CHEM 565 and CHEM/BIOCHEM 665
BIOPHYSICAL CHEMISTRY

University of Wisconsin-Madison
- Spring 2020 -

LECTURE: 9:55 – 10:45 a.m. MTRF, B371 Chemistry

LECTURER: Prof. Silvia Cavagnero
Office: 5357 Chemistry
Phone: 262-5430
Email: cavagnero@chem.wisc.edu

OFFICE HOURS: M, F 10:55 - 11:55 a.m. and by appointment
Location: rm. 5357 Chemistry

TEACHING ASSISTANT: Miranda Mecha
Office: rm. B221 Chemistry
Email: mmecha@wisc.edu

TA OFFICE HOURS: T, R 11:00 - 11:50 a.m., and by appointment
Location: rm. B221 Chemistry

COURSE WEB SITE: https://canvas.wisc.edu/courses/174976
use your UW login and password to access Canvas,
click on the Chem665:Biophysical Chemistry icon to
enter the class web site

INTRODUCTION
CHEM 565/CHEM 665/BIOCHEM 665 is an introductory class on equilibrium thermodynamics and chemical kinetics with emphasis to biological applications. Issues of particular interest are the concept of entropy, enthalpy and free energy, the kinetics of complex reactions, the non-covalent forces that determine protein and nucleic acid stability (particularly the hydrophobic effect, electrostatic interactions and the hydrogen bond) and the folding and misfolding kinetics of proteins and nucleic acids.

OFFICIAL COURSE DESCRIPTION
Equilibrium thermodynamics, chemical kinetics, and transport properties, with emphasis on solution behavior and applications to biological macromolecules in solution. For students interested primarily in the biological applications of physical chemistry.
**Requisites:** CHEM 327 or 329; MATH 222; Physics 201 or 207; BIOCORE 303, or BIOCHEM 501 or concurrent registration, or consent of instructor. Not for credit for those who have taken CHEM 561

**Course Designations:** Advanced level; physical science breadth; counts as L&S credit

**Instructional mode:** Face-to-face

**NUMBER OF CREDITS AND CREDIT-HOUR POLICY STANDARDS**
This is a 4-credit course. The course meets the credit-hour policy standard by offering 4 weekly lectures, with the expectation that students will work on course learning activities for about 2 hours out of classroom for every class period. Learning activities include a 1-hr weekly discussion meeting, reading, studying, problem sets, two exams, and a final exam. Both the instructor and the TA will have 2 weekly office hrs each to facilitate and foster student learning.

**LEARNING OUTCOMES**
The expected learning outcomes of this course are the acquisition of a thorough knowledge of the fundamental principles of thermodynamics and kinetics and their applications to biological systems. The primary objective of this course is to enable students gain a deep understanding and, in some cases acquire predictive power, on how chemical and biological processes work.

**TEXTBOOK AND OTHER REQUIRED MATERIAL**
2. Handouts distributed in class or uploaded on the class web site.
3. An inexpensive non-programmable calculator (e.g., Texas Instruments TI-30Xa or an equivalent device). It should have capabilities for square roots, logarithms and exponential operations. The calculator will be used on exams and homework assignments. A programmable calculator will not be allowed during exams.

**ADDITIONAL USEFUL READING**
Barrick, *Biomolecular Thermodynamics: From Theory to Application (Foundations of Biochemistry and Biophysics)*, Taylor and Francis, 1st edition, 2017;
Eisenberg and Crothers, *Physical Chemistry with Applications to the Life Sciences*, Addison-Wesley, 1979;
Cantor and Schimmel, *Biophysical Chemistry, Volumes 1, 2 and 3*, Freeman, 1980;
Hammes, *Thermodynamics and Kinetics for the Biological Sciences*, Wiley & Sons, 2000;
Fersht, *Structure and Mechanism in Protein Science: A Guide to Enzyme Catalysis and Protein Folding*, Freeman, 1999;
Klotz and Rosenberg, *Chemical Thermodynamics*, Wiley & Sons, 1994;
Jencks, Catalysis in Chemistry and Enzymology, Wiley & Sons, 1975;
Klotz, Ligand-Receptor Energetics, Wiley & Sons, 1997;
Weber, Protein Interactions, Chapman & Hall, 1992;
Espenson, Chemical Kinetics and Reaction Mechanisms, McGraw Hill, 1995;
Crothers, Bloomfield, Tinoco, Nucleic Acids, Structures, Properties and Functions,

