Faculty of Science Course Syllabus  
Department of Biochemistry & Molecular Biology  
BIOC 4701/5701  
Enzymes  
Winter Term, 2020

Instructor: Dr. Stephen L. Bearne (Tupper 9J)

Lectures: 8:30 – 10:00 (Tuesday & Thursday) in Tupper theatre D

Laboratories: None

Tutorials: None

Course Description

What gives the cell its life and personality are enzymes. They govern all body processes; malfunction of even one enzyme can be fatal. Nothing in nature is so tangible and vital to our lives as enzymes, and yet so poorly understood and appreciated by all but a few scientists.

Arthur Kornberg
For the Love of Enzymes, 1989

Fundamental principles of enzyme catalysis and its regulation will be examined. Use of tools such as steady-state and pre-steady-state kinetics, isotope effect measurements, site-directed mutagenesis, spectroscopy, x-ray crystallography, and mechanism-based inhibitors to study the architecture and mechanism of action of enzyme active sites will be presented. The catalytic mechanism and transition state stabilization will be considered in detail for selected enzymes that have been well-characterized structurally. Classic and current papers in the literature will be reviewed so that the experimental and conceptual approaches used may be critically appraised.

The lectures are designed to present the theory of selected topics in enzymology. Problem sets based on articles from the biochemical literature will serve to provide specific examples of the concepts introduced in the lectures. The problem sets will be assigned every two weeks. Since there is not a laboratory component associated with this course, the problem sets will be quite detailed and students are expected to work on them over the two-week period (i.e., not the night before they are due!). Each student will write an essay and present an oral presentation (30 min) based on their essay topic. Essay topics may be chosen from the list provided or in consultation with the course instructor. Attendance at presentations is mandatory. All students will be responsible for lecture material, assigned readings, problem sets, and material presented during the student seminars.

Course Prerequisites
BIOC 3700.03; or (CHEM 3601.03 and CHEM 2301.03), all with a grades of B or higher or instructor's consent

Course Objectives/Learning Outcomes
1. Account for why a given ligand may be bound tightly by an enzyme or covalently modify an enzyme (transition state analogues).
2. Explain how given techniques (spectroscopy, radioactivity, HPLC) may be used to measure enzyme activity in direct or indirect assays.
3. Given a pH-dependent kinetic mechanism, derive an initial velocity equation and sketch the plot of kinetic constants as a function of pH.
4. Given the kinetic mechanism (with or without inhibition), derive an initial velocity equation using either the steady-state assumption or the rapid equilibrium approach.
5. Show how entropic contributions lead to huge intramolecular rate enhancements.
6. Given the kinetic parameters for an enzyme-catalyzed reaction and the corresponding nonenzymatic reaction, calculate the efficiency, rate enhancement, proficiency, and extent of transition state stabilization.
7. Given the steady-state velocity expression for a multisubstrate enzyme, predict the product inhibition pattern and binding order in the presence of fixed and variable substrate concentrations.
8. Derive the steady-state velocity equation for a given kinetic mechanism for a multisubstrate enzyme using the King-Altman method.
9. Identify uniform and differential binding from site-directed mutagenesis studies or substrate mutilation studies to discern the role of residues in transition state and ground state binding.
10. Given an enzyme mechanism, design a reversible or irreversible inhibitor.
11. Given an irreversible inhibitor, design an experiment to determine the efficiency of inactivation and the binding affinity.

Course Materials
Course website: BrightSpace (https://dal.brightspace.com)

Additional References in Enzymology:

**GENERAL**
(Volumes XIX *(QU 135 B79 1990)* and XX *(QU 135 B79 1992)*, *Mechanisms of Catalysis* are particularly good.)

**MECHANISMS**
ASSAYS AND PURIFICATION

KINETICS

Course Assessment

Please note: Alterations may be necessary in the event of a flu pandemic.

<table>
<thead>
<tr>
<th>Component</th>
<th>Weight (% of final grade)</th>
<th>Date</th>
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<tbody>
<tr>
<td>1st Midterm</td>
<td>15%</td>
<td>February 11, 2020</td>
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<tr>
<td>2nd Midterm</td>
<td>15%</td>
<td>March 17, 2020</td>
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<tr>
<td>Problem Sets</td>
<td>30%</td>
<td>(~ every 2 weeks)</td>
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<tr>
<td>Graduate Student Essay &amp; Oral Presentation</td>
<td>n/a</td>
<td>Feb. 27, 2020</td>
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<tr>
<td>Final exam (3 h)</td>
<td>40%</td>
<td>(Scheduled by Registrar)</td>
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<tr>
<td>Conversion of numerical grades to Final Letter Grades follows the Dalhousie Common Grade Scale‡</td>
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<tr>
<td>A+ (90-100)</td>
<td>B+ (77-79)</td>
<td>C+ (65-69)</td>
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<tr>
<td>A (85-89)</td>
<td>B (73-76)</td>
<td>C (60-64)</td>
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<tr>
<td>A– (80-84)</td>
<td>B– (70-72)</td>
<td>C– (55-59)</td>
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‡In accord with the Faculty of Science recommendation, grades will be rounded up from 0.5 within the intervals between letter grades.
Course Policies on Missed Examinations/Mid-terms and Assignments

