

CHEM 4423W Syllabus

Foundations of Chemical Biology Laboratory

Instructor: Erin E. Carlson

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Teaching Assistants: TBD

Laboratory: 494 Kolthoff Hall

Course Credits: Two credit hours; 3 hours of lab per week and 50 min lecture

Microcomputer Lab: 101D Smith Hall, Phone: (612) 624-3372
www.chem.umn.edu/services/microlab/

Prerequisites: Organic Chemistry II 2302 or Organic Chemistry II for the Life Sciences 2304 and Organic Laboratory 2311

Required Materials:

Bound laboratory notebook (available at Univ. bookstore)

Safety goggles (bring your own, or buy at Smith 249 General Chemistry stockroom).

Lab coat is also recommended (available at Univ. bookstore)

Recommended Textbook: Essentials of Chemical Biology: Structure and Dynamics of Biological Macromolecules, Andrew Miller and Julian Tanner, John Wiley & Sons, 2008, ISBN 978-0-470-84531-8 and related literature.

Moodle Site: moodle.umn.edu

Use this resource to download course material, post results from each experiment, upload reports and answer sheets, and keep track of grades.

Course Overview: Chemical biology is a rapidly developing field at the interface of chemical and biological sciences. Generally speaking, Chemical Biology deals with how chemistry can be applied to manipulate and study biological problems using a combination of experimental techniques ranging from organic chemistry, analytical chemistry, biochemistry, molecular biology, biophysical chemistry and cell biology. Students will perform experiments to highlight many of the major techniques and concepts used in modern Chemical Biology research, including experiments that emphasize the clear connections between the material that they are taught in the classroom/laboratory and experimental science, health, disease and medical research.

Objectives:

1. Apply the knowledge you learned in organic chemistry in a biological context.
2. Learn experimental skills used in chemical biology such as protein purification, biopolymer synthesis and purification, microscopy, protein-ligand characterization, protein/peptide mass spectrometry.
3. Learn about several available online and university resources important to interdisciplinary science including Pymol, PDB, Pubmed, ExPASy, Department of Chemistry Mass Spectrometry Lab.
4. Evaluate experimental data through basic statistical analysis.
5. Participate in the evaluation of data collected by the entire lab section.
6. Prepare high-quality figures and technical reports based on the formatting of a premier chemical biology journal, *ACS Chemical Biology* (<http://pubs.acs.org/journal/acbcct>).

Lab Experiments:

Labs	Weeks	Major Concepts	Reference Materials
Lab Introduction	1	Familiarization, check-in, micropipette tutorial, preparing solutions	
Lab Basic Techniques	2	Spectrophotometry, serial dilutions, buffers	
Lab Module A – β-Lactamase	5 weeks	<i>These proteins are a major source of antibiotic resistance</i>	(1)
Part 1 – Protein Production Day 1 – Anion Exchange Chromatography		Protein purification, anion exchange	
Part 2 – Protein Production Day 2 – Quantify Enzyme Activity and Protein Concentration		Activity assay, protein concentration determination	
Part 3 – Protein Production Day 3 - Assess protein purity and identity		SDS-PAGE and protein MS (MALDI)	
Part 4 – Enzyme kinetics and inhibitor assessment		Colorimetric or fluorescence assay for enzyme kinetics, inhibition, inhibitor structure/development, natural products as drugs	
Part 5 - Catch-up and molecular docking on known inhibitors, modeling design of new inhibitors		Molecular modeling, protein-ligand interaction visualization (covalent drug)	
Lab Module B - Lysozyme	3 weeks		
Part 1 – Complete Docking and		Protein structure determination	(2)

Protein Crystallization (set up trays)			
Part 2 – Examine crystals under microscope, Modeling of Protein with Inhibitor		Protein structure determination, molecular modeling, protein-ligand interaction visualization	(3)(4)
Part 3 - Protein modification and assessment by SDS-PAGE and mass spectrometry		Bioconjugation, chemoselectivity, protein mass spectrometry (MALDI), protein gel electrophoresis	(5)(6)
Lab Module C – Peptide Synthesis	3 weeks		
Part 1 – Peptide Synthesis		Biopolymer synthesis, microscale reactions	
Part 2 (2 weeks) – Purification of peptide by HPLC and characterization by MS		Polar molecule purification, peptide MS/MS for sequence determination	(7, 8)
Lab Module D – Cancer Cell Cytotoxicity	2 weeks		
Part 1 - Assess the cytotoxicity of various substances against cancer cell lines		Cell-based assay (live/dead; affects of drugs)	(5)
Part 2 – Visualization of tubulin perturbation by microscopy		Cell-based assay, mechanism of action, microscopy, fluorescent read-out/localization, natural product (taxol)	(9)

Lab Schedule: Working groups of two persons will be formed after the first lab meeting. Each group will work on the assigned experiments from Week 3 to Week 15.

