CHM 441: Biological Chemistry I

Professor: Linda Columbus
Time: Tuesday and Thursday 11:00 AM – 12:15 PM
Place: Ruffner Hall G004A
Text: Biochemistry by Garrett and Grisham
Prerequisites: One year of organic chemistry.
Office Hours: Monday at 2PM, Wed at 4PM, and Friday at 11AM
Class Website: Toolkit site for CHEM441-1 Fall 2007
Email: columbus@virginia.edu
Who am I?

• B.A. in Chemistry from Smith College
• Ph.D. in Biochemistry and Molecular Biology from UCLA
• Postdoctoral fellow at The Scripps Research Institute
• My research focuses on the structure and dynamics of membrane proteins involved in bacterial pathogenesis using NMR, EPR, and X-ray crystallographic techniques.
Your TA
What is CHEM441?

CHM441, Biological Chemistry I, introduces the components of biological macromolecules and the principles behind their observed structures. The structure, properties, and functions of nucleic acids, proteins, lipids, and carbohydrates will be the focus of the course with an additional emphasis on large cellular assemblies such as the ribosome.
• The key to doing well and learning the material in this class is to read each assignment before coming to class so that the lecture is the second time that you are thinking about the material. The exams will be based on the problem sets. Therefore, if you do and understand all the problem sets, then you will do well.

• I encourage you to form a study group of about 5 people and meet at least once a week to compare notes from the class.

• Repeated exposure to the course material is critical to doing well.

• Use the material on the publisher’s website (http://www.brookscole.com/cgi-wadsworth/course_products_wp.pl?fid=M20b&product_isbn_isbn=0030223180&discipline_number=12) to review material and test your understanding.
Grading

Problem Sets 100 pts
Pop Quizzes 200 pts
Projects 200 pts
Exam I 100 pts
Exam II 100 pts
Final Exam 300 pts
Total 1000 pts

There will be a chance to earn up to 200+ pts extra credit (>20% of the total grade).

Grades:

A+ ≥ 1000 pts
A 999 – 900 pts
B+ 875 – 899 pts
B 825 – 874 pts
B- 800 – 824 pts
C 700 – 799 pts
Policies

- Problem Sets will be graded as Pass or Fail. Only 1 question (chosen randomly) will be graded for each problem set. Problem sets 5, 9, and 13 will not be collected; however, the material will be on the exams. All the solutions to the problem set will be posted on the class website.

- There will be no make-up exams. If there is an emergency that will keep you from taking an exam, you must contact me via email as soon as you are aware that you will miss the exam. The final exam will be in three portions. The first two portions will correspond to Exam I and Exam II material. The grade on the corresponding portion of the final will be used in the place of the missed exam.

- If you think a mistake has been made in grading your exam, please submit the exam to be re-graded; however, the entire exam will be re-graded. To submit an exam to be re-graded, bring the exam directly to me with a typed sheet that clearly identifies the question(s) that you think is incorrectly graded and describes why you believe it is incorrect. This needs to be done within 24 hours of receiving the graded exam. A bit of advice, if the number of points that are in contention is less than 2% of your total grade (20 pts) it is likely not worth the risk to have the entire exam re-graded. Instead, it would be better to do one of the extra credit assignments.
• **Review Sessions** - Q & A format.
  Therefore, come prepared with questions if you want to benefit from the session. There will be a review session on:
  10/1 at 7PM for Exam I 
  11/5 at 7PM for Exam II 
  12/12 and 12/13 at 7PM for the Final Exam

• **Extra Credit**
  1. Choose as class topic, find a recent article in the scientific literature, and review the findings in two pages (worth 25 pts). Be sure to cite your sources.

  2. Exam 1: The extra credit question will be about the “The Double Helix” and worth 10 pts.

  3. Exam 2: The extra credit question will be a question about the discovery of the $\alpha$-helix and will be worth 5 pts.

  4. Attend one of the Friday Chemistry Seminar at 4:00 P.M. in Room 304 Chemistry Building, email me a few sentences summarizing the seminar (not just the name and title) and you will receive 10 pts extra credit. [http://www.virginia.edu/chem/newsandevents/seminars/](http://www.virginia.edu/chem/newsandevents/seminars/)
“real science you’re not too worried about the right answer…Real science recognizes that you have an advantage over practically any other human enterprise because what you are after – call it truth or understanding – waits patiently while you screw up.”

“You have to be confused, before you can reach a new level of understanding anything.”

