McMaster University | Biochemistry & Biomedical Sciences

We recognize and acknowledge that McMaster University meets and learns on the traditional territories of the Mississauga and Haudenosaunee nations, and within the lands protected by the "Dish With One Spoon" wampum, an agreement amongst all allied Nations to peaceably share and care for the resources around the Great Lakes.

Biochemistry and Biomedical Sciences 3Z03 - Structural Determination and Analysis of Macromolecules 2024 Winter Term

Instructor: Dr. Sara Andres | **Microsoft Teams:** @andressn

Office: MDCL 2325 | **Office Hours:** By Appointment

Teaching Assistants

- Caitlin Doubleday doubledc@mcmaster.ca
- Harman Dev devh1@mcmaster.ca
- Sahil Karnani karnanis@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. ***I will post all announcements both on A2L and Microsoft Teams.***

Questions

- For any and all questions, please use the "Questions" channel in Microsoft Teams.
- If you prefer to direct message, direct message **ALL 3 TAs first**. You will get a faster answer if you message all 3 at once.
- 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 Teams message– we're human and get a lot of messages, so there's a good chance we may have missed it!

Course Information

- Tuesdays 2:30pm – 3:20pm, T13 127
- Wednesdays 2:30-3:20 pm , PC 155
- Friday 4:30-5:20 pm, PC 155

Materials & Fees

There are no textbooks required for this course, however there are great resources available online (YouTube has great videos!) 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! **A laptop with internet connection *and mouse* are required to carry out assignments, follow-along in hands-on learning, and for the final project.**

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 lectures on cryo-electron microscopy, small-angle x-ray scattering, nuclear magnetic resonance, and artificial intelligence. 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 refine, analyze and present protein structures.

Prerequisite(s): One of BIOCHEM 2BB3, BIOCHEM 3G03, or ISCI 2A18 A/B

Course Learning 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?)

What to Expect in Class

Mondays will be hands-on learning, with skills needed for the assignments. Wednesdays and Fridays will be more theory-based, with interactive lecture. Be sure to bring your mouse for Mondays! All main details about the course (assignments, course content, quizzes, marks, etc.) will be on Avenue2Learn. So, A2L is the central hub for all information; Microsoft Teams will be used for communication: contacting the TAs, myself and/or your team for the group project. Classes will be recorded and posted after class for those who are unable to attend in person due to sickness, conflicts, etc. However, I strongly encourage attendance particularly for Monday with the hands-on learning.

Virtual Course Delivery (if needed)

To follow and participate in virtual classes it is expected that you have reliable access to the following:

- A computer that meets performance requirements found here.
- An internet connection that is fast enough to stream video.
- Computer accessories that enable class participation, such as a microphone, speakers and webcam when needed.

If you think that you will not be able to meet these requirements, please contact uts@mcmaster.ca as soon as you can. Please visit the Technology Resources for Students page for detailed requirements. If you use assistive technology or believe that our platforms might be a barrier to participating, please contact Student Accessibility Services, sas@mcmaster.ca, for support.

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 assignments. **ALTERNATELY**: Both Phenix and Coot will be accessible through the computer labs at McMaster, which can be accessed by a virtual desktop.

Program	Purpose	Website
X11	May be needed to run Phenix, Coot if you have a Mac. Try installing Phenix and Coot first.	https://www.xquartz.org/
Phenix	For x-ray structure solution, refinement, analysis – choose “Latest official release”.	https://www.phenix-online.org/download/

	Note: **First click "obtain a password for downloading Phenix"**	
Coot	Works with Phenix, for x-ray refinement, analysis, if not installed automatically with phenix. We will go through this in a Friday tutorial class!	For Windows: https://bernhardcl.github.io/coot/ For Mac: Install Homebrew: https://brew.sh/ Then, https://scottlab.ucsc.edu/xtal/wiki/index.php/Stand-Alone_Coot
Virtual Desktop	To access Phenix and Coot instead of installing on your own computer. See "How to Connect".	https://uts.mcmaster.ca/services/teaching-and-learning/computer-labs/
Pymol	Protein structure analysis, figures and movies. **MAKE SURE TO REGISTER YOUR EDUCATIONAL COPY!**	https://pymol.org/edu/?q=educational/
FoldIt	For Assignment 1	https://fold.it/
BioRender (optional)	For making figures for other assignments. There are limitations to the free version, but it will be sufficient for this course.	https://biorender.com/
Canva (optional)	For making illustrations for an assignment.	https://www.canva.com/education/students/

