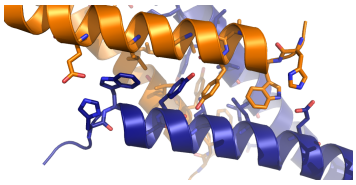


Biochemistry and Biomedical Sciences 3Z03:
Structural Determination and Analysis of Macromolecules

CONTACT INFORMATION

Instructor

Dr. Sara Andres andressn@mcmaster.ca Office: MDCL 2325
Office hours: By appointment only

Teaching Assistants

Lucas Koechlin koechlil@mcmaster.ca
Tim Klein kleint1@mcmaster.ca

Course Website

Course information will be posted on Avenue2Learn. If the course is not visible on your Avenue page, please contact the instructor. Please check regularly for any announcements pertaining to the course. ***Note: I use this a lot to post updates on the class.***

QUESTIONS

- For any and all questions, please contact your TAs by email, using the subject line "3Z03 question".
- Note that we will do our best to respond within 24 hrs to your questions, however if you haven't heard from us after 24 hrs, please send a follow-up email – we're human and get a lot of emails, so there's a good chance we may have missed it!

COURSE INFORMATION

In OUR Course

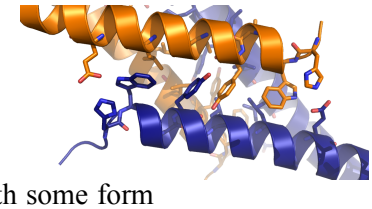
- Every voice matters
- Every individual is treated with respect, dignity and equality
- We will establish a safe, inviting and caring environment so we can share our thoughts and ideas with one another and learn from each other
- Everyone shares the responsibility for making our course a POSITIVE, engaging, respectful and fun environment.

Course Description

This course is designed to be an introduction to the methods used in determining protein and macromolecular structures, with an emphasis on x-ray crystallography, but also with short lectures on cryo-electron microscopy, small-angle x-ray scattering, and nuclear magnetic resonance. In addition to the methods, we also want to highlight how to interpret protein structure data (what does the structure tell us, is the data any good?) and do a practical component, with hands-on learning of how to solve, refine, analyze and present protein structures.

What to Expect in Class

These are looooooooong classes. Classes are 3 hours,. I can't talk that long (ok, I can, but I don't want to, and you probably don't want me to either), so we'll mix it up. If there's a quiz scheduled, we'll start with that (~20 minutes), followed by some lecture. We'll have a ~15



minute break mid-way (stand-up, stretch, move around) and then we'll continue with some form of hands-on or active learning. Also, I get that this is right over lunch hour, so I fully endorse you eating and drinking during the class. Please be considerate, though, and clean up after yourself; also, please don't bring any strong smelling foods (i.e. re-heated fish or Stilton cheese). As delicious as they may be, some people are sensitive to smells (myself included) and this won't be conducive to learning.

Course Objectives

1. Describe the basic theory and applications of structural biology methods.
2. Employ structural biology software to analyze and interpret data
3. Create high-quality structural images to tell a story (Science can be art!)
4. Evaluate the quality of structural data (Is the data good enough to make conclusions?)
5. Analyze protein structure (What does it tell us?)

Prerequisites

One of BIOCHEM 2BB3, BIOCHEM 3G03, or ISCI 2A18 A/B

MATERIALS AND FEES

Textbooks

There are no textbooks required for this course, however there are great resources available online and in the primary literature, and books available through the library (both digital and hard copy) for further understanding of the topics covered. See the last page for a list of resources. Feel free to explore!

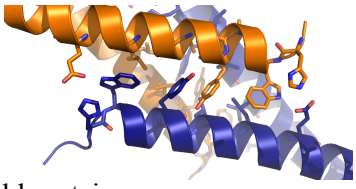
Computers and Software

A laptop (Windows, Mac or Linux-based) is required for this course, capable of running the software below. All the software required for group projects is freely available online. Please download all the programs onto your laptop and bring them to class, as we will be learning the software during class together, in preparation for your group projects. **If you do not have access to a computer for class use, please contact the instructor immediately so that alternate arrangements can be made.**

