Course Syllabus – STBIO 430

Course Information

Course Number: STBIO 430 WI21
Course Name: X-Ray Crystallography
Term: WI 2021
Start Date: 01/05/2021
End Date: 03/26/2021
Credits: 3.0

Meeting Days / Times

Tuesdays and Thursdays, 8:15-9:45am PT / 11:15am-12:45pm ET
(See Calendar in Canvas for the most up-to-date schedule.)

Location

Online via Zoom

Course Managers

Role	Last Name	First Name	Email Address
Instructor	Johnson	Jack	jackj@scripps.edu
TA	Ferguson	James	ferguson@scripps.edu

Course Description

The crystallography course describes the theoretical foundations of crystallography, covering all the areas described in the syllabus. The specific lecture titles provide additional details of the course content. The main purpose is to describe what goes on within the sophisticated crystallography programs used for modern crystal structure determination. While there is an effort to provide some practical experience in crystal structure solution, the main focus is on theory. The successful student will have a firm grasp of all aspects of crystallography and crystal structure determination.

Program Learning Outcomes

By the end of the program, students will have accomplished these objectives:
PLO1: Original Research – graduate students are expected to develop the skills critical for generating high-quality research output. This would include absorbing, recalling, and contextualizing scientific knowledge, evaluating scientific information and data, creating testable hypotheses and investigating hypotheses, mastering scientific tools and techniques, displaying ethical behavior, and receiving and giving feedback.

PLO2: Communication – graduate students are expected to demonstrate the oral, written, and media skills to effectively communicate the impact of a study or a body of work to the greater scientific community and to the public at large using a number of methods.
PLO3: Critical Thinking – graduate students are expected to develop a self-directed process to analyze information, form opinions or judgments, and use this process to improve the quality of their scientific thoughts, navigate problems, and make informed decisions.
PLO4: Intellectual Curiosity – graduate students are expected to acquire the capacity to build their intellectual curiosity and demonstrate problem solving approaches that serve their professional growth and ability to impact a field.
PLO5: Career and Professional Development – graduate students are expected to develop a variety of transferable skillsets throughout their graduate experience, including management and leadership, inclusiveness, resilience, scientific rigor, collaboration, accountability, time management, teamwork, networking, and career planning.

Course Learning Outcomes

Upon completion of this course students will be able to:
CLO1: Describe the theoretical foundations of crystallography.
CLO2: Understand the properties and symmetry of crystals.
CLO3: Interpret and understand x-rays and their properties.
CLO4: Describe and detect diffracted x-rays as well as the geometry of diffractions.
CLO5: Understand the intensity of scattered radiation.
CLO6: Comprehend the uses of fourier syntheses, transformations, and series in crystallography.
CLO7: Have a working knowledge of the Heavy Atom Method and Patterson Techniques.
CLO8: Describe and understand Isomorphous Replacement.
CLO9: Describe and understand Molecular Replacement.
CLO10: Identify and interpret Anomalous scattering and MAD Phasing.
CLO11: Understand structure refinement.

Course Materials

Required: Rupp (2009). Biomolecular Crystallography: Principles, Practice, and Application to Structural Biology. ISBN: 978-0815340812.
The text and references used for hand out material are given at the end. Handout material for each lecture will be provided as PDF files prior to class.

Instructor Policies

PART I Crystals, X-rays, Diffraction

-Overview of Course in X-ray Diffraction
Lecture dealing with optical diffraction, semi quantitative development of the Fourier

transform, reciprocal lattice, weighted reciprocal lattice and the principles of image processing of electron micrographys. Ref. G,L,R, Chapt. 1; Holmes & Blow, pp. 115-134 (Handout).

-Mathematical Review for X-ray Diffraction
Review of Vector and Matrix algebra, complex numbers and Fourier Series as applied to crystallography. Ref. Sherwood Chapt. 2, Chapt. 5; S & J Chapt. 8.

-Properties of Crystals
What is a crystal? The description of the lattice, crystal directions, lattice planes, Miller indices, interfacial angles, unit cell and lattice parameters, molecular weight determination. Ref. G,L,R, Chapts 2,5,15; Sherwood Chapt. 3; S & J Chapt. 2 & 4; Woolfson, Chapt. 1; McPherson, Chapt. 5; B & J Chapt. 3; L & P Chapt. 1

-X-rays and Properties
History and production of X-rays including continuous spectrum, wavelength distribution, short wavelength limit; dependence on tube current, voltage and target materials. Characteristic spectrum, excitation potential, lines, Mosley's Law. Absorption, filtered and monochromatic radiation. Syncrhotron Radiation Ref. S & J Chapt. 1; Cullity Chapt. 1; Sherwood Chapt. 14; L. & P. Appendix 4.