Attendance: Attendance in lab, for the entire lab period, is required. Missing more than 15 minutes of a lab period will be considered an absence. In the case of a true emergency, serious illness, university-related trip that prevents a student from attending a lab meeting, an **excused absence may be granted**. To obtain an excused absence, students must contact Professor Carlson as soon as circumstances allow, to discuss the nature of the emergency, and eventually to provide documentation. **ONLY ONE** excused absence will be granted during the course of the semester. The average score of the student's other work will replace the zero for the day. If extenuating circumstances prevent a student from attending more than one lab period, a meeting must be scheduled immediately to discuss any options available. If any absence is unexcused, it will reduce your final laboratory grade by 5%, in addition to the missing points for the day. After 3 absences, whether partial or full, an automatic F is earned in lab.

University Athletes and Military Personnel: If you are a member of a varsity team at the University and will be traveling during the semester, or will have military duty that conflicts with more than one lab period, you are responsible for contacting the instructor or staff in Smith 115 in order to be moved to a lab section that minimizes scheduling conflicts.

Reference Texts: Available through Walter Library Reserve

Introduction to Bioorganic Chemistry and Chemical Biology, David Van Vranken and Gregory Weiss, Garland Science, Taylor & Francis Group, LLC, 2013, and related literature.

Experiments in the Purification and Characterization of Enzymes: A Laboratory Manual, Thomas A. Crowley and Jack Kyte, Elsevier, 2014, and related literature.

Fundamental Laboratory Approaches for Biochemistry and Biotechnology: 2nd (second) Edition, Alexander J. Ninfa, Wiley, John & Sons, 2010.

Additional Resources Online:

How to write a scientific paper:

1) How to Write a Paper in the Scientific Journal Style and Format (Greg Anderson, Bates College). Gives information on the structure of a paper and its parts. Important, though: different journals require different parts in papers. Fit Greg's advice to your needs.

<http://abacus.bates.edu/%7Eganderso/biology/resources/writing/HTWtoc.html>

2) UW-Madison Writing Center Science Writer's Handbook. More advice on structure of scientific papers. <http://writing.wisc.edu/Handbook/ScienceReport.html>

Pre-Lab Lectures: These lectures will be used to discuss the syllabus, review and introduce new concepts, provide laboratory logistics, discuss data analysis from previous experiments, and interpret results obtained by the entire class.

Laboratory notebooks: A laboratory notebook per student is required to write annotations related to experiments conducted in the laboratory throughout the semester. Prior to starting a laboratory experience, the notebook must include calculations needed and notes on the procedure that will be followed that day. During the laboratory experience, the student must fill up tables prepared for data collection and tabulation and write observations that will help prepare the lab report. After the lab experience, the student will complete the data analysis, add graphs and images, and write conclusions.

Lab Reports: Instructions to prepare lab reports and answer sheets will be provided on the Moodle site. Four lab reports will be required. Each will describe a lab module that includes several weeks of experimentation. Each report will be about 10 pages in length, including the supporting documentation. The course grades will be based on the progress that is assessed largely (~70%) through the series of written lab reports. These must meet "journal style" standards for presentation, style, and clarity. The percentage of the written report that is graded on the writing style itself will be ~20%.

Answer sheets and lab reports for a given experiment are due seven days later at 11:00 AM, after the completion of the last experiment included in the report. Each report and lab sheet must be submitted electronically as a PDF file. In addition, some numeric values from the report will be

submitted to databases accessible through the Moodle site. These databases will be used for discussions during pre-lab sessions.

Points will be taken off when reports or sheets are late (based on time stamp in the Moodle Site). The respective grade will be reduced by 20% the first 24 hours of being late and then reduced 10% per additional workday of being late. The instructor may waive a late penalty to those presenting a strong and legitimate reason (illness, serious accident, etc.; not my computer crashed) for not submitting the lab report on time. There is no excuse for a “failure to communicate” in advance of a deadline.

Quizzes: There will be oral quizzes during the lab sessions to assess knowledge on the fundamentals of the techniques and instrumentation being used that day.

