

**CHEM 588B: Macromolecular Crystallography  
Spring 2018**

**1. Basic Information**

Time: M 2:00-3:20 pm  
Location: SGM 307  
Unit Value: 2 units  
Grading: Letter Grade  
Instructor: Prof. Vadim Cherezov  
Contact info: Email: [cherezov@usc.edu](mailto:cherezov@usc.edu)  
Phone: (213) 821-1464  
Office: TRF119  
Office Hours: By appointment  
Prerequisites: CHEM 488 or instructor's permission.  
Class Web Page: Blackboard

**2. Course Overview**

Advanced techniques and methods in X-ray crystal structure determination of biological macromolecules with emphasis on practical work.

**3. Course Description**

The importance of single-crystal X-ray diffraction in structural biology is evident, with over 100,000 structures deposited in the Protein Data Bank (PDB). This success can be attributed to major breakthroughs and improvements in recombinant protein expression, stabilization and crystallization, developments of new X-ray sources, crystallographic hardware and software used for X-ray structure determination, allowing the determination of crystal structures for challenging macromolecules and their complexes, previously deemed too difficult to crystallize. This course will introduce students to the most common crystallization approaches and crystallographic software tools, and cover the necessary techniques and methods to handle biomolecular structure determinations.

The course will combine lectures with practical work, meaning that students will perform data processing, structure solutions and structure refinements using real world X-ray diffraction datasets. The use of structural databases in research will be covered as well.

**4. Course Goals and Learning Objectives**

The goal of this course is for you to become familiar with and acquire the techniques and methods of X-ray structure determination, as applied to biological macromolecules (i.e., proteins and nucleic acids). You will become familiar with modern crystallographic software tools such as the CCP4 suite, Phenix, Buster, HKL, XDS, SHELX, Coot, and Pymol. You will also learn how to access and use the Protein Data Bank (PDB) and other crystallographic databases.

This class is designed to be hands-on. You will try crystallizing a test protein. You will process real X-ray diffraction data sets and subsequently solve and refine the crystal structure. You will also be introduced to advanced topics such as problematic structures, low resolution, structural disorder, twinning, pseudo-symmetry.

After successfully completing this course, you will be able to:

- Design a macromolecular structure determination project.
- Prepare protein for crystallization, set up crystallization trials, detect initial crystal hits, optimize crystal growth and harvest crystals for data collection.
- Select an appropriate strategy for diffraction data collection.
- Process diffraction data sets, solve, refine and validate the structure.
- Visualize, manipulate and use crystal structures for gaining mechanistic insights into protein function and generation of new hypotheses.

## 5. Textbooks

Required:

Rodes, G. 2016. *Crystallography Made Crystal Clear. A guide for users of macromolecular models*. 3<sup>rd</sup> Edition, Academic Press.

Recommended:

Rupp, B. 2009. *Biomolecular Crystallography. Principle, practice and application to structural biology*. 1<sup>st</sup> Edition, Garland Science.

## 6. Supplementary Textbooks and References

- McPherson, A. 2016. *Introduction to Macromolecular Crystallography*. 2<sup>nd</sup> ed., Wiley-Blackwell.
- McPherson, A. 1999. *Crystallization of Biological Macromolecules*. 1<sup>st</sup> ed., Cold Spring Harbor Laboratory Press.
- Branden, C, and Tooze, J. 1999. *Introduction to Protein Structure*. 2<sup>nd</sup> ed. Garland Science
- Bergfors, TM. 2009. *Protein Crystallization*. 2<sup>nd</sup> ed., International University Line.
- Petsko, GA, and Ringe, D. 2003. *Protein Structure and Function (Primers in Biology)*. 1<sup>st</sup> ed., Sinauer Associates, Inc.
- Hahn, T. 2005. *International Tables for Crystallography Volume A: Space-group symmetry*, 5<sup>th</sup> ed., Springer.

## 7. Reasons for Taking this Course

Macromolecular Crystallography is the most successful technique in structural biology to date that provides three-dimensional structural information about biological molecules at atomic resolution. This structural information is critical for understanding the mechanisms of action of biological macromolecule and designing specific ligands to modulate their function.

For a long time, X-ray crystallography remained a highly specialized technique that was inaccessible to the average undergraduate or even the postgraduate. With the development of more and more sophisticated diffractometers, the steady rise in computing power, and the advances in crystallographic computer software, macromolecular X-ray crystallography has become a very powerful method to gain insight and understanding structure and function of biological molecules. While X-ray diffraction is now seen as a routine method, it is essential to have a good grasp of the process of crystal structure determination and be able to evaluate crystallographic results and data.

## 8. Technological Proficiency and Hardware/Software Required

As this class is very hands-on and you will carry-out crystal structure refinements, you should have a personal computer or a laptop and be familiar with Windows and/or OS X. All software used during the course is freely available or covered by a campus license.

