From Atoms to Molecules Biochem 729, Section 006

MWF 8:50-9:40AM 1116 DeLuca Biochemistry Building

This course is required for first semester IPiB graduate students. Topics covered include protein structure and folding, protein dynamics, biological catalysis, membrane structure and assembly, nucleic acid structure and folding, and bioenergetics. Each topic includes discussion of the primary literature, hypothesis generation, experimental design, data, analysis and interpretation underlying the facts in the textbook. The goal is to help students transition from undergraduate consumers of knowledge to graduate students and future independent scientists who will discover and add new knowledge.

Objectives

- To develop basic knowledge of the chemical principles underlying the structure, dynamics, interaction, and function of biological molecules.
- To learn how to design experiments to test a particular hypothesis.
- To learn how experimental data is analyzed, interpreted, tested and shared.
- To understand how biochemical knowledge develops from experimental data.

Textbook:

The Molecules of Life: Physical and Chemical Principles,
Kuriyan, Konforti & Wemmer, 2013

Note: Chapters 7-10.C cover basic physical chemistry principles. I assume that you know this material, but please review it if your background is weak in this area.

Assignments: Are due at the beginning of class on the assigned due date!

Grading: Problem sets and quizzes assigned by instructors (20%)
Paper presentation and written review (20%)
Three take-home midterm exams (20% each)

I expect that you will attend the IPiB retreat (all day on 9/7) and Biochemistry seminars (3:30 pm on Mondays in 1211 HF DeLuca Biochemical Sciences Building).

Accommodations:

Students with documented disabilities can register with the Disability Support Services office. Please inform me about specific accommodation needs at the start of the course.

Students without documented disabilities who may need specific accommodations should contact me to set up a conference to discuss specific needs.

Protein Structure (Rayment)

9/5 Examining protein structure: the PDB
9/7 IPiB Retreat – No class. Go to the retreat!
9/10 Assessing the quality of a crystal structure
9/12 Structure determination by CryoEM
9/14 Comparison of X-ray and CryoEM
9/17 Structure determination by NMR (Henzler-Wildman)
9/19 Protein structure prediction and design (Raman)
9/28 Directed evolution of proteins (Romero)

Student Presentations:

9/24 Lockless & Ranganathan. Evolutionarily conserved pathways of energetic connectivity in protein families. *Science* **286,**295-299 (1999).

Protein Synthesis & Folding (Henzler-Wildman)

9/26 Monitoring protein folding
9/21 Folding thermodynamics
10/1 Folding kinetics & intermediates
10/3 What does "unfolded" really mean? IDPs

Student Presentations:

10/8 Kerner, *et al.*Proteome-wide analysis of chaperonin-dependent protein folding in Escherichia coli. *Cell***122,**209–220 (2005).

Midterm 1 ***due 10/12***

Protein Dynamics (Katie)

10/10 MD simulations
10/12 Time and length scales of motion & experimental methods
10/15 Single molecule vs ensemble methods
10/17 Dynamics & entropy

Protein-Ligand Interaction (Henzler-Wildman)

10/19 Monitoring protein-ligand interaction
10/22 Thermodynamics of protein-ligand interaction
10/24 Kinetics of protein-ligand interaction
10/26 Affinity vs specificity

Catalysis (Rayment)

10/29 Enzyme Kinetics: Michaelis Menten
10/31 Enzyme Inhibition
11/2 Catalysis Theory
11/5 Catalysis Chemistry
11/7 Allostery
11/9 Kinases
11/12 Pre-steady state kinetics

Midterm 2 ***due 11/14***

Nucleic Acid Structure & Folding (Butcher)

11/14 DNA structure
11/16 RNA structure
11/19 RNA folding
11/21 Ribozymes

Student Presentations:

11/26 Nguyen, *et al*. Evolutionary drivers of thermoadaptation in enzyme catalysis. *Science* **355** 289-294 (2017).

Membrane Structure & Assembly (Henzler-Wildman)

11/28 Lipids & membrane material properties

11/30 Lipid phases, cholesterol, lipid composition *in vivo*

12/3 Membrane protein structure and folding

Energy in Biology (Henzler-Wildman)

12/5 ATP-driven machines

12/7 Electrical energy – action potentials and channels

12/10 Secondary active transport

Student Presentations:

12/12 Omabegho, *et al*. Controllable Molecular Motors Engineered from Myosin and RNA. *Nature Nanotechnology* **13,** 34-40 (2018).

Midterm 3 ***due 12/12***

Paper Presentation Guidelines

Assignment: (20 points total)

You must individually write a 2-page review that includes both a summary and critique of your assigned paper. The summary and critique should be distinct. You must first accurately summarize the scientific work before you can critique it. This is due on the day of your assigned paper discussion. (10 points)

With partners, you will jointly present the paper to the class using powerpoint slides or other similar presentation software. Be sure to present background information to place the research in context, the data contained in the figures and tables of the paper, and your evaluation of the authors interpretation and conclusions. (10 points)

Guidelines:

When you are a practicing scientist, you will often read papers that are not directly in your area of expertise, or which assume knowledge you never learned in a class. In this situation you will need to teach yourself the necessary background information by reading references cited in the introduction to the paper, asking experienced scientists for good review articles in the field, or reading textbook chapters on the topic. You will need to do the same here in order to write your review and present your paper to your classmates.

While you should critically evaluate the paper yourself and with your partners, you are welcome to discuss the background and details of technical approaches with other members of your rotation lab, other students, or faculty so that you can confidently evaluate the assigned paper.

When evaluating your assigned paper, consider the following questions when preparing both your paper and your presentation:

Summary

- What is the significance of the work? How does this fit into previous knowledge? What gap in knowledge are the authors trying to address?
- What is the hypothesis that the authors are trying to test?
- What is innovative about this work – either in the technical methods used or the way of thinking about the problem?
- What experimental method(s) do the authors use to address their hypothesis?
- What results were obtained?
- What is the authors' interpretation of their results and what is their conclusion?

Critique

- Is the experimental method appropriate? Is it the best approach? If not, what could be done better?
- Are there any critical flaws? Missing controls?
- Any potential sources for bias in the experimental design or interpretation?
- Does the data presented by the authors directly or indirectly address the hypothesis? Does the data refute the hypothesis or is it consistent with the hypothesis? Do the results justify the authors interpretation and conclusions?
- Did the authors consider other relevant results and prior data in the literature?
- Do the results suggest new research directions or new research questions? What experiments would you do next to follow up?

If you have questions please come talk to an instructor.