Welcome to BCMB / BIOL / CHEM 3100 Introductory Biochemistry

Please pick up handouts
(duplicate sets at both ends of the front desk).

INSTRUCTORS FOR THIS COURSE

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INTRODUCTORY BIOCHEMISTRY
BCMB/BIOL/CHM 3100
Fall Semester 2019

***10:10-11:00 AM, Mon. Wed. & Fri,
Room C127 - Life Sciences

***Breakout Session: 5:00-5:50 PM,
Tues. Room C127 – Life Sciences

COURSE TEXT:
**Biochemistry: A Short Course, Fourth Edition, John L Tymoczko,
Jeremy M. Berg, Gregory J. Gatto, Jr. and Lubert Stryer, W.H. Freeman
and Company, New York, 2019

See Syllabus for important information about the course

• Partial Class Notes will be available on the class website at least one day prior to lecture (have these printed out for lecture)

• Class website (see syllabus for website)
http://www.ccrc.uga.edu/~dmohnen/bcmb3100/list.html

• Grading: 100% from 4 exams
  (you have the opportunity to add up to 2 points to your grade if you turn in all requested homework, group and other assignments)

• You are strongly encouraged to form study groups

• Any handouts/exams not picked in the breakout session, will be available in the BCMB office (B Tower Life Sciences)
Tips for doing well in BCMB/BIOL/CHEM3100

• Read the chapter **BEFORE CLASS**
  
  *Skim* chapter (look at figures!)
  Bring partial notes to class and write on them
  *Read* in detail
  *Reread* and integrate information from the notes and
  from the text. Pay attention to major concepts.

• **Keep up!**

• **Work at the material every day**

• **Form study groups and meet regularly**

• **Complete homework by the due date and bring it to the**
  **breakout session.**

• **Bring calculator to all exams and breakout sessions. You may**
  **NOT use pencils, blue or red ink for the exam. YOU MUST**
  **USE BLACK PEN FOR THE EXAMS!!**

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**BIOCHEMISTRY**

"... the central goal of the science of biochemistry is to determine how
the collections of inanimate molecules found in living organisms
interact with each other to constitute, maintain, and perpetuate
the living state."

*from Biochemistry, Albert L. Lehninger, 1975*

Biochemistry is the study of the molecular basis of life. It is an
empirical, reductionist, and rapidly evolving discipline.
Partial Class Notes for BCMB 3100 - Chapter 1

BCMB 3100 - Lecture 1

- **History of BIOCHEMISTRY**
- Important functional groups
- Four types of macromolecules in living organisms

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**HISTORY OF BIOCHEMISTRY**

1800’s: *vitalism*

1770-1774 – Joseph Priestly -

1773 – Hilaire Marin Rouelle -

1828 - Friedrich Wöhler -

\[ \text{NH}_4(OCN) \xrightarrow{\text{Heat}} \text{H}_2\text{N} \equiv \text{C} - \text{NH}_2 \] (1.1)
1862 - Louis Pasteur –

1897 - Edvard & Hans Buchner - DEATH OF VITALISM.

1890 - Emil Fisher: lock & key model

1891 - configuration of d-glucose

Early 1900s - 1st biochemistry departments established.

1926 - James B. Sumner –

1930s - Linus Pauling & Robert Corey : x-ray

1950s - 3D structure of 1st proteins by x-ray crystallography
   Max Perutz –
   John Kendrew -
1953 - James Watson & Francis Crick –

Current biochemical generalization regarding living things
1.
2.
3.
4. The Central Dogma of life information flow:

BCMB 3100 - Chapters 1 & 2

• History of BIOCHEMISTRY
• **Important functional groups**
• Four types of macromolecules in living organisms
See ALSO TEXT TABLE 2.1

