Structural and Physical Biochemistry

CHE 474/674 (Fall 2018) – 3 credits

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Teaching Assistants (TAs)

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Lecture: 9:30-10:50 am on Tuesdays and Thursdays in LSB 105
TA Office Hours: 5-6 pm on Mondays in LSB 215 (computer room) and Thursday 7-8 pm in CST 1-019 (recitation / problem solving session)
Prof. Office Hours: 1-2:30 pm on Fridays in 3rd floor CST conference room (3-014G CST)

Course Description:

CHE 474/674 covers basic physical chemistry for the undergraduate biochemistry/physical science majors and graduate students with interests in the biochemical sciences. The course begins with a discussion of interactions between biological molecules in solution, the laws of thermodynamics, chemical equilibrium and the application of the 1st and 2nd laws of thermodynamics to biochemical systems (e.g. binding). Part II of the course addresses important physical and structural properties of DNA/RNA/proteins (e.g. DNA melting, self-association mechanisms), and ligand binding experiments. Part III will briefly review chemical kinetics as applied to biological systems. The remainder of the course covers bonding in chemistry using quantum mechanics and analyzes the optical properties and absorption spectra of biological macromolecules. If time permits, we will discuss further uses of quantum mechanics to understand biomolecular NMR.

In addition to discussing the physical and chemical properties of biological systems, students in CHE 474/674 will use the biomolecular modeling program Pymol in a computer laboratory to analyze structures of drugs, proteins, and DNA/RNA. In addition to viewing and analyzing structures, Pymol has some basic building tools for small molecules and peptides. In a final assignment, Pymol will be used to make figures of biological molecules that are incorporated into a short scientific paper describing the nature and function of a small molecule-macromolecule interaction.

Learning Objectives:

1) You will be able to analyze macromolecular structures of proteins and nucleic acids in detail using molecular visualization tools.
2) You will be able to explain in writing the laws of thermodynamics, specifically the relationships involving internal energy, free energy, heat, work, and entropy.
3) You will be able to apply thermodynamic equations **to solve problems** involving chemical and physical equilibria of biological molecules including proteins and nucleic acids.
4) You will be able to use a combination of thermodynamics, molecular structure, and non-covalent interactions to understand protein/RNA folding, and DNA melting.
5) You will be able to use and apply the principles of chemical kinetics to reaction schemes and enzymes.
6) You will be able to use the concepts of quantum mechanics to understand electron configurations of atoms, molecular orbitals, and molecular bonding and structure.
7) You will be able to apply the principles of quantum mechanics to understand the molecular basis of optical spectroscopies including UV and fluorescence.

Required Text:
Physical Chemistry. Principles and Applications in Biological Sciences, 5th. ed., Tinoco, Sauer, Wang, Puglisi, Harbison and Rovnyak, Pearson Education, Inc., Upper Saddle River, NJ, 2014. This text is available at the bookstore, together with its online resources. You may also buy (or rent) this book from other sources such as Amazon (ISBN 978-0136056065). Keep in mind that the final exam is scheduled for December 10 if you decide to rent this textbook. I personally recommend getting a hard copy to keep, as this is a good resource if you plan to continue in the biomolecular sciences.

Resource Texts:
In addition to the main text, I will occasionally use resources from other texts including:

- *Biochemistry*, latest edition (Berg, Stryer). This text, which is mainly descriptive, covers the structure and function of DNA, RNA, and proteins.
- *Biochemistry,* Mathews, C. K., et al., Addison Wesley Longman, Inc., San Francisco, latest edition. This physically oriented general biochemistry text covers many topics addressed in CHE 474/674.

Grading:
Exams 1-3: Each is worth 16%
Final Exam: 22%
Group Work: 5%
Pymol Homeworks 1 - 3: 5% each
Pymol Homework 4: 10%

The grading scale will be such that the average score will represent a B- or C+, to be determined. All letter-grade numerical boundaries will be chosen to minimize assignments of different letter grades to two students whose performance is essentially identical. Completion of any incomplete will require taking the missed exam(s) in Fall 2019, which is the next time this course will be offered.

Students enrolled in CHE 674 can expect a greater number and more challenging questions on exams as well as more demanding homework assignments than their CHE 474 counterparts. Separate grading scales will be used for CHE 474 and CHE 674.