Program	Purpose	Website
X11	May be needed to run Phenix, Coot. Try installing Phenix and Coot first.	https://www.xquartz.org/
Phenix	For x-ray structure solution, refinement, analysis	https://www.phenix-online.org/download/
Coot	Works with Phenix, for x-ray refinement, analysis	If Windows: use WinCoot through CCP4 For Mac: https://www.phenix-online.org/download/other.html
Pymol	Protein structure analysis, figures and movies	https://pymol.org/edu/?q=educational/
FoldIt	For Assignment 1	https://fold.it/portal/

COURSE ASSESSMENT

Grade Breakdown and Due Dates



FoldIT Assignment (4% of final grade): FoldIT is an online game to learn how to fold proteins. Completing the introductory tasks highlight critical components of protein folding and are important concepts to know when solving crystal structures. **Due February 25, 9 a.m.**

Quizzes (25% total of final grade): 6 quizzes will be held at the **BEGINNING** of each lecture from **Jan 14 – Feb 25**, worth 5% each, based on material inclusive of all previous classes. Quizzes will be no more than 10 questions, and will be a mix of multiple choice, matching, fill-in-the-blank and short answer (like 2 sentences short!). The final grade will be calculated **based on your top 5 best scores**. If you miss a test (with or without filing MSAF), that test will be dropped automatically.

Summary Reports (30% total of final grade): 3 summary reports will be completed throughout the semester, detailing the progress of the group project. **EACH** student must hand in their own individual summary report on Avenue2Learn. Each report is worth 10%. **Due as outlined below.**

Group Project (40% total of final grade) : This project will include a final presentation to the class on your protein. 20% will be for the powerpoint slides, 15% for the actual presentation, 5% for answering questions. This is the equivalent of a final exam; please keep this in mind if considering a Late Withdrawal as per University policies.

***SPECIAL NOTE ON THE GROUP PROJECT:** You will need to create a group of 4 and submit the names of your group members to **both** TAs by January 21st, midnight. If you cannot find a group, please email the TAs who will assign you to a group.

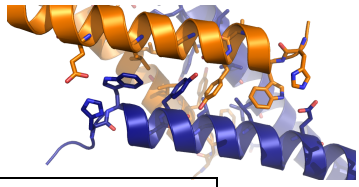
Attendance at Presentations (1% of final grade): Attendance will be taken at the start of the presentation lectures to ensure that everyone is present. 0.5% per presentation class attended.

Course Evaluation (0.5% BONUS): If 90% of the class completes the course evaluation, everyone will receive a 0.5% bonus on their final mark. This could be the difference between an 11 or 12!

You have **one week** after a test or assignment has been completed and the results released to contact the course instructor to report an issue, *ie* incorrect addition. Please make sure to take a good look at your results once they are released.

CLASS AND EVALUATION SCHEDULE

Date	Topic	Evaluation
January 7	**Introduction and X-ray crystallography Part 1** – Crystallization, software installation, intro to FoldIT and the PDB website	
January 14	**X-ray crystallography Part 2** – Data collection: Spacegroup, Bragg's Law, Ewald's sphere, processing data. Proteomics	Quiz
January 21	**X-ray crystallography Part 3** – Phase determination: MR, SAD/MAD, SIR/MIR, direct methods, solving the phase problem (and your structure!) with Phenix; also how to import your data files with Phenix	Quiz; **Submit names of your group members**
January 28	**X-ray crystallography Part 4** – Model Building and Refinement: How to get the best structure, R and Rfree values, Phenix and Coot to refine, Ligand Fitting, Pymol to present your structure	Quiz
February	**X-ray crystallography Part 5** – Model validation and analysis of	Quiz



4	your structure: Ramachandran plots and protein geometry, crystallography statistics and what the structure tells us	
February 11	**Other cool structural techniques**: Cryo-electron microscopy, Small-angle x-ray scattering, Nuclear magnetic resonance, Atomic Force Microscopy	Quiz; Summary Report 1 **Due at 11:59 pm**
February 18	**No classes – reading week. Enjoy ☺ Play some FoldIT ☺**	
February 25	**Group Project** : Focus on structure solution, model building, refinement	Quiz; **FoldIT due 9 am**
March 3	**Group Project**: Continue refinement/validation and begin analysis.	Summary Report 2 **Due at 11:59 pm**
March 10	**Group Project:** Finish analysis; start working on your story (presentation, figures/movies).	
March 17	**Group Project:** Continue working on your story (presentation, figures/movies).	Summary Report 3 **Due at 11:59 pm**
March 24	**Presentations –** Everyone present; random draw for order of presentation	Final evaluation
March 31	**Presentations –** Everyone present; random draw for order of presentation	Final evaluation