Missed midterms:
A student who misses a midterm test due to illness must notify the instructor as soon as possible, and must submit a Student Declaration of Absence Form through the course Brightspace page within three (3) calendar days following the last day of absence. A make-up midterm will normally be written within 7 calendar days after the missed midterm. Absence for non-medical reasons is not ordinarily acceptable unless prearranged with the professor. A missed examination for which no satisfactory arrangement has been made will be given a mark of zero. Absence for non-medical reasons is not ordinarily acceptable unless prearranged with the instructor. A missed evaluation component (including assignments, essays, and oral presentations) for which no satisfactory arrangement has been made will be given a mark of zero.

The Student Declaration of Absence form can only be submitted up to two (2) separate times per course during a term and only for absences of 3 days or shorter. Students who exceed one or both of these limits, must inform their course instructor and course coordinator and will be required to register with an Advisor at Student Academic Success (SAS). If students have recurring short-term absences and do not register with SAS, it is at the instructors’ discretion to disallow any further Student Declarations and deny alternate coursework arrangements.

Please refer to the link below for further information on the University policy regarding Long-term absence:

https://www.dal.ca/dept/university_secretariat/policies/academic/missed-or-late-academic-requirements-due-to-student-absence.html

Missed Final exam:
A student who misses the final examination due to illness must notify the course coordinator or department office within 48 h to provide a medical certificate (see Dalhousie Calendar, section 16.8). Absence for non-medical reasons is not acceptable. If necessary, a make-up final examination will be held at or shortly after the end of the official exam period, and typically before May 1. Students who need to write a makeup exam for medical or other reasons are expected to be available during this period.
Course Content

LECTURE OUTLINE 2020*

SECTION I: ENZYME KINETICS

- Jan. 7    Fundamental Concepts of Kinetics.
- Jan. 16   Altering Enzyme Activity: Tight Binding Inhibitors and Time-Dependent Inhibition 1.
- Jan. 21   Altering Enzyme Activity: Tight Binding Inhibitors and Time-Dependent Inhibition 2.

Presentation of Graduate Student Essay Topics

- Jan. 23   Altering Enzyme Activity: Active Site-directed Reversible Inhibitors.

Assignment of Graduate Student Essay Topics

- Feb. 4    Multisubstrate Systems 1: Steady-state Equations / King-Altman Method.
- Feb. 6    Multisubstrate Systems 2: Steady-state Equations / King-Altman Method.
- Feb. 11   MID-TERM TEST I (material up to and including pH effects)
- Feb. 13   Multisubstrate Systems 3: Inhibition Studies and Binding Order.
- Feb. 18   Study Break
- Feb. 20   Study Break
- Feb. 25   Kinetic Isotope Effects 1 (GRADUATE STUDENT ESSAYS DUE)
- Feb. 27   GRADUATE STUDENT PRESENTATIONS & Kinetic Isotope Effects 2

SECTION II: CATALYSIS, MECHANISM, AND ENZYME ARCHITECTURE

- Mar. 3    Enzyme Efficiency, Rate Enhancements, and Transition State Stabilization.
- Mar. 5    Principles of Catalysis: Effective Molarity and Entropy.
- Mar. 10   Principles of Catalysis: Mechanisms.
- Mar. 17   MID-TERM TEST II (from multisubstrate systems kinetics to principles of catalysis)
- Mar. 19   Transition State Stabilization: Structural Alterations to the Protein and Transition State Analogue Inhibitors.
- Mar. 26   Architecture of Enzymes and Their Active Sites: Three-dimensional Structure of Triosephosphate Isomerase.
- Apr. 7    no classes
- Apr. 8    EXAMINATIONS BEGIN

* LECTURE SCHEDULE MAY BE ALTERED DEPENDING ON TIME CONSTRAINTS AND THE TIME REQUIRED TO COVER SPECIFIC TOPICS
OFFICE HOURS
Office: Tupper 9-J2
Phone: 494-1974
e-mail: sbearne@dal.ca

By appointment. (In general, I do not answer questions addressed to me via e-mail except to arrange an appointment time.) Please feel free to drop by my office at anytime to arrange an appointment or discuss course material.

