# MCB*6370 Protein Structural Biology and Bioinformatics

Winter 2024
Section(s): 01

Department of Molecular and Cellular Biology
Credit Weight: 0.50
Version 1.00 - January 05, 2024

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# 1 Course Details

## 1.1 Calendar Description

This course explores structural biology from three perspectives: 1) the fundamental concepts in structural biology; 2) the methods used to determine structures (including x-ray crystallography, NMR, electron microscopy, and computational modeling); 3) the bioinformatic concepts and tools used to compare, contrast and assign biochemical function to protein structures and sequences. The course emphasizes building a conceptual and practical skill set that will be applicable to any structure related problem.

## 1.2 Course Description

**Course synopsis:**

This course will explore the relationship between protein sequence and three-dimensional structure. Students will gain experience with critical assessment of recent protein structure journal articles and the tools and methodology required for modeling, docking, and designing protein structure.

**Objectives:**

Mastery of PyMOL for analysing structures and generating figures

Analysis of protein sequences and structures using diverse sequence and structural bioinformatics tools

Understanding and applying ab initio protein structure modelling and other modelling tools

Understanding of the methods used to generate experimental structures

Critical analysis of contemporary primary literature

Mastering scientific writing

Practice of oral presentation skills

**Recommended background:** The course is designed for students who have met the requirements for entry to the M.Sc. or Ph.D. programs of the Department of Molecular and Cellular Biology, having completed a B.Sc. degree or the equivalent, preferably in a field that is focused on biology at a sub-cellular level. It is expected that students have a good working knowledge of basic biochemistry, including a familiarity with the main concepts of protein structures.

**Assignment groups:** The PyMOL, bioinformatics and modelling exercises and main structure analysis assignment will be completed individually. If enrolment is high, there will likely not be enough class time to discuss one paper per student. Consequently, the journal club papers may be presented either individually, or in groups of two to three. In the case of group

presentations, students can suggest groupings, or the instructor will help to match unpaired students.

### 1.3 Timetable

Mondays 1:30 to 4:30 p.m.

Class meetings will be conducted in person in SSC 3317.

Attendance of lectures in person is required.

### 1.4 Final Exam

There is no final exam for this course.

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## 2 Instructional Support

### 2.1 Instructional Support Team

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| **Instructor:** | Matthew Kimber |
| **Email:** | mkimber@uoguelph.ca |
| **Telephone:** | +1-519-824-4120 x52568 |
| **Office:** | SSC 2254 |
| **Office Hours:** | Meetings available by prior email appointment, either in person or over videoconference. |

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## 3 Learning Resources

### 3.1 Course resources

Lectures will be the primary means of communication. All lecture notes will be uploaded to the course's courselink site prior to the lecture; similarly, tutorials will be posted and all written assignments will be submitted through courselink.

Students will be accessing papers through the University of Guelph library.

Students need access to a reasonably capable computer (5 years old should be fine) and an

internet connection to use Pymol and complete bioinformatics exercises. Students will need a gmail account in order to be able to access Alphabet's computational cloud.

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# 4 Learning Outcomes

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# 5 Teaching and Learning Activities

## 5.1 Lecture

**Topics:**

| Week | Topics | Content | Tutorials | Assignments |
|---|---|---|---|---|
| 1 | Introduction<br>Protein Structure Fundamentals (part 1) | Forces and thermodynamics<br>Amino acid properties | PyMOL tutorial | |
| 2 | Protein Structure Fundamentals (part 2) | Secondary structure<br>Tertiary structure<br>Oligomerization<br>Membrane proteins<br>IUPs | | PyMOL image #1 |
| 3 | Protein Structure fundamentals (part 3) | Protein states<br>Protein Dynamics<br>Structure-function relationships<br>Binding and catalysis<br>Gene Ontology | Sequence bioinformatics tutorial | PyMOL image #2 |

