



BIOC*4540 Enzymology

Winter 2021

Section(s): C01

Department of Molecular and Cellular Biology

Credit Weight: 0.75

Version 1.00 - January 08, 2021

1 Course Details

1.1 Calendar Description

This is a laboratory-intensive course where the topics studied include enzyme active sites and the mechanisms of enzyme action; enzyme kinetics and regulation; recombinant proteins and site-directed mutagenesis as tools for understanding enzymes.

Pre-Requisites: BIOC*3560 (may be taken concurrently), BIOC*3570

1.2 Course Description

This is a required Biochemistry fourth-year course on the subject of Enzyme Structure, Function and Mechanism. It features a laboratory component (5 laboratory modules) and an Independent Study where the students research an enzyme of choice and present a PowerPoint seminar with a partner.

1.3 Timetable

- Lectures: Tuesday and Thursday @ 10:00 – 11:20 via Zoom (virtual)
- Laboratory sections will be held during your scheduled lab period via Zoom (virtual)

1.4 Final Exam

The Final Exam is scheduled for April 23, 2021 from 11:30 am - 1:30 pm (on-line).

2 Instructional Support

2.1 Instructional Support Team

Instructor: Rod Merrill
Email: rmerrill@uoguelph.ca
Telephone: +1-519-824-4120 x53806
Office: Remote
Office Hours: By appointment

Lab Co-ordinator: Colin Cooper
Email: ccoope08@uoguelph.ca
Office: Remote
Office Hours: By Appointment

2.2 Teaching Assistants

Teaching Assistant: Brianna Ball
Email: ballb@uoguelph.ca
Office Hours: Brianna will work as a Laboratory Teaching Assistant for the course.

Teaching Assistant: Kyle Pimentel
Email: kpimente@uoguelph.ca
Office Hours: Kyle will work as a Laboratory Teaching Assistant for the course.

Teaching Assistant: Tanisha Teelucksingh
Email: tteeluck@uoguelph.ca
Office Hours: Tanisha will be working as a Laboratory Teaching Assistant for the course.

3 Learning Resources

3.1 Required Resources

Computer with internet access (Equipment)

This course will be offered in an alternate format (remotely); a computer with an internet connection is required.

3.2 Recommended Resources

Principles in Biochemistry (Readings)

- No single textbook is sufficient for the lecture material but Lehninger: Principles in Biochemistry (Lehninger 5th, 6th, or 7th editions) Chapter 6 serves as the basis for basic enzyme understanding and theory and this chapter should be read and carefully studied.

- On reserve

3.3 Additional Resources

Introduction to Proteins: Structure, Function, and Motion (Textbook)

Amit Kessel, Nir Ben-Tal (2018) Introduction to Proteins: Structure, Function, and Motion, 2nd Edition (Chapman and Hall, CRC; published April 11, 2018)

- on reserve

Structure and Mechanism in Protein Science: A Guide to Enzyme Catalysis and Protein Folding, Series in Structural Biology (Textbook)

Alan Fersht (2017) Structure and Mechanism in Protein Science: A Guide to Enzyme Catalysis and Protein Folding, Series in Structural Biology – vol. 9 (2017), World Scientific Co. Pte. Ltd, Hakensack, New Jersey.

- on reserve

Enzymes: Biochemistry, Biotechnology and Clinical Chemistry (Textbook)

Trevor Palmer (2007) Enzymes: Biochemistry, Biotechnology and Clinical Chemistry, 2nd edition, Albion Press.

- on reserve

3.4 Note

- A number of related texts have been placed on reserve as resources and to provide background information on the various topics discussed in the course (see Course Subject Outline).
- The Adobe Acrobat (*.pdf) files for each Powerpoint lecture will be available for download from the Courselink website and each lecture will be made available at least 2 weeks before the specified lecture date.

3.4 Additional Texts

- All indicated additional texts, papers and treatises are available at the Reserve Desk at the library on two hour loan.

4 Learning Outcomes

Objectives: (i) To integrate the practical aspects of enzymology with the kinetic theories to provide a mechanistic overview of enzyme activity and regulation in cells; (ii) to prepare students to confidently and competently work with enzyme systems in both Academia and Industry; and (iii) to give students the experience to research an enzyme topic, prepare and deliver a PowerPoint lecture.