Course Overview and Assessment

Grade Breakdown and Due Dates

FoldIT Assignment (3% 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 and analyzing crystal structures. **Due February 1, 11:59 pm.**

Quizzes (20% total of final grade): 5 quizzes will be held outside of class hours, on Avenue2Learn for a 3hr period of time each week (exact time TBD as a class) from **Jan 22 – March 1**, worth 5% each, based on

material inclusive of all previous classes. Quizzes will be short, and will be a mix of multiple choice, matching, fill-in-the-blank, short and long answer. The final grade will be calculated **based on your top 4 best scores**. If you miss a test (**no MSAF required if only missing 1 quiz**), that test will be dropped automatically. Quizzes are 20 minutes in length.

Protein Stories (Mid-term Assignment) (30% total of final grade): Working in a group, create a children's story on a protein of your choosing. This will be an illustrated storybook style, where illustrations need to incorporate PyMol figures and the story needs to centre on the protein's structure and function. Further details are in the assignment. **Checkpoint 1 – Jan 25, Checkpoint 2 – Feb 15, Final submission Due Feb 29, all due dates by 11:59 pm.**

AI and the Written Report (17% total of final grade): A written report with 2 checkpoints and a final submission with limited use of ChatGPT as outlined in the assignment, to help improve writing, describing a protein structure of the student's choosing. **EACH** student must hand in their own individual summary report on Avenue2Learn. **Checkpoints and final assignment are due as follows: 1st checkpoint– Feb 8, 2nd checkpoint - March 7, final submission– March 21, all by 11:59 pm.** Note that you can always hand in something EARLY ☺.

Protein Refinement, Analysis and AlphaFold (Final Project) (30% total of final grade) : This project will include multiple checkpoints with hands-on learning, followed by a choice of a final pre-recorded 15-min presentation or written report. All groups will present a short 3 minute presentation during the final classes. Additional details are in the assignment. This is the equivalent of a final exam; please keep this in mind if considering a Late Withdrawal as per University policies**. Due Dates (exact dates TBD):** **Checkpoint 1 (week 2 of group project), Checkpoint 2 (week 3 of group project), Final Report or Presentation (4 days before presentations), 3 min presentation (final week of class)**

***Special Note on the Two Group Projects:** You will need to create a group of 4 and submit the names of your group members on Avenue2Learn by **January 22nd, 11:59 pm**. If you cannot find a group, *please contact the TAs who will assign you to a group*. This group will also be used during class time for in-class activities. **Optional**: If you would prefer to not work in a group and complete one or both group projects individually, please contact Dr. Andres. Evaluations will follow the same rubrics, but evaluation will take into consideration the work is being completed by an individual instead of a group of 4.

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 TA who marked the assignment first, and then course instructor, if additional discussion is required to report an issue, *ie* incorrect addition. Please make sure to take a good look at your results once they are released.

A note on quizzes, assignments and assessments

To be explicitly clear in my expectations for all graded material:

•It is your responsibility to know the McMaster Academic Integrity Policy

•Quizzes are meant to be completed individually

•All written answers and all written assignments must be in your own words

•Quizzes are meant to be done without any additional aids (for example, but this is not an exhaustive list: notes, internet, AI software)

•However, as we are not using proctoring software, the quizzes are written such that if you look things up, you will be unable to finish the quiz in time.

- For written assignments that are individual (i.e. short reports):
  - It is your responsibility to know McMaster's Academic Integrity Policy
  - All written assignments must be in your own words.
  - Assignments are meant to be done individually, but you can talk to others for ideas, for help, for proof-reading, just not to do the whole assignment for you.