General formulas - **Organic compounds**

(a) *Organic compounds*

<table>
<thead>
<tr>
<th>Functional group</th>
<th>Formula</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>R—OH</td>
<td>R—C—H</td>
</tr>
<tr>
<td>Aldehyde</td>
<td>R—C=H</td>
<td>R—C—R₁</td>
</tr>
<tr>
<td>Ketone</td>
<td>R—C=O</td>
<td>R—C—OH</td>
</tr>
<tr>
<td>Carboxylic acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiol (Sulphhydryl)</td>
<td>R—SH</td>
<td>R—NH₂</td>
</tr>
<tr>
<td>Primary Amines</td>
<td>R₁—NH</td>
<td>R₁—NH₂</td>
</tr>
<tr>
<td>Secondary Amines</td>
<td>R—N—R₂</td>
<td>R₁—NH₃</td>
</tr>
<tr>
<td>Tertiary Amines</td>
<td></td>
<td>R₁—N—R₂</td>
</tr>
</tbody>
</table>

1. Under most biological conditions, carboxylic acids exist as carboxylate anions: R—C=O⁻
2. Under most biological conditions, amines exist as ammonium ions: R—NH₃, R—NH₂, and R—NH—R₂.

---

General Formulas - **Functional groups**

(b) *Functional groups*

<table>
<thead>
<tr>
<th>Functional group</th>
<th>Formula</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyl</td>
<td>—OH</td>
<td>—C—R</td>
</tr>
<tr>
<td>Acyl</td>
<td></td>
<td>—C—R</td>
</tr>
<tr>
<td>Carbonyl</td>
<td></td>
<td>—C—O⁻</td>
</tr>
<tr>
<td>Carboxylate</td>
<td></td>
<td>—C—O⁻</td>
</tr>
<tr>
<td>Sulphhydryl (Thiol)</td>
<td>—SH</td>
<td>—NH₂ or —NH₃</td>
</tr>
<tr>
<td>Amino</td>
<td></td>
<td>—O—P—O⁻</td>
</tr>
<tr>
<td>Phosphate</td>
<td></td>
<td>—P—O⁻</td>
</tr>
<tr>
<td>Phosphoryl</td>
<td></td>
<td>—P—O⁻</td>
</tr>
</tbody>
</table>
General Formulas - Linkages

(c) Linkages in biochemical compounds

<table>
<thead>
<tr>
<th>Linkage</th>
<th>Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ester</td>
<td>(-\overset{\circ}{\text{C}}-\overset{\circ}{\text{O}}-\text{C})</td>
</tr>
<tr>
<td>Ether</td>
<td>(-\overset{\circ}{\text{C}}-\overset{\circ}{\text{O}}-\overset{\circ}{\text{C}})</td>
</tr>
<tr>
<td>Amide</td>
<td>(-\overset{\circ}{\text{N}}-\overset{\circ}{\text{C}})</td>
</tr>
<tr>
<td>Phosphate ester</td>
<td>(-\overset{\circ}{\text{C}}-\overset{\circ}{\text{O}}-\overset{\circ}{\text{P}}-\overset{\circ}{\text{O}})</td>
</tr>
<tr>
<td>Phosphoanhydride</td>
<td>(-\overset{\circ}{\text{O}}-\overset{\circ}{\text{P}}-\overset{\circ}{\text{O}}-\overset{\circ}{\text{O}})</td>
</tr>
</tbody>
</table>

BCMB 3100 - Chapter 1

- History of BIOCHEMISTRY
- Important functional groups
- Four types of macromolecules in living organisms
There are four types of molecules in living cells:

The basic macromolecular compartments of living things are_________

____________cells contain no nucleus or intracellular membranes and are usually unicellular (bacteria and archaea)

____________cells contains membrane-bound organelles: nucleus, ER, Golgi, mitochondria, lysosomes, peroxisomes, chloroplasts (animals, plants fungi, protists)

Biochemists concentrate on certain “model” organisms for their studies.

Prokaryote: E. coli
**Eukaryote:** humans, mice, rats, yeast, arabidopsis, drosophila

**Eukaryotic cell (plant)**

![Diagram of a plant cell](image1.png)

**Eukaryotic cell (animal)**

![Diagram of an animal cell](image2.png)

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Figure 1.12
Biochemistry: A Short Course, Second Edition
© 2013 W. H. Freeman and Company
Viruses

- Adenovirus: Viruses consist of a nucleic acid molecule surrounded by a protein coat. [NOTE: viruses are not living. They require living cells to propagate.]