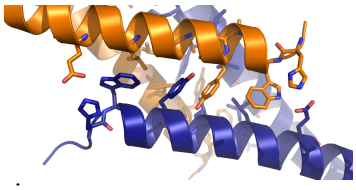
COURSE EXPECTATIONS and UNIVERSITY POLICIES

Missed Work
If you are absent from the university for a minor medical reason, lasting fewer than 5 days, you may report your absence, one per term, without documentation, using the McMaster Student Absence Form (http://www.mcmaster.ca/msaf/). Absences for a long duration or for other reasons must be reported to the Associate Dean of Science office, with documentation, and relief may not necessarily be granted. After filling out the MSAF you must immediately contact your course instructor (normally within 2 working days) by email to learn what relief may be granted for the work you have missed and relevant details for submission or location of make-up test or assignment. Please note that the MSAF may not be used for term work worth 25% or more.

Late Work
Work submitted after the deadline will suffer a loss of 10% per 24 hr period.

Remarking Work
If you would like to have any work regraded, please adhere to the Department of Biochemistry and Biomedical Sciences "Regrading Policy" available at the following website under regarding requests and use the associated form, both of which can be found here:
https://healthsci.mcmaster.ca/biochem/education/undergraduate/forms-and-procedures

Changes to the Course Outline
The instructor and University reserve the right to modify elements of the course during the term. The University may change the dates and deadlines for any or all courses in extreme circumstances. If either type of modification becomes necessary, reasonable notice and communication with the students will be given with explanation and opportunity to comment on changes. It is the responsibility of students to check their McMaster email accounts and course websites weekly during the term and to note any changes.
Academic Integrity



You are expected to exhibit honesty and use ethical behaviour in all aspects of the learning process. Academic credentials you earn are rooted in principles of honesty and academic integrity. **It is your responsibility to understand what constitutes academic dishonesty.** Academic dishonesty is to knowingly act or fail to act in a way that results or could result in unearned academic credit or advantage. This behaviour can result in serious consequences, e.g. the grade of zero on an assignment, loss of credit with a notation on the transcript (notation reads: "Grade of F assigned for academic dishonesty"), and/or suspension or expulsion from the university. For information on the various types of academic dishonesty please refer to the *Academic Integrity Policy*, located at https://secretariat.mcmaster.ca/university-policies-procedures- guidelines/
The following illustrates only three forms of academic dishonesty:

- plagiarism, e.g. the submission of work that is not one's own or for which other credit has been obtained.
- improper collaboration in group work.

copying or using unauthorized aids in tests and examinations.

Academic Accommodation of Students with Disabilities
Students with disabilities who require academic accommodation must contact Student Accessibility Services (SAS) at 905-525-9140 ext. 28652 or sas@mcmaster.ca to make arrangements with a Program Coordinator. For further information, consult McMaster University's *Academic Accommodation of Students with Disabilities* policy.

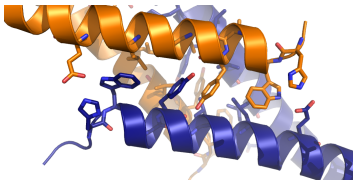
Requests for Relief for Missed Academic Term Work
McMaster Student Absence Form (MSAF): In the event of an absence for medical or other reasons, students should review and follow the Academic Regulation in the Undergraduate Calendar "Requests for Relief for Missed Academic Term Work".

Academic Accommodation for Religious, Indigenous or Spiritual Observances (RISO)
Students requiring academic accommodation based on religious, indigenous or spiritual observances should follow the procedures set out in the RISO policy. Students should submit their request to their Faculty Office ***normally within 10 working days*** of the beginning of term in which they anticipate a need for accommodation or to the Registrar's Office prior to their examinations. Students should also contact their instructors as soon as possible to make alternative arrangements for classes, assignments, and tests.

Extreme Circumstances
The University reserves the right to change the dates and deadlines for any or all courses in extreme circumstances (e.g., severe weather, labour disruptions, etc.). Changes will be communicated through regular McMaster communication channels, such as McMaster Daily News, A2L and/or McMaster email.