ACCOMMODATION POLICY FOR STUDENTS
Students may request accommodation as a result of barriers related to disability, religious obligation, or any characteristic protected under Canadian Human Rights legislation. The full text of Dalhousie’s Student Accommodation Policy can be accessed here: http://www.dal.ca/dept/university_secretariat/policies/academic/student-accommodation-policy-wef-sep-1--2014.html

Students who require accommodation for classroom participation or the writing of tests and exams should make their request to the Advising and Access Services Centre (AASC) prior to or at the outset of the regular academic year. More information and the Request for Accommodation form are available at www.dal.ca/access.

ACADEMIC INTEGRITY
Academic integrity, with its embodied values, is seen as a foundation of Dalhousie University. It is the responsibility of all students to be familiar with behaviours and practices associated with academic integrity. Instructors are required to forward any suspected cases of plagiarism or other forms of academic cheating to the Academic Integrity Officer for their Faculty.

The Academic Integrity website (http://academicintegrity.dal.ca) provides students and faculty with information on plagiarism and other forms of academic dishonesty, and has resources to help students succeed honestly. The full text of Dalhousie’s Policy on Intellectual Honesty and Faculty Discipline Procedures is available here: http://www.dal.ca/dept/university_secretariat/academic-integrity/academic-policies.html

STUDENT CODE OF CONDUCT
Dalhousie University has a student code of conduct, and it is expected that students will adhere to the code during their participation in lectures and other activities associated with this course. In general: “The University treats students as adults free to organize their own personal lives, behaviour and associations subject only to the law, and to University regulations that are necessary to protect

- the integrity and proper functioning of the academic and non-academic programs and activities of the University or its faculties, schools or departments;
- the peaceful and safe enjoyment of University facilities by other members of the University and the public;
- the freedom of members of the University to participate reasonably in the programs of the University and in activities on the University's premises;
- the property of the University or its members.”

The full text of the code can be found here: http://www.dal.ca/dept/university_secretariat/policies/student-life/code-of-student-conduct.html
SERVICES AVAILABLE TO STUDENTS

The following campus services are available to help students develop skills in library research, scientific writing, and effective study habits. The services are available to all Dalhousie students and, unless noted otherwise, are free.

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<thead>
<tr>
<th>Service</th>
<th>Support Provided</th>
<th>Location</th>
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<tbody>
<tr>
<td>General Academic Advising</td>
<td>Help with - understanding degree requirements and academic regulations - choosing your major - achieving your educational or career goals - dealing with academic or other difficulties</td>
<td>Killam Library Ground floor Rm G28 Bissett Centre for Academic Success</td>
<td>In person: Killam Library Rm G28 By appointment: - e-mail: <a href="mailto:advising@dal.ca">advising@dal.ca</a> - Phone: (902) 494-3077 - Book online through MyDal</td>
</tr>
<tr>
<td>Dalhousie Libraries</td>
<td>Help to find books and articles for assignments Help with citing sources in the text of your paper and preparation of bibliography</td>
<td>Killam Library Ground floor Librarian offices</td>
<td>In person: Service Point (Ground floor) By appointment: Identify your subject librarian (URL below) and contact by email or phone to arrange a time: <a href="http://dal.beta.libguides.com/sb.php?subject_id=34328">http://dal.beta.libguides.com/sb.php?subject_id=34328</a></td>
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<tr>
<td>Studying for Success (SFS)</td>
<td>Help to develop essential study skills through small group workshops or one-on-one coaching sessions Match to a tutor for help in course-specific content (for a reasonable fee)</td>
<td>Killam Library 3rd floor Coordinator Rm 3104 Study Coaches Rm 3103</td>
<td>To make an appointment: - Visit main office (Killam Library main floor, Rm G28) - Call (902) 494-3077 - email Coordinator at: <a href="mailto:sfs@dal.ca">sfs@dal.ca</a> or - Simply drop in to see us during posted office hours All information can be found on our website: <a href="http://www.dal.ca/sfs">www.dal.ca/sfs</a></td>
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<td>Writing Centre</td>
<td>Meet with coach/tutor to discuss writing assignments (e.g., lab report, research paper, thesis, poster) - Learn to integrate source material into your own work appropriately - Learn about disciplinary writing from a peer or staff member in your field</td>
<td>Killam Library Ground floor Learning Commons &amp; Rm G25</td>
<td>To make an appointment: - Visit the Centre (Rm G25) and book an appointment - Call (902) 494-1963 - email <a href="mailto:writingcentre@dal.ca">writingcentre@dal.ca</a> - Book online through MyDal We are open six days a week See our website: writingcentre.dal.ca</td>
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