1. Biochemistry, and thermodynamics

Jianhan Chen
Office Hour: M 1:30-2:30PM, Chalmers 034
Email: jianhanc@ksu.edu
Office: 785-2518

Overall Course Setup

• **Time & Location:** MWF 12:30-1:20 pm, Burt 114
• **Instructors:**
  – **Section I:** Jianhan Chen, 034 Chalmers, 532-2518, jianhac@ksu.edu
  – **Section II:** Larry Davis, 062 Chalmers, 532-6124, ldavis@ksu.edu
  – **Section III:** Gerald Reek, 203 Burt, 532-6117, reeck@ksu.edu
• **1-h Exams:** please mark your calendar and plan accordingly
  – Section I: Sep 28 (M) during the class time
  – Section II: Nov 2 (M) during the class time
  – Section III: Dec 16 (Wed) 4:10-6:00 PM (In the finals week)
• **Grading:** 100 points each section; the final letter grades for the entire course will be determined by adding the scores from all three sections and grading on a curve.
Section I Overview

- Focus: proteins and protein structure
- Aug 24 (M) – Sept 28 (M)
- Mostly cover Chapters 1-2, 4-7
- Redacted PowerPoint slides will be available on KSOL
  – Be prepared to take good notes during lectures
- Office hours: M 1:30 – 2:30 PM, Chalmers 034
  – Or by appointment

- 1 Quiz: 10 points, Sept 4 (Friday)
- 1 Essay assignment: 20 points, due Sept 25
- 1 exam: 70 points, Sept 28 (Monday)
  - No make-up: please plan your schedule accordingly

Schedule (tentative):

<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Book Chapters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aug 24</td>
<td>Review of thermodynamics; water</td>
<td>1, 2</td>
</tr>
<tr>
<td>Aug 26</td>
<td>Acid-base reactions</td>
<td>2</td>
</tr>
<tr>
<td>Aug 28</td>
<td>Amino Acids</td>
<td>4</td>
</tr>
<tr>
<td>Aug 31</td>
<td>Amino Acids/Peptides</td>
<td>4, 5</td>
</tr>
<tr>
<td>Sep 2</td>
<td>Protein Primary Structure</td>
<td>5</td>
</tr>
<tr>
<td>Sep 4</td>
<td>10 min Quiz, Protein Secondary Structure</td>
<td>6</td>
</tr>
<tr>
<td>Sep 7</td>
<td>UNIVERSITY HOLIDAY (Labor Day)</td>
<td></td>
</tr>
<tr>
<td>Sep 9</td>
<td>Protein Tertiary and Quaternary Structure</td>
<td>6</td>
</tr>
<tr>
<td>Sep 11</td>
<td>Protein Stability and Folding</td>
<td>6</td>
</tr>
<tr>
<td>Sep 14</td>
<td>Molecular mechanics</td>
<td>class notes</td>
</tr>
<tr>
<td>Sep 16</td>
<td>Molecular modeling and simulation</td>
<td>class notes</td>
</tr>
<tr>
<td>Sep 18</td>
<td>Oxygen-binding proteins</td>
<td>7</td>
</tr>
<tr>
<td>Sep 21</td>
<td>Muscle Proteins</td>
<td>7</td>
</tr>
<tr>
<td>Sep 23</td>
<td>Protein Purification</td>
<td>5</td>
</tr>
<tr>
<td>Sep 25</td>
<td>Protein Sequencing</td>
<td>5</td>
</tr>
<tr>
<td>Sep 28</td>
<td>Section 1 Exam</td>
<td></td>
</tr>
</tbody>
</table>

(c) Jianhan Chen
Which of the following fields is biochemistry NOT relevant to?

A. Immunology  
B. Nutrition  
C. Kinesiology  
D. Waste management  
E. Brewing

Which of the following elements is most abundant (in % weight) in the human body?

A. H  
B. O  
C. N  
D. C  
E. Both H and C are equally abundant
To what class does the following compound belong?

A. Lipid
B. Carbohydrate
C. Amino acid
D. Nucleotide

Which of the following functional groups does the compound shown NOT contain?

A. amino
B. carboxyl
C. hydroxyl
D. aldehyde
To what class of molecule does the following belong?

A. Carbohydrate
B. Lipid
C. Amino acid
D. Nucleotide

BIOCH 755: Biochemistry I

Jianhan Chen
Office Hour: M 1:30-2:30PM, Chalmers 034
Email: jianhanc@ksu.edu
Office: 785-2518
Biochemistry

• Chemistry of life
  – Chemical nature and structure of biological molecules
  – Interaction of biomolecules
  – Synthesis and degradation of biomolecules (metabolism)
  – Energy generation and consumption
  – Regulation of biomolecules
  – Genetic information storage, translation, and propagation

• Highly interdisciplinary
• Direct implication in heath and medicine

1.1: Introduction to the Chemistry of Life

• **Key Concepts 1.1:**
  – Biological molecules are constructed from a limited number of elements.
  – Certain functional groups and linkages characterize different types of biomolecules.
  – During chemical evolution, simple compounds condensed to form more complex molecules and polymers.
  – Self-replicating molecules would have been subject to natural selection.
Human Body Mass Composition

