Rutgers University – New Brunswick, Spring 2021

# Chem 482 / 582: Chemical Biology

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Course Location and Time: TBD

## General Description

Chemical biology is an emerging interdisciplinary field at the interface of chemistry and biology. This dynamic field involves topics that are built on both basic and applied research, all geared toward advancing life science, biotechnology, and medicine. Primary methodology in chemical biology is to investigate, implement, mimic, or manipulate biological systems using functional small molecules that are produced via synthetic organic chemistry. Design principles of experiments often make use of the relative reactivity or biomolecular interactions of small molecules within cellular or physiologically relevant environments. Experimental results are typically obtained by advanced analytical techniques, including spectrophotometric measurements and bioimaging. This course will teach the fundamentals (both theories and techniques) of chemical biology from a chemist's perspective.

## Prerequisites

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

## Course Material

A specific textbook is not required. The course will follow the lecture notes provided by the instructor. These lecture notes are periodically updated based on the new information gathered from the most recent scientific literature. The most recent developments in the field of chemical biology cannot be properly covered in any single textbook. Therefore, the students are advised to study the lecture notes primarily. These lecture notes will be available free of charge at the beginning of the course. *To get more insight on a specific topic, the students are encouraged to refer to the recommended supportive textbooks and online sources.*

## Recommended 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*, 7$^{th}$ edition, Cold Spring Harbor Laboratory Press.

ISBN-13: 978-0-321-76243-6; ISBN-10: 0-321-76243-6

- Hermanson, G. T., *Bioconjugate Techniques*, 3rd edition, Academic Press
  ISBN: 978-0-12-382239-0

- Blackburn, G. M. and Gait, M., *Nucleic Acids in Chemistry and Biology*, 3rd edition, RCS Publishing.
  ISBN: 0-85404-654-2

## Recommended 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

## Course Grading

The overall grade will be determined based on the followings:

- Two mid-term exams (100 pts each, 200 pts total)
- Research Article Presentation (100 pts)
  Students will carry out a 15-min presentation of a recent and comprehensive research article using PowerPoint slides. At the end of the presentation, there will be a 5- to 10-min of Q/A session. Students are strongly encouraged to engage with the presentations and ask questions.
- Final exam (200 pts)
  This exam will be comprehensive. In addition to the fundamental concepts, some of the key knowledge covered throughout the article presentations will also be included.

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

## Lecture Attendance

Students are expected to attend all classes; if you expect to miss a class due to legitimate reasons, students 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.

## 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

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

There are no makeup mid-term exams. 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. Unexcused missed exams will result in a score of zero (0) for that exam. For excused exams, the score will be temporarily assigned as zero (0) and will be replaced by the average of the other exams including the final.

## 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 – 3 | **M1:** The Central Dogma |
| 4 – 6 | **M2:** Nucleic Acids |
| 7 – 9 | **M3:** Proteins |
| 10 | *Mid-term Exam 1, covering* **M1** – **M3** |
| 11 | *Discussion on Exam 1 (solutions and strategies)* |
| 12 – 14 | **M4:** Small-Organic-Molecule Regulators and Inhibitors |
| 15 – 16 | **M5:** Bioconjugate Chemistry and Applications in Chemical Biology |
| 17 | *Mid-term Exam 2, covering* **M4** – **M5** |
| 18 | *Discussion on Exam 2 (solutions and strategies)* |
| 19 | **M6:** Photochemistry and Applications in Chemical Biology |
| 20 – 21 | **M7:** Chemical Tools for Biomolecular Imaging |
| 22 – 23 | Research Article Presentations |
| 24 | *Final Exam, covering* **M1** – **M7** *and presentations* |
| 25 | *Discussion on Exam 1 (solutions and strategies)* |

## Learning Goals

Students will learn to describe, analyze, rationalize and apply technical and core concepts related to the *Central Dogma*, nucleic acids, proteins, small-organic-molecule regulators and inhibitors, bioconjugate chemistry and applications in chemical biology, photochemistry and applications in chemical biology, chemical tools for biomolecular imaging. These concepts will be taught in individual modules, and the details of the specific learning goals for each specific module are described below.

### M1. The Central Dogma

Replication, transcription and translation of the genetic information
Role of organic chemistry in understanding the central dogma
Functionality and catalysis induced by bio-macromolecules
Organic molecules that might have led to the emergence of information transfer.
Chirality in biologically relevant building blocks

### M2. Nucleic Acids

Structural features of DNA, RNA and non-biological nucleic acids (e.g., TNA, PNA)
Nomenclature and synthesis of nucleobases, nucleosides and nucleotides
H-bonding properties (e.g., Watson-Crick, Hoogsteen, wobble) and tautomerization of nucleobases

Solid-phase organic synthesis of nucleic acids
Chemical modifications and metabolic labeling of nucleic acids.
Functional nucleic acids (e.g., ribozymes)
    Natural nucleic acid enzymes
    Laboratory-evolved nucleic acid enzymes (e.g., ligases, aptamers, Diels-Alderase) and *in vitro* selection techniques

**M3. Proteins**

Structural features of proteins
Nomenclature and chemical properties of amino acids
Classