Instructor(s): Dr. Jan K. Rainey (Tupper 10N), Dr. Stephen L. Bearne (Tupper 9J), Paul Briggs (Lab Instructor, Tupper 8J)

Lectures: 8:30 – 9:30 (Monday, Wednesday & Friday) in Chemistry 223, supplemented by online review lectures for Dr. Rainey’s material.

Laboratories: 1 x 3 h (Tuesday 14:35–17:25)

Tutorials: Offered in place of traditional lectures as detailed in Lecture Outline (Rainey) or as supplemental learning opportunities (Bearne).

Course Description
This course covers structural and functional properties of biomolecules, including the physical bases for their characterization, thermodynamic principles of protein folding and biomolecular interactions, and the kinetics and mechanisms of enzyme catalysis.

Course Prerequisites
BIOC 2300.03, 2610.03, CHEM 2401.03, and CHEM 2402.03 (all with a grade of B– or higher), or instructor’s consent

Course Objectives/Learning Outcomes
1. Discriminate between and calculate the roles of entropy, enthalpy, and molecular interactions in protein stability, folding and ligand binding.
2. Given the architecture of an enzyme active site, write a mechanism and show how general acid/base, covalent, or electrophilic catalysis may occur.
3. Given the kinetic mechanism (with or without inhibition), derive an initial velocity equation using either the steady-state assumption or the rapid equilibrium approach.
4. Draw the structure of a peptide with defined stereochemistry at a given pH.
5. Given the substrates, products, and cofactors for a particular class of enzyme-catalyzed reaction, write a mechanism for the reaction.
6. Analyze implications of molecular spectroscopy (absorption, emission, CD, NMR) results on polypeptide structure and environment in direct context of the physical basis of the technique in question.
7. Given an enzyme mechanism, design a reversible or irreversible inhibitor.
8. Apply peptide bond properties and hydrogen-bonding to predict primary and secondary structuring preferences.
9. Present and analyze experimental data in a prescribed format for a formal scientific report.
10. Demonstrate proficiency in biochemical laboratory techniques, including liquid handling, pH measurements, visible range spectroscopy, enzyme assays and determination of kinetic parameters, thin layer chromatography, protein isolation and quantification, and SDS-PAGE.
Course Materials
Course website:  http://www3.biochem.dal.ca/3700/

Additional References:

**BIOPHYSICAL CHEMISTRY**


**KINETICS & ENZYME CHEMISTRY**
GENERAL TEXTBOOKS

Course Assessment

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<tr>
<th>Component</th>
<th>Weight (% of final grade)</th>
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<tr>
<td>1st Midterm</td>
<td>15%</td>
<td>October 5, 2018</td>
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<tr>
<td>2nd Midterm</td>
<td>15%</td>
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<tr>
<td>Laboratory Reports**</td>
<td>30%</td>
<td>(As scheduled in Lab)</td>
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<tr>
<td>Final exam**</td>
<td>40%</td>
<td>(Scheduled by Registrar)</td>
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Please note: Alterations may be necessary in the event of a flu pandemic.

Conversion of numerical grades to Final Letter Grades follows the Dalhousie Common Grade Scale

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<tr>
<td>F</td>
<td>(&lt;50)</td>
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Course Policies

**YOU MUST PASS BOTH THE FINAL EXAM AND THE LABORATORY COMPONENT TO PASS THE COURSE**

Note: The final examination:
(i) may include questions based on laboratory experiments and
(ii) is not restricted solely to material subsequent to the midterms.

Department of Biochemistry & Molecular Biology Policy for Students repeating a BIOC course with an integral lab component (BIOC 3300, BIOC 3400, BIOC 3700):
Students who have previously taken BIOC 3300, BIOC 3400, or BIOC 3700 and passed the laboratory component will not be allowed to retake the lab component if they redo the course. The previous lab marks will be used to assign the grade for the lab component based on the weight given to this component in the prospectus for the course in the year it is retaken.
Department of Biochemistry & Molecular Biology Policy on missed examinations/mid-terms and assignments:

A student who misses an evaluation component of the course (midterm test, assignment, presentation, lab, etc.) due to illness should, if possible, notify the instructor, course coordinator, or department office either prior to, or within 48 h of the scheduled time or due date for that component. The student must also submit a Student Declaration of Absence Form (through the course Brightspace page or to their instructor via e-mail) within three (3) calendar days following the last day of absence. Special ‘make-up’ tests (if offered) will normally be written within 7 calendar days after the missed test. Absence for non-medical reasons is not ordinarily acceptable unless prearranged with the instructor. A missed evaluation component 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. Students who exceed this limit must inform their course instructor(s) 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 instructor(s)’ discretion to disallow any further Student Declarations and deny alternate coursework arrangements.

