

BB481 / 581 Molecular Biophysics I: Macromolecular Structure

Fall 2019

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Day, Time and Location	Mondays, Wednesdays & Fridays 1:00 – 1:50 pm, LInC 200 Office Hours: Thursdays 11:00 am – 12:00 noon, and by appointment, ALS 2143 (office)
Course Objectives	This course provides an introduction to structural biology, the discipline focused on understanding the structural properties of biological macromolecules – especially proteins and nucleic acids – and relating them to their function. The course introduces students to the vocabulary and tools of this discipline, covering both the fundamental physicochemical principles governing the structure and function of biological macromolecules and a selected set of widely used experimental and theoretical approaches to their characterization. This is done through lectures, and textbook and literature readings. Graduate students receive additional experience in scientific reading, writing and presentation through a literature-based term project.
Learning Resources	Assigned readings and articles from the literature. Recommended Text and Readings: <i>“Principles of Physical Biochemistry, 2nd Ed.”</i> by van Holde, Johnson, and Ho <i>“Envisioning Information”</i> , <i>“The Visual Display of Quantitative Information”</i> , <i>“Visual Explanations: Images and Quantities, Evidence and Narrative”</i> , <i>“The Cognitive Style of PowerPoint”</i> , <i>“Beautiful Evidence”</i> by Edward Tufte <i>“Entropy and Art”</i> , <i>“Visual Thinking”</i> by Rudolf Arnheim <i>“The Elements of Graphing Data”</i> , <i>“Visualizing Data”</i> by William Cleveland <i>“Data Points”</i> , <i>“Visualize This”</i> by Nathan Yau BB Departmental and CGRB Seminars, alternate Wednesday, 3:00 – 4:00pm, ALS 4001
Course Policies	Prerequisites: BB 450 / 550 or BB 490 / 590 Incompletes: Take this course only if you plan to finish it in a timely manner (during this term). An "Incomplete" will only be given when there is a strong and compelling case for doing so (e.g., health reasons, military commitment).

Learner Outcomes

When confronted with a biochemical phenomenon, students should be able to rationalize how to examine, model, and analyze the system and effectively communicate the results. Through taking this course, successful students will (unless otherwise noted each outcome applies to both BB481 and BB581):

- 1) Understand the breadth of the discipline of structural biology and the importance of knowing molecular structure for understanding mechanism in biology.
- 2) Acquire the technical language for techniques used in structural biology and be able to recall key elements of these techniques, including the concepts behind the experiments and the types of results obtained.
- 3) Understand the fundamental thermodynamic principles governing protein and nucleic acid folding and stability as well as molecular recognition.)
- 4) Be able to apply the above concepts with the principles of logic to solve realistic, specific problems in structural biology and to understand and critically evaluate research papers in this field.
- 5) Be able to use databases, computational tools and other online resources effectively.
- 6) Intelligently analyze, interpret and appraise the soundness of research findings (which involves being able to make basic order-of-magnitude estimates), and demonstrate the ability to produce quality critical analysis. (BB 581)

N.B. Actually, everyone should be able to examine, model, analyze and effectively communicate all their observations and experiences!

Learner Expectations

First and foremost, I expect everyone to respect one another. Among other things, this means that only one person speaks at a time, no cell phone usage in class, and that each of you put forth an honest effort in class. Arrive to class on time every day, prepared and with all necessary materials, ready to discuss the topic for the day.

I hope that this class will be very active and expect each of you to participate as much as possible. Don't be afraid to ask questions or make mistakes – both are key in helping you understand the subject material. This course will require you to spend time each week reading the assigned material and participating in classroom discussions.

Course Evaluation

Fulfillment of the student learning outcomes will be assessed through three exams, one project and four assignments. In the case of BB 581 an additional written assignment. The assessment will be based on your scores as follows:

	BB 481	BB 581
Stereoimage assignment (Monday, September 30 th), 10 points	2.2 %	2 %
Reciprocal space video (Monday, October 7 th), 35 points	7.8 %	7 %
Exam #1 (Friday, October 11 th), 75 points	16.7 %	15 %
Reciprocal space critiques (Monday, October 21 st), 20 points	4.4 %	4 %
Exam #2 (Wednesday, October 30 th), 75 points	16.7 %	15 %
Homology Modeling project (Wed., November 13 th), 50 points	11.1 %	10 %
Exam #3 (Wednesday, November 20 th), 75 points	16.7 %	15 %
Seminar writeup (Wednesday, November 27 th), 35 points	7.8 %	7 %
BB581 Term Project (Friday, November 29 th), 50 points	–	10 %
Final Exam (7:30 am, Friday, December 13 th), 75 points	16.7 %	15 %

Stereoimage assignment (10 points)

