CH 8990 03 – Methods in Biophysical Chemistry
Course Syllabus

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Course Description

Many of the advances in modern biochemistry have occurred because of the intense effort scientists have devoted to studying proteins and protein function. By applying the principles of physical chemistry to biological systems, we have learned much about the chemistry of life, and we have started to understand the molecular basis of human disease. This class is designed to build upon an undergraduate background in physical chemistry and biochemistry; in it, we will study the behavior of proteins, and we will learn about several techniques that are commonly used to study protein structure and function. We will also focus on how mathematical models can be used to describe protein behavior, and we will discuss in depth how those models can be related to experimental observables. When you have completed the course, you will be able to design and interpret experiments for studying proteins, and you will be able to apply biophysical concepts to understand how these molecules work.

Meeting Times / Attendance

The course will meet Monday, Wednesday, and Friday from 5:00 to 5:50 PM in Hand Lab 3324. Because of the interactive nature of the lectures, attendance is mandatory for the course. Please contact the instructor if you must miss a class meeting.

Two exams will be given throughout the course, and these will be scheduled outside of class. The times and dates of these exams will be determined so all students can be present.

Course Format

The primary format for the course will be lecture; however, students will also have an opportunity to present journal-club discussions throughout the course. The lecture notes will be written on the board during the class, and occasionally PowerPoint slides or other visual aids will be used to supplement the course materials. These slides will be made available upon request, but in general you will be responsible for taking your own notes during class.

The journal discussions will occur on most Fridays during the semester. During each class period, two articles will be discussed: an older "classic" article and a newer article describing the current state of protein research. Students will be selected to lead a class discussion on one of the two articles, and all students will lead the journal presentation at least once during the semester (more details are given below).

Reading / Textbook

The primary textbook for the class is *Principles of Physical Biohemistry: Principles and Applications in the Biological Sciences* by van Holde, Johnson, and Ho (2006 Pearson Education, Inc., ISBN 0-13-046427-9). In addition, we will use *An Introduction to Error Analysis: The Study*

of Uncertainties in Physical Measurements by Taylor (1996 University Science Books, ISBN 0-93-570275-X) to discuss models and model fitting. These books are available in the bookstore, but it may be cheaper for you to purchase them online (try www.addall.com). Readings from these books will be assigned throughout the course, and it is expected that you come to class having read the material.

In addition, the following texts may provide helpful information to supplement what is covered in the course. Many of these are classic biophysics text books and are worth having in your library if you plan to continue with biophysical research. You can often find them available used or on-line.

- Tinoco, Sauer, Wang, and Puglisi. (2003) *Physical Chemistry: Principles and Applications in the Biological Sciences.* Prentice Hall, Inc.
- Cantor and Schimmel (1980) *Biophysical Chemistry*. (Parts I, II, and III) W. H. Freeman and Company.
- Rule and Hitchens (2005) *Fundamentals of Protein NMR Spectroscopy*. Springer.
- Rhodes (2006) *Crystallography Made Crystal Clear: A Guide for Users of Macromolecular Models.* Academic Press.
- Glusker and Trueblood (2010) *Crystal Structure Analysis: A Primer*. Oxford University Press.
- Atkins and de Paula. (2009) *Physical Chemistrry*. W. H. Freeman and Company.
- Berg, Tymoczko, and Stryer. (2010) *Biochemistry*. W. H. Freeman and Company.

Grade Distribution

The grades for the course will be calculated according to the table below. Although attendance is not explicitly included, the instructor will deduct 5 percentage points from your final course grade if you have more than three unexcused absences.

Course Component	Percentage
Exams (2)	40%
Homework (7)	35%
Programing Assignment	10%
In-Class Presentation(s)	15%

If the distribution of grades necessitates it, the final grades will be curved. However, if all students do well, they should not expect to receive poor grades simply because of a forced bell curve on the final distribution. Students are encouraged to concentrate on learning, which has lifelong benefits, rather than grades, which are useful to your mid-twenties at best. No student who has shown discipline in pursing educational excellence will fail this course.