4.1 Course Learning Outcomes

By the end of this course, you should be able to:

1. Analyse and plot enzyme kinetic data and study the effect of pH on the kinetic activity of the enzyme.
 2. Learn how to use Bioinformatic tools and software, including PyMOL to study and analyze enzyme structure and function.
 3. Perform a literature research on a specific enzyme topic
 4. Prepare and deliver a Powerpoint seminar to your peers
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5 Teaching and Learning Activities

5.1 Course Subject Outline

I. ENZYMES AS CATALYSTS (Lehninger Ch 6; Fer Ch 2, 3, 4, 6; Palm Ch 1, 6, 8, 16)

- Lect#1: Introduction and History of Enzymes
 - Historical aspects
 - Discovery of enzymes
 - Chemistry of enzymes
 - Function and importance
 - Enzymes in biotechnology
- Lect#2: Enzyme Purification and Assay
 - Initial velocity measurements
 - Assay types
 - Enzyme units of activity
 - Turnover number and properties
 - Purification and assessment
 - Methods for measurements
- Lect#3: Michaelis-Menten Kinetics
 - Introduction

- Assumptions
- Derivation
- Description of v_o versus $[S_o]$
- Michaelis constant (K_M)
- Specificity/substrate constant (SpC)
- Lect#4: Graphical Analysis of Kinetic Data, pH, Temp Dependence and Allosteric Enzymes
 - Graphical analysis
 - Lineweaver-Burk Analysis
 - Hanes-Woolf Analysis
 - Eadie-Hofstee Analysis
 - Direct Linear Plot (Eisenthal/Cornish-Bowden Plot)
 - Nonlinear Curve Fitting
 - pH-dependence of Michaelis-Menten Enzymes
 - Temperature-dependence of enzyme reactions
 - Allosteric enzymes
- Lect#5: Enzyme Classification, Characteristics and Properties
 - Classification
 - Catalytic power and specificity
 - Enzymes as catalysts
 - Enzyme - substrate interactions
 - lock & key model
 - induced fit model
 - transition state model
 - quantum tunnelling model
 - Enzymes as proteins
 - Enzyme cofactors
- Lect#6: Enzyme Inhibition and Kinetics
 - Classification of Inhibitors
 - Reversible
 - Irreversible
 - Iodoacetamide
 - DIFP
 - Suicide substrates
 - Classification of Reversible Inhibitors
 - Competitive

- Uncompetitive
 - Noncompetitive
 - Substrate
- Lect#7: Single Molecule Enzymology
 - Movies of single enzymes
 - Advantages of Single Molecule Studies
 - Applications of Single Molecule Studies
 - Following enzymes in real time
 - ATP Synthase with tethered actin
 - ATP Synthase mechanism
 - Myosin-V
 - Kinesin motor attached to a fluorescent bead
 - Single Molecule Studies of Cholesterol Oxidase
 - β -galactosidase: a model Michaelis-Menten enzyme?
- Lect#8: Multi-substrate Reactions and Substrate Binding Analysis
 - Multi-substrate reactions
 - Cleland convention
 - Ordered and random mechanisms
 - Sequential and nonsequential mechanisms
 - Sequential
 - Nonsequential
 - Substrate Binding Analysis
 - Single Binding Site Model
 - Binding Data Plots
 - Direct Plot
 - Reciprocal Plot
 - Scatchard Plot
 - Determination of Enzyme-Substrate Dissociation Constants
 - Kinetics
 - Equilibrium Dialysis
 - Equilibrium Gel Filtration
 - Ultracentrifugation
 - Spectroscopic Methods

II. MECHANISM OF ENZYME CATALYSIS (Lehninger Ch 6; Fer Ch 2, 9; Palm Ch 10, 11)

- Lect#9: Enzyme Mechanisms-I
 - Reaction Mechanisms and Catalysis
 - Enzyme-transition state complementarity
 - Structure-activity correlations
 - Transition state analogues
 - Catalytic antibodies
 - Summary
 - Preferential transition state binding
 - Transition state theory
 - Proximity effect
 - Acid-base catalysts
- Lect#10: Enzyme Mechanisms II
 - Covalent catalysis
 - Metal ion catalysis
 - Electrostatic catalysis
 - Low barrier H-bonds
 - Structural flexibility
- Lect#11: Enzyme Mechanisms-III: Techniques for Drug Discovery
 - Drug Design
 - Techniques of Drug Discovery
 - Complexity of Drug Discovery
 - SARs and QSARs
 - Structure-based Drug Design
 - Combinatorial Chemistry and High-Throughput Screening
 - Introduction to Pharmacology
 - Pharmacokinetics
 - Toxicity and Adverse Reactions Eliminate Most Drug Candidates
 - Phase I
 - Phase II
 - Phase III
 - Drug Candidate Statistics
 - Cytochrome P450 Metabolizes Drugs
 - Many Drugs are Enzyme Inhibitors
 - Sulfadruugs
 - Viagra
- Lect#12: Active Site Investigations I