-Geometry of Diffraction
Reflection from a set of planes (Bragg's Law). The reciprocal lattice, definition of reciprocal vectors, properties, conditions for constructive interference. Laue Equations, Ewald Sphere, Equivalence between Ewald Shpere and Bragg's Law. Ref. G,L,R, Chapt 3; Sherwood Chapt. 8; S & J Chapt. 2; Woolfson, Chapt. 3; B & J Chapt. 5.1 - 5.10; L. & P. Chapt. 3.

-Detection of Diffraction
Camera geometries - oscillation, rotation, Weissenberg cameras, precision photography, diffractometers, cell parameter measurements, intensity measurements. Ref. G,L,R, Chapt 7; S & J Chapt. 5, 6; Woolfson, Chapt. 5; Sherwood, Chapt. 14; B & J Chapt. 9; L. & P. Chapt. 3.

PART II Symmetry, Diffraction, Amplitude measurements, Fourier series, Phase determination, Structure refinement, Protein crystals, Isomorphous replacement,

-Symmetry of Crystals
Definition of symmetry, point groups, point group algebra, plane groups, Bravais lattices, crystal systems, Laue Classes, space groups, systematic absences and space group determination. Ref. G,L,R, Chapt 4; S & J Chapt. 3; Woolfson, Chapt. 1; Sherwood Chapt. 3; B & J Chapt. 4; L. & P. Chapt. 2

-Intensity of Scattered Radiation
Superposition of waves. Scattering of X-rays from non-crystalline materials. The scattering factor and temperature factor. Scattering from crystals. The sodium chloride problem.

Systematic absences. Ref. G,L,R, Chapt 7; Stout and Jensen, Chapt. 8; Woolfson, Chapt. 2 & 3; Sherwood, Chapt. 4, 6, 7, 8, 9; G & T Chapt. 5; L. & P. Chapt. 4, 5.

-Uses of Fourier Series in Crystallography
Representation of electron density using Fourier Series. The structure factor and electron density as reciprocal Fourier transforms. Calculation of fourier Series, Beevers Lipson Strips. Structure Solution in outline. Ref. G,L,R, Chapt 6; Stout and Jensen, Chapt. 8, 9; Woolfson, Chapt. 4; Sherwood, Chapt. 5, 9; L. & P. Chapt. 6.

-The Phase Problem and Its Solution
Discussion of the phase problem. The heavy atom method. The Patterson (vector) map. Heavy atom determination from the Patterson. Ref. G,L,R Chapt 8,9; Stout and Jensen, Chapt. 10; Woolfson, Chapt. 8, Sec. 3; Sherwood, Chapt. 11, 12; L. & P. Chapt. 6.4.

-Intensity Statistics and Patterson Methods
Polarization and Lorentz factors. The temperature and scale factors (Wilson Plot). Effect of symmetry on intensity distribution. Modification of Patterson maps (sharpening). The Patterson superposition method. Ref. G,L,R, Chapt. 8; Stout and Jensen, chapt. 7, 10, 14; Woolfson, Chapt. 7, Sec. 5, Chapt. 8, Sec. 3; Sherwood, Chapt. 11, 12, Sec. 1;; L. & P. Chapt. 6.4.4.

-Refinement
Structure refinement by difference Fourier and Least Squares methods. Use of constrained and restrained least squares. Ref. G,L,R, Chapt 10; Stout and Jensen, chapt. 16; L. & P. Chapt. 7.4

-Properties of Protein Crystals
Factors affecting solubility of proteins. Crystallization techniques. Solvent of Crystallization. Ref. G,L,R, Chapts 2,15; B & J Chapt. 3; McPherson, Chapt. 5.

-Isomorphous Replacement
Isomorphous replacement in centric and acentric structures. Harker Construction. Phase probability curves most probable phase, best phase, lack of closure, figure of merit. Ref. G,L,R, Chapt. 8; B & J Chapt. 6; McPherson, Chapt. 6, 10; Woolfson, Chapt. 8, Sec. 4; L. & P. Chapt 6.48.

PART III Molecular replacement, MAD phasing, Structure analysis

-Patterson Methods
Difference Pattersons. Heavy atom location. Anamolous difference Pattersons. Rotation function, vector search procedures. Ref.G,L,R, Chapt. 8; B & J Chapt. 11;.

-Molecular Replacement
The Orientation Problem, The translation problem. Calculation of Phases. Ref. G,L,R, Chapt 8; B & J Chapt. 16.

-MAD Phasing
Anomalous Scattering. Friedel's Law. Multiwavelength Anomalous Dispersion. Ref. Drenth, Chapter 9; Blow. Chapter 8.

-Structure Solution of a Protein, Its Display and Meaning
Summary of structure determination. Display of structure, Graphics Display System. Primary, Secondary Tertiary Structures of Proteins. Protein Structures. Ref. G,L,R, Chapts 9,12,16,17; Ref. B & J Chapt. 2, 13; McPherson, Chapt. 11.