Exams

Two exams will be given during the semester. Although referred to as a "midterm" and a "final," the exams will not be cumulative. Each exam will count 25% toward your final grade. The exam format may be varied, and you should not expect the exams to be entirely multiple-choice. Because of the limited class time available for exams, the exams will be given outside of class, at a time that is convenient for all students in the class. At the discretion of the instructor, one or both exams may be "take-home." While the emphasis of each exam will be the material presented during class, you will also be tested on the assigned readings, including the journal presentations. There will be no cumulative final exam for the class.

Homework

Throughout the course, you will have seven bi-weekly problem sets to test you on the material taught. You will also have a long-term computer-based assignment to ensure that you learn a programming language. These assignments are graded and constitute 45% of your final course grade. Assignments will be graded on both completeness and correctness: for a majority of the problems, you will receive credit if you have shown effort and are mostly correct. Because of this, you should show all your work so that the instructor can follow your line of reasoning.

The first assignment (HW0) will be a programming assignment that requires you to learn a programming language to parse and process a protein structure file. You will have several months to complete this assignment, and if you do not know how to program, you should begin learning *immediately*.

Sloppy or illegible homework assignments will not be given credit! You are responsible for submitting assignments that are easy to follow with justification given for each answer. If you cannot write legibly, type your answers. If there are large portions of your assignment that are crossed out or out of order, re-copy it to make it neater and easier to follow. Your assignments should be organized and stapled when you come to class.

The assignments will be collected at the beginning of the class period when they are due (see the schedule below). Late assignments will not be accepted unless prior arrangements have been made with the instructor.

Presentations

Several times during the semester, students will be required to lead a journal article discussion. These discussions will occur on Fridays, and two articles will be discussed during the lecture. The journal article discussions have several goals: First, for the presenter, it is a valuable opportunity to develop public speaking and teaching skills. Second, it is a chance to see where current work in protein biophysics is directed. Finally, it is a chance to look back at several classic papers and understand the context leading up to significant discoveries in protein science.

The rubric for grading journal article presentations is attached at the end of the syllabus. The presentation grade will account for 15% of your final grade, and if you present multiple times, your presentation grades will be averaged. Depending on the size of the class, some students may present multiple times. If you have presented more than twice, your lowest presentation grade will be dropped from the average.

You are welcome to present your journal articles however you like: if you are comfortable using PowerPoint slides, a computer will be made available to you (or you can bring your own computer). Alternatively, if you'd like to lead a discussion from the board, that's okay too, although it is recommended that you select some figures from the articles to discuss using the overhead display. Either way, **your presentation should last 15-20 minutes with 5-10 minutes additional for discussion.**

On the flip side, you should come to journal club having read the material deeply. Simply skimming the journal articles is not sufficient! The material covered in the journal articles will appear on your exams, regardless of whether the speaker has done a satisfactory job of presenting the material. I reserve the right to call on students directly if no one is willing to participate in discussion afterward.

Office Hours

Office hours Tuesdays and Wednesdays at 9 am in my office (Hand Lab 3310). Other times are available by appointment. You are welcome and encouraged to stop by my office to discuss the course material at any time, but I may need to reschedule our meeting if I am busy.

Course Web Page

The web page for this course is located at http://fitzkee.chemistry.msstate.edu/ch8990/. Please check this site frequently for course updates. You will be able to find PDF copies of this syllabus and other important course materials at this site.

Academic Integrity

Group work and collaboration is encouraged in this course, but all students are expected to complete their own assignments and submit their own work. Failure to do so not only cheats the system, but also diminishes your own understanding of the material. Instances of plagiarism and cheating will be addressed according to the Student Honor Code. In severe cases of academic dishonesty, students will be dropped from the class with an XF grade and will be required to take a class in academic integrity to have the "X" sanction removed. You are encouraged to read the Student Honor Code, available on the Honor Code Office website, http://www.honorcode.msstate.edu/.

Supplemental Reading

In the course schedule on the following pages, several places indicate additional reading to be completed before lecture (e.g "Reading #1"). These readings represent important papers that you should understand in addition to your textbooks. In most cases, you will be able to download these documents from the web; however, in some cases where a digital copy is not readily available you will receive a PDF of the document via email.

