**CHEM 588a: Advanced Practical X-ray Structure Determination of Small Molecules**

# Basic Information

Time: Wednesday, 10:00 – 11:20 am

Location: SGM 307

Unit Value: 2 units

Grading: Letter Grade Instructor: Professor Ralf Haiges

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Office: ACB 201 Office Hours: By appointment

Prerequisites: CHEM 488 or instructor’s permission. Class Web Page: <http://chemmac1.usc.edu/588a/>

# Course Overview

Advanced techniques and methods in small molecule X-ray crystal structure determination. Emphasis on practical and laboratory work.

# Course Description

The importance of single-crystal X-ray diffraction is ever increasing which can be seen by the almost exponentially increasing amount of published crystal structures. An important role in this development can be attributed to major improvements in the crystallographic hardware and software used for X-ray structure determination, allowing the determination of crystal structures for previously deemed “unusable” samples. This course will introduce students to the most often used crystallographic software tools and cover the necessary techniques and methods to handle difficult structure determinations.

The course is very hands-on, meaning that students will perform data processing, structure solutions and structure refinements for actual samples using real world X-ray diffraction datasets. The use of structural databases in research will be covered as well.

# 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 “small” molecules (i.e., those with up to approx. 100 non-hydrogen atoms in the asymmetric unit of the crystal). You will become familiar with modern crystallographic software tools such as the Bruker APEX suite, ShelX, ShelXle, Platon, ORTEP, Olex2 and Mercury. You will also learn how to access and use the Cambridge Structure Database (CSD) as well as the Inorganic Crystal Structural Database (ICSD).

This class is designed very hands-on. You will be presented with real world X-ray diffraction data sets that you will process and subsequently solve and refine the crystal structure. You will also be introduced to advanced topics such as problematic structures, structural disorder, twinning, superstructures and modulated structures.

After successfully completing this course, you will able to:

* + Carry-out actual laboratory work in X-ray structure determination.
  + Process X-ray diffraction data, solve and refine a wide range of crystal structures without relying on the “full-auto” mode of crystallographic software.
  + Treat problematic and formally “unsolvable” structures with disorder, twinning modulation and supercells.

# Textbooks

This course will not have any formal prescribed textbooks. Materials from the supplementary resources listed below will be used from time to time.

# Supplementary Textbooks and References

* + Peter Müller et al., *Crystal Structure Refinement A Crystallographer’s Guide to SHELXL*, Oxford Science Publications 2005 (IUCr Texts on Crystallography 8)
  + Theo Hahn, *International Tables for Crystallography Volume A: Space-group symmetry*, 5th ed., Springer 2005
  + Mark Ladd and Rex Palmer, Structure Determination by X-ray Crystallography: Analysis by X-rays and Neutrons, 5th ed., Springer 2013
  + W. Massa, *Crystal Structure Determination*, 2nd ed., Springer 2004
  + Bob B. He, *Two-Dimensional X-Ray Diffraction*, Wiley 2009
  + Maureen M. Julian, *Foundations of Crystallography with Computer Applications*, 2nd ed., CRC Press, 2014
  + Jenny P. Glusker, Kenneth N. Trueblood, *Crystal Structure Analysis A Primer*, 3rd ed., Oxford Science Publications 2010 (IUCr Texts on Crystallography 14)
  + Christopher Hammond, *The Basics of Crystallography and Diffraction*, 4th ed., Oxford Science Publications 2015 (IUCr Texts on Crystallography 21)
  + Dennis W. Bennett, *Understanding Single-Crystal X-Ray Crystallography*, Wiley-VCH 2010
  + Richard Tilley, *Crystals and Crystal Structures*, Wiley 2006
  + Alexander J. Blake et al., *Crystal Structure Analysis Principle and Practice*, Oxford Science Publications 2009 (IUCr Texts on Crystallography 13)
  + Carmelo Giacovazzo et al., *Fundamentals of Crystallography*, 2nd ed., Oxford Science Publications 2002 (IUCr Texts on Crystallography 7)

# Reasons for Taking this Course

Crystals and the understanding of crystals play a vital role in many subjects, among them mineralogy, inorganic, organic and physical chemistry, physics, metallurgy, materials science, geology, geophysics, biology, and medicine. Practically all information about the molecular structure of matter at atomic resolution is the result of crystallographic analysis. Diffraction methods have contributed to our fundamental understanding of minerals and ceramics, and to the design of material properties, pharmaceuticals and engineered enzymes. It is essential to understand and appreciate the origins of molecular structural information and the biological, chemical and physical implications derived from this information.

Crystallography underscores the importance of interdisciplinary science directly and tangibly affects all our lives through advances in biosciences up to space-age high tech materials development.

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, X-ray crystallography has become a very powerful method to gain insight and understanding of physical properties and reaction behavior of compounds and materials. 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.

# Technological Proficiency and Hardware/Software Required

As this class is very hands-on and you will carry-out crystal structure refinements, you should be familiar with Windows and/or OS X. You need to have access to a computer running Windows 7 or higher. Most software used during the course is freely available or covered by a campus license.

# Classroom policy

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

# Tentative Schedule of Classes

* + **Week 1:**

Overview, Outline of the crystal structure determination process.

# Week 2:

Introduction to ShelX and refinement of a straight forward crystal structure.

# Week 3:

Crystallographic databases

# Week 4:

The X-ray diffractometer, background theory for data collection*.*

# Week 5:

Symmetry and space group determination: the orientation matrix, unit cell parameter and crystal system of the sample.

# Week 6:

Reduction of X-ray diffraction data: data integration and absorption correction.

# Week 7:

Structure solution through intrinsic phasing, direct methods, and Patterson methods.

# Week 8:

Why does my structure not refine? The importance of the unit cell.

# Week 9:

The nuts and bolts of absolute structure determination.

# Week 10:

Is there order in disorder? How to treat disorder.

# Week 11:

A look beyond Bruker APEX and ShelX: Other software packages.

# Week 12:

Problematic structures I: Wrong atom types, strong absorption,

# Week 13:

Problematic structures II: How to deal with multi-domain crystal specimen.

# Week 14:

Problematic structures III: Twinning.

# Week 15:

Structure report: Computation and validation of structural parameters.

# Grading

Your final grade will be based on homework and one project assignment, as follows:

|  |  |
| --- | --- |
| Grade Breakdown | Proportion |
| Project | 50 % |
| Homework | 50 % |
| Total | 100 % |

* 1. *Course grade*: The course grade is computed on the individual assessment grades using the indicated percentages. The letter grade is assigned on a straight scale: 90% and above leading to A, 80%-89.9% leading to B, etc. Pluses and minuses are assigned by dividing each range in corresponding halves (A, A-) or thirds (B+, B, B-, C+,…).

# 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](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](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, w](http://dornsife.usc.edu/ali)hich 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> 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*](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.