Course Evaluation Schedule (subject to change with advance notice)

Week	Topic (Subject to change)	Evaluation
January 8-12	**Introduction and AlphaFold** – Course expectations, assignments, intro to FoldIT and the PDB website, AlphaFold, software installation	
January 15-19	**Analyzing Protein Structure** What does it mean, tools for analysis, PyMol for analysis and figures	
January 22	**Submit names of your group members by 11:59 pm or contact Dr. Andres if you wish to work individually**	

January 22-26	**X-ray Crystallography Part I, Quiz 1** The practical side of crystallization and data collection, with a dash of theory Final help on software installation	Quiz 1
Jan 25	**Protein Stories Checkpoint 1 due at 11:59pm**	Protein Stories
Jan 29 – Feb 2	**X-ray Crystallography Part II, Quiz 2** Solving the phase problem – theoretically and practically during the tutorial, with Phenix (and the start of model building)	Quiz 2
Feb 1	**FoldIT due 11:59pm**	**FoldIT due 11:59pm**

Date	Topic (Subject to change)	Evaluation
February 5-9	**X-ray Crystallography Part III, Quiz 3** Model building, refinement and validation – in theory and practice using Phenix and Coot	Quiz 3
February 8	**Written report Part 1 due at 11:59 pm**	**Written report part 1 due at 11:59pm**
Feb 15	**Protein Stories Checkpoint 2 due at 11:59pm**	
February 12-16	**Cryo-Electron Microscopy and Nuclear Magnetic Resonance Spectroscopy, Quiz 4** What they are, how they work, the information they can give; practice using Phenix and Coot for Model Validation	Quiz 4
February 19-23	**No classes – reading week. Enjoy ☺ Play some FoldIT ☺**	
Feb 26 – March 1	**Small Angle X-ray Scattering and Atomic Force Microscopy, Quiz 5** What they are, how they work, the information they can give; further practice with Phenix and Coot before the group project starts	Quiz 5
Feb 29	**Protein Stories due at 11:59 pm**	**Protein Stories due at 11:59 pm**
March 4 -8	**Group Project** : Focus on refinement and AlphaFold mutation **Tutorial:** Examples/suggested outlines of 3 min and 15 min presentations	

March 7	**Written report part 2 at 11:59 pm**	**Written report part 2 due at 11:59 pm**
March 11-15	**Group Project**: Continue refinement/validation and begin analysis of wildtype and mutant protein	
March 17	**Group Project check-in on A2L by 11:59 pm**	**Group Project check-in on A2L by 11:59 pm**
March 18-22	**Group Project:** Finish analysis; start working on your story (presentation, figures/movies).	
March 21	**Written report part 3 at 11:59 pm**	**Written report due at 11:59 pm**
March 25-April 5	**Group Project:** Finish it up!	
April 5 (depending on number of presentations)	**Group Project Recording or Report DUE, uploaded to TEAMS, at 11:59 pm** **Make sure to watch or read assigned presentations before next class**	**Group Project DUE on Teams 11:59 pm**
April 8-10 (depending on number of presentations)	**3-minute Presentations, Q&A Sessions** IN-PERSON	**Final evaluation in-class**

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.

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 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.

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.

Courses with An On-Line Element

In this course we will be using Avenue to Learn (A2L) and Microsoft Teams. 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.

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.

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.

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 the McMaster Office of Academic Integrity's webpage.

Conduct Expectations

As a McMaster student, you have the right to experience, and the responsibility to demonstrate, respectful and dignified interactions within all 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.

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.

Research Ethics -N/A

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.

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!

Congratulations on reading this far into the course outline. The first student to email Dr. Andres at andressn@mcmaster.ca and give the phrase "Answers to many questions can be found in the course outline" will receive a $5 Amazon gift card. Individuals are only eligible for 1 prize during the 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 / σ I	##(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 (°)	