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| | Sequence Bioinformatics (part 1) | BLAST<br>Sequence databases | | |
| 4 | Sequence Bioinformatics (part 2) | MSA<br>Phylogenetic trees<br>Gene annotation | | PyMOL image #3<br>Journal Club #1 |
| 5 | Structural Bioinformatics | Structure superposition<br>CONSURF<br>PISA – oligomeric states<br>Chemi-informatics | Structural bioinformatics tutorial | Sequence bioinformatics exercise<br>Journal Club #2 |
| 6 | Computational Methods | Molecular dynamics<br>Homology modelling<br>Rosetta<br>AlphaFold | Colabfold tutorial | Structural bioinformatics exercise<br>Journal Club #3 |
| | **READING WEEK** | | | |
| 7 | Cryo-electron microscopy | | | Journal Club #4<br>Modelling exercise |
| 8 | X-ray crystallography | | | Journal Club #5 |

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|---|---|---|---|---|
| 9 | NMR | | | Journal Club #6 |
| 10 | | | | Journal Club #7 |
| 11 | No lecture | | | Structural assignment due<br>Structural analysis assignment: Presentations |
| 12 | No lecture | | | Structural analysis assignment: Presentations |

*Schedule is for guidance only and is subject to change depending on the rate at which we proceed through the material, and the final enrolment numbers.

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# 6 Assessments

**Foundational exercises:**

A core goal of this course is to teach students how to visualize, analyze and communicate protein structures and sequences. Students will complete a series of detailed tutorials, each of which emphasizes a different core skill in protein analysis.

1) **Protein visualization in PyMol**: Protein structure visualization is an extremely important skill in structural biology. Students will complete a comprehensive tutorial on how to use the very powerful, general-purpose macromolecular structure viewing, analysis and documenting program PyMol. They will then complete a series of mini-assignments that will test their ability to closely reproduce figure panels from recently published structure papers from publicly available PDB files and other resources.

2) **Sequence Bioinformatics skills**: students will complete a tutorial introducing key sequence bioinformatics programs, and complete an analysis of a protein sequence using the skills learned.

3) **Structural Bioinformatics skills**: students will complete a tutorial introducing key structural bioinformatics programs, and complete an analysis of a protein structure using the skills learned.

4) **Ab initio structure modelling**: Students will complete a tutorial on using the open source AlphaFold implementation ColabFold, and model a structure.

**Journal Club Presentations:**

Each student will present a research paper which focuses on some particular protein bioinformatics or structure-function relations problem, with all students participating in a discussion of the work. One or two students will be assigned to lead the discussion, and should be deeply familiar with the paper, have done any additional reading required to understand the material being analysed, and should be looking to stimulate a meaningful discussion with their peers. The primary focus should be on this discussion; the leader may optionally use PowerPoint or PyMOL to show figures from the paper, the whiteboard, etc. if they feel that it helps foster the discussion, but these materials will not be the focus of the evaluation. All students are expected to be able to meaningfully discuss the content of the paper, and therefore need to be familiar with its content and have done some further reading into the background to the problem. Students are expected to have informed opinions about the methodology, its applicability to the problem, the quality of the results obtained and the appropriateness of the interpretation.

**Structure Analysis Paper:**

The final assignment for the course is a structure annotation assignment. Students will be allowed to choose a protein or protein complex they are interested in (or have one assigned), subject to the restriction that no detailed structure-function analysis is currently available in the literature. Students will build a model of the structure using ColabFold, and then analyse the structure and sequence using bioinformatics tools (including, but not limited to, those

discussed in class), and searches of the literature and public databases. This analysis will be centered on generating a publication quality analysis of sequence-structure-function relations in this protein, with original figures and concrete hypothesis that could, in principle, be experimentally tested. The results of this analysis will be presented as a scientific manuscript, and presented as a talk to the class.

