Lecture 3  
Wednesday, January 09, 2008

1. Foundations

- pH and the Henderson - Hasselbalch Equation
- Biochemical buffers

2. Protein Composition and Structure

- Amino acids and peptides.
- Peptide titrations
- Secondary and tertiary structures.

<table>
<thead>
<tr>
<th>Chemical Group</th>
<th>pKa Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$-CO$_2$ in peptide</td>
<td>3.5</td>
</tr>
<tr>
<td>Sidechain CO$_2$ (Glu and Asp)</td>
<td>4.5</td>
</tr>
<tr>
<td>Imidazole (Histidine)</td>
<td>6.5 (HIGHLY VARIABLE)</td>
</tr>
<tr>
<td>Sulfhydryl (-SH in Cysteine)</td>
<td>8.5</td>
</tr>
<tr>
<td>Phenol (tyrosine)</td>
<td>10.0</td>
</tr>
<tr>
<td>$\alpha$-amino group</td>
<td>8.5</td>
</tr>
<tr>
<td>Sidechain amino (lysine)</td>
<td>10.0</td>
</tr>
<tr>
<td>Guanidinyl (arginine)</td>
<td>12</td>
</tr>
</tbody>
</table>
D. pH & buffers.

General rxn

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

\[ \text{BH}^+ \rightleftharpoons \text{B} + \text{H}^+ \]

- histidine
- alkaloids
- chemical buffers

Equil. const.

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

\[ pK_a = -\log K_a \]

Low pH means strong acid.

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

High pH means weak acid.

Calculate solution pH.
Example 1. Calculate pH of a 0.01 M solution of an acid with \( pK_a = 4.76 \)

\[ \ce{H+} + \ce{A^-} \rightleftharpoons \ce{H2A} + \ce{H+} \]

Write equilibrium constant:

\[ K_a = \frac{[\ce{H+}][\ce{A^-}]}{[\ce{H2A}]} \]

Let \( x = [\ce{H+}] = [\ce{A^-}] \)

\[ [\ce{H2A}] = 0.01 - x \]

To get \( K_a \) from \( pK_a \):

\[ K_a = 10^{-pK_a} = 10^{-4.76} = 1.74 \times 10^{-5} \]

Plug in variables:

\[ K_a = 1.74 \times 10^{-5} = \frac{x - x}{0.01 - x} \]

Use quadratic equation to solve for \( x \).
\[ q = \frac{q^2 + bx + c}{x^2 + 1.74 \times 10^{-5} x - 1.74 \times 10^{-7}} \] (conc. \( q \))

\[ [H^+] = -K_a \pm \frac{\sqrt{K_a^2 + 4(1.01)K_a}}{2} \]

\[ [H^+] = ? \]

\[ pH = -\log [H^+] = 3.39 \]


From \( K_a = \frac{[H^+][A^-]}{[HA]} \), derive \( H-H \) eqn.

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

Alternative form

\[ \frac{[A^-]}{[HA]} = 10^{pH - pK_a} \]

\[ pH = pK_a + \log \frac{[A^-]}{[HA]} \]
allows us to calculate pH given pKa and ratio of unprotonated forms of an acid.

uses:
calc. pH given pKa and ratio
calc. pKa given pH and ratio
calc. ratio given pH and pKa.

Example 2:

If muscle cell pH = 6.8, what is ratio of $ \text{HPO}_4^{2-} : \text{H}_2\text{PO}_4^{-} \ (\text{pK}_a = 7.20)$?

\[
\frac{[A^-]}{[HA]} = 10^{\text{pH} - \text{pK}_a} = 10^{6.8 - 7.2} = 10^{-0.4}
\]

\[
= 0.4
\]
Buffers:

Many biochemicals have ionizable groups:

\[ R-O-P-O^{-} \]

\[ R-O^{-} \]

\[ R-NH_{3}^{+} \]

Changing pH could have a deleterious effect on biochemistry & life.

Cells & blood are buffer

Buffer is a compound that resists changes in pH.

- Act like proton sponges.

\[ H_{2}PO_{4}^{-} \rightarrow HPO_{4}^{2-} + H^{+} \]

\[ K_a \approx 7.20 \]
- protect against large changes in pH.

Protein Composition & Function

a. amino acids.
   - any compound that contains both an acid (carboxyl group) and an amino functional group.
     - found in proteins
     - act as neurotransmitters
     - signalling molecules
In proteins, have \( \alpha \)-amino acids.

\[
\begin{array}{c}
\text{R} \\
\text{NH}_2 \\
\end{array} + \begin{array}{c}
\text{R} \\
\text{CO}_2 \end{array} \]

Other amino acids are \( \beta \), \( \gamma \)

\[
\begin{array}{c}
\text{R} \\
\text{NH}_2 \\
\end{array} \quad \gamma \text{-amino butyrate} \\
\text{GABA.}
\]

\( \alpha \)-amino acids are:

\( L \)-isomer predominates

all \( \alpha \)-acids are \( L \)
in proteins in humans

\( D \)-isomers do exist; in bacteria toxic to humans
ii. Ionizable.

\[ \text{R-} \text{NH}_3^+ \xrightarrow{\text{low pH}} \text{R-} \text{NH}_3 \xrightarrow{\text{physiol. pH}} \text{R-} \text{NH}_2 \text{CO}_2^- \xrightarrow{\text{high pH}} \text{R-} \text{CO}_2^- \]

\( pK_a \approx 3.4 \)

\( pK_a \approx 6.5 \)

Biological ion

iii. Can be distinguished by their "R" groups.

- In proteins, 20 typical amino acids.
- Play many roles in proteins:
  - Structural
  - Binding interface
  - Serve as chemical catalysts

Consequently, 20 R groups fairly different
group are based on chemical properties.

1. Hydrophobic amino acids:

- Alanine: Ala
- Valine: Val
- Leucine: Leu
- Isoleucine: Ile
- Methionine: Met
- Glycine: Gly
- Proline: Pro

2. Polar:

- Serine: Ser
- Threonine: Thr
- Glutamine: Gln
- Asparagine: Asn
- Cysteine: Cys

3. Basic:

- Lysine: Lys
- Arginine: Arg
- Histidine: His
4. Acidic

- Glutamate  Glu  E
- Aspartate  Asp  D

5. Aromatic

- Phenylalanine  Phe  F
- Tyrosine  Tyr  Y
- Tryptophan  Trp  W

* Know structures & pK_a's for these 7 amino acids.

\[
\text{Cys.} \quad \overset{\text{S-S}}{\longrightarrow} \quad \overset{\text{Amino Acids}}{\text{pK}_a = 8.5} \quad \overset{\text{Base}}{\text{pK}_a = 6.5}
\]