COURSE INFORMATION

Lectures. During lectures we will discuss principles and illustrate them with examples. You should take your own notes during lecture and it is important that you come to class to learn from the instructor and be interactive. Attendance is mandatory. A set of lecture notes taken by a Teaching Assistant (TA) will be available on the web (see course website above), in case you had to occasionally miss any of the lectures. Please be sure to turn your cell phones off during lecture so that you can focus on learning the material.

Lecture Schedule. The Biophysical Chemistry (CHEM 565/665) lectures are on Mondays, Tuesdays, Thursdays and Fridays at 9:55 am. Please check the course outline (which follows) for a detailed schedule of the lectures.

Textbook. The textbook supplements the lectures. It provides background material for the lectures and also works out many relevant examples. In addition, at the end of each chapter are a number of problems. For an understanding of the material in this course it is important to solve as many of these problems as possible. Plan to buy your own textbook as you will need it very often during the semester. A reference copy of the textbook is available for consultation in the Steenbock and College libraries. The Steenbock library also contains a copy of the Additional Useful Reading material listed above.

Problem Sets. For each chapter a set of especially relevant problems is assigned. The formation of study groups for working on problems is strongly encouraged. Difficulties with any problems should be discussed with your TA in the discussion sessions. Unless otherwise stated in the syllabus, the problem sets are usually handed in on Fridays and are due the following Friday of the following week. Hand in your worked-out problem sets in class by 9:55 a.m. (i.e., right before Friday class) on the due date. Graded problem sets will be typically distributed during the Wednesday Discussion Sessions and answer keys will be posted on Canvas after the due date. Please check the course outline (which follows) for a detailed schedule of the problem set due dates.

Discussion Sessions. Discussion sessions are primarily for review and problem solving relevant to the recent lecture material. Your TA will go over some examples similar to the assigned problems. You should be prepared when you come to discussion session. Ask specific questions to your TA and plan to be interactive. Discussion sessions are on Wednesdays, at either 9:55 am in room 2373, at 11:00 am in room 2311, or at 12:05 pm in room 2311.
**Exams.** There will be three one-hour exams, and a two-hour final exam. Check the Course Outline (which follows) for the examination dates and times. The exams will primarily be based on the material presented in the lectures, and on material illustrated by the assigned problems. No make-up exams will be given. The final exam will be comprehensive, covering topics from the entire semester.

**Special Requirement for Students Taking the Class as Chem/Biochem 665: Oral Presentations.** All students taking the course as Chem/Biochem 665 are required to deliver one oral-presentation on a topic chosen from the following list:

(a) The effect of molecular crowding and non-specific binding on protein structure and conformation;
(b) The effect of salts on protein and nucleic acid stability;
(c) The preferential interaction coefficient and the effect of cosolutes on protein stability;
(d) The role of friction in protein folding kinetics: Kramer’s reaction rate theory and comparisons with transition-state and Arrhenius theories;
(e) The concept of cooperativity in protein folding and unfolding;
(f) The thermodynamic, kinetic and structural role of molecular chaperones;
(g) The mechanism of protein aggregation and its relations to neurodegenerative diseases;
(h) Isothermal titration calorimetry (ITC) and the measurement of enthalpy and entropy contributions upon ligand binding in protein-protein and protein-ligand interactions;
(i) Experimental methods to detect protein hydration and the role of hydration in macromolecule structure and function.
(k) Sickle cell anemia, fibril formation and nucleation kinetics.
(m) The mechanism of cotranslational protein folding.
(m) Liquid-liquid phase separations in live cells.