- Kinetic Studies
- Variation of substrate concentration
- Variation of substrate structure
- Reversible inhibition
- Variation of pH
- Pre-steady state kinetics
- Detection of Intermediates
- X-ray Crystallographic Studies
- NMR for Protein Structure Determination
- Lect#13: MID-TERM EXAMINATION (during class time) Tue, Mar 2, 2021
- Lect#14: Active-Site Investigations II
 - Chemical modifications of active-site side-chains
 - applications
 - Super-reactive side-chains
 - Suicide substrates
 - Interpretation of chemical modification experiments
 - Criteria for establishment of side-chain involvement in catalysis
- Lect#15: Enzyme Engineering and Design
 - Protein Engineering
 - Engineering Technology
 - Engineering Methods
 - Engineering proteins to be more stable enzymes
 - Engineering a more stable T4 lysozyme
 - Disulfide bonds increase T4 lysozyme stability
 - Helix stabilization (capping) of T4 lysozyme
 - Incorporation of Non-Canonical Amino Acids (NCAA) into Proteins
 - Protein Engineering by Combinatorial Methods
 - Machine-learning-guided directed evolution for protein engineering

III. CASE STUDY ENZYMES/INDEPENDENT PROJECT/SEMINAR (Starting Tue, Mar 11, 2021)

- Lect#16: Student Presentations (n = 3 presentations, groups of 2 students)
- Lect#17: Student Presentations (n = 3 presentations, groups of 2 students)
- Lect#18: Student Presentations (n = 3 presentations, groups of 2 students)
- Lect#19: Student Presentations (n = 3 presentations, groups of 2 students)
- Lect#20: Student Presentations (n = 3 presentations, groups of 2 students)

- Lect#21: Student Presentations (n = 3 presentations, groups of 2 students)
- Lect#22: Student Presentations (n = 3 presentations, groups of 2 students)
- Lect#23: Student Presentations (n = 3 presentations, groups of 2 students)
- Lect#24: Course Review

Fer = Ferst; Lehninger = Lehninger 7th ed., Palm = Palmer

6 Assessments

6.1 Marking Schemes & Distributions

Name	Scheme A (%)
Mid-term	20
Laboratory	25
Independent Study/Seminar	25
Participation	5
Final exam	25
Total	100

6.2 Assessment Details

Midterm (20%)

Date: Tue, Mar 2, 10:00 AM - 11:20 AM, In class

- There will be a Mid-term Examination (80 min, in class-time) involving multiple choice and short answer questions.
- There are no alternate exams offered since the Mid-term will be given in class time.
- The final grade can be based entirely on the Final Exam (and other components) only if reasons for missing the Mid-term exam are adequately documented.
- Both exams are required!
- Students who score a significantly higher grade on the Final Exam, compared with the Mid-term Exam, may receive a higher weighting of the Final Exam (Mid-term: 10%, Final: 40%), at my discretion. A significantly higher grade is one that is 25 percentage points higher.

Laboratory Component (25%)

Date: Remote

Lab periods will begin the week of January 11th during your scheduled day of the week.

Lab Reports will be monitored with anti-plagiarism software (Turnitin)

Independent Study/Seminar (25%)