Course Organization: Structural and Physical Biochemistry, CHE 474/674, consists of four components: lecture, exams, practice problems, and Pymol homework assignments.

I. Lecture: The lecture material in the course is collected from the texts, selected research articles, other publications and graphics obtained from websites and the published literature. The early part of the course applies basic principles learned in general chemistry to **problem solving** in physical biochemistry. As the course progresses, more emphasis is placed on the physical and structural aspects of biological systems, and detailed chemical kinetic analyses. The lecture material for the final portion of the course covers basic quantum mechanics, absorption, and fluorescence spectroscopy.

For the lecture portion of the course, students are expected to take detailed notes and review them after each lecture. Supplemental information will be presented throughout the course. Most of this will be posted as short PDFs on Blackboard. They will contain subject matter germane to questions given on exams in the course.

In order to preserve the learning environment, it is my policy that cell phones, computers or other electronic devices be hidden from view, inaudible and not in any way be in use.

Since violating this rule is rude to the lecturer and distracting to fellow students, violators will be asked to leave the lecture room.

II. Group Work: Occasionally, we will conduct group work sessions as part of lecture or as take-home assignments between class sessions. These will constitute groups of four or five students working together to solve between one and three problems.

III. Practice Problems: CHE 474/674 has an extensive series of "practice problems" with solutions posted on Blackboard. These problems are designed to prepare you for the exams in the course, and **requires use of your own graphing or scientific calculator.** A good strategy for working out the solution to a practice problem is to read the lecture notes that apply and, if necessary, consult appropriate sections in one or more of the above texts. If after doing so, the approach to solving the problem is not obvious, consult the solution that is posted on Blackboard. Since an exam questions will often be related to but not identical to the practice problems, understanding the scientific logic behind the setup of a solution is more important than memorizing the solution to a specific problem. ***Working out the solutions to practice problems should be started early and it should be continuous and on-going throughout the course. Saving this task for the night before the exam is not a good way to obtain a high grade on the exam. No points toward a grade in the course are allotted for solving the practice problem sets.*** Consulting "hard copies" or electronic versions of the solutions to the practice problems *during* exams is academic dishonesty and is strictly forbidden.

IV. Examinations: Three exams, each weighted 16% of the final grade, will be given on the dates and time (9:30 AM to 10:50 AM), indicated in the syllabus. These exams, referred to as "hourly" exams, cover the material for the various parts of the course. Typically, each hourly exam consists of 7-8 questions with most questions requiring a numerical solution (**use of a scientific or graphing calculator**). The final exam, which is given on the date and time set by the University, is comprehensive, and accounts for 22% of the grade in the course. The final exam generally consists of 9-11 questions in a similar format to the individual exams. The exams may have an attached section that gives formulas, relationships, and other data that are important for answering questions on the exam.

During exams, cell phones and PDAs with phone and text messaging capabilities must be hidden from view and inaudible during the exam. *If a student is observed using a cell phone or PDA during the exam, a grade of zero will be given for the exam.*

Examination Policies: The dates and times (9:30 AM to 10:50 AM) for the three hourly exams are as indicated in the syllabus. **There is no possibility to make up an hourly exam in CHE 474/674.** A student presenting a *valid excuse* (defined below) who has missed one hourly exam, can have the averages of the remaining two hourly exams used as the score for the missed hourly exam. *In order to receive a passing grade in CHE 474/674, a student must take the comprehensive final exam.* A student who fails to take the comprehensive final exam at the scheduled date and time, may gain the right to take a make-up final exam (2 hours in length) provided that a valid excuse is presented.

A valid excuse: A valid excuse is a written and dated document that is presented to the instructor *within three days of the missed exam*. A valid medical excuse must *be signed by a physician* and it must be evident from the excuse that the student was unable to write

the exam at the specified date/time. A valid student-athlete excuse is an official document provided to the instructor by the Athletic Office stating the reason for the absence.

V. Homework Assignments:

There are four (4) homework assignments in the course which collectively constitute 25% of the total grade in the course. For all assignments, each student is given his or her own structure which must be constructed, manipulated and/or analyzed using the molecular visualization program, Pymol. **Each enrolled student will have FREE access to the full version of Pymol, courtesy of the SU Chemistry department.** Pymol can be downloaded and used on your own desktop/laptop (Windows, Mac OS X or Linux). If you do not have access to a computer, please let me know by the end of the first week.