Course Content

*LECTURE OUTLINE*

Note: Dr. Rainey's component of the course includes some online lectures reviewing key concepts from prerequisite courses alongside in-class lectures and tutorials. Students are responsible for material in both the online and in-class components and in-class discussion will build upon the online material. Additional online lectures may be produced upon request.

**Online material for Dr. Rainey's section will be provided via the BIOC 3700 Brightspace site.**

**PROTEIN CHEMISTRY AND 1°-4° STRUCTURE (JKR)**

Online review lectures (1&2) – Acid-base equilibria & amino acids.

Sept. 04 (W) 1  **Amino acids & peptide bonds.** Amino acid stereochemistry. Peptide bond formation & properties.

Sept. 06 (F) 2  **Polypeptides.** Peptide bond formation & properties.

Sept. 09 (M) 3  **Secondary structure.** Helices.

Sept. 11 (W) 4  **Secondary structure & fibrous proteins.** β-structures & introduction to fibrous proteins.

Sept. 13 (F) 5  **Fibrous protein & globular protein structure.** Fibrous proteins, 3° & 4° structuring.

Sept. 16 (M) 6  **Tutorial 1.** Expanding on lectures 1-5.

**OPTICAL SPECTROSCOPY & STRUCTURAL BIOLOGY OF PROTEINS (JKR)**

Sept. 18 (W) 7  **Spectroscopy background.** Quantum mechanical background for optical & NMR spectroscopy.

Sept. 20 (F) 8  **Optical spectroscopy 1.** Absorption spectroscopy & circular dichroism.

Sept. 23 (M) 9  **Optical spectroscopy 2.** CD & emission spectroscopy.

Sept. 25 (W) 10  **Optical spectroscopy 3.** Emission spectroscopy.

**Online lecture (3) – NMR chemical shifts – moving from small molecules to proteins.**

Sept. 27 (F) 11  **Structural biology 1.** NMR spectroscopy.

Sept. 30 (M) 12  **Structural biology 2.** X-ray crystallography and cryo-electron microscopy.
Oct. 02 (W)  13  Tutorial 2. Expanding on lectures 7-12.
Oct. 04 (F)  14  1st MIDTERM (covering lectures 1-13).

Macromolecular Thermodynamics, Stability & Folding (JKR)

Online review lectures (4-6) – Fundamental thermodynamics.

Oct. 07 (M)  15  Thermodynamics. Spontaneity & equilibria.
Oct. 09 (W)  16  Intra/intermolecular interactions. Forces holding together molecules and complexes.
Oct. 11 (F)  17  Protein folding. Factors influencing folding & relation to thermodynamics & stability.
Oct. 14 (M)  18  THANKSGIVING DAY – NO CLASSES

Enzyme Kinetics (SLB)

Oct. 16 (W)  18  Fundamental kinetics 1. Rate equations.
Oct. 18 (F)  19  Fundamental kinetics 2. Progress curves and graphs of initial rates.
Oct. 21 (M)  20  Enzyme kinetics 1. Rapid equilibrium and steady-state kinetics.
Oct. 23 (W)  21  Enzyme kinetics 2. Enzyme assays and analysis of kinetic data.
Oct. 25 (F)  22  Enzyme kinetics 3. Inhibition models and determination of inhibition constants (K_i).

Enzyme Catalysis & Mechanism (SLB)

Oct. 28 (M)  23  Reactivity of amino acids revisited. Side chain chemistry, covalent modification.
Oct. 30 (W)  24  General acid-base catalysis 1. How slow are nonenzymatic reactions and why?
  Transition state stabilization.
Nov. 01 (F)  25  General Acid-Base Catalysis 2. Mechanisms of isomerases.
Nov. 04 (M)  26  2nd MIDTERM (covering lectures 14-25)
Nov. 06 (W)  27  Promoting hydrolysis reactions 1. Covalent catalysis.
Nov. 08 (F)  28  Promoting hydrolysis reactions 2. Electrophilic catalysis.
Nov. 11 (M)  29  STUDY BREAK – NO CLASSES
Nov. 13 (W)  30  STUDY BREAK – NO CLASSES
Nov. 15 (F)  31  STUDY BREAK – NO CLASSES
Nov. 18 (M)  32  Design of enzyme inhibitors. TS analogues, suicide inhibitors, activity profiling.
Nov. 20 (W)  33  Stabilization of carbanions 1. Pyridoxal phosphate as a coenzyme.
Nov. 22 (F)  34  Dr. Rainey. Pre-exam review
Nov. 25 (M)  35  Stabilization of carbanions 2. Thiamine pyrophosphate as a coenzyme.
Nov. 27 (W)  36  Redox reactions 1. NAD+ as a coenzyme.
Nov. 29 (F)  37  Redox reactions 2. FAD as a prosthetic group with coenzyme function.
Dec. 02 (M)  38  Bond-forming reactions 1. Biotin as a prosthetic group.
Dec. 03 (M)  39  Bond-forming reactions 2. Phosphoryl transfers and positional isotope exchange.
Dec. 05 (Th)  40  EXAMINATIONS BEGIN

