

**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

1. Dill & Bromberg, *Molecular Driving Forces*, 2nd edition, Garland Science, 2011.
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;
Van Holde, Johnson and Ho, *Principles of Physical Biochemistry*, Prentice Hall, 1998;
Tinoco, Sauer, Wang and Puglisi, *Physical Chemistry: Principles and Applications in Biological Sciences*, Pearson Education, 2001;
Jackson, *Molecular and Cellular Biophysics*, Cambridge Univ. Press, 1st edition, 2006;
Cantor and Schimmel, *Biophysical Chemistry, Volumes 1, 2 and 3*, Freeman, 1980;
Serdyuk, Zaccai, Zaccai, *Methods in Molecular Biophysics*, Cambridge, 2007;
Daune, *Molecular Biophysics: Structures in Motion*, Oxford Un. Press, 2nd edition, 2006;
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;
Connors, *Chemical Kinetics, The study of Reaction Rates in Solution*, VCH, 1990;
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*, Mc Graw Hill, 1995;
Creighton, *Proteins: Structures and Molecular Properties*, Freeman & Co., 1992;
Crothers, Bloomfield, Tinoco, *Nucleic Acids, Structures, Properties and Functions*,
University Science Books, 2000.

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.
- (l) The mechanism of *in vitro* protein folding.
- (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 %
<u>Final Exam</u>	<u>25 %</u>
Total	100 %

CHEM/BIOCHEM 665 STUDENTS:

Exam I	16 %
Exam II	16 %
Exam III	16 %
Oral Presentation	12 %
Class Attendance	5 %
Homework Questions	10 %
<u>Final Exam</u>	<u>25 %</u>
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

<u>DATE</u>	<u>TOPIC</u>	<u>CHAPTER</u>	<u>NOTES ON PROBLEM SETS</u>
T Jan 21	Principles of Probability	1	
R Jan 23	Principles of Probability	1	
F Jan 24	Principles of Probability	1	Problem Set #1 Assigned
M Jan 27	Principles of Probability	1	
T Jan 28	Principles of Probability	1	
R Jan 30	Principles of Probability	1	
F Jan 31	Predicting Equilibrium in Chemistry and Biology	2	Problem Set #1 Due Problem Set #2 Assigned

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 Problem Set #3 Assigned
M Feb 10	Random Walks in Biophysics:	--	
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	Problem Set #3 Due No Problem Set Assigned This Week
M Feb 17	Exam I (9:55 am, 1 hr, room TBA) <i>Note: there will be no class today</i>		
T Feb 18	Thermodynamic Driving Forces (TA lecture)	6	
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 Problem Set #5 Assigned
M March 2	Lab Conditions & Free Energies	8	
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

M Mar 9	The Boltzmann Distribution Law (TA lecture)	10	
T Mar 10	The Boltzmann Distribution Law Pre-exam minireview/Q-A session (TA lecture)	10	
R Mar 12	Exam II (9:55 am, 1 hr, room TBA) <i>Note: there will be no class today</i>		
F Mar 13	Noncovalent inter-molecular interactions (Guest lecture by Prof. Sandro Mecozzi)		Problem Set #6 due Problem Set #7 Assigned
M Mar 16	Spring Break	--	
T Mar 17	Spring Break	--	
R Mar 19	Spring Break	--	
F Mar 20	Spring Break	--	
M Mar 23	Temperature and Heat Capacity	12	
T Mar 24	Chemical Equilibria	13	
R March 26	Chemical Equilibria	13	
F March 27	Chemical Equilibria	13	Problem Set #7 due Problem Set #8 assigned
M March 30	Chemical Equilibria	13	
T March 31	Chemical Equilibria	13	
R Apr 2	Hot Topics in Biophysics I: Protein Stability, Folding and the Hydrophobic effect		
F Apr 3	Hot Topics in Biophysics I: Protein Stability, Folding and the Hydrophobic Effect, Thermal Unfolding	--	No problem set due today
M Apr 6	Hot topics in Biophysics II: Practical Biophysical	--	

Chemistry – Burial of Surface Area
and Relations to Protein Folding and
Ligand Binding

T Apr 7	Hot topics in Biophysics III: Practical Biophysical Chemistry -- Protein Unfolding Titrations and Effect of Denaturing Agents	--	
R Apr 9	Hot topics in Biophysics IV: Partition Coefficient, Hydration, Preferential Interaction Coefficient and Solute Effects on Protein Stability	16	
F Apr 10	Hot topics in Biophysics V: Net charge and hydrophobicity in biomolecular structure: the amazing world of folded and intrinsically disordered proteins (IDPs)	--	No problem set due today
M Apr 13	Physical Kinetics (and Vector Calculus Handout)	17	
T Apr 14	Physical Kinetics	17	
R Apr 16	Physical Kinetics	17	
F Apr 17	Microscopic Dynamics	18	Problem Set #8 Due Problem Set #9 Assigned
M Apr 20	Chemical Kinetics	19	
T Apr 21	Chemical Kinetics	19	
R Apr 23	Chemical Kinetics Pre-exam minireview/Q-A session	19	
F Apr 24	665-Student Oral Presentations	--	Problem Set #9 Due
M Apr 27	Exam III (9:55 am, 1 hr, room TBA) <i>Note: there will be no class today</i>		
T Apr 28	665-Student Oral Presentations	--	

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) <i>Note: the final exam will cover all the material taught during the semester</i>	