.15 (pK&lt;sub&gt;a&lt;/sub&gt;)</td>
</tr>
<tr>
<td>Formic acid</td>
<td>1.78 × 10⁻⁴</td>
<td>4.75</td>
</tr>
<tr>
<td>Sarcosine acid</td>
<td>6.17 × 10⁻⁴</td>
<td>4.21 (pK&lt;sub&gt;a&lt;/sub&gt;)</td>
</tr>
<tr>
<td>Ornithine</td>
<td>5.37 × 10⁻⁶</td>
<td>6.27 (pK&lt;sub&gt;a&lt;/sub&gt;)</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>1.74 × 10⁻⁵</td>
<td>4.76</td>
</tr>
<tr>
<td>Salicylic acid</td>
<td>2.29 × 10⁻⁵</td>
<td>5.64 (pK&lt;sub&gt;a&lt;/sub&gt;)</td>
</tr>
<tr>
<td>2-(N-Morpholino)ethanesulfonic acid (MIES)</td>
<td>8.13 × 10⁻⁵</td>
<td>6.06</td>
</tr>
<tr>
<td>HCO&lt;sub&gt;3&lt;/sub&gt;⁻</td>
<td>4.47 × 10⁻⁷</td>
<td>6.35 (pK&lt;sub&gt;a&lt;/sub&gt;)</td>
</tr>
<tr>
<td>Piperazine-N,N'-bis(2-hydroxy-2-ethylaminofluorine) (PHEPSE)</td>
<td>1.74 × 10⁻⁷</td>
<td>6.76</td>
</tr>
<tr>
<td>H&lt;sub&gt;2&lt;/sub&gt;CO&lt;sub&gt;3&lt;/sub&gt;</td>
<td>1.61 × 10⁻⁶</td>
<td>6.82 (pK&lt;sub&gt;a&lt;/sub&gt;)</td>
</tr>
<tr>
<td>3-(N-Morpholino)propanesulfonic acid (MOPS)</td>
<td>7.05 × 10⁻⁶</td>
<td>7.15</td>
</tr>
<tr>
<td>N,N'-bis(2-hydroxyethyl)propane-N'-2-ethylaminofluorine acid (HEPESE)</td>
<td>3.90 × 10⁻⁶</td>
<td>7.47</td>
</tr>
<tr>
<td>Trichloroethyl(aminomethane) Trio</td>
<td>8.32 × 10⁻⁶</td>
<td>8.08</td>
</tr>
<tr>
<td>Boric acid</td>
<td>5.75 × 10⁻¹⁰</td>
<td>9.24</td>
</tr>
<tr>
<td>NH₃</td>
<td>3.82 × 10⁻⁹</td>
<td>9.29</td>
</tr>
<tr>
<td>Glycine (amino group)</td>
<td>1.66 × 10⁻⁹</td>
<td>9.78</td>
</tr>
<tr>
<td>HCO&lt;sub&gt;3&lt;/sub&gt;⁻</td>
<td>4.48 × 10⁻¹⁰</td>
<td>10.31 (pK&lt;sub&gt;a&lt;/sub&gt;)</td>
</tr>
<tr>
<td>Piperazine</td>
<td>9.98 × 10⁻¹⁰</td>
<td>11.11</td>
</tr>
<tr>
<td>HEPES</td>
<td>4.17 × 10⁻¹³</td>
<td>12.36 (pK&lt;sub&gt;a&lt;/sub&gt;)</td>
</tr>
</tbody>
</table>

*The pH for the overall reaction CH₃COOH + H₂O ⇌ H₃COO⁻ + H<sup>⁺</sup> and see Box 2-2.

### 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

\[ \text{H}_3\text{PO}_4 \rightleftharpoons \text{H}^+ + \text{H}_2\text{PO}_4^- \rightleftharpoons \text{H}^+ + \text{HPO}_4^{2-} \rightleftharpoons \text{H}^+ + \text{PO}_4^{3-} \]

\( pK_1 \quad pK_2 \quad pK_3 \)

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?

\[ \text{pH} = pK_a + \log [A^-]/[HA] \]

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

-3.5 = log \([A^-]/[HA]\)
Ionization of Water

Example 2:
What is the ratio of $[\text{A}^-]/[\text{HA}]$ for a weak acid with a $pK_a = 6.0$ at pH 2.5?