Be sure to see text (Chapters 1 & 2) for:

* SI for size units & terminology
  
  ^ Note: one angstrom (Å) = 0.1 nm !!!

* subcellular organization

* types of organic compounds, linkages and functional groups (Table 2.1)

in vivo versus in vitro
BCMB 3100 - Chapter 2

- Properties of the solvent of life: water
- Four types of noncovalent interactions
- Review of acid-base concepts, pKa

WATER

- 60%-90% of most cells and tissues is water
- water is the solvent of life
- it is ESSENTIAL to understand the chemical properties of water in order to understand how molecules react in water
**Polarity of Small Molecules**

- Water and ammonia each have a permanent dipole while CO$_2$ does not.
Water molecules have a high affinity for each other

- Water is __________
- Water forms hydrogen bonds _______
  ______________________
- Attraction between slightly negative O and slightly positive H
- H bonds are directional (more stable when linear)
Hydrogen bonding by a water molecule

• A water molecule can form up to __________________

• Hydrogen bonds shown in green

• Water is partly ordered, H-bonds continually form & break, average 3.4 H-bonds in liquid water

Water is an excellent solvent for polar molecules and molecules that ionize

* It weakens electrostatic forces & H-bonds by _____________________________

* it forms oriented _____________ around ions
Fig. 2.3

* life depends on the ability of water to dissolve polar molecules. A high [ ] of these molecules can coexist with water

*Molecules that dissolve readily in water are called

Glucose is an example of a very soluble molecule since it has five hydroxyl groups and a ring oxygen which can hydrogen bond with water

Different short-chain alcohols have different solubility in water

Fig. 2.3
*Some polar interactions, however, are essential. Biological systems have created water free microenvironments where polar interactions have maximal strength

*Molecules that are nonpolar (e.g. hydrocarbons) do not dissolve in water. They are called ________________

*Nonpolar molecules or groups tend to cluster together in water = __________________________

[Diagram: C6H14 (hexane) molecules in water, labeled as hexane and water, with two clustered hexane molecules shown in a box.]

See Fig 2.9

Nonpolar solute molecules are driven together in water NOT because they have a high affinity for each other BUT ____________________________

________________________.

Water that surrounds nonpolar molecules is more restricted in its interaction with other water molecules.

Thus, there is a net gain in entropy when the nonpolar groups aggregate and water is freed from an ordered state.

Second Law of Thermodynamics: “The total entropy of a system and its surrounding always increases in a spontaneous process.”
Are all molecules hydrophilic or hydrophobic?

________________: molecules that are both hydrophilic and hydrophobic

Sodium dodecyl sulfate (SDS)

- A synthetic detergent
- A 12-carbon tail
- Polar sulfate group

Challenge of the Week

We are in the early stages of a “Freshwater Crisis” (Scientific American, August 2008; https://www.unwater.org/water-facts/scarcity/)

Today one out of six people (> 1 billion) have inadequate access to water.

By 2050, as much as ¾ of the earth’s population could face scarcities of water.

What is minimum amount of water each person requires per year for drinking, hygiene and growing food?

Water is minimum amount of drinking water each person requires per year?

What are the symptoms of dehydration?

How long can a human exist without drinking water?

PLEASE HAVE ANSWER TO TURN IN FOR BREAKOUT NEXT TUESDAY.
BCMB 3100 – Chapter 2

• Properties of the solvent of life: water
• **Four types of noncovalent interactions**
• Review of acid-base concepts, pKa

There are four types of noncovalent bonds (reversible molecular interactions)

*  
*  
*  
*  
*  
*
**Charge-charge interactions** - ______________________

* Charge-charge interaction: also called ionic bond, salt linkage, salt bridge, ion pair, electrostatic attraction

*In an optimal electrostatic attraction, distance between oppositely charge groups is ________ (compare to 1.54Å in C-C bond)

Electrostatic bond: potentially strongest noncovalent interaction: ____________________


**Hydrogen bonds:**

* **Hydrogen donor:** atom to which H is more tightly associated. O-H, N-H

* **Hydrogen acceptor:** atom to which H is less tightly associated. O or N The acceptor has partial negative charge that attracts H atom.