## 9. Classroom policy

Electronic communication devices (phones, blackberries, and similar) must be turned off or placed away during lectures.

## 10. Tentative Schedule of Classes

- **Week 1:**  
An overview of macromolecular crystallography. A general outline of the crystal structure determination process.
- **Week 2:**  
Protein crystallization. Properties of protein crystals, crystallization methods.
- **Week 3:**  
Special case of membrane proteins.
- **Week 4:**  
Diffraction data collection. Geometric principles of diffraction. X-ray sources. Oscillation method. Serial crystallography.
- **Week 5:**  
X-ray diffraction data processing I. Indexing and Integration.
- **Week 6:**  
X-ray diffraction data processing II. Scaling and Merging.
- **Week 7:**  
*Midterm Exam.* Structure solution methods.
- **Week 8:**  
Structure solution I. Molecular replacement.
- **Week 9:**  
Structure solution II. Isomorphous replacement.
- **Week 10:**  
Structure solution III. Anomalous scattering.
- **Week 11:**  
Map inspection and model building.
- **Week 12:**  
Structure refinement.
- **Week 13:**  
Difficult structures. Low resolution. Disorder. Twinning. Pseudo-symmetry.
- **Week 14:**  
Structure analysis, validation and presentation.
- **Week 15:**  
Protein Data Bank. What structures can and can't tell us. Future outlook of macromolecular crystallography.

## 11. Grading

Your final grade will be based on one midterm, one final exam, and homework assignments, as follows:

Grade Breakdown	Proportion
Final Exam	30 %
Midterm Exam	20 %
Homework	50 %
Total	100 %

11.1 *Examinations:* The midterm and final exams are closed book tests for which you are only required to bring a calculator, a ruler, and a pen. The final exam covers the course material studied during the entire semester (that is, it is a cumulative test) and uses a combination of multiple choice and free response questions. Students who are not able to attend the examination must notify the instructor before the test.

### **Date of the Midterm Exam:**

February 19, 2018

### **Date of the Final Exam:**

May 7, 2018

11.2 *Homework:* The homework consists of practical problems and exercises related to different stages of structure determination process. Homework is due at the beginning of class on the day specified in class. Solutions to the homework will be posted on the class web page a few days after the due date such that homework that is more than two days late will not be accepted. (Students will receive a zero on that particular homework assignment.)

11.3 *Course grade:* The course grade is computed based on the weighted average of the individual assessments using the indicated percentages.

94-100%	A
89-93%	A-
84-88%	B+
79-83%	B
74-78%	B-
69-73%	C+
64-68%	C
59-63%	C-
54-58%	D+
49-53%	D
40-48%	D-
<40%	F

## Statement on Academic Conduct and Support Systems

### Academic Conduct

Plagiarism – presenting someone else’s ideas as your own, either verbatim or recast in your own words – is a serious academic offense with serious consequences. Please familiarize yourself with the discussion of plagiarism in *SCampus* in Section 11, *Behavior Violating University Standards* <https://scampus.usc.edu/1100-behavior-violating-university-standards-and-appropriate-sanctions>. Other forms of academic dishonesty are equally unacceptable. See additional information in *SCampus* and university policies on scientific misconduct, <http://policy.usc.edu/scientific-misconduct>.

Discrimination, sexual assault, and harassment are not tolerated by the university. You are encouraged to report any incidents to the *Office of Equity and Diversity* <http://equity.usc.edu> or to the *Department of Public Safety* <http://adminopsnet.usc.edu/department/department-public-safety>. This is important for the safety of the whole USC community. Another member of the university community – such as a friend, classmate, advisor, or faculty member – can help initiate the report, or can initiate the report on behalf of another person. *The Center for Women and Men* <http://www.usc.edu/student-affairs/cwm/> provides 24/7 confidential support, and the sexual assault resource center webpage <http://sarc.usc.edu> describes reporting options and other resources.

### Support Systems

A number of USC’s schools provide support for students who need help with scholarly writing. Check with your advisor or program staff to find out more. Students whose primary language is not English should check with the *American Language Institute* <http://dornsife.usc.edu/ali>, which sponsors courses and workshops specifically for international graduate students. *The Office of Disability Services and Programs* [http://sait.usc.edu/academicsupport/centerprograms/dsp/home\\_index.html](http://sait.usc.edu/academicsupport/centerprograms/dsp/home_index.html) provides certification for students with disabilities and helps arrange the relevant accommodations. If an officially declared emergency makes travel to campus infeasible, *USC Emergency Information* <http://emergency.usc.edu> will provide safety and other updates, including ways in which instruction will be continued by means of blackboard, teleconferencing, and other technology.