Rutgers University – New Brunswick

Chemical Biology (Chem 482 / 582) Syllabus

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Course Location: CCB 1203 (Busch Campus)

General Description

Chemical biology is an exciting and rapidly emerging field that constantly brings new advancements to life sciences, biotechnology, and medicine. Research in chemical biology aims to investigate, manipulate, or mimic biological systems by means of molecular tools and to develop smart molecular designs with clinical potential. The design principles and implications of these molecular tools are geared toward understanding a complex biological phenomenon or developing platforms that display biologically useful functions. This course will cover the fundamentals (both theory and technique) of chemical biology and the research strategies from a chemist's perspective.

Prerequisites

01:160:308 or 01:160:316; 11:115:403 or 01:694:407, or permission from instructor.

Course Material

A specific textbook is not required, as it is challenging to adequately cover the quickly progressing field of chemical biology. Therefore, this course will follow the lecture notes that are periodically updated to reflect the most recent scientific literature, including peer-reviewed research and review articles. The lecture notes will be available free of charge at the beginning of the course. In addition, practice questions will be provided periodically. Students are advised to attend all the classes and study the lecture notes, designated articles, and practice questions. To get more insight on the basic concepts, students can refer to the following *supportive textbooks* and *online sources*.

Supportive Textbooks

- Van Vranken, D. and Weiss, G., *Introduction to Bioorganic Chemistry and Chemical Biology*, 1st edition, Garland Science.
  ISBN-13: 978-0815342144; ISBN-10: 0815342144
- Watson, J. D. et al., *Molecular Biology of the Gene*, 7th edition, Cold Spring Harbor Laboratory Press.
  ISBN-13: 978-0-321-76243-6; ISBN-10: 0-321-76243-6

- Blackburn, G. M. and Gait, M., *Nucleic Acids in Chemistry and Biology*, 3rd edition, RCS Publishing.
  ISBN: 0-85404-654-2
- Hermanson, G. T., *Bioconjugate Techniques*, 3rd edition, Academic Press
  ISBN: 978-0-12-382239-0

Supportive Online Sources

Protein Data Bank (PDB), Rutgers and UCSD: https://www.rcsb.org/pdb/home/home.do
E-book by Tom Brown / ATDBio Ltd: http://www.atdbio.com/nucleic-acids-book

Office Hours

Instructor will provide office hours for 2 hours per week. Further details will be given in the beginning of the course.

Lecture Attendance

Students are required and expected to attend all classes in person under normal circumstances. Attendance will be taken every class and will be used for the course grade determination. A total of 25 points will come from full attendance throughout the semester. Students anticipating to miss a class due to legitimate reasons must use the University absence reporting website https://sims.rutgers.edu/ssra/ to indicate the date and reason for the absence. An email is automatically sent to the instructor.

Course Grading

The overall grade will be determined based on the followings:

- Attendance (25 pts total)
- Two mid-term exams (100 pts each, 200 pts total). Midterm exams will be given in person, not online.
- Research Article Presentation (100 pts total)
  Each student will make a PowerPoint presentation of a research article from the recent literature. *There is no requirement to submit a written report.* To determine which article to present, a two-step protocol will be followed: **1)** The student will identify 3 conceptually different publications from the prominent chemical biology journals (*Nature Chemical Biology*, *Cell Chemical Biology*, *ACS Chemical Biology*). Note that these journals, along with most other scientific journals, can be accessed through the Rutgers library portal using a NetID. **2)** The instructor will evaluate these 3 selected articles and determine which specific one that the student will present depending on the suitability of the work for the concepts covered in the class and the scope of other potential presentations. Presentations

will be given in person, not online. Students will carry out a 15-min presentation using PowerPoint slides. Upon completion, there will be a 5- to 10-min of Q/A session. The audience is strongly encouraged to carefully listen to each presentation and ask questions.

- Final exam (175 pts total)
  Final exam will be given in person, not online. This exam will be comprehensive. In addition to the fundamental concepts covered during the lectures, at least one question will come from the designated research article presented by the students.

Grade	A	B+	B	C+	C	D	F
Points	500–425	424–375	374–325	324–300	299–275	274–250	≤ 249

Academic Integrity

All assignments (presentation slides, midterm and final exams) submitted for credit in Chem 482 / 582 should reflect individual scholarship. While teamwork is encouraged, students can **never copy others' answers**. Academic dishonesty and violation of academic integrity will have consequences in strict accordance with the Rutgers University Academic Integrity Policy. A copy of the Academic Integrity Policy, which went into effect on September 1, 2013, can be found at:
http://studentconduct.rutgers.edu/student-conduct-processes/academic-integrity/

Student-Wellness Services

Counseling, ADAP & Psychiatric Services (CAPS): (848) 932-7884 / 17 Senior Street, New Brunswick, NJ 08901/ http://health.rutgers.edu/medical-counseling-services/counseling/**.** CAPS is a University mental health support service that includes counseling, alcohol and other drug assistance, and psychiatric services staffed by a team of professionals within Rutgers Health services to support students' efforts to succeed at Rutgers University. CAPS offers a variety of services that include: individual therapy, group therapy and workshops, crisis intervention, referral to specialists in the community, and consultation and collaboration with campus partners.