* Distance between 2 electronegative atoms involved in hydrogen bond = __________

*Hydrogen bond energy ranges from __________

*Hydrogen bonds are _________________
Hydrogen bonding between hydrogen acceptor and hydrogen donor

Some biologically important H-bonds

**Fig. 2.4**
Van der Waals bonds: non-specific attractive force important when any two atoms are _______________. Most important when numerous atoms in one molecule come close to atoms in another molecule

* ________________ than electrostatic & H-bonds

* the distribution of electric charge around an atom changes with time

*Thus, at any instant charge distribution is asymmetric. This asymmetry around one atom encourages similar asymmetry in electric distribution around neighboring atoms, leads to attraction

*Attraction is distance dependent: most strong at ________________

\[
\text{Van der Waals contact distance: } 2.4-4.0\text{Å} \\
\text{Van der Waals contact radius: } 1.2-2.0\text{Å} \\
\text{Van der Waals bond energy: } 0.4-4 \text{ kJ/mol} \text{ (~1 kcal/mol). Only slightly larger than the average thermal energy of molecules at RT (0.6 kcal/mol)}
\]

Effect of internuclear separation on van der Waals forces

- Strongly repulsive at short internuclear distances, very weak at long internuclear distances
- Van der Waals attraction is maximal when two atoms are separated by their van der Waals radii
- Van der Waals contact radius: 1.2-2.0Å
- Van der Waals contact distance: 2.4-4.0Å
- Van der Waals bond energy: 0.4-4 kJ/mol (~1 kcal/mol). Only slightly larger than the average thermal energy of molecules at RT (0.6 kcal/mol)
Hydrophobic attractions

* weak interactions: ___________________

* Interactions between nonpolar molecules due to tendency of water to bond strongly to itself

* __________________________________

________________ is the major driving force for folding of macromolecules, binding of substrates to enzymes, & formation of membranes
Noncovalent interactions in biomolecules

- Charge-charge interactions
- Hydrogen bonds
- Van der Waals interactions
- Hydrophobic interactions

Water is a weak **NUCLEOPHILE**

* __________: electron rich group due to a negative charge or to unshared pairs of electrons*

* **Nucleophiles tend to** __________to positively charged or electron deficient groups known as electrophiles*

* **Most common** biological nucleophiles contain __________

* __________ makes hydrolysis (cleavage of a bond such as anhydrides or peptide bonds by water) a potential problem*

* **Nonbeneficial hydrolysis in organisms is prevented by:**
  - biopolymer stability at physiological pH
  - inactive or inaccessible storage of hydrolases
  - two step biosynthetic reactions using nucleophiles other than water
  - shielding water sensitive intermediates in enzyme active site
BCMB 3100 – Chapter 2

- Properties of the solvent of life: water
- Four types of noncovalent interactions
- **Review of acid-base concepts, pKa**

### Review of Acid-Base Concepts

#### Ionization of Water (1)

Water dissociates into hydronium ($\text{H}_3\text{O}^+$) and hydroxyl ($\text{OH}^-$) ions

$$\text{H}_2\text{O} + \text{H}_2\text{O} \rightarrow \text{H}_3\text{O}^+ + \text{OH}^-$$

(write $\text{H}^+$ rather than $\text{H}_3\text{O}^+$ for simplicity)

$$\text{H}_2\text{O} \Leftrightarrow \text{H}^+ + \text{OH}^-$$

**Equilibrium constant (Keq)**

$$\text{Keq} = \frac{[\text{H}^+][\text{OH}^-]}{[\text{H}_2\text{O}]}$$

$$[\text{H}_2\text{O}] = 55.5\text{M} \quad \text{Keq}_{\text{water}} = 1.8 \times 10^{-16} \text{M}$$
**Ionization of Water (2)**

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

Since [water] (i.e. 55.5M) changes little by ionization, the equilibrium constant of water (Kw) can be simplified:

\[
\text{Keq} = \frac{[\text{H}^+][\text{OH}^-]}{[\text{H}_2\text{O}]}
\]

\[
1.8 \times 10^{-16} \text{ M} = \frac{[\text{H}^+][\text{OH}^-]}{55.5\text{ M}}
\]

\[
\text{Kw} = [\text{H}^+][\text{OH}^-] \quad (\text{Kw = ion product of water})
\]