Grading

3 Lab Answer Sheets 10 pts (3-4 pts each)

4 Full Reports 72 pts (18 pts each)

6 Quizzes 18 pts (3 pts each)

Total: 100 pts

Final Grade: This course is not graded on a curve. As shown below, the final grade for the course is directly determined from the total number of points that are accumulated throughout the semester. Due to the structure of the course, “I” grades cannot be granted.

Final Grade Total Points

A 85 – 100

A- 80 – 84.9

B+ 75 – 79.9

B 70 – 74.9

B- 65 – 69.9

C 60 – 64.9

D 50 – 59.9

F < 50.0

Safety: The Department of Chemistry promotes a culture of safety in the laboratory. Although general safety instructions will be provided during the first lab session (Check-in Day), each student working in a chemistry lab is strongly encouraged to visit <http://www.chem.umn.edu/services/safety/> to get acquainted with the Chemical Hygiene Plan in the department.

All personnel must wear personal protective equipment (safety goggles and no open shoes) at all times while working in the lab. Wearing a laboratory coat or old clothing is highly recommended.

Prior to each experiment, you are responsible for reviewing the material safety data sheets (MSDS) for chemicals that you will be utilizing on that day. See <http://www.ilpi.com/msds/>. Other safety considerations are described in the Moodle site.

E-mail: All students and instructors should be reachable at their University-wide e-mail accounts. If you normally use a departmental or private e-mail account, you should set up your University-wide account to automatically forward messages to this other address. You can do this most easily through the account settings page.

Reference Texts: Although the instructor will lecture on various topics related to the experiments you do in this lab, it will often be your responsibility to find appropriate reference materials. This means chemical biology, biochemistry and organic chemistry textbooks, handbooks, encyclopedias, and original literature (i.e. journal articles). SciFinder Online (<http://scifinder.cas.org/>), the search tool for the American Chemical Society's Chemical Abstracts Service, is an excellent tool for searching for journal articles on a particular topic. To use SciFinder Online, you will need to register (<http://tinyurl.com/scifinderumn>) with your umn.edu email address. You can also usually access journal articles directly from a SciFinder search by clicking "Get Full Text". To read the articles online, you will either need to be using a computer with a UMN IP address, access them via the U of M Libraries website (<http://www.lib.umn.edu/#journals> to search), or use a virtual private network (VPN) tunnel. (Go to <http://www.oit.umn.edu/vpn/> to download the software needed to do this, and to learn more.)

Important Policy Statements

Student Conduct Code: The University seeks an environment that promotes academic achievement and integrity, that is protective of free inquiry, and that serves the educational mission of the University. Similarly, the University seeks a community that is free from violence, threats, and intimidation; that is respectful of the rights, opportunities, and welfare of students, faculty, staff, and guests of the University; and that does not threaten the physical or mental health or safety of members of the University community.

As a student at the University you are expected adhere to Board of Regents Policy: *Student Conduct Code*. To review the Student Conduct Code, please see: [http://regents.umn.edu/sites/default/files/policies/Student Conduct Code.pdf](http://regents.umn.edu/sites/default/files/policies/Student%20Conduct%20Code.pdf).

Note that the conduct code specifically addresses disruptive classroom conduct, which means "engaging in behavior that substantially or repeatedly interrupts either the instructor's ability to teach or student learning. The classroom extends to any setting where a student is engaged in work toward academic credit or satisfaction of program-based requirements or related activities."

Any student found performing unauthorized experiments or behaving in an unsafe manner in the laboratory may be removed from the laboratory at any time. Whether or not behavior is unsafe is at the discretion of the instructors, and this includes failure to properly respond to instructions in a timely manner. Removal from the laboratory may be for a period of time as short as the remainder of the current lab period or as long as the remainder of the course itself, depending on circumstances.

Disability Accommodations: The University of Minnesota is committed to providing equitable access to learning opportunities for all students. Disability Services (DS) is the campus office that collaborates with students who have disabilities to provide and/or arrange reasonable accommodations. If you have, or think you may have, a disability (e.g., mental health, attentional, learning, chronic health, sensory, or physical), please contact DS at 612-626-1333 to arrange a confidential discussion regarding equitable access and reasonable accommodations.

If you are registered with DS and have a current letter requesting reasonable accommodations, please contact Professor Carlson as early in the semester as possible to discuss how the accommodations will be applied in the course. For more information, please see the DS website, <https://diversity.umn.edu/disability/>.