Living Matter Consists of Few Elements

<table>
<thead>
<tr>
<th>Element</th>
<th>Dry Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>61.7</td>
</tr>
<tr>
<td>N</td>
<td>11.0</td>
</tr>
<tr>
<td>O</td>
<td>9.3</td>
</tr>
<tr>
<td>H</td>
<td>5.7</td>
</tr>
<tr>
<td>Ca</td>
<td>5.0</td>
</tr>
<tr>
<td>P</td>
<td>3.3</td>
</tr>
<tr>
<td>K</td>
<td>1.3</td>
</tr>
<tr>
<td>S</td>
<td>1.0</td>
</tr>
<tr>
<td>Cl</td>
<td>0.7</td>
</tr>
<tr>
<td>Na</td>
<td>0.7</td>
</tr>
<tr>
<td>Mg</td>
<td>0.3</td>
</tr>
</tbody>
</table>

*Calculated from Frieden, E., Sci. Am. 227(1), 54–55 (1972).*
Biological Polymers

- Biological macromolecules are polymers: formed through condensation reactions of various monomers
- Two extremely important outcomes:
  - Exponentially increase in the chemical versatility ($N^M$)
  - Possibility of replication (information storage, propagation & evolution)!

### TABLE 1.3 Major Biological Polymers and Their Component Monomers

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Monomer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein (polypeptide)</td>
<td>Amino acid</td>
</tr>
<tr>
<td>Nucleic acid (polynucleotide)</td>
<td>Nucleotide</td>
</tr>
<tr>
<td>Polysaccharide (complex carbohydrate)</td>
<td>Monosaccharide (simple carbohydrate)</td>
</tr>
</tbody>
</table>

Table 1.3 © 2013 John Wiley & Sons, Inc. All rights reserved.
Condensation and Hydrolysis

\[
\begin{align*}
\text{Condensation} & \quad \text{Hydrolysis} \\
\text{H}_2\text{O} & \quad \text{H}_2\text{O}
\end{align*}
\]

Dehydration takes place here

Peptide group

Replication: Mutation & Evolution

Transcription DNA→RNA
Post-transcription RNA→mRNA
Translation mRNA→Polypeptide
Degradation
Aggregation
Regulation

Post-translation (Covalent Modification) (Chaperones) (Cofactors)
Typical Animal Cell

Life Obeys Thermodynamics
1.3. Thermodynamics

- **Key Concepts 1.3:**
  - Energy must be conserved, but it can take different forms.
  - In most biochemical systems, enthalpy is equivalent to heat.
  - Entropy, a measure of a system’s disorder, tends to increase.
  - The free energy change for a process is determined by the change in enthalpy and the change in entropy \((\Delta G = \Delta H - T \Delta S)\).
  - A spontaneous process occurs with a decrease in free energy.
  - The free energy change for a reaction can be calculated from the temperature and the concentrations and stoichiometry of the reactants and products \((\Delta G = -RT \ln K_{eq})\).
  - Biochemists define standard state conditions as a temperature of 25°C, a pressure of 1 atm, and a pH of 7.0.
  - Organisms are nonequilibrium, open systems that constantly exchange matter and energy with their surroundings.
  - Enzymes increase the rates of thermodynamically favorable reactions.

---

Measuring Internal Energy

- Only changes can be measured
  \[
  \Delta E = q - w \\
  dE = \delta q - \delta w 
  \]

- If only \(P \, dV\) work (expansion or contraction) done:
  \[
  dE = \delta q - PdV \\
  = \delta q \quad \text{if constant } V \\
  \Delta E = q_v 
  \]

  - Heat exchange measured at constant volume (without other types of work done) is the internal energy change!
First Law of Thermodynamics

- **Conservation of energy**: heat (q), work (w), and (internal) energy (E)

\[ \Delta E = q - w \]
\[ dE = \delta q - \delta w \]

- **Internal energy (E)**
  - **State Function**: depends only on the state, regardless of the path of arrival
  - Microscopically: multiple contributions including: kinetic, vibrational, rotational, (chemical) bonding, non-bonded interaction, nuclei (typically not relevant in chemistry/biochemistry) components
  - Macroscopically: only definable on relative scale (see Eq above)

What about heat measured in more “natural” settings with constant pressure?

- Most (biochemical) experiments done on open systems with PV work exchange with environment:

\[ dE = \delta q - PdV \]
  - Heat exchange no longer measures internal energy change!

- Need to introduce the concept of **enthalpy**: \( H = E + PV \)
  - Heat exchange measured at constant pressure (without other types of work done) is the enthalpy change!

- Biochemical reactions in solution (NPT condition)
  - Volume change is minimal (\( \Delta V \sim 0 \))
  - \( dH = dE + P\Delta V \sim dE \)
  - That is, enthalpy is more or less equivalent to internal energy
Energy dictates the direction of many processes ...
but not always

“Ideal Gas”

\[ \Delta E = 0 \]

Entropy instead of energy dictates the direction here!