Using your computer, a digital camera, or your smartphone, create a three-dimensional image of your choosing. To create your 3D image, take a picture, shift the camera at least 2.5 inches to the right (or left) and take another picture, doing your best not to shift the image. These two pictures represent what your right and left eye sees individually. You will then need to place these two images side by side using a photoediting program. Post your composition to the course Canvas site. Please format your composition for cross-eyed viewing. The photos you take must be static – anything moving in your images will destroy the 3D “illusion”. **Late submissions will not be accepted.**

Reciprocal Space video and critiques (35/20 points)

The concept of “reciprocal space” is important to the understanding of x-ray crystallography and to why it works as an “imaging” technique despite the absence of a refocusing lens. However, just because it is important (or maybe because it is?) doesn’t mean it is easy to understand. In fact, it can be quite difficult to understand, mainly because there is no direct physical interpretation that can be made based on your experiences. For this assignment, you will think about what “reciprocal space” is and film a short (4-5 minutes in length, maximum!) video using a camera or smartphone explaining your understanding of reciprocal space. It is not expected that you will understand this concept perfectly, nor are Hollywood-level production values expected. What is expected,

however, is an honest attempt at explaining this difficult concept.

Each of you will be randomly assigned four submitted videos to watch and review. Each of your reviews should consist of some comments and a numerical score (1-5).

Your comments should follow the "TAG" format:

"T" - tell them something you liked about the video

"A" - ask a question about the content

"G" - give some advice

The score you assign should be in the 1-5 range where "5" is best. An "average" video should be given a score of "3", whereas a sub-par video should receive a "1" and an outstanding video should receive a "5". (If you think all three of the videos you watch are "outstanding", that means "outstanding" is your "average" and they should all be given a "3". You should be watching the videos and scoring according to the content and explanation of reciprocal space and whether or not it is clearly described or explained. Do not score the videos based on production values, or the "slickness" of the video. The reviews can be read by the video submitter, but are anonymous.

Your grade for the reviews will depend on the comments and scores you submit, not on the comments and scores you receive on your video. The score you receive for your video will depend on the comments and scores you receive from your peers as well as my assessment. **Late submissions of either the video or the critiques will not be accepted.**

Homology Modeling project (50 points)

There are times where having a structure of the protein you are studying would be useful. But, as you well know, not all proteins have had their structures solved. In these cases, one depends on homology modeling to generate a tentative structure based on sequence similarities to proteins with known structures. Oftentimes the homology modeling is based on proteins with only 40% or less sequence homology. Here you will be simulating such a case by pretending the structure of your protein of choice does not exist and you will assess how well your protein can be homology modeled. Specific details for this project will be posted on the course Canvas site. **Ten points/day will be deducted for late submissions.**

Seminar Writeup (35 points)

Hopefully, over the years you have been taking advantage of being at OSU by attending some of

the seminars put on by the various departments on campus. Experts in their field (well, if not expert, at least very proficient) are invited to OSU and they present and discuss interesting research results and insights coming out of their laboratories. Open to anyone interested in attending, and often with refreshments before or after the seminar! For this assignment, you will choose a seminar to attend, then within a week of the seminar date submit online a one page summary of the seminar.

Your summary must include:

- the date, speaker name and affiliation, seminar title and inviting department
- the key results and conclusions
- a brief “justification” of how the seminar is related to biophysics (could be the system being studied, techniques that were used, implications of the results, etc.)
- what you found most interesting and why
- something you liked about the presentation
- something you didn’t like about the presentation
- an appropriately detailed question that you would like to ask the speaker about their research, results, or future work

The seminar you choose to summarize is entirely up to you, and can be from any department on campus, for example, from Biochemistry & Biophysics, Chemistry, CGRB, Pharmacy, EHSC or CVM. Scheduled seminars for this term can be found on each of the departments’ websites. The only major caveats to selecting a seminar are that it not be given by a student, and that it takes place before Wednesday, November 13th (which means the deadline for submitting your summary is the Wednesday before Thanksgiving). If you have any concerns about the appropriateness of a seminar for this assignment, please contact me. **Ten points/day will be deducted for late submissions.**

BB 581 Term Project (50 points)

Each student must choose and have approved an original scientific publication that will be the subject of their term project. *The publication must be a recently published primary report of a theoretical or experimental biophysical study of a biomacromolecule using one or more of the methods covered in this*

course. The article chosen must have an explicit and informative methods section (either in the article or as supplementary material that is available). The project will result in a short written report due during the last week of the class.