The topics will be presented mini-lecture (12 min total, 3 minutes for questions), out of a unique powerpoint file. Small catchy demos during the presentation are encouraged. Oral presentations should contain clear connections to the material studied in class during the semester and further in-depth insights. Plan to talk to Prof. Cavagnero well in advance (within a week after Exam I) to discuss your group’s choice of special topic. The special topic will be presented to the class during the last two weeks of class according to the class schedule below. Powerpoint presentations are recommended. Your grade will be determined in part by a grade assigned by the instructor during your presentation and in part by a peer review of your slides about one week ahead of the presentation date.

**HONESTY AND VIOLATIONS OF PROPER CONDUCT**
Perhaps needless to write, in this class it is expected that you will be 100% honest. Academic misconduct of any type, as defined at: https://conduct.students.wisc.edu/academic-misconduct/ will not tolerated under any circumstances.

**GRADES**
This course will be graded on a maximum of 100 % divided as follows:
CHEM/BIOCHEM 565 STUDENTS:
Exam I 20 %
Exam II 20 %
Exam III 20 %
Class Attendance 5 %
Homework Questions 10 %
Final Exam 25 %
Total 100 %

CHEM/BIOCHEM 665 STUDENTS:
Exam I 16 %
Exam II 16 %
Exam III 16 %
Oral Presentation 12 %
Class Attendance 5 %
Homework Questions 10 %
Final Exam 25 %
Total 100 %

Your course grade will be determined by the total number of points you have accumulated.

**Extra Credit Points.** Up to 2 % extra credit (in addition to the total 100 %) will be assigned to students who provide, on a voluntary basis, a written outline containing detailed comments on the textbook typos and unclear statements. This outline is due on Wednesday, May 6 by 9 am and should be emailed to Silvia in word (not PDF) format.