At 25°C, \(\text{Kw is } 1.0 \times 10^{-14} \text{ M}^2\)

---

**Definition of Acid & Base**

Acid = proton donor \hspace{1cm} Base = proton acceptor

Conjugate Acid \hspace{1cm} Conjugate Base

acid \hspace{1cm} \text{H}^+ + \text{base}

acetic acid \hspace{1cm} \text{H}^+ + \text{acetate}

\(\text{CH}_3\text{-COOH} \hspace{1cm} \text{H}^+ + \text{CH}_3\text{-COO}^-\)

ammonium ion \hspace{1cm} \text{H}^+ + \text{ammonium}

\(\text{NH}_4^+ \hspace{1cm} \text{H}^+ + \text{HN}_3\)

*The above are conjugate acid-base pairs*
The pH of a solution is a measure of the concentration of H⁺

The pH Scale

- **pH** is defined as the negative logarithm of the concentration of H⁺

\[
pH = -\log [H^+] = \log \frac{1}{[H^+]}\]

(Søren Peter Lauritz Sørensen, 1909)

---

**Acid-Base behavior in Water**

Note: Since the ion product for water (Kw) is constant (i.e. 1.0 x 10⁻¹⁴ M²), the product of [H⁺] and [OH⁻] is always 1.0 x 10⁻¹⁴ M², thus as an acid is dissolved in water, the [OH⁻] decreases and vice versa.

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

<table>
<thead>
<tr>
<th>pH</th>
<th>[H⁺] (M)</th>
<th>[OH⁻] (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>10⁻¹⁴</td>
</tr>
<tr>
<td>1</td>
<td>10⁻¹</td>
<td>10⁻¹³</td>
</tr>
<tr>
<td>2</td>
<td>10⁻²</td>
<td>10⁻¹²</td>
</tr>
<tr>
<td>3</td>
<td>10⁻³</td>
<td>10⁻¹¹</td>
</tr>
<tr>
<td>4</td>
<td>10⁻⁴</td>
<td>10⁻¹⁰</td>
</tr>
<tr>
<td>5</td>
<td>10⁻⁵</td>
<td>10⁻⁹</td>
</tr>
<tr>
<td>6</td>
<td>10⁻⁶</td>
<td>10⁻⁸</td>
</tr>
<tr>
<td>7</td>
<td>10⁻⁷</td>
<td>10⁻⁷</td>
</tr>
<tr>
<td>8</td>
<td>10⁻⁸</td>
<td>10⁻⁶</td>
</tr>
<tr>
<td>9</td>
<td>10⁻⁹</td>
<td>10⁻⁵</td>
</tr>
<tr>
<td>10</td>
<td>10⁻¹⁰</td>
<td>10⁻⁴</td>
</tr>
<tr>
<td>11</td>
<td>10⁻¹¹</td>
<td>10⁻³</td>
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<td>12</td>
<td>10⁻¹²</td>
<td>10⁻²</td>
</tr>
<tr>
<td>13</td>
<td>10⁻¹³</td>
<td>10⁻¹</td>
</tr>
<tr>
<td>14</td>
<td>10⁻¹⁴</td>
<td>1</td>
</tr>
</tbody>
</table>

Kw = ion product of water
pH values for some fluids

- Lower values are acidic fluids
- Higher values are basic fluids

Acid Dissociation Constants of Weak Acids

- Strong acids and bases dissociate completely in water

\[ \text{HCl} + \text{H}_2\text{O} \rightarrow \text{Cl}^- + \text{H}_3\text{O}^+ \]

- Cl\(^-\) is the conjugate base of HCl
- H\(_3\)O\(^+\) is the conjugate acid of H\(_2\)O
Acid Dissociation Constants of Weak Acids

Acetic acid is a weak acid

• Weak acids and bases do not dissociate completely in H₂O

\[
\text{CH}_3\text{COOH} \quad \xrightleftharpoons{K_a} \quad \text{H}^+ + \text{CH}_3\text{COO}^- \\
\text{Acetic acid} \quad \text{(weak acid)} \quad \text{Acetate anion} \quad \text{(conjugate base)}
\]

Equilibrium constant = \( K_a = [H^+] [A^-] / [HA] \)

The equilibirum constant for the dissociation of a proton from an acid in water is called the **acid dissociation constant**, \( K_a \).