**Turnitin:**

In this course, your instructor will be using Turnitin, integrated with the Courselink Dropbox tool, to detect possible plagiarism, unauthorized collaboration or copying as part of the ongoing efforts to maintain academic integrity at the University of Guelph. All submitted assignments will be included as source documents in the Turnitin.com reference database solely for the purpose of detecting plagiarism of such papers. Use of the Turnitin.com service is subject to the Usage Policy posted on the Turnitin.com site.

## 6.1 Marking Schemes & Distributions

**Mini assignments:**

PyMol exercises: 7%

Sequence Bioinformatics: 7%

Structural bioinformatics: 6%

ColabFold exercise: 5%

**Journal Club:**

Presentation: 15%

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| Participation: | 10% |

**Structural Annotation:**

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| Written | 40% |
| Oral Presentation | 10% |

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# 7 Department of Molecular and Cellular Biology Statements

## 7.1 Academic Advisors

If you are concerned about any aspect of your academic program:

- Make an appointment with a program counsellor in your degree program. B.Sc. Academic Advising or Program Counsellors

## 7.2 Academic Support

If you are struggling to succeed academically:

- Learning Commons: There are numerous academic resources offered by the Learning Commons including, Supported Learning Groups for a variety of courses, workshops related to time management, taking multiple choice exams, and general study skills. You can also set up individualized appointments with a learning specialist. http://www.learningcommons.uoguelph.ca/
- Science Commons: Located in the library, the Science Commons provides support for physics, mathematic/statistics, and chemistry. Details on their hours of operations can be found at: http://www.lib.uoguelph.ca/get-assistance/studying/chemistry-physics-help and http://www.lib.uoguelph.ca/get-assistance/studying/math-stats-help

## 7.3 Wellness

If you are struggling with personal or health issues:

- Counselling services offers individualized appointments to help students work through personal struggles that may be impacting their academic performance. https://www.uoguelph.ca/counselling/
- Student Health Services is located on campus and is available to provide medical attention. https://www.uoguelph.ca/studenthealthservices/clinic
- For support related to stress and anxiety, besides Health Services and Counselling Services, Kathy Somers runs training workshops and one-on-one sessions related to stress management and high performance situations. http://www.selfregulationskills.ca/

## 7.4 Personal information

Personal information is collected under the authority of the University of Guelph Act (1964), and in accordance with Ontario's Freedom of Information and Protection of Privacy Act (FIPPA) http://www.e-laws.gov.on.ca/index.html. This information is used by University officials in order to carry out their authorized academic and administrative responsibilities and also to establish a relationship for alumni and development purposes.

For more information regarding the Collection, Use and Disclosure of Personal Information policies please see the Undergraduate Calendar. (https://www.uoguelph.ca/registrar/calendars/undergraduate/current/intro/index.shtml)

## 7.5 Course Offering Information Disclaimer

Please note that course delivery format (face-to-face vs online) is subject to change up to the first-class day depending on requirements placed on the University and its employees by public health bodies, and local, provincial and federal governments. Any changes to course format prior to the first class will be posted on WebAdvisor/Student Planning as they become available.

# 8 University Statements

## 8.1 Email Communication

As per university regulations, all students are required to check their e-mail account regularly: e-mail is the official route of communication between the University and its students.

## 8.2 When You Cannot Meet a Course Requirement

When you find yourself unable to meet an in-course requirement because of illness or compassionate reasons please advise the course instructor (or designated person, such as a teaching assistant) in writing, with your name, id#, and e-mail contact. The grounds for Academic Consideration are detailed in the Undergraduate and Graduate Calendars.