**COURSE OUTLINE**

<table>
<thead>
<tr>
<th>DATE</th>
<th>TOPIC</th>
<th>CHAPTER</th>
<th>NOTES ON PROBLEM SETS</th>
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<tbody>
<tr>
<td>T Jan 21</td>
<td>Principles of Probability</td>
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<td>R Jan 23</td>
<td>Principles of Probability</td>
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<td>F Jan 24</td>
<td>Principles of Probability</td>
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<td>M Jan 27</td>
<td>Principles of Probability</td>
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<td>T Jan 28</td>
<td>Principles of Probability</td>
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<td>Problem Set #1 Assigned</td>
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<tr>
<td>R Jan 30</td>
<td>Principles of Probability</td>
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<tr>
<td>F Jan 31</td>
<td>Predicting Equilibrium in Chemistry and Biology</td>
<td>2</td>
<td>Problem Set #1 Due</td>
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<td>Problem Set #2 Assigned</td>
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M Feb 3  Heat, Work & Energy  3
T Feb 4  Heat, Work & Energy  3
R Feb 6  Brief math review, Random Walks in Biophysics  
F Feb 7  Random Walks in Biophysics  --  Problem Set #2 Due  
M Feb 10 Random Walks in Biophysics:  --  Problem Set #3 Assigned  
T Feb 11 Multivariate Calculus  4  
R Feb 13 Entropy & the Boltzmann Law  5  
F Feb 14 Entropy & the Boltzmann Law Pre-exam minireview/Q-A session  5  
M Feb 17 **Exam I** (9:55 am, 1 hr, room TBA)  
*Note: there will be no class today*
T Feb 18 Thermodynamic Driving Forces  6  *(TA lecture)*
R Feb 20 Thermodynamic Driving Forces  6  
F Feb 21 The logic of Thermodynamics  7  Problem Set #4 Assigned  
M Feb 24 The logic of Thermodynamics  7  
T Feb 25 Lab Conditions & Free Energies  8  
R Feb 27 Lab Conditions & Free Energies  8  
F Feb 28 Lab Conditions & Free Energies  8  Problem Set #4 Due  
M March 2 Lab Conditions & Free Energies  8  Problem Set #5 Assigned  
T Mar 3 Maxwell’s Relations and Mixtures  9  
R Mar 5 Maxwell’s Relations and Mixtures  9  
F Mar 6 The Boltzmann Distribution Law  10  Problem Set #5 Due  
*Problem Set #6 Assigned*
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<tr>
<th>Date</th>
<th>Topic</th>
<th>Days</th>
<th>Notes</th>
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<tr>
<td>M Mar 9</td>
<td>The Boltzmann Distribution Law</td>
<td>10</td>
<td>TA lecture</td>
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<tr>
<td>T Mar 10</td>
<td>The Boltzmann Distribution Law Pre-exam minireview/Q-A session</td>
<td>10</td>
<td>TA lecture</td>
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<td>R Mar 12</td>
<td><strong>Exam II</strong> (9:55 am, 1 hr, room TBA)</td>
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<td>Note: there will be no class today</td>
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<td>F Mar 13</td>
<td>Noncovalent inter-molecular interactions</td>
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<td>(Guest lecture by Prof. Sandro Mecozzi)</td>
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<td>M Mar 16</td>
<td>Spring Break</td>
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<td>T Mar 17</td>
<td>Spring Break</td>
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<td>R Mar 19</td>
<td>Spring Break</td>
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<td>F Mar 20</td>
<td>Spring Break</td>
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<tr>
<td>M Mar 23</td>
<td>Temperature and Heat Capacity</td>
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<td>T Mar 24</td>
<td>Chemical Equilibria</td>
<td>13</td>
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<td>R March 26</td>
<td>Chemical Equilibria</td>
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<td>F March 27</td>
<td>Chemical Equilibria</td>
<td>13</td>
<td>Problem Set #7 due</td>
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<td>Problem Set #8 assigned</td>
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<td>M March 30</td>
<td>Chemical Equilibria</td>
<td>13</td>
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<tr>
<td>T March 31</td>
<td>Chemical Equilibria</td>
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<td>R Apr 2</td>
<td>Hot Topics in Biophysics I: Protein Stability, Folding and the Hydrophobic effect</td>
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<tr>
<td>F Apr 3</td>
<td>Hot Topics in Biophysics I: Protein Stability, Folding and the Hydrophobic Effect, Thermal Unfolding</td>
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<td>No problem set due today</td>
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<td>M Apr 6</td>
<td>Hot topics in Biophysics II: Practical Biophysical</td>
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<td>T Apr 7</td>
<td>Hot topics in Biophysics III: Practical Biophysical Chemistry -- Protein Unfolding Titrations and Effect of Denaturing Agents</td>
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<tr>
<td>R Apr 9</td>
<td>Hot topics in Biophysics IV: Partition Coefficient, Hydration, Preferential Interaction Coefficient and Solute Effects on Protein Stability</td>
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<td>F Apr 10</td>
<td>Hot topics in Biophysics V: Net charge and hydrophobicity in biomolecular structure: the amazing world of folded and intrinsically disordered proteins (IDPs)</td>
<td>-- No problem set due today</td>
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<td>M Apr 13</td>
<td>Physical Kinetics (and Vector Calculus Handout)</td>
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<td>T Apr 14</td>
<td>Physical Kinetics</td>
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<td>R Apr 16</td>
<td>Physical Kinetics</td>
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<td>F Apr 17</td>
<td>Microscopic Dynamics</td>
<td>18 Problem Set #8 Due</td>
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<td>Problem Set #9 Assigned</td>
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<td>M Apr 20</td>
<td>Chemical Kinetics</td>
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<td>T Apr 21</td>
<td>Chemical Kinetics</td>
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<td>R Apr 23</td>
<td>Chemical Kinetics</td>
<td>19 Pre-exam minireview/Q-A session</td>
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<td>F Apr 24</td>
<td>665-Student Oral Presentations</td>
<td>-- Problem Set #9 Due</td>
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<td>M Apr 27</td>
<td><strong>Exam III</strong> (9:55 am, 1 hr, room TBA)</td>
<td>Note: there will be no class today</td>
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<tr>
<td>T Apr 28</td>
<td>665-Student Oral Presentations</td>
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</table>
R Apr 30  665-Student Oral Presentations  --
F May 1  665-Student Oral Presentations  --
T May 5  **FINAL EXAM** (2:45 pm – 4:45 pm, room TBA)
*Note: the final exam will cover all
the material taught during the semester*