The Henderson-Hasselbalch Equation

• Defines the pH of a solution in terms of:
  
  (1) The \( pK_a \) of the weak acid

\[ pK_a \text{ is pH at which an acid is half dissociated} \]
\[ pK_a \text{ is a measure of acid strength} \]

(2) Concentrations of the weak acid (HA) and conjugate base (A⁻)

\[
\text{pH} = pK_a + \log \frac{[A^-]}{[HA]}
\]
**Buffering Power:** An acid-base conjugate pair resists changes in pH of a solution (i.e. it acts as a buffer). A weak acid has most effective buffering capability in +/- one pH unit of its pKa.

**Titration curve of acetic acid (CH₃COOH)**

- Titration curves are used to determine pKₐ values

---

**Ionization constants and pKₐ of some biochemically important compounds**

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Structure</th>
<th>$K_a$</th>
<th>pKₐ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetic acid</td>
<td>H₃C—COOH</td>
<td>$1.74 \times 10^{-5}$</td>
<td>4.76</td>
</tr>
<tr>
<td>Citric acid</td>
<td>OH</td>
<td>$8.12 \times 10^{-4}$</td>
<td>3.09</td>
</tr>
<tr>
<td></td>
<td>HOOC—CH₂—CH₂—CH₂—COOH</td>
<td>$1.77 \times 10^{-3}$</td>
<td>4.75</td>
</tr>
<tr>
<td></td>
<td>COOH</td>
<td>$3.89 \times 10^{-6}$</td>
<td>5.41</td>
</tr>
<tr>
<td>Citric acid</td>
<td>OH</td>
<td>$6.45 \times 10^{-3}$</td>
<td>2.19 (COOH)</td>
</tr>
<tr>
<td></td>
<td>HOOC—CH₂—CH₂—CH₂—COOH</td>
<td>$5.62 \times 10^{-5}$</td>
<td>4.25 (COOH)</td>
</tr>
<tr>
<td></td>
<td>NH₃⁺</td>
<td>$2.14 \times 10^{-10}$</td>
<td>9.67 (NH₃⁺)</td>
</tr>
<tr>
<td>Lactic acid</td>
<td>H₂C—CH—COOH</td>
<td>$1.38 \times 10^{-4}$</td>
<td>3.86</td>
</tr>
<tr>
<td>Pyruvic acid</td>
<td>H₂C—C—COOH</td>
<td>$3.16 \times 10^{-3}$</td>
<td>2.50</td>
</tr>
<tr>
<td>Succinic acid</td>
<td>HOOC—CH₂—CH₂—COOH</td>
<td>$6.46 \times 10^{-3}$</td>
<td>4.19</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$3.31 \times 10^{-6}$</td>
<td>5.48</td>
</tr>
</tbody>
</table>

Note: Some molecules have more than one ionizable group.

Source: After T. M. Devlin et al., *Textbook of Biochemistry with Clinical Correlations*, 6th ed. (Wiley-Liss, 2005), Table 1.5.
**Fig. 2.13**

Titration curve of acetic acid made by adding acid equivalents

\[ \text{CH}_3\text{COO}^- + \text{H}^+ \rightarrow \text{CH}_3\text{COOH} \]

**Fig. 2.14**

Midpoint of titration

\[ pK_a = 9.25 \]
\[ [\text{NH}_4^+] = [\text{NH}_3] \]

Buffering regions:

- \( pK_a = 6.86 \)
- \( \text{NH}_3 \)
- \( \text{H}_2\text{PO}_4^- \)
- \( \text{HPO}_4^{2-} \)
- \( \text{NH}_4^+ \)
- \( \text{H}_2\text{PO}_4^- \)
- \( \text{HPO}_4^{2-} \)
- \( \text{NH}_3 \)
- \( \text{H}_2\text{PO}_4^- \)
- \( \text{HPO}_4^{2-} \)