The list of readings is given below:

1. Kuriyan, Konforti, and Wemmer. *The Molecules of Life*, Chapter 1. Available for free at the Garland Science website: http://www.garlandscience.com/product/isbn/9780815341888

2. Johnson, M. L. (1992) *Anal. Biochem.* **206**: 215.

3. Dill, K. A. (1990) *Biochemistry.* **29**: 7133.

4. Rose, G. D., *et al*. (2006) *PNAS*. **103:** 16623.

5. Dill, K. A. and Chan, H. S. (1997) *Nat. Sturct. Biol.* **4:** 10.

6. Zanni, M. T., and Hochstrasser, R. M. (2001) *Curr. Op. Struct. Biol.* **11**: 516.

7. Wütrich, K. (2003) *J. Biomol NMR.* **27**: 13.

8. Lewis, E. A. and Murphy, K. P. (2005) *Meth. Mol. Biol.* **305:**1.

9. Cantor and Schemmel. *Biophysical Chemistry Part II: Techniques for the Study of Biological Structure and Function*. Chapter 13. Will be provided in class.

Additional readings may be assigned throughout the course.

Schedule of Topics

Week 1			
Date	**Description**	**Reading**	**Assignment**
January 13	Introduction; Protein Structure I	VH: 1.1-1.3 Reading #1	HW0 (out) HW1 (out)
January 15	Protein structure II	VH: 1.5	
January 17	DNA structure	VH: 1.5-1.6	
Week 2			
Date	**Description**	**Reading**	**Assignment**
January 20	No Class – Martin Luther King, Jr. Day		
January 22	Review of uncertainties and experimental error	T: Chapt. 1-5	
January 24	Fitting models to data	T: Chapt. 8, 12 Reading #2	
Week 3			
Date	**Description**	**Reading**	**Assignment**
January 27	Macromolecular forces I	VH: 3.1-3.2 Reading #3	HW1 (due) HW2 (out)
January 29	Macromolecular forces II	VH: 3.3	
January 31	**Journal Discussion:** • Rose, *et al*. (1985) *Science*. **229:** 834-838. • Berkholz, *et al*. (2012) *PNAS*. **109**: 449-453.		
Week 4			
Date	**Description**	**Reading**	**Assignment**
February 3	Computational simulations	VH: 3.4	
February 5	Protein folding	Reading #4 Reading #5	
February 7	**Journal Discussion:** • Lazaridis & Karplus. (1999) *JMB*. **288**: 477-487. • Cooper, S. *et al.* (2010) *Nature.* **466**: 756.		

Week 5			
Date	**Description**	**Reading**	**Assignment**
February 10	Statistical mechanics	VH: 4.1-4.2	HW2 (due) HW3 (out)
February 12	Helix-coil theory	VH: 4.4	
February 14	**Journal Discussion:** • Scholtz, J. M. *et al.* (1995) *PNAS*. **92**: 185. • Aksel, T. *et al.* (2011) *Structure*. **19**: 349.		
Week 6			
Date	**Description**	**Reading**	**Assignment**
February 17	Review of quantum mechanics I	VH: 8.1-8.2	
February 19	Review of quantum mechanics II	VH: 8.3	
February 21	Interactions between light and matter	VH: 8.4-8.5	
Week 7			
Date	**Description**	**Reading**	**Assignment**
February 24	UV-Visible spectroscopy	VH: 9.1	HW3 (due) HW4 (out)
February 26	UV spectroscopy of proteins, introduction to infrared spectroscopy	VH: 9.2	
February 28	**Journal Discussion:** • Pace, C. N. *et al.* (1995) *Prot. Sci.* **4**: 2411. • Kim, Y. S. *et al.* (2008) *PNAS*. **105**: 7720.		
Week 8			
Date	**Description**	**Reading**	**Assignment**
March 3	IR Spectroscopy	Reading #6	
March 5	Circular dichroism and optical activity	VH: 10.1-10.2	
March 7	**Journal Discussion:** • Kim, *et al*. (2005) *J Phys. Chem. C.* **109**: 7511. • Khan, M. Q. *et al*. (2010) *PNAS* **107**: 19808		