Crisis Intervention:
http://health.rutgers.edu/medical-counseling-services/counseling/crisis-intervention/
Report a Concern: http://health.rutgers.edu/do-something-to-help/

Violence Prevention & Victim Assistance (VPVA): (848) 932-1181 / 3 Bartlett Street, New Brunswick, NJ 08901 / www.vpva.rutgers.edu/**.** The Office for Violence Prevention and Victim Assistance provides confidential crisis intervention, counseling and advocacy

for victims of sexual and relationship violence and stalking to students, staff and faculty. To reach staff during office hours when the university is open or to reach an advocate after hours, call 848-932-1181.

Exam Regrade Requests

All student complaints about grades will be managed in close agreement with University Policies and Procedures. Students wishing to file a complaint about an exam grade or the course grade should initiate all attempts to resolve the matter through discussion with the Instructor. Such a discussion shall be NO LATER than one week after the exam in question is posted. If the issue cannot be satisfactorily resolved this way, the instructor will direct the student to the Vice-Chair of the Undergraduate Program (for Chem 482) or the Vice-Chair of the Graduate Program (for Chem 582). Student may specify in writing the basis for the complaint and request a review by the Vice-Chair and the Department Chair. A written complaint must be submitted to the department chair no later than (a) two weeks after notification of a disputed exam grade for disputed exam grades or (b) four weeks after the end of the exam period for that semester. For all appeals, and for additional information, please be sure follow these policies on grading as specified: https://sasoue.rutgers.edu/policies-resources/grading/53-policies-resources/125-grade-appeals

Exam Conflict

Certain scheduled Rutgers activities may take precedence over class activities for students who are formally registered to participate in those activities (see also RU Common Hour Exam Policies). If a student has an exam conflict between an examination and a scheduled activity, that students **MUST notify the instructor, by email 2 weeks before such conflict(s)**, so that alternative arrangements can be made. These arrangements may include, for example, an earlier or a later assessment. An exam conflict will be treated as if the student has missed the exam due to a legitimate reason (see below). A student with final exam conflict will be allowed to take a make-up exam. The exact date and location will be announced later.

Missed Exam

Exams must be taken at the scheduled times. Only excusable reasons will be considered (e.g. illness or family emergency). **To be excused from an exam, students must fill out a self-reported absence form,** available at https://sims.rutgers.edu/ssra, and **MUST notify the instructor, by email at least 48 hours before the exam**, so that alternative arrangements can be made. These arrangements may include, for example, an earlier or a later assessment. Unexcused missed exams will result in a score of zero (0) for that exam.

Special Needs

Any student requiring extra time and/or other unusual testing accommodations must provide documentation supporting their circumstances and **MUST notify the instructor.** ALL requests for extending time and/or other special accommodations for exams must be handled through the Office of Disability Services (https://ods.rutgers.edu) The office of Disability Services will be responsible for all necessary proctoring arrangements.

Course Outline

Class #	Modules
1	Introduction to the Course (Brief overview of **Modules 1**–**7**)
2 – 3	**M1:** The Central Dogma and Chemical Origins of Biology
4 – 6	**M2:** Chemistry and Function of Oligonucleotides and Nucleic Acids
7 – 9	**M3:** Chemistry and Function of Peptides and Proteins
10	Mid-term Exam 1, covering **M1**–**M3**
11	Discussion of Exam 1 (solutions and strategies)
12 – 14	**M4:** Small-Molecule Regulators and Inhibitors
15 – 16	**M5:** Bioconjugate Chemistry
17	Mid-term Exam 2, covering **M4**–**M5**
18	Discussion of Exam 2 (solutions and strategies)
19 – 20	**M6:** Photochemistry
20 – 21	**M7:** Chemical Tools for Biomolecular Imaging and Diagnostics
22 – 24	Research Article Presentations
25 – 26	Review of **M1**–**M7** and Practice Questions
27	Final Exam, covering **M1**–**M7** and a research article covered in the student presentations (class #22 or 23)
28	Discussion of Final Exam (solutions and strategies)

Learning Goals

Students will learn to describe, analyze, and rationalize technical and core concepts regarding prebiotic chemistry, enzymatic and non-enzymatic synthesis of genetic polymers, nucleic acids chemistry, peptides and proteins, small-molecule regulators and inhibitors that serve as therapeutics, bioconjugate chemistry, photochemistry,

photopharmacology, design principles of molecular tools for biomolecular imaging and diagnostics. These concepts will be taught via individual modules, and the details of the learning goals for each specific module are outlined below. Students are expected to build a strong theoretical foundation on these concepts and encouraged to support their learning process by reading the recommended articles (first author surname, *journal abbreviation*, **publication year**, first page number) listed below each respective module. These articles can be accessed through the Rutgers library portal using a NetID.