Phosphate

- \( pK_a = 5.86 \)
- \( 5.86 \)
- \( 5.86 \)
- \( 5.86 \)
- \( 5.86 \)

Acetate

- \( pK_a = 3.76 \)
- \( 3.76 \)
- \( 3.76 \)
- \( 3.76 \)
- \( 3.76 \)

CH$_3$COOH

\[ [\text{CH}_3\text{COOH}] = [\text{CH}_3\text{COO}^-] \]
\[ pK_a = 4.76 \]

OH$^-$ added (equivalents)

0.1 0.3 0.5 0.7 1.0

Percentage titrated

0 50 100
Dissociation constants and pKₐ values of weak acids in aqueous solutions at 25°C

<table>
<thead>
<tr>
<th>Acid</th>
<th>K_a (M)</th>
<th>pKₐ</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCOOH (Formic acid)</td>
<td>1.77 x 10⁻⁴</td>
<td>3.8</td>
</tr>
<tr>
<td>CH₃COOH (Acetic acid)</td>
<td>1.76 x 10⁻⁵</td>
<td>4.8</td>
</tr>
<tr>
<td>CH₃CHOHCOOH (Lactic acid)</td>
<td>1.37 x 10⁻⁴</td>
<td>3.9</td>
</tr>
<tr>
<td>H₃PO₄ (Phosphoric acid)</td>
<td>7.52 x 10⁻³</td>
<td>2.2</td>
</tr>
<tr>
<td>H₂PO₄⁻ (Dihydrogen phosphate ion)</td>
<td>6.23 x 10⁻⁸</td>
<td>7.2</td>
</tr>
<tr>
<td>HPO₄²⁻ (Monohydrogen phosphate ion)</td>
<td>2.20 x 10⁻¹³</td>
<td>12.7</td>
</tr>
<tr>
<td>H₂CO₃ (Carbonic acid)</td>
<td>4.30 x 10⁻⁷</td>
<td>6.4</td>
</tr>
<tr>
<td>HCO₃⁻ (Bicarbonate ion)</td>
<td>5.61 x 10⁻¹¹</td>
<td>10.2</td>
</tr>
<tr>
<td>NH₄⁺ (Ammonium ion)</td>
<td>5.62 x 10⁻¹⁰</td>
<td>9.2</td>
</tr>
<tr>
<td>CH₃NH₂⁺ (Methylenammonium ion)</td>
<td>2.70 x 10⁻¹ⁱ</td>
<td>10.7</td>
</tr>
</tbody>
</table>

Equilibrium constant = K_a = [H⁺][A⁻]/[HA]

Titration curve for phosphoric acid (H₃PO₄)

The phosphate buffer system contributes to intracellular buffering.
The pH of the blood is regulated primarily by the CO₂-carbonic acid-bicarbonate buffer system. Human Blood plasma is ~pH 7.4.

Blood plasma of mammals has a remarkably constant pH of 7.4.

1 mL 10 M HCl

Physiological saline pH 7, 1 liter (0.15 M NaCl)

pH 2

Blood plasma pH 7.4, 1 liter

pH 7.2

How???
Bicarbonate Buffer System for Blood. Percentages of carbonic acid and its conjugate bases as a function of pH (pH of blood plasma ~7.4)

CO₂ (Gaseous) ⇌ CO₂(aqueous) ⇌ Carbonic acid H₂CO₃ ⇌ Bicarbonate ion HCO₃⁻ ⇌ Carbonate ion CO₃²⁻

pKₐ = 6.4
pKₐ = 10.2

[H₂CO₃ includes dissolved CO₂ (i.e. CO₂(aq)), H₂CO₃⁺ is used to represent the two species]
Proteins (hemoglobin) & inorganic phosphate also contribute to intracellular buffering

Build up of H⁺ from the tissues

Regulation of the pH of blood in mammals

Alkalosis (e.g. hyperventilation)
Aqueous phase of blood cells passing through capillaries in lung
Air space in lung