The written report must be in your own words and be explicitly organized as follows:

- 1) *Introduction* (1 paragraph) – Includes what questions the researchers were hoping to answer in this study (the hypothesis they were testing), why is that of interest, and (briefly) the strategies that they used to obtain the results.
 - 2) *Key methods* (1-5 paragraphs) – This section includes a description of each key method used, the principles behind it, what assumptions are made and what information can be obtained. This section IS NOT a summary of what experiments were done or how they were done; rather, it is an explanation in your own words of the principles behind the approaches used and what information they deliver. Focus on the molecular biophysics approaches only; cloning, protein expression and protein purification, etc. should be skipped.
 - 3) *Key results* (1 paragraph) – This section is a brief fairly technical description of the basic results reported by the authors (not their interpretation or your interpretation!)
 - 4) *Interpretation and Conclusions* (1 paragraph) – This section is a brief summary of the substantive conclusions reported by the authors (not the results and not your opinions!)
 - 5) *Critique* (3 paragraphs) – This is your opinion of the work in terms of strengths and weaknesses and value. Focus the first paragraph on strengths and things you agree with, the second on weaknesses and the third on your opinion about the work.
 - 6) *References* (not counted in page limits) – References should be kept to a minimum, but references from which specific information was used must be referred to in the text and included in a single spaced bibliography. References used to help you understand methods do not need to be cited. In the text, references should be inserted in the form of numbers in square brackets [#], with references numbered in the order of appearance. The format of the cited references should follow the APA (American Psychological Association) format.
 - 7) *Figures* – One optional page with drawn or photocopied/scanned (give citation) figures you refer to in your text that are not in the original article. This page does not count toward the page limits.
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Deadlines and Details:

- 1) The written report must be no more than 3 pages single-spaced and typed in 12 point Times, Times New Roman, or 11 point Arial font.
- 2) Your chosen paper must be approved by 3 pm, Friday, November 1st, and a paper copy is to be provided to me.
- 3) The written report is due by noon, Friday, November 29th. The completed paper is to be submitted via the course's Canvas website. Ten points/day will be deducted for late papers.

Grading:

The project will be worth 50 points, distributed as follows:

- 5 points for meeting the November 1st deadline for paper selection (all or none);
- 45 points for the written report: 5, 10, 7, 7, and 10 points for sections 1–5, respectively, and 6 points for overall grammar and style.

Ten points/day will be deducted for late papers.

Outline of Schedule

Topic	Readings	
	van Holde, <i>et. al.</i>	Karplus
Basic concepts of macromolecular structure	Chap. 1	Chap. 2
Structure determination by x-ray crystallography	Chap. 6	Chap. 3
Structure determination by NMR spectroscopy	Chap. 12	Chap. 3
Structure determination by cryo-electron microscopy	–	–
Molecular thermodynamics	Chaps. 2, 3, 4.1	Chaps. 5, 2, 6
Protein energy landscapes and hydrogen exchange	Pgs. 684-690	Chap. 6
Mass spectrometry	Chap. 15	–
Optical spectroscopy	Chaps. 9, 10, 11	–
Single molecule methods	Chap. 16	–

<p>Statement Regarding Students with Disabilities</p>	<p>Please note: “Accommodations for students with disabilities are determined and approved by Disability Access Services (DAS). If you, as a student, believe you are eligible for accommodations but have not obtained approval please contact DAS immediately at 541-737-4098 or at http://ds.oregonstate.edu. DAS notifies students and faculty members of approved academic accommodations and coordinates implementation of those accommodations. While not required, students and faculty members are encouraged to discuss details of the implementation of individual accommodations.”</p>
<p>Reach Out for Success</p>	<p>University students encounter setbacks from time to time. If you encounter difficulties and need assistance, it’s important to reach out. Consider discussing the situation with an instructor or academic advisor. Learn about resources that assist with wellness and academic success at http://oregonstate.edu/ReachOut. If you are in immediate crisis, please contact the Crisis Text Line by texting OREGON to 741-741 or call the National Suicide Prevention Lifeline at 1-800-273-TALK (8255).</p>
<p>University Rules on Civility and Honesty</p>	<p>The University statement on student conduct and community standards can be found at: http://studentlife.oregonstate.edu/code.</p> <p><i>Cheating or plagiarism by students is subject to the disciplinary process outlined in the Statement of Expectations for Student Conduct (http://studentlife.oregonstate.edu/studentconduct/offenses-0)</i></p> <p>Students are expected to be honest and ethical in their academic work. Academic dishonesty is defined as an intentional act of deception in one of the following areas:</p> <ul style="list-style-type: none"> ◆ Cheating – use or attempted use of unauthorized materials, information or study aids ◆ Fabrication – falsification or invention of any information ◆ Assisting – helping another commit an act of academic dishonesty ◆ Tampering – altering or interfering with evaluation instruments and documents ◆ Plagiarism – representing the words or ideas of another person as one’s own <p>Behaviors disruptive to the learning environment will not be tolerated and will be referred to the Office of Student Conduct for disciplinary action.</p> <p><i>“The goal of Oregon State University is to provide students with the knowledge, skill and wisdom they need to contribute to society. Our rules are formulated to guarantee each student’s freedom to learn and to protect the fundamental rights of others. People must treat each other with dignity and respect in order for scholarship to thrive. Behaviors that are disruptive to teaching and learning will not be tolerated, and will be referred to the Student Conduct Program for disciplinary action. Behaviors that create a hostile, offensive or intimidating environment based on gender, race, ethnicity, color, religion, age, disability, marital status or sexual orientation will be referred to the Affirmative Action Office.”</i></p>