Second and Third Laws of Thermodynamics

- **Law of increasing entropy**: entropy must increase in an irreversible process
- Many other forms in different contexts
  - “No process is possible whose sole result is the transfer of heat from a body of lower temperature to a body of higher temperature” (Rudolf Clausius)
  - “No process is possible in which the sole result is the absorption of heat from a reservoir and its complete conversion into work”. (Lord Kevin)
  - …

- Existence of absolute zero temperature \((T = 0\ K)\)
- **Third law of thermodynamics**: \(S = 0\) at \(T = 0\) for perfect crystals.
Entropy

- A measure of internal heat content, or, the unavailability of a system’s energy to do work \((S=q_{rev}/T)\).
- The physical meaning of entropy is only provided in the context of statistical mechanics
  - A statistical measure of the probability for a given macro state (left equation)
  - A measure of uncertainty (from information theory) (right equation)

\[ S = k_B \ln W \quad \quad S = -k_B \sum_i p_i \ln p_i \]

- \(k_B\): Boltzmann’s constant
- \(W\): number of microscopic state
- \(p_i\): probability of a microscope state

Free Energy & Spontaneous Processes

- Both enthalpy and entropy matter (normal/NPT condition)
- **Gibbs free energy**: \(\Delta G = \Delta H - T \Delta S\)
- Free energy decreases in a spontaneous process.

<table>
<thead>
<tr>
<th>(\Delta H)</th>
<th>(\Delta S)</th>
<th>(\Delta G = \Delta H - T \Delta S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>+</td>
<td>The reaction is both enthalpically favored (exothermic) and entropically favored. It is spontaneous (exergonic) at all temperatures.</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>The reaction is enthalpically favored but entropically opposed. It is spontaneous only at temperatures below (T = \Delta H/\Delta S).</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>The reaction is enthalpically opposed (endothermic) but entropically favored. It is spontaneous only at temperatures above (T = \Delta H/\Delta S).</td>
</tr>
<tr>
<td>+</td>
<td>-</td>
<td>The reaction is both enthalpically and entropically opposed. It is nonspontaneous (endergonic) at all temperatures.</td>
</tr>
</tbody>
</table>

Table 1-4
© 2015 John Wiley & Sons, Inc. All rights reserved.

(c) Jianhan Chen
Enthalpy and Entropy Compensation

- $\Delta G = \Delta H - T\Delta S$
- Consider an example of protein folding:

\[ \Delta H_f < 0 \quad \Delta S_f < 0 \]

1. Low temperature, $\Delta G_f = \Delta H_f - T\Delta S_f < 0$ (folding)
   (the favored state is not the more “random” denatured state!)
2. At folding temperature $T_m$, $\Delta G_f = 0$ ($p_f = p_u = 0.5$)
3. High temperature, $\Delta G_f = \Delta H_f - T\Delta S_f > 0$ (unfolding)

Equilibrium Constant

- Remember that given a reaction:
  \[ A + B = C + D \]
  the quantity: $K = [C][D]/[A][B]$ is a constant that is commonly referred to as an “equilibrium constant”. But why a constant?
- **Proof:**
  - First, needs to define a “standard state” (commonly 298K, 1atm, 1M).
    Then for a solution with a concentration $[A]$,
    \[ G = G^0 + RT \ln ([A]/[A]^0) = G^0 + RT \ln [A] \]
  - Therefore,
    \[ \Delta G = \Delta G^0 + RT \ln ([C][D]/[A][B]) \]
  - At equilibrium, $\Delta G = 0$. Thus,
    \[ \Delta G^0 + RT \ln ([C][D]/[A][B]) = 0 \]
    \[ \Delta G^0 = -RT \ln K \]
    \[ K = [C][D]/[A][B] = \exp(-\Delta G^0/RT) \]
Thermochemistry

- Experimental determination of the thermodynamic parameters such as $\Delta G$, $\Delta H$ and $\Delta S$.
- $\Delta G$ can be directly calculated from $K_{eq}$
  - Often done by fitting to a titration curve
  - Require choosing a measurable that responds to binding or (bio-)chemical reaction
- Determination of $\Delta H$ and $\Delta S$
  - Van’t Hoff Relationship
  - Calorimetry
  - Theory and simulation: not reliable at quantitative level

Van’t Hoff Relationship

- The classical approach, require multiple measurements of $K_{eq}$ at different temperatures and certain assumptions

$$\ln K_{eq} = \frac{\Delta G^0}{RT} = -\frac{\Delta H^0}{RT} + \frac{\Delta S^0}{R}$$

- Assuming that $\Delta H$ and $\Delta S$ are temperature independent (often a strong assumption in biochemical/biophysical processes)
- “safer” to calculate $\Delta S=(\Delta H-\Delta G)/R$
Summary

- Biochemistry
- Organic nature of biomolecules
- Biopolymers
- Key concepts of thermodynamics

- Coming up: water and what is special about it
Which of the following is not true for biochemical standard conditions?

A. The concentrations of reactants and products is 1M.
B. The concentration of hydrogen ions is 1M.
C. Temperature is 25°C/298K.
D. Pressure is 1 atmosphere.