Biophysical Methods I: Practical Macromolecular Crystallography

Tuesday & Thursday, **8:00 - 9:15 am**, Chem **169**

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Office hours: By appointment

Prerequisites: None/By consent of instructor
Required Textbook: Biomolecular Crystallography ISBN: 978-0-8153-4081-2
Bernhard Rupp Price: $72.50 (used, Amazon.com)

Course Policies

University Policies located online at http://www.uwm.edu/Dept/SecU/SyllabusLinks.pdf
Lectures and other resources will be made available via the **D2L** system (https://uwm.courses.wisconsin.edu/)

Expectations

In terms of background knowledge, students should have a solid foundation in biochemistry and at least a working knowledge of protein structure (*e.g.* the types of 2° structures, knowing all 20 amino acids by 1- and 3-letter code as well as their structures). If you do not know much about protein structure it will be helpful to read Chapter 2 of the Rupp text. A well-developed understanding of physical chemistry—especially thermodynamics and the physical basis of inter- and intramolecular interactions—will be also be helpful. Finally, there is no avoiding mathematics in diffraction, so at least a rudimentary knowledge of calculus is assumed. While not necessary for success in the course, some of the hands-on portions will be much more accessible if the student is familiar with the Linux operating system.

Attendance

It is expected that students will attend all lectures, observe basic courtesy, participate in discussions, and complete all assignments given.

Course goals

- To understand the entire process of macromolecular structure determination, from protein production all the way through to structure validation and analysis. You should be able, by the end of the course, to independently determine a structure for an "easy protein" like lysozyme.
- To be able to critically interpret structural data, which requires a thorough knowledge of (a) what structures can tell us about a protein's function and (b) the limitations of single-crystal diffraction.
- To be able to read and evaluate protein structure research articles and to communicate effectively in oral format.

Grading

Your grade in this course will be based on two 90-minute exams (30% each), a formal in-class presentation (30%) and general participation/engagement in the lectures and hands-on exercises (10%).

***TENTATIVE* Lecture Schedule**

9/5 Introduction: Course goals, grading, administrative details; Why crystallography? What can structures tell us and what are the limitations? What is a crystal? Properties of crystals, their assembly (crystal growth) and morphology

9/7 Practical aspects of crystallization: The phase diagram; Types of crystallization experiments, methods for identifying and optimizing crystallization conditions.

9/12 Hands-on crystallization experiments (class meets in Chem 380; Check on experiments between the 11th and 15th).

9/14 Crystal geometry: repeating lattices and symmetry.

9/19 Space groups.

9/21 Through the looking glass: The reciprocal lattice.

9/26 X-ray scattering.

9/28 Diffraction geometry I.

10/3 Diffraction geometry II.

10/5 X-ray absorption and review for midterm.

10/10 Exam I

10/17 Reciprocal space (because too much is never enough).

10/19 Statistics and probability in the analysis of diffraction data.

10/24 Collection of single crystal X-ray diffraction data I: Radiation sources, detectors, and ancillary equipment.

10/26 Fundamentals of data collection.

10/27 Field trip to Marquette for data collection.

10/31 Field trip to Marquette for data collection.

11/2 Intro to Linux and data processing software.

11/7 Hands-on data processing (meet in Chem 380).

11/9 Phasing: Difference Fourier, molecular replacement, heavy atom methods, MAD/SAD.

11/14 Hands-on phasing (meet in Chem 380).

11/16 Hands-on model building and refinement (meet in Chem 380).

No class on 11/21

11/28 Model analysis and validation.

11/30 Student presentations.

12/5 Student presentations.

12/7 Student presentations.

12/12 Student presentations, review for final.

12/14 Exam 2