- Dudley Herschbach
  Professor of Chemistry, Harvard University
  Nobel Prize 1986
Projects

• Projects are designed to help you learn the language and tools of biochemistry so that you can read and write about topics that interest you. Communication is very important in science. Scientists publish papers, present lectures about their research, and teach all of which requires well-developed verbal and writing skills. I will provide an outline of what I expect for the format and organization.
Expectations

- respect the honor code

- Respect each other

- Communicate with your TA respectfully
  - She/He is here to help you and I not to serve us

- Be responsible
  - Hand in assignments on time
  - Read and study the material
  - Do not fall behind

- Enjoy yourself
Questions?
Chapter 1
Diversity of Living Systems
Inorganic Precursors

Metabolites

Building Blocks

Macromolecules

Supramolecular Complexes

Organelles

Cells

Tissue

Hierarchical organization of a cell and organism
A bacterial cell

1. Plasma membrane
2. Cell wall
3. Cytoplasmic membrane
4. Nucleoid
5. Flagella
An animal cell – make sure you can identify these organelles and know their functions.

Compare eukaryotic and prokaryotic cells.
A plant cell – make sure you can identify these organelles and know their functions.
Which of the following is a characteristic of a prokaryotic organism?

A. posses a nucleus bounded by a nuclear membrane
B. frequently contains a chitin-derived cell wall
C. partly relies on glycolysis for ATP synthesis
D. contains a variety of organelles
Outline of the class

1. H₂O
   Why would I start the class with H₂O?
# The Approximate Chemical Composition of a Bacterial Cell

<table>
<thead>
<tr>
<th></th>
<th>% of total cell weight</th>
<th># of types of each molecule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>70</td>
<td>1</td>
</tr>
<tr>
<td>Inorganic ions</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>Sugars and precursors</td>
<td>1</td>
<td>250</td>
</tr>
<tr>
<td>Nucleotides and precursors</td>
<td>0.4</td>
<td>100</td>
</tr>
<tr>
<td>Amino acids and precursors</td>
<td>0.4</td>
<td>100</td>
</tr>
<tr>
<td>Fatty acids and precursors</td>
<td>1</td>
<td>50</td>
</tr>
<tr>
<td>Other small molecules</td>
<td>0.2</td>
<td>~300</td>
</tr>
<tr>
<td>Macromolecules (proteins,</td>
<td>26</td>
<td>~3000</td>
</tr>
<tr>
<td>nucleic acids and</td>
<td></td>
<td></td>
</tr>
<tr>
<td>polysaccharides)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Outline of the class

1. $\text{H}_2\text{O}$
2. Nucleic acids
3. Proteins

The book chapters are ordered differently, why did I choose this order?
The “central dogma” of life:

Transcription: DNA → RNA

Translation: RNA → protein
The “central dogma” of life

- DNA → RNA → protein

- Transfer RNA (tRNA)
- Ribosomal RNA (rRNA)
- Messenger RNA (mRNA)
- Many other RNAs!!!
The “central dogma” of life

DNA ⇌ RNA → protein
The "central dogma" of life:

Center for Computational Visualization
University of Texas at Austin
presents
Outline of the class

1. $\text{H}_2\text{O}$
2. Nucleic acids
3. Proteins
4. Carbohydrates
5. Lipids/membranes
6. Assemblies
Chapter 2
Water: The Medium of Life
What do you see when you hear the word water or H$_2$O?
H$_2$O

- High surface tension
- High boiling point
- High melting point
- High heat of vaporization

**Bent structure makes it polar**
Non-tetrahedral bond angles
H-bond donor and acceptor
Potential to form four H-bonds per water

Dipole moment

Covalent bond length = 0.095 nm

Van der Waals radius of oxygen = 0.14 nm

Van der Waals radius of hydrogen = 0.12 nm
**WATER**

Two atoms, connected by a covalent bond, may exert different attractions for the electrons of the bond. In such cases the bond is polar, with one end slightly negatively charged ($\delta^{-}$) and the other slightly positively charged ($\delta^{+}$).

Although a water molecule has an overall neutral charge (having the same number of electrons and protons), the electrons are asymmetrically distributed, which makes the molecule polar. The oxygen nucleus draws electrons away from the hydrogen nuclei, leaving these nuclei with a small net positive charge. The excess of electron density on the oxygen atom creates weakly negative regions at the other two corners of an imaginary tetrahedron.

**WATER STRUCTURE**

Molecules of water join together transiently in a hydrogen-bonded lattice. Even at 37°C, 15% of the water molecules are joined to four others in a short-lived assembly known as a “flickering cluster.”

The cohesive nature of water is responsible for many of its unusual properties, such as high surface tension, specific heat, and heat of vaporization.

**HYDROGEN BONDS**

Because they are polarized, two adjacent $\text{H}_2\text{O}$ molecules can form a linkage known as a hydrogen bond. Hydrogen bonds have only about 1/20 the strength of a covalent bond.

Hydrogen bonds are strongest when the three atoms lie in a straight line.
Amphipathic molecules

The sodium salt of palmitic acid: Sodium palmitate
(Na⁺OOC(CH₂)₁₄CH₃)

Polar head
Nonpolar tail

micelle
Samples of which of the following molecules will exhibit the strongest intermolecular interactions?

