CHEM 565 and CHEM/BIOCHEM 665
BIOPHYSICAL CHEMISTRY

SYLLABUS

- Spring 2023 -

LECTURE: 9:55 – 10:45 a.m. MTRF, in-person
(required attendance, see also Appendix for health/emergency-related needs)
Location: room 1435 New Chemistry Building (North Tower)

DISCUSSION: on W, in-person
9:55 – 10:45 a.m. (disc. 301, in 2425 Sterling Hall);
11:00 – 11:50 a.m. (disc. 302, in 2333 Sterling Hall);
12:05 – 12:55 p.m. (disc. 303, in 2333 Sterling Hall)
(required attendance: one discussion section per week, see also Appendix for health/emergency-related needs)

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

PROF OFFICE HOURS: M, F 10:55 - 11:55 a.m. and by appointment
Location: room 6449 New Chemistry Building (North Tower)
(see also Appendix for health/emergency-related needs)

TEACHING ASSISTANT: Shapla Ummay Mahfuza
Office: N.A.: reach your TA by email or in person during her office hours in room 6449 New Chemistry Building (North Tower)
Email: shapla@wisc.edu

TA OFFICE HOURS: T, R 10:55 - 11:55 a.m., and by appointment
Location: room 6449 New Chemistry Building (North Tower)
(see also Appendix for health/emergency-related needs)

COURSE WEB SITE: https://canvas.wisc.edu/courses/328738
Click the link above. Alternatively, you can use your UW login and password to access Canvas, then click on the "Chem665: Biophysical Chemistry (001) SP23" icon to enter the class web site

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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.

> **Prerequisites:** 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:** In-person, with synchronous required attendance

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.

INCLUSIVENESS, FAIRNESS AND BIAS PREVENTION

This course welcomes all students that meet the prerequisites, regardless of ethnicity, nationality and cultural background. Every effort will be made to make the class environment inclusive, welcoming and fair, to render all assignments as equitable as possible, and to promote cooperation and bas prevention among students, as well as among students and professor, and among students and TA. In case you were to experience any type of bias, please do not hesitate to reach out to Silvia, your TA and/or any other university resources. Every effort will be made to help you feel welcome!

SPECIAL ACCOMMODATIONS

In case you need special accommodations, please touch base with the McBurney Center (https://mcburney.wisc.edu/) and keep Silvia informed. Every effort will be made to help you and to take your needs into account.

PANDEMIC-RELATED CONSIDERATIONS

- There are no covid-related university rules, this semester. Therefore mask-wearing during lecture is not required. On the other hand, you are welcome to wear a mask if you wish.
- If you experience COVID-19-related symptoms, do not come to class and get tested as soon as possible. In case of positive COVID-19 test results follow the advice of your physician and let Silvia and the TA know that you need to quarantine (you do not have to explain why). Appropriate accommodations for missed classes will be made. See additional guidelines and helpful advice at: https://covidresponse.wisc.edu/

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. Attendance will be taken during class (see Appendix for details). Please be sure to turn your cell phones off during lecture so that you can focus on learning the course 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 week on Friday. Electronically submit your worked-out problem sets by 9:55 a.m. of the due date (i.e., right before Friday class). Instructions on how to submit problem sets electronically are available in the Appendix. Graded problem sets will typically be available by the following Wednesday's 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 in-person on Wednesdays, at either 9:55 am, 11:00 am or 12:05 pm. See page 1 of this document for locations. Note: discussion sessions will not be recorded. The Appendix also lists additional information.

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: Written Reports. All students taking the course as Chem/Biochem 665 are required to prepare a written report on a topic chosen from the following list:

(a) Thermodynamics and kinetics of prion proteins
(b) Kinetic trapping in protein folding
(c) The effect of molecular crowding and non-specific binding on protein structure and conformation
(d) The effect of salts on protein and nucleic acid stability
(e) The preferential interaction coefficient and the effect of cosolutes on protein stability
(f) The role of friction in protein folding kinetics: Kramer's reaction rate theory and comparisons with transition-state and Arrhenius theories
(g) The concept of cooperativity in protein folding and unfolding

(h) The thermodynamic, kinetic and structural role of molecular chaperones
(i) The mechanism of protein aggregation and its relations to neurodegenerative diseases
(j) Isothermal titration calorimetry (ITC) and the measurement of enthalpy and entropy contributions upon ligand binding in protein-protein and protein-ligand interactions
(k) Experimental methods to detect protein hydration and the role of hydration in macromolecule structure and function
(l) Sickle cell anemia, fibril formation and nucleation kinetics
(m) The mechanism of cotranslational protein folding
(n) Liquid-liquid phase separations in live cells
(o) Specific case studies illustrating the concept of "energy coupling" in biology

Additional topic choices related to thermodynamics or kinetics are also possible. Consult with Silvia if you would like to propose an alternative topic. Details on the format and requirements for the written report will be made available and posted on CANVAS separately.