Courses with an On-Line Element
In this course we will be using Avenue to Learn (A2L). Students should be aware that, when they access the electronic components of this course, private information such as first and last names, user names for the McMaster e-mail accounts, and program affiliation may become apparent to all other students in the same course. The available information is dependent on the technology used. Continuation in this course will be deemed consent to this disclosure. If you have any questions or concerns about such disclosure please discuss this with the course instructor.

Conduct Expectations



As a McMaster student, you have the right to experience, and the responsibility to demonstrate, respectful and dignified interactions within all of our living, learning and working communities. These expectations are described in the *Code of Student Rights & Responsibilities* (the "Code"). All students share the responsibility of maintaining a positive environment for the academic and personal growth of all McMaster community members, **whether in person or online**.
It is essential that students be mindful of their interactions online, as the Code remains in effect in virtual learning environments. The Code applies to any interactions that adversely affect, disrupt, or interfere with reasonable participation in University activities. Student disruptions or behaviours that interfere with university functions on online platforms (e.g. use of Avenue 2 Learn, WebEx or Zoom for delivery), will be taken very seriously and will be investigated. Outcomes may include restriction or removal of the involved students' access to these platforms.

Authenticity/Plagiarism Detection
Some courses may use a web-based service (Turnitin.com) to reveal authenticity and ownership of student submitted work. For courses using such software, students will be expected to submit their work electronically either directly to Turnitin.com or via an online learning platform (e.g. A2L, etc.) using plagiarism detection (a service supported by Turnitin.com) so it can be checked for academic dishonesty.

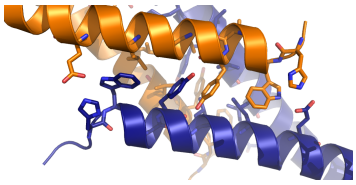
Students who do not wish their work to be submitted through the plagiarism detection software must inform the Instructor before the assignment is due. No penalty will be assigned to a student who does not submit work to the plagiarism detection software. **All submitted work is subject to normal verification that standards of academic integrity have been upheld** (e.g., on-line search, other software, etc.). For more details about McMaster's use of Turnitin.com please go to www.mcmaster.ca/academicintegrity.

Courses With An Online Element
Some courses may use on-line elements (e.g. e-mail, Avenue to Learn (A2L), LearnLink, web pages, capa, Moodle, ThinkingCap, etc.). Students should be aware that, when they access the electronic components of a course using these elements, private information such as first and last names, user names for the McMaster e-mail accounts, and program affiliation may become apparent to all other students in the same course. The available information is dependent on the technology used. Continuation in a course that uses on-line elements will be deemed consent to this disclosure. If you have any questions or concerns about such disclosure please discuss this with the course instructor.

Copyright and Recording
Students are advised that lectures, demonstrations, performances, and any other course material provided by an instructor include copyright protected works. The Copyright Act and copyright law protect every original literary, dramatic, musical and artistic work, **including lectures** by University instructors.

The recording of lectures, tutorials, or other methods of instruction may occur during a course. Recording may be done by either the instructor for the purpose of authorized distribution, or by a student for the purpose of personal study. Students should be aware that their voice and/or image may be recorded by others during the class. Please speak with the instructor if this is a concern for you.

Online Proctoring
Some courses may use online proctoring software for tests and exams. This software may require students to turn on their video camera, present identification, monitor and record their computer



activities, and/or lock/restrict their browser or other applications/software during tests or exams. This software may be required to be installed before the test/exam begins.

Collaboration Policy

This course focuses on teamwork and collaboration. This is because science and almost all careers rely heavily on teamwork and sharing of ideas. Care must be taken to ensure equal distribution of work ethic and acknowledgement of individual ideas and creativity whenever collaborating with anyone. This is not only respectful but also fair. Additionally, it allows for a free-flowing, creative environment where individual ideas are proposed and acknowledged properly. This always gives rise to individual and team empowerment, productivity, optimism and a sense of contribution. Only wonderful things can happen when you acknowledge each other's contributions