A. O₂
B. N₂
C. CO₂
D. H₂O
HYDROGEN ION EXCHANGE

Positively charged hydrogen ions (H⁺) can spontaneously move from one water molecule to another, thereby creating two ionic species.

\[
\begin{align*}
\text{H}_2\text{O}^{-} + \text{H}_2\text{O} & \rightleftharpoons \text{H}_3\text{O}^+ + \text{OH}^- \\
\end{align*}
\]

The equilibrium constant for this reaction is given by:

\[
K_a = \frac{[\text{H}^+][\text{-COO}^-]}{[\text{-COOH}]}.
\]

ACIDS

Substances that release hydrogen ions into solution are called acids.

\[
\begin{align*}
\text{HCl} & \rightarrow \text{H}^+ + \text{Cl}^- \\
\text{hydronium ion} & \text{hydrogen ion} \\
\text{(water acting as a weak base)} & \text{(strong acid)} \\
\end{align*}
\]

Many of the acids important in the cell are only partially dissociated, and they are therefore weak acids—for example, the carboxyl group (−COOH), which dissociates to give a hydrogen ion in solution.

\[
\begin{align*}
\text{−COOH} & \rightleftharpoons \text{H}^+ + \text{−COO}^- \\
\text{(weak acid)} & \\
\end{align*}
\]

Note that this is a reversible reaction.

BASES

Substances that reduce the number of hydrogen ions in solution are called bases. Some bases, such as ammonia, combine directly with hydrogen ions.

\[
\begin{align*}
\text{NH}_3 + \text{H}^+ & \rightarrow \text{NH}_4^+ \\
\text{ammonium ion} & \\
\end{align*}
\]

Other bases, such as sodium hydroxide, reduce the number of H⁺ ions indirectly, by making OH⁻ ions that then combine directly with H⁺ ions to make H₂O.

\[
\begin{align*}
\text{NaOH} & \rightarrow \text{Na}^+ + \text{OH}^- \\
\text{(strong base)} & \\
\end{align*}
\]

Many bases found in cells are partially dissociated and are termed weak bases. This is true of compounds that contain an amino group (−NH₂), which has a weak tendency to reversibly accept an H⁺ ion from water, increasing the quantity of free OH⁻ ions.

\[
\begin{align*}
\text{−NH}_2 + \text{H}^+ & \rightleftharpoons \text{−NH}_3^+ \\
\end{align*}
\]

The acidity of a solution is defined by the concentration of H⁺ ions it possesses. For convenience we use the pH scale, where

\[
pH = -\log_{10}[\text{H}^+]
\]

For pure water

\[
[H^+] = 10^{-7} \text{ moles/liter}
\]
• What is the pH of 0.1 M solution of formic acid?
• Table 2.4 gives acid dissociation constants. HCOOH \( K_a = 1.78 \times 10^{-4} \)
Henderson-Hasselbalch Equation Relates pH and $pK_a$ of an Acid-Base System

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

Equilibrium constant, $K_a$

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

Take the log of both sides

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

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

Substitute

\[ \text{pH} = pK_a + \log \frac{[\text{A}^-]}{[\text{HA}]} \]
Example of the application of the Henderson-Hasselbalch Eqn.

• What is the pH of a solution that contains 0.1 M acetic acid (CH\textsubscript{3}COOH) and 0.12 M sodium acetate (Na\textsuperscript{+}CH\textsubscript{3}COO\textsuperscript{-})? The pKa of acetic acid is 4.76.
Titration Curves

Titration curve is the plot of the pH of a solution as incremental amounts of hydr dioxide ions (or protons) are added.
Titration Curve for lactic acid
Titration curve for phosphoric acid
Study Aids

Buffers

- Buffers are solutions that resist changes in pH as acid and base are added.
- Most buffers consist of a weak acid and its conjugate base.
- The plot of pH versus base added is flat near the $pK_a$.
- Buffers can only be used reliably within a pH unit of their $pK_a$. 

![Buffer diagram](image-url)
The bicarbonate blood buffering system

Respiratory alkalosis (hyperventilation)

Respiratory acidosis (hypoventilation)

The $pK_a$ of carbonic acid is 3.77 (at 25 °C) and 3.57 (at 37 °C), but the pH of blood plasma is 7.4 – how does this buffer system work?
Blood buffering system
Properties of common buffers

![Graph showing pH and pKₐ values for various buffers.]

<table>
<thead>
<tr>
<th>Buffer</th>
<th>pH 5.5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
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<tbody>
<tr>
<td>MES</td>
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<td>BIS-TRIS</td>
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<tr>
<td>BICINE</td>
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</tbody>
</table>

Useful pH range of selected biological buffers (25°C, 0.1 M)

- **pKₐ**
  - MES: 6.1
  - BIS-TRIS: 6.5
  - PIPES: 6.8
  - BES: 7.1
  - MOPS: 7.2
  - TES: 7.4
  - HEPES: 7.5
  - TEA: 7.8
  - TRICINE: 8.1
  - BICINE: 8.3
Overview

• Properties of water
• Weak acids and bases
• Titration curves
• Henderson-Hasselbalch Eqn
• Buffers