HONESTY AND VIOLATIONS OF PROPER CONDUCT

Importantly, it is expected that you will be 100% honest in this class. 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 %
Written Report	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 Monday, May 8 by 10 am (firm deadline) and should be emailed to Silvia in word (not PDF) format.

COURSE OUTLINE

DATE	TOPIC	CHAPTER	NOTES ON PROBLEM SETS
T Jan 24	Principles of Probability	1	
R Jan 26	Principles of Probability	1	
F Jan 27	Principles of Probability	1	Problem Set #1 Assigned
M Jan 30	Principles of Probability	1	
T Jan 31	Principles of Probability	1	
R Feb 2	Principles of Probability	1	
F Feb 3	Predicting Equilibrium in Chemistry and Biology	2	Problem Set #1 Due Problem Set #2 Assigned
M Feb 6	Heat, Work & Energy	3	
T Feb 7	Heat, Work & Energy	3	
R Feb 9	Brief math review, Random Walks in Biophysics	--	
F Feb 10	Random Walks in Biophysics	--	Problem Set #2 Due Problem Set #3 Assigned
M Feb 13	Random Walks in Biophysics:	--	
T Feb 14	Multivariate Calculus	4	
R Feb 16	Entropy & the Boltzmann Law	5	
F Feb 17	Entropy & the Boltzmann Law Pre-exam minireview/Q-A session	5	Problem Set #3 Due No Problem Set Assigned This Week
M Feb 20	**Exam I** (9:55 am, 1 hr in class)		
T Feb 21	Thermodynamic Driving Forces *Online Lecture*	6	
R Feb 23	Thermodynamic Driving Forces	6	

F Feb 24	The logic of Thermodynamics	7	Problem Set #4 Assigned
M Feb 27	The logic of Thermodynamics	7	
T Feb 28	Lab Conditions & Free Energies	8	
R Mar 2	Lab Conditions & Free Energies	8	
F Mar 3	Lab Conditions & Free Energies	8	Problem Set #4 Due Problem Set #5 Assigned
M March 6	Lab Conditions & Free Energies	8	
T Mar 7	Maxwell's Relations and Mixtures	9	
R Mar 9	Maxwell's Relations and Mixtures	9	
F Mar 10	The Boltzmann Distribution Law	10	Problem Set #5 Due No Problem Set Assigned This Week
M Mar 13	*No class, spring Break*		
T Mar 14	*No class, spring Break*		
R Mar 16	*No class, spring Break*		
F Mar 17	*No class, spring Break*		
M Mar 20	The Boltzmann Distribution Law	10	
T Mar 21	The Boltzmann Distribution Law Pre-exam minireview/Q-A session	10	
R Mar 23	**Exam II** (9:55 am, 1 hr, in class)		
F Mar 24	Temperature and Heat Capacity	12	Problem Set #6 Assigned
M Mar 27	Chemical Equilibria *In-class Lecture by TA*	13	
T Mar 28	Chemical Equilibria *In-class Lecture by TA*	13	
R Mar 30	Chemical Equilibria	13	

F Mar 31	Chemical Equilibria	13	Problem Set #6 Due Problem Set #7 Assigned (Long Problem Set)
M Apr 3	Chemical Equilibria	13	
T Apr 4	Hot Topics in Biophysics I: Protein Stability and Folding	--	
R Apr 6	Hot Topics in Biophysics I: Protein Stability, Folding and the Hydrophobic Effect	--	
F Apr 7	Hot Topics in Biophysics I: the Hydrophobic Effect and Thermal Unfolding	--	
M Apr 10	Hot topics in Biophysics II: Practical Biophysical Chemistry – Burial of Surface Area and Relations to Protein Folding and Ligand Binding	--	
T Apr 11	Hot topics in Biophysics III: Practical Biophysical Chemistry -- Protein Unfolding Titrations and Effect of Denaturing Agents	--	
R Apr 13	Hot topics in Biophysics IV: Partition Coefficient, Preferential Interaction Coefficient and Solute Effects on Protein Stability	16	
F Apr 14	Hot topics in Biophysics V: Net Charge and Hydrophobicity in Biomolecular Structure: the Amazing World of Folded and Intrinsically Disordered Proteins (IDPs)	--	Problem Set #7 Due Problem Set #8 Assigned
M Apr 17	Hot topics in Biophysics VI: 'Free-Energy Coupling and Thermo Wizardry': How to Make the Impossible Happen	--	