Attendance Statement

Students are expected to attend all classes. Students who are unable to attend class must seek permission for an excused absence from the course director or teaching assistant. Unapproved absences or late attendance for three or more classes may result in a lower grade or an "incomplete" for the course. If a student has to miss a class, he or she should arrange to get notes from a fellow student and is strongly encouraged to meet with the teaching assistant to obtain the missed material.

Scientific and Professional Ethics

The work you do in this course must be your own. Feel free to build on, react to, criticize, and analyze the ideas of others but, when you do, make it known whose ideas you are working with. You must explicitly acknowledge when your work builds on someone else's ideas, including ideas of classmates, professors, and authors you read. If you ever have questions about drawing the line between others' work and your own, ask the course professor who will give you clear guidance. Exams must be completed independently. Any collaboration on answers to exams, unless expressly permitted, may result in an automatic failing grade and possible expulsion from the Graduate Program.

Technology Requirements and Support

For issues related to Canvas, please contact the Graduate Office by email at: gradprgm@scripps.edu or by phone at: 858-784-8469.

Course Grading

Grading is in accordance with the academic policies of the Skaggs Graduate School. The breakdown of grading is as follows:

- Exam I: 30%
- Exam II: 35%
- Exam III: 35%

Grade Point	Letter Grade	
4.00	A	Outstanding achievement. Student performance demonstrates full command of the course subject matter and evinces a high level of originality and/or creativity that far surpasses course expectations.
3.67	A-	Excellent achievement. Student performance demonstrates thorough knowledge of the course subject matter and exceeds course expectations by completing all requirements in a superior manner.
3.33	B+	Very good work. Student performance demonstrates above-average comprehension of the course subject matter and exceeds course expectations on all tasks as defined in the course syllabus. There is notable insight and originality.
3.00	B	Satisfactory work. Student performance meets designated course expectations and demonstrates understanding of the course subject matter at an acceptable level.
2.67	B-	Marginal work. Student performance demonstrates incomplete understanding of course subject matter. There is limited perception and originality.
2.33	C+	Unsatisfactory work. Student performance demonstrates incomplete and inadequate understanding of course subject matter. There is severely limited or no perception or originality. Course will not count toward degree.
2.00	C	Unsatisfactory work. Student performance demonstrates incomplete and inadequate understanding of course subject matter. There is severely limited or no perception or originality. Course will not count toward degree.
0.00	I	Incomplete is assigned when work is of passing quality but is incomplete for a pre-approved reason. Once an incomplete grade is assigned, it remains on student's permanent record until a grade is awarded.
0.00	P	Satisfactory work. Student performance demonstrated complete and adequate understanding of course subject matter. Course will count toward degree.
0.00	F	Unacceptable work/Failure. Student performance is unacceptably low level of knowledge and understanding of course subject matter. Course will not count toward degree. Student may continue in program only with permission of the Dean.
0.00	W	Withdrew from the course with Dean's permission beyond the second week of the term.

- All courses will be recorded and maintained in the student's permanent academic record; only courses that apply towards the degree will appear on the academic transcript. Non-credit or audited courses will not appear on the transcript.
- 4 core courses taken for a letter grade (pass = B- or higher for a core course)
- 2 elective courses taken pass/fail (pass = A, B, C for an elective)

Course Schedule:

Date	Details
Tue Jan 5, 2021	Overview I and II (Johnson)
Thu Jan 7, 2021	Properties of Crystals I and II (Johnson)
Tue Jan 12, 2021	X-rays and their Properties (Johnson)
Thu Jan 14, 2021	Geometry of Diffraction I and II (Johnson)
Tue Jan 19, 2021	Detection of Diffracted X-rays I and II (Johnson)
Thu Jan 21, 2021	Symmetry and Symmetry of Crystals (Johnson)
Tue Jan 26, 2021	Exam I
Thu Jan 28, 2021	Intensity of Scattered Radiation I and II and III (Johnson)
Tue Feb 2, 2021	Fourier Syntheses and Transforms (Johnson)
Thu Feb 4, 2021	Fourier Series; Electron Density; Structures (Johnson)
Tue Feb 9, 2021	Heavy Atom Method; Patterson Techniques (Johnson)
Thu Feb 11, 2021	Isomorphous Replacement I (Johnson)
Tue Feb 16, 2021	Isomorphous Replacement II (Johnson)
Thu Feb 18, 2021	Exam II
Tue Feb 23, 2021	Molecular Replacement I (Johnson)
Thu Feb 25, 2021	Molecular Replacement II (Johnson)
Tue Mar 2, 2021	Anomalous Scattering and MAD Phasing I (Johnson)
Thu Mar 4, 2021	MAD Phasing II (Johnson)
Tue Mar 9, 2021	Refinement (Johnson)
Thu Mar 11, 2021	Exam III