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

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

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

antilog of -3.5 is $3.2 \times 10^4$; therefore:

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

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

0.002% dissociated.

If the initial total $[\text{HA}]$ was 0.1 M, then $[\text{HA}] + [\text{A}^-] = 0.1$ and $[\text{A}^-] = 0.1 - [\text{HA}]$. Substitution of this

value for $[\text{A}^-]$ into the ratio gives:

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

$[\text{HA}] = 0.1/1.00032 = 0.09997 \text{ M}$ and $[\text{A}^-] = 0.00032 \text{ M}$

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

$\text{HA} \rightleftharpoons \text{H}^+ + \text{A}^-$

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

---

Ionization of Water

Example 3:
Histidine is an important amino acid and the imidazole group can dissociate at physiological pH. There is
an equilibrium with HHis$^+$ and His$^-$;

$\text{HHis}^+ \rightleftharpoons \text{His}^- + \text{H}^+$

What is the pH of a 0.1 M solution of HHis$^+$Cl?
Ionization of Water

Example 3:
Histidine is an important amino acid and the imidazole group can dissociate at physiological pH. There is an equilibrium with HHis° and His⁺;

\[ HHis° \leftrightarrow His^+ + H^+ \]

What is the pH of a 0.1 M solution of HHisCl?

For this we need to return to the equilibrium constant for this reaction:

\[ K_e = [HHis^+] \times [H^+] / [HHis] \]

which has a \( pK_a \) of 6.0. From the reaction we know that for every HHis° formed from the dissociation/ionization reaction, there is one H⁺ produced. Therefore, the equilibrium expression reduces to:

\[ K_e = [H^+] \times [HHis] \]

If you take the –log of both sides you get:

\[ pK_e = 2pH – \log([HHis^+]) \]. Solving for pH:

\[ pH = \frac{pK_a + \log([A^-])}{2} \]

Therefore, the approximate pH of this 0.1 M solution will be 3.5. You can calculate the %dissociation of HHis at this pH and see that it is 3% dissociated and therefore the amount of HHis° from the 0.1 M initial concentration of HHis° is small and would tend to decrease the pH slightly from 3.5 as you have more H⁺ produced. However, you can reuse these values for the fraction dissociated and the concentrations of each as described in example 2 and calculate another pH in an iterative fashion. You can also do this using the quadratic equation as described in one of the suggested problems in the book.

Biological Buffer Systems

- Maintenance of intracellular pH is vital to all cells.
  - Enzyme-catalyzed reactions have optimal pH.
  - Solubility of polar molecules depends on H-bond donors and acceptors.
  - Equilibrium between CO₂ gas and dissolved H₂CO₃ and HCO₃⁻ depends on pH.

- Buffer systems in vivo are mainly based on:
  - phosphate, concentration in millimolar (mM) range
  - bicarbonate, important for blood plasma; blood pH = 7.40

EXAMPLE: Clinical Importance

\[ HCO_3^- + H^+ \leftrightarrow H_2CO_3 \]

\[ pK_a = 6.1 \]

\begin{align*}
\text{Bicarbonate} & = 24 \text{ mM} \\
\text{Carbonic Acid} & = 1.2 \text{ mM}
\end{align*}

Patient comes to ER with hyperventilation and acidosis (pH = 7.03; [CO₂] = 1.1 mM)

What is the [HCO₃⁻] and what % is used?

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

\[ 7.03 = 6.1 + \log \left( \frac{[HCO_3^-]}{[H_2CO_3]} \right) \]

\[ 0.93 = \log \left( \frac{[HCO_3^-]}{[CO_2]} \right) \]

\[ 8.5 = [HCO_3^-]/[CO_2] \]

\[ 8.5 = [CO_2]/1.1 \]

\[ 9.36 \text{ mM} = [HCO_3^-] \]

What do you do?