T Apr 18	Physical Kinetics (and Vector Calculus Handout)	17	
R Apr 20	Physical Kinetics	17	
F Apr 21	Chemical Kinetics	19	Problem Set #8 Due Problem Set #9 Assigned
M Apr 24	Chemical Kinetics	19	
T Apr 25	Chemical Kinetics	19	
R Apr 27	Chemical Kinetics	19	
F Apr 28	Chemical Kinetics	19	Problem Set #9 Due
M May 1	Chemical Kinetics	19	
T May 2	Chemical Kinetics	19	
	Pre-exam minireview/Q-A session		
R May 4	**Exam III** (9:55 am, 1 hr, in class)		
F May 5	End-of-semester review/Q-A session --		
Sun May 7	**FINAL EXAM** (12:25 pm – 2:25 pm, location TBA) *Note: the final exam will cover all the material taught during the semester*		

APPENDIX

Additional Practical Details

LECTURES (IN-CLASS MEETINGS)

How lecture time works:
Chem 565/665 will be **in-person** this semester. In-**person attendance is required and will count towards your grade** (see Syllabus). Attendance will be monitored during random lectures a few times during the semester. Note: the lectures will not be recorded.

How in-person attendance will be monitored:
In-person attendance is required and will count toward your grade. We will take attendance with a sign-in sheet that will be at the classroom entrance. We will show you where it is on the first day of class. Please sign that sheet next to your name either when you enter class or when you leave.

What do I do if I am occasionally unable to attend lecture in person?
While lecture is mandatory and in person, it is possible that you may occasionally have health issues, some type of emergency, or other compelling reasons for occasionally not being able to attend lecture or discussion. If this is the case, we will be happy to help. If you are occasionally unable to attend lecture, send an email ($\geq$ 24 hr notice is preferred) to your TA (and cc Silvia) asking to be excused. Please note that a regular, recurrent conflict with another class time throughout the semester is not considered an excused absence. If you are excused from attending in person, you will not get any attendance penalties.

Important lecture guidelines:
We are excited to have this class in the new chemistry building! This space is set up differently from a traditional lecture hall. Therefore, there are a few things we want you to keep in mind for class in this space:

1. Enter the classroom from outside the building. You cannot enter the classroom by going through the other chemistry buildings (e.g. Daniels, Mathews, or Shain). If you want to go to a different chemistry building after class, you will need to exit the building and re-enter an entrance of the building you want to go to.
2. There are tables set up with eight chairs around each table. Sit with only four people at a table, and do not sit directly next to another student, when possible, to allow for adequate physical distancing.
3. Do not move the tables or chairs.
4. Do not walk near the podium at the front of the classroom. There are wires around there we do not want you to trip over.
5. Be careful and aware of the wires at your table. Do not kick them or step on them.
6. The tables have outlets on top of them. Feel free to use these to charge your laptop or phone during lecture.

7. The tables have microphones on top of them. Please use the microphone whenever you would like to ask a question, so Silvia can hear you. Otherwise, leave them turned off.

How to ask questions during lecture (in-class meeting):
Raise your hand as during regular pre-pandemic times. Silvia will call on you to ask your question. Please say your name upfront during the first 5-6 weeks of class (for easy identification) and use the microphone on your table to ask your question, so that Silvia can hear you. Note that the microphone button needs to remain continuously pressed, while you ask your question.

HOMEWORK AND EXAMS

How to submit homework assignments:
All homework assignments will be submitted as pdf documents onto Canvas. To turn in your homework, start by generating a single PDF file with your worked-out problem set. Then go to CANVAS, click on "Assignments" on the left. Then click on the most recent problem set and select a file with your homework to upload.

Exams: Exams will be in-person during class time. Exact exam policies will be communicated later in the semester.