Undergraduate Calendar - Academic Consideration and Appeals
https://www.uoguelph.ca/registrar/calendars/undergraduate/current/c08/c08-ac.shtml

Graduate Calendar - Grounds for Academic Consideration
https://www.uoguelph.ca/registrar/calendars/graduate/current/genreg/index.shtml

Associate Diploma Calendar - Academic Consideration, Appeals and Petitions
https://www.uoguelph.ca/registrar/calendars/diploma/current/index.shtml

## 8.3 Drop Date

Students will have until the last day of classes to drop courses without academic penalty. The deadline to drop two-semester courses will be the last day of classes in the second semester. This applies to all students (undergraduate, graduate and diploma) except for Doctor of Veterinary Medicine and Associate Diploma in Veterinary Technology (conventional and alternative delivery) students. The regulations and procedures for course registration are available in their respective Academic Calendars.

Undergraduate Calendar - Dropping Courses
https://www.uoguelph.ca/registrar/calendars/undergraduate/current/c08/c08-drop.shtml

Graduate Calendar - Registration Changes
https://www.uoguelph.ca/registrar/calendars/graduate/current/genreg/genreg-reg-regchg.shtml

Associate Diploma Calendar - Dropping Courses
https://www.uoguelph.ca/registrar/calendars/diploma/current/c08/c08-drop.shtml

## 8.4 Copies of Out-of-class Assignments

Keep paper and/or other reliable back-up copies of all out-of-class assignments: you may be asked to resubmit work at any time.

## 8.5 Accessibility

The University promotes the full participation of students who experience disabilities in their academic programs. To that end, the provision of academic accommodation is a shared responsibility between the University and the student.

When accommodations are needed, the student is required to first register with Student Accessibility Services (SAS). Documentation to substantiate the existence of a disability is required; however, interim accommodations may be possible while that process is underway.

Accommodations are available for both permanent and temporary disabilities. It should be noted that common illnesses such as a cold or the flu do not constitute a disability.

Use of the SAS Exam Centre requires students to make a booking at least 14 days in advance, and no later than November 1 (fall), March 1 (winter) or July 1 (summer). Similarly, new or changed accommodations for online quizzes, tests and exams must be approved at least a week ahead of time.

For Guelph students, information can be found on the SAS website

https://www.uoguelph.ca/sas

For Ridgetown students, information can be found on the Ridgetown SAS website
https://www.ridgetownc.com/services/accessibilityservices.cfm

## 8.6 Academic Integrity

The University of Guelph is committed to upholding the highest standards of academic integrity, and it is the responsibility of all members of the University community-faculty, staff, and students-to be aware of what constitutes academic misconduct and to do as much as possible to prevent academic offences from occurring. University of Guelph students have the responsibility of abiding by the University's policy on academic misconduct regardless of their location of study; faculty, staff, and students have the responsibility of supporting an environment that encourages academic integrity. Students need to remain aware that instructors have access to and the right to use electronic and other means of detection.

Please note: Whether or not a student intended to commit academic misconduct is not relevant for a finding of guilt. Hurried or careless submission of assignments does not excuse students from responsibility for verifying the academic integrity of their work before submitting it. Students who are in any doubt as to whether an action on their part could be construed as an academic offence should consult with a faculty member or faculty advisor.

Undergraduate Calendar - Academic Misconduct
https://www.uoguelph.ca/registrar/calendars/undergraduate/current/c08/c08-amisconduct.shtml

Graduate Calendar - Academic Misconduct
https://www.uoguelph.ca/registrar/calendars/graduate/current/genreg/index.shtml

## 8.7 Recording of Materials

Presentations that are made in relation to course work - including lectures - cannot be recorded or copied without the permission of the presenter, whether the instructor, a student, or guest lecturer. Material recorded with permission is restricted to use for that course unless further permission is granted.

## 8.8 Resources

The Academic Calendars are the source of information about the University of Guelph's procedures, policies, and regulations that apply to undergraduate, graduate, and diploma programs.

Academic Calendars
https://www.uoguelph.ca/academics/calendars

## 8.9 Illness

Medical notes will not normally be required for singular instances of academic consideration,

although students may be required to provide supporting documentation for multiple missed assessments or when involving a large part of a course (e.g.. final exam or major assignment).

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