* LECTURE SCHEDULE MAY BE ALTERED DEPENDING ON TIME CONSTRAINTS AND THE TIME REQUIRED TO COVER SPECIFIC TOPICS
University Policies and Statements

This course is governed by the academic rules and regulations set forth in the University Calendar and by Senate

Academic Integrity
At Dalhousie University, we are guided in all of our work by the values of academic integrity: honesty, trust, fairness, responsibility and respect (The Center for Academic Integrity, Duke University, 1999). As a student, you are required to demonstrate these values in all of the work you do. The University provides policies and procedures that every member of the university community is required to follow to ensure academic integrity.
Information: https://www.dal.ca/dept/university_secretariat/academic-integrity.html

Accessibility
The Advising and Access Services Centre is Dalhousie's centre of expertise for student accessibility and accommodation. The advising team works with students who request accommodation as a result of a disability, religious obligation, or any barrier related to any other characteristic protected under Human Rights legislation (Canada and Nova Scotia).
Information: https://www.dal.ca/campus_life/academic-support/accessibility.html

Student Code of Conduct
Everyone at Dalhousie is expected to treat others with dignity and respect. The Code of Student Conduct allows Dalhousie to take disciplinary action if students don't follow this community expectation. When appropriate, violations of the code can be resolved in a reasonable and informal manner—perhaps through a restorative justice process. If an informal resolution can't be reached, or would be inappropriate, procedures exist for formal dispute resolution.

Diversity and Inclusion – Culture of Respect
Every person at Dalhousie has a right to be respected and safe. We believe inclusiveness is fundamental to education. We stand for equality. Dalhousie is strengthened in our diversity. We are a respectful and inclusive community. We are committed to being a place where everyone feels welcome and supported, which is why our Strategic Direction prioritizes fostering a culture of diversity and inclusiveness
Statement: http://www.dal.ca/cultureofrespect.html

Recognition of Mi’kmaq Territory
Dalhousie University would like to acknowledge that the University is on Traditional Mi’kmaq Territory. The Elders in Residence program provides students with access to First Nations elders for guidance, counsel and support. Visit the office (Rm 3037, McCain Building), e-mail (elders@dal.ca) or leave message (902-494-6803).
Information: https://www.dal.ca/campus_life/communities/indigenous.html

Important Dates in the Academic Year (including add/drop dates)
https://www.dal.ca/academics/important_dates.html

University Grading Practices
https://www.dal.ca/dept/university_secretariat/policies/academic/grading-practices-policy.html

Student Resources and Support

Advising
General Advising https://www.dal.ca/campus_life/academic-support/advising.html
Science Program Advisors: https://www.dal.ca/faculty/science/current-students/academic-advising.html
Indigenous Student Centre: https://www.dal.ca/campus_life/communities/indigenous.html
Black Advising Centre: https://www.dal.ca/campus_life/communities/black-student-advising.html
International Centre: https://www.dal.ca/campus_life/international-centre/current-students.html

Academic supports
Library: https://libraries.dal.ca/
Writing Centre: https://www.dal.ca/campus_life/academic-support/writing-and-study-skills.html
Studying for Success: https://www.dal.ca/campus_life/academic-support/study-skills-and-tutoring.html
Copyright Office: https://libraries.dal.ca/services/copyright-office.html

Other supports and services
Student Health Services: https://www.dal.ca/campus_life/health-and-wellness/health-services/services.html
Counselling: https://www.dal.ca/campus_life/health-and-wellness/counselling.html
Student Advocacy: https://www.dsu.ca/dsas

Safety
Research Lab Safety
Biosafety: https://www.dal.ca/dept/safety/programs-services/biosafety.html
Chemical Safety: https://www.dal.ca/dept/safety/programs-services/chemical-safety.html
Radiation Safety: https://www.dal.ca/dept/safety/programs-services/radiation-safety.html

Scent-Free Program: https://www.dal.ca/dept/safety/programs-services/occupational-safety/scent-free.html