All homework assignments will be available on Blackboard. The material submitted for grading will generally consist of digital files of molecules built/analyzed using Pymol plus a brief word document. These items are to be uploaded to Blackboard. Deadlines for homework assignments HW-1, HW-2, and HW-3 are 11:59 PM EST/EDT on the date indicated in the syllabus. If errors are discovered on an assignment after it has been submitted to Blackboard, it is possible to resubmit a corrected version of the assignment to Blackboard ***so long as the resubmission has ALL of the parts of the assignment (even those parts that did not require correction) and is submitted to Blackboard before the deadline. It is your responsibility to ensure this is the case.***

The final homework assignment, HW-4, the "Mini-Project", is a written scientific report that is modeled after Journal of Molecular Biology journal articles. An important emphasis of HW-4 is the use of embedded figures/images that were created using Pymol. HW-4 is submitted for grading as a PDF document via Blackboard.

The grading scale for "on time" submissions (as determined by the 9 PM "time stamp" on the document) for all homework assignments is 0 to 100%. If the student fails to submit the homework assignment or any part of it on time, the assignment will be considered "late" and a grading scale 0-75% will be applied. Assignments (HW1-3) submitted more than one week after the due date and time will receive a score of zero. *There is no "late" grading scale for the final homework assignment (HW-4, the mini project) which is due on the date/time specified*. The weightings for the homework assignments in the course are, HW1-3 (5% for each), HW4, the *Mini-Project*, (10%).

Educational use of student work: I intend to use academic work that you complete this semester in subsequent semesters for educational purposes. Before using your work for that purpose, I will either get your written permission or render the work anonymous by removing all your personal identification.

Academic Integrity:
Syracuse University's Academic Integrity Policy reflects the high value that we, as a university community, place on honesty in academic work. The policy defines our expectations for academic honesty and holds students accountable for the integrity of all work they submit. Students should understand that it is their responsibility to learn about course-specific expectations, as well as about university-wide academic integrity expectations. The policy governs appropriate citation and use of sources, the integrity of work submitted in exams and assignments, and the veracity of signatures on attendance sheets and other verification of participation in class activities. The policy also prohibits students from submitting the same work in more than one class without receiving written authorization in advance from both instructors. Under the policy, students found in

violation are subject to grade sanctions determined by the course instructor and non-grade sanctions determined by the School or College where the course is offered as described in the Violation and Sanction Classification Rubric. SU students are required to read an online summary of the University's academic integrity expectations and provide an electronic signature agreeing to abide by them twice a year during pre-term check-in on MySlice. For more information and the complete policy, see http://academicintegrity.syr.edu.

Complete academic honesty is expected of all students. Any incidence of academic dishonesty, as defined by the SU Academic Integrity Policy (see http://academicintegrity.syr.edu), will result in both course sanctions and formal notification of the College of Arts & Sciences. In this course, all submitted writings, calculations, and/or graphical work that counts towards the grade must be the creation of individual students, and not the result of a partnership or group effort; no student may receive help from any other student during in-class written examinations.

Disability Accommodations:
If you believe that you need accommodations for a disability, please contact the Office of Disability Services (ODS), located at 804 University Avenue, third floor, or go to the ODS website at http://disabilityservices.syr.edu, and click current students tab to register on-line. You may also call (315) 443-4498 for an appointment to discuss your needs and the process for requesting accommodations. ODS is responsible for coordinating disability-related accommodations and will issue "Accommodation Letters" to students as appropriate. Since accommodations may require early planning and are not provided retroactively, please contact ODS as soon as possible. Syracuse University values diversity and inclusion; we are committed to a climate of mutual respect and full participation. Our goal is to create learning environments that are useable, equitable, inclusive and welcoming. If there are aspects of the instruction or design of this course that result in barriers to your inclusion or accurate assessment or achievement, we invite any student to meet with us to discuss additional strategies beyond accommodations that may be helpful to your success.

Faith-based Observances:
SU's policy, found at http://supolicies.syr.edu/emp_ben/religious_observance.htm, recognizes the diversity of faiths represented among the campus community and protects the rights of students, faculty, and staff to observe religious holy days according to their tradition. An online notification process is available through MySlice/Student Services/Enrollment/My Religious Observances from the first day of class until the end of the second week of class, September 7.