- Commencing with Lecture#16 (**March 11, 2021**), we will have three Powerpoint presentations per lecture period with each seminar being a group effort (two students per team). The presentations will be 15 min in length followed by a 5-min question period. Each team member will receive an **identical mark** for the presentation, including the ability to answer questions--this activity is meant to be a team-effort and not two individuals presenting separately. Therefore, choose your partner wisely since you must work well with your partner to make the best team-based presentation possible! The independent study/seminar is worth 25%; additionally there is a 5% participation mark. Therefore, it is important to help each other and to work as a team! It is paramount to remember that anything that you include or say during your presentation is open to questions from the audience and, so you should ensure that you fully understand it. A seminar rubric will be used for evaluation of the seminars. Dr. Merrill, Dr. Cooper and the TAs will complete evaluation forms on each presentation. The comments/feedback will be given, but not the marks until all the presentations have been completed. A grade of 5% (participation mark) will also be given for seminar preparation (following the time-line, not last minute) and participation in the question period (details to follow later).
- Students must form a two-person team by **Jan 22nd, 2021** and the team must decide upon a case-study enzyme for their presentation and clear the topic with Dr. Merrill by **Jan 29th, 2021** (4 pm). The lecture/seminar dates are: Mar 11, 16, 18, 23, 25, 30 and Apr 1, 6 and 8. Dr. Cooper will schedule the presentation dates for all the teams through Courselink. Some research and preparation time will be given during the Enzymology lab sessions (see Dr. Cooper for details). If you are unable to present your seminar on the scheduled date, a separate written project/assignment will be given.

Participation (5%)**Final Exam (25%)**

Scheduled by the registrar's office, see WebAdvisor for details.

- The examination component of the Final Grade can be based entirely on the Final Exam only if reasons for missing the Mid-term exam are adequately documented.
 - Both exams are required!
 - The Final Exam is cumulative and will cover all lectures, including the research seminars.
 - Students who score a significantly higher grade on the Final Exam, compared with the Mid-term Exam, may receive a higher weighting of the Final Exam (Mid-term: 10%, Final: 40%), at my discretion. A significantly higher grade is one that is 25 percentage points higher.
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7 Course Statements

7.1 Instructor & Course Evaluation

As part of the evaluation process in the Department of Molecular and Cellular Biology, written comments on the Course and/or the Instructors' teaching performance may be sent to the Chair, Department of Molecular and Cellular Biology, at any time. Such letters must be signed. Departmental Evaluations will also be conducted near the end of the semester. Copies of evaluations will be made available to the Instructor after submission of the final grade.

7.2 Course Add and Drop

Notification is not needed for dropping the course before the DROP deadline (last day of class, Apr 12, 2021). Program approval is only needed for drops and adds if your category is "Special" or "Provisional".

7.3 Recording of Lecture Materials

By enrolling in a course, unless explicitly stated and brought forward to their instructor, it is assumed that students agree to the possibility of being recorded during lecture, seminar or other "live" course activities, whether delivery is in-class or online/remote.

If a student prefers not to be distinguishable during a recording, they may:

1. turn off their camera
2. mute their microphone
3. edit their name (e.g., initials only) upon entry to each session
4. use the chat function to pose questions.

Students who express to their instructor that they, or a reference to their name or person, do not wish to be recorded may discuss possible alternatives or accommodations with their instructor.

7.4 Online Behaviour

Inappropriate online behaviour will not be tolerated. Examples of inappropriate online behaviour include:

- Posting inflammatory messages about your instructor or fellow students
- Using obscene or offensive language online
- Copying or presenting someone else's work as your own
- Adapting information from the Internet without using proper citations or references
- Buying or selling term papers or assignments
- Posting or selling course materials to course notes websites
- Having someone else complete your quiz or completing a quiz for/with another student
- Stating false claims about lost quiz answers or other assignment submissions
- Threatening or harassing a student or instructor online
- Discriminating against fellow students, instructors and/or TAs
- Using the course website to promote profit-driven products or services
- Attempting to compromise the security or functionality of the learning management system
- Sharing your user name and password
- Recording lectures without the permission of the instructor

8 Department of Molecular and Cellular Biology

Statements

8.1 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](#)

8.2 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>

8.3 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/>

8.4 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>)

9 University Statements

9.1 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.

9.2 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>

9.3 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>

9.4 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.

9.5 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 book their exams at least 7 days in advance and not later than the 40th Class Day.

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>

9.6 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>

9.7 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.

9.8 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>

9.9 Disclaimer

Please note that the ongoing COVID-19 pandemic may necessitate a revision of the format of course offerings and academic schedules. Any such changes will be announced via CourseLink and/or class email. All University-wide decisions will be posted on the COVID-19 website (<https://news.uoguelph.ca/2019-novel-coronavirus-information/>) and circulated by email.

9.10 Illness

The University will not normally require verification of illness (doctor's notes) for fall 2020 or winter 2021 semester courses. However, requests for Academic Consideration may still require medical documentation as appropriate.