Late Withdrawal

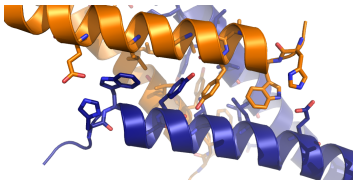
McMaster University provides a Late Withdrawal option to assist students who have become irretrievably behind in a course. Students who have fallen behind with assignments and/or are not prepared to write final examinations (or equivalent) in one or more courses are encouraged to make use of this option and must contact their Academic Advisor in the Faculty/Program Office. Students will work with their Academic Advisor to discuss the situation and what steps they can take to prevent a recurrence. The maximum number of units for which students may request a Late Withdrawal is 18 units throughout their undergraduate degree. Students may request a Late Withdrawal, without petition, no later than the last day of classes in the relevant Term. However, it is important to note that:

- Requests for Late Withdrawal cannot be made in courses for which the final exam (or equivalent) has been attempted or completed. This also includes courses where a final grade has been assigned (e.g. clinical courses).
- Such requests will be cancelled or revoked if it is determined that the student attempted or completed the final exam (or equivalent).
- Students cannot use the Late Withdrawal option for courses in which they are under investigation or for which they have been found guilty of academic dishonesty. Course(s) approved for Late Withdrawal will be:
    - Assigned a non-numeric grade of LWD, in lieu of an alpha/numerical grade
    - Excluded from the calculation of the GPA
    - Ineligible for tuition refund

Approval of a late withdrawal is final, and requests to be re-enrolled in the withdrawn course(s) will not be considered. A withdrawal will not preclude students from enrolling in the course(s) in a subsequent term.

FINAL NOTES

We hope that during this course you will come to appreciate structural biology and understand its impact on the world around you. Throughout the course we'll hand out course evaluations. These are very important to us – they let us know what you like, what you don't like, and how we can make this course even better! If you ever have any questions or suggestions about the course or even science in general, please don't hesitate to contact us through one of the methods under instructor information – we are always happy to share our perspective on the scientific world! Here's to a great semester!



RESOURCES

At the library

Crystallography Made Crystal Clear: A guide for users of macromolecular models by Gale Rhodes – digital copy

Biomolecular Crystallography: principles, practice and application to structural biology by Bernhard Rupp – hard copy

Introduction to Macromolecular Crystallography by Alexander McPherson – digital and hard copy

Online Resources (a very small sampling of what is available)

Crystallography
Structural Overview, with a focus on crystallography:
http://www.proteinstructures.com/index.html (Go to experimental tab)

X-ray crystallography explained with links to each step of the process:
http://my.yetnet.ch/dergutemensch/crystallography/phasedetermination.htm

Another great course on x-ray crystallography, with lots of detail:
http://www-structmed.cimr.cam.ac.uk/course.html

Tutorial on iMosflm: https://www.mrc-lmb.cam.ac.uk/harry/imosflm/ver711/documentation/tutorial.html

Pymol help: https://www.pymolwiki.org/index.php/Practical_Pymol_for_Beginners
More Pymol help: https://pymolwiki.org/index.php/Category:Tutorials

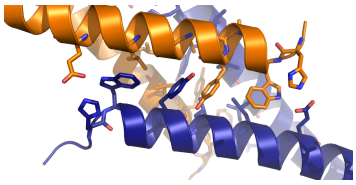
Phenix information: https://www.phenix-online.org/documentation/phenix_gui.html

SAXS
SAXS overview: http://biosaxs.com/technique.html

SAXS Review: (Don't get bogged down by the equations).
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3962079/

EM
Cryo-EM brief history: https://www.fei.com/life-sciences/history-of-cryo-em/
Biological applications: https://www.nature.com/articles/nature19948

CRYSTALLOGRAPHY TABLE



(adapted from https://www.nature.com/nature/for-authors/formatting-guide)

Data collection and refinement statistics (molecular replacement)

	Crystal 1 name
Data collection	
Space group	
Cell dimensions	
a, *b*, *c* (Å)	42.08, 86.93, 86.24
α, β, γ (°)	118.11, 99.65, 95.47
Resolution (Å)	##(high res shell) *
R_{sym} or R_{merge}	##(high res shell)
I / σI	##(high res shell)
$CC_{1/2}$	##(high res shell)
Completeness (%)	##(high res shell)
Redundancy	##(high res shell)
Refinement	
Resolution (Å)	
No. reflections	
R_{work} / R_{free}	
No. atoms	
Protein	
Ligand/ion	
Water	
B-factors	
Protein	
Ligand/ion	
Water	
R.m.s. deviations	
Bond lengths (Å)	
Bond angles (°)	