Mental Health and Stress Management: As a student you may experience a range of issues that can cause barriers to learning, such as strained relationships, increased anxiety, alcohol/drug problems, feeling down, difficulty concentrating and/or lack of motivation. These mental health concerns or stressful events may lead to diminished academic performance and may reduce your ability to participate in daily activities. University of Minnesota services are available to assist you. You can learn more about the broad range of confidential mental health services available on campus via the Student Mental Health Website: <http://www.mentalhealth.umn.edu>.

Sexual Harassment: "Sexual harassment" means unwelcome sexual advances, requests for sexual favors, and/or other verbal or physical conduct of a sexual nature. Such conduct has the purpose or effect of unreasonably interfering with an individual's work or academic performance or creating an intimidating, hostile, or offensive working or academic environment in any University activity or program. Such behavior is not acceptable in the University setting. For additional information, please consult Board of Regents Policy:

<http://regents.umn.edu/sites/default/files/policies/SexHarassment.pdf>

Equity, Diversity, Equal Opportunity, and Affirmative Action: The University provides equal access to and opportunity in its programs and facilities, without regard to race, color, creed, religion, national origin, gender, age, marital status, disability, public assistance status, veteran status, sexual orientation, gender identity, or gender expression. For more information, please consult Board of Regents Policy:

http://regents.umn.edu/sites/default/files/policies/Equity_Diversity_EO_AA.pdf.

Scholastic Dishonesty: You are expected to do your own academic work and cite sources as necessary. Failing to do so is scholastic dishonesty. Scholastic dishonesty means plagiarizing; cheating on assignments or examinations; engaging in unauthorized collaboration on academic work; taking, acquiring, or using test materials without faculty permission; submitting false or incomplete records of academic achievement; acting alone or in cooperation with another to falsify records or to obtain dishonestly grades, honors, awards, or professional endorsement; altering, forging, or misusing a University academic record; or fabricating or falsifying data, research procedures, or data analysis. (Student Conduct Code: http://regents.umn.edu/sites/default/files/policies/Student_Conduct_Code.pdf) In this course, direct copying of assignments or fabricating lab data will be considered dishonest and the proper sanctioning guidelines will be followed (<http://www.oscai.umn.edu/integrity/faculty/Sanctioning%20Guidelines.pdf>). If it is determined that a student has cheated, he or she may be given an "F" or an "N" for the course, and may face additional sanctions from the University. For additional information, please see: <http://policy.umn.edu/Policies/Education/Education/INSTRUCTORRESP.html>.

The Office for Student Conduct and Academic Integrity has compiled a useful list of Frequently Asked Questions pertaining to scholastic dishonesty: <http://www1.umn.edu/oscai/integrity/student/index.html>. If you have additional questions, please clarify with Professor Carlson or the TAs.

Makeup Work for Legitimate Absences: Students will not be penalized for absence due to unavoidable or legitimate circumstances. Such circumstances include verified illness, participation in intercollegiate athletic events, subpoenas, jury duty, military service, bereavement, and religious observances. For complete information, see: <http://policy.umn.edu/Policies/Education/Education/MAKEUPWORK.html>.

Appropriate Student Use of Class Notes and Course Materials: Taking notes is a means of recording information but more importantly of personally absorbing and integrating the educational experience. However, broadly disseminating class notes beyond the classroom community or accepting compensation for taking and distributing classroom notes undermines instructor interests in their intellectual work product while not substantially furthering instructor and student interests in effective learning. Such actions violate shared norms and standards of the academic community. For additional information, please see: <http://policy.umn.edu/Policies/Education/Education/STUDENTRESP.html>.

Conflict Resolution: The instructor and TA are willing to settle disagreements as quickly and amicably as possible. If you need assistance please contact the Office of Conflict Resolution (<http://www.sos.umn.edu/>).

FERPA Compliance: In this class, our use of technology will make students' names visible within the course Moodle website, but only to other students in this class. Since we are using a secure, password-protected course website, this will not increase the risk of identity theft or

spamming for anyone in the class. If you have concerns about the visibility of your name, please contact Prof. Carlson for further information.

If you feel you are having troubles or concerns about the class, please feel free to contact Prof. Carlson or the TA's; we want you to have a positive learning experience in this course. If you feel for any reason that we are not taking your concerns seriously, and that this is negatively impacting your learning, the Student Dispute Resolution Center (<http://www.sos.umn.edu/>) makes both informal (ombudsman) and formal (advocate) representatives within the University available for students to share their concerns with.