CHE 474/674 Tentative Course Schedule (Fall 2018)

L	Day	M	D	Topic	Notes
1	Tuesday	8	28	Non-covalent Interactions, Proteins. Practice Problems 1 (PP1) Assign HW-1: Getting Started with Pymol	Ch 3 pp. 80-87, Ch 12 pp. 463-480
2	Thursday	8	30	1st Law of Thermodynamics / Hess's Law	Ch 2 pp. 13-24, 26-31, 39-41
3	Tuesday	9	4	2nd Law of Thermodynamics / Chemical Potential Practice Problems 2	Ch 3 pp. 55-64, Ch 4 pp. 102-108
4	Thursday	9	6	Gibbs Free Energy and Equilibria / Thermodynamics of Protein Folding	Ch 3 pp. 72-75, Ch 4 pp. 115-119, 133-135
	Monday	9	10	Pymol HW-1 due 11:59 PM. Assign HW-2: Torsion angles of DNA / RNA / proteins	
5	Tuesday	9	11	Thermodynamics of Protein Folding and Aggregation	Ch 4 pp. 115-119, 133-135 and notes
6	Thursday	9	13	RNA Structure, Folding and Equilibria	Ch 5 pp. 176-180
7	Tuesday	9	18	Nucleic Acids, Structure, and Properties Practice Problems 3	Ch 3 pp. 83-87, Ch 8 pp. 286-295
	Thursday	9	20	Exam 1	PP1, PP2 and notes
8	Tuesday	9	25	Physical Properties of Nucleic Acids Melting	Ch 5 pp. 179-180
9	Thursday	9	27	Thermodynamics of DNA Melting	notes
	Monday	10	1	Pymol HW-2 due 11:59 PM. Assign HW-3: Structures of DNA/RNA	
10	Tuesday	10	2	Monomer/Dimer Associations Equilibrium Dialysis	Ch 5 pp. 176-180
11	Thursday	10	4	Equilibrium Dialysis / Scatchard Equation Practice Problems 4	Ch 5 pp. 180-184, 186-188, Ch 6 pp. 208-213
12	Tuesday	10	9	Ligand Binding & Cooperativity	Ch 4 pp. 139-140, Ch 5 pp. 180-184, 186-188, Ch 6 pp. 208-213
13	Thursday	10	11	Acid/Base Equilibria	Ch 4 pp. 129-138
	Tuesday	10	16	Exam 2	PP3, PP4 and notes
14	Thursday	10	18	Review of Chemical Kinetics Practice Problems 5	Ch 9 pp. 305-321
15	Tuesday	10	23	Rate Laws, Equilibrium	Ch 9 pp. 305-321, 325-326, 333-334

16	Thursday	10	25	Introduction to Quantum Mechanics and the Schrodinger Equation Practice Problems 6	Ch 11 pp. 408-423
17	Tuesday	10	30	1D Particle in a Box	Ch 11 pp. 423-429
	Wednesday	10	31	Pymol HW-3 due 11:59 PM. Assign HW-4: Mini-Project	
18	Thursday	11	1	1D Particle in a Box and Problems	Ch 11 pp. 423-429
19	Tuesday	11	6	2D/3D Particle in a Box	notes
20	Thursday	11	8	Absorption Spectroscopy of Proteins and Nucleic Acids	Ch 13 pp. 502-507
21	Tuesday	11	13	Absorption Spectroscopy and Equilibrium	Ch 13 pp. 502-507 and notes
	Thursday	11	15	Exam 3	PP5, PP6 and notes
	Tuesday	11	20	THANKSGIVING BREAK – NO CLASS	
	Thursday	11	22	THANKSGIVING BREAK – NO CLASS	
22	Tuesday	11	27	Hydrogen Atom and Hybridization	Ch 11 pp. 434-444
	Wednesday	11	28	Pymol HW-4 Mini-Project due 11:59 PM.	
23	Thursday	11	29	Molecular Structure and Molecular Orbitals	Ch 12 pp. 453-461
24	Tuesday	12	4	Fluorescence	Ch 13 pp. 507-520
25	Thursday	12	6	Fluorescence / Biomolecular NMR	Ch 14 pp. 539-547 and notes
	Monday	12	10	CUMULATIVE FINAL EXAM 12:45 – 2:45 PM, LSB 105	PP1 – PP6, all notes