M1. The Chemical Origins of Cellular Systems

- Replication, transcription, and translation of the genetic information
- Role of organic chemistry in understanding the central dogma
- Chirality in biologically relevant building blocks
- Structure-based function and catalysis of biomacromolecules
- Organic molecules that might have led to the emergence of information transfer.

Recommended Articles: Joyce, *Nature* **2002**, p214; Wu, *Nat. Rev. Chem* **2017**, 0068; Szostak, *Angew. Chem. Int. Ed.* **2017**, p11037.

M2. Chemistry and Function of Oligonucleotides and Nucleic Acids

- Structural features of DNA, RNA, and non-biological nucleic acids (e.g., TNA, PNA, NP-DNA)
- Nomenclature and synthesis of nucleobases, nucleosides and nucleotides
- H-bonding properties and tautomerization of nucleobases
- Solid-phase chemical synthesis of nucleic acids
- Chemical modifications and metabolic labeling of nucleic acids.
- Functional nucleic acids (e.g., aptamers and nucleic acid enzymes: ribozymes)
- Laboratory evolution of functional nucleic acids
- Advantages of unnatural nucleic acids (artificial genetic polymers)

Recommended Articles: Deck, *Nat. Chem.* **2011**, p603; Chaput, *Acc. Chem. Res*. **2021**, p1056; Neubacher, *Angew. Chem. Int. Ed.* **2019**, p1266.

M3. Chemistry and Function of Peptides and Proteins

- Structural features of polypeptides and proteins
- Nomenclature and chemical properties of amino acids
- Enzymatic synthesis of peptides and proteins
- Bioorthogonal peptide bond formation

- In-solution chemical synthesis of peptides
- Solid-phase chemical synthesis of peptides
- Incorporation of unnatural amino acids into proteins

Recommended Articles: Lang, *Chem. Rev.* **2014**, p4764; Shah, *Chem. Sci.* **2014**, p446.

M4. Molecular Regulators, Inhibitors, and Degraders

- Interactions between organic molecules and nucleic acids.
- Synthetic drug molecules that work by stalling replication or translation (e.g., organic / organometallic intercalators, unnatural nucleoside agents)
- Interactions between organic molecules and proteins (small-molecule inhibitors of protein enzymes)
- The role of synthetic organic chemistry in developing small-molecule drugs (synthesis of complex therapeutic molecules and diversity-oriented synthesis: build-couple-pair)
- Targeted protein degradation and proteolysis-targeted chimeras (PROTACs)
- Targeted RNA degradation and ribonuclease targeting chimeras (RiboTACs)

Recommended Articles: Kim, *Biol Chem* **2008**, p1; Paige, *Science* **2011**, p642; Hansen, *Mol. Cell* **2002**, p117; Nielsen, *Angew. Chem. Int. Ed.* **2008**, p48; Schreiber, *Cell* **2021**, p3; Békés, *Nat. Rev. Drug Discov.* **2022**, p181; Meyer, *J. Am. Chem. Soc.* **2022**, p21096.

M5. Bioconjugate Chemistry

- Chemoselectivity and cytocompatibility in reaction design
- Ligation, cycloaddition (e.g., Diels-Alder reaction, copper-mediated and copper-free click chemistry, tetrazine ligation), 1,4-addition (conjugate or Michael addition), and other relevant bioorthogonal conjugation reactions

Recommended Articles: Lang, *Chem. Rev.* **2014**, p4764; Lang, *Nat.Chem.* **2012**, p298; Li, *J. Am. Chem. Soc.* **2013**, p4996.

M6. Photochemistry

- The basic concepts of photochemistry (Jabłoński diagram, quantum efficiency, brightness, quenching and photobleaching)
- Organic molecule designs that leverage photochemistry
- Photoisomerism and design principles of photoswitchable molecular probes

- Photopharmacology

Recommended Articles: Lavis, *ACS Chem. Biol.* **2014**, p855; Hüll, *Chem. Rev.* **2018**, p10710.

M7. Chemical Tools for Biomolecular Imaging and Diagnostics

- Organic fluorophores for imaging (bio)molecules *in vitro* and *in vivo* (their classification, synthesis, and biological application)
- Nucleic acid-derived imaging technologies (trafficking RNA or metabolites in cells and applications in nano/biotechnology)
- Molecular tools designed for super-resolution microscopy
- CRISPR/Cas-based detection of pathogens

Recommended Articles: Lavis, *ACS Chem. Biol.* **2014**, p855; Möckl, *J. Am. Chem. Soc.* **2020**, p17828; Singh*, ACS Chem. Biol.* **2018**, p1785; Kaminski*, Nat. Biomed. Eng.* **2021**, p643.