Spring Break (Research Week)			
Date	**Description**	**Reading**	**Assignment**
March 10	No Class – Spring Break		
March 12	No Class – Spring Break		
March 14	No Class – Spring Break		
Week 9			
Date	**Description**	**Reading**	**Assignment**
March 17	Circular dichroism and proteins, singular value decomposition		HW0 (due) HW4 (due) HW5 (out)
March 19	Introduction to fluorescence	VH: 11.1-11.5	
March 21	**Journal Discussion:** • Meeker, A. K. *et al.* (1996) *Biochemistry.* **35**: 6443. • Schuller, B. *et al.* (2004) *PNAS.* 102: 2754.		
Week 10			
Date	**Description**	**Reading**	**Assignment**
March 24	Fluorescence quenching, FRET	VH: 11.6-11.8	
March 26	Fluorescence polarization	VH: 11.9-11.10	
March 28	Introduction to NMR I	VH: 12.1-12.2	
Week 11			
Date	**Description**	**Reading**	**Assignment**
March 31	Introduction to NMR II	VH: 12.5-12.6	HW5 (due) HW6 (out)
April 2	Fourier transforms and spectral processing		
April 4	NMR Relaxation	VH: 12.3-12.4	

Week 12			
Date	**Description**	**Reading**	**Assignment**
April 7	Multidimensional NMR spectroscopy on proteins	VH: 12.7-12.8	
April 9	Methods for determining structure by NMR spectroscopy	Reading #7	
April 11	**Journal Discussion:** • Shen, Y. *et al*. (2008) *PNAS*. **105**: 4685. • Zhou, Y. *et al*. (2008) *Mol. Cell.* **31**: 896.		
Week 13			
Date	**Description**	**Reading**	**Assignment**
April 14	Isothermal Titration Calorimetry I	Reading #8	HW6 (due) HW7 (out)
April 16	Isothermal Titration Calorimetry II		
April 18	No Class – Good Friday		
Week 14			
Date	**Description**	**Reading**	**Assignment**
April 21	X-Ray crystallography I	VH: 6.1-6.3 Reading #9	
April 13	X-Ray crystallography II	VH: 6.4-6.5	
April 25	X-Ray crystallography III		
Week 15			
Date	**Description**	**Reading**	**Assignment**
April 28	Class discussion/extra lecture day		HW7 (due)
April 30	**Journal Discussion:** • Ben-Shem, A. *et al*. (2011) *Science*. **334**: 1524. • Lang. *et al.* (2014) *PNAS*. **111**: 237.		
May 1	No Class – Reading Day		

JOURNAL PRESENTATION RUBRIC

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Category	Evaluation Criteria	Max. Score	Student Score
Presentation Content	**Presentation Fidelity** • Student understands questions asked by the article • Student can explain at least one (preferably two or more) figures from the article	20	
	Presentation Emphasis • Background: not too much, not too little • Student focuses on important topics: figure, tables, etc. • Less time is spent on unimportant details / methodology	10	
	Scientific Accuracy • At least one reference to course material • No scientific inaccuracies in the presentation	15	
	Organization • Presentation flows logically • Clear introduction and summary of what is covered	5	
Speaking Skills	**Speaker Clarity** • Speaker doesn't mumble, projects and is easily understood • Speaker doesn't simply read the slides	10	
	Spoken English • Speaker shows a command of the English language • No grammatical problems with spoken English	5	
Technical Merit	**Presentation Mechanics** • Slides are appropriately chosen and helpful to audience • Talk flows smoothly; no abrupt transitions • Presentation does not go over time (15-20 minutes)	10	
	A/V Aids • No complete sentences on slides • Handwriting is clear (for written talks) • Images are clear and professional, with pixelated images • Student shows mastery of presentation software	10	
Audience Interaction	**Question and Answer Session** • Student can candidly answer questions about the paper • Student is polite and receptive to audience feedback • Student can facilitate a discussion if no questions are forthcoming	10	
	Real-Time Response to Audience • Student recognizes confusion in the audience and addresses it appropriately • Student can elaborate on a slide during the talk if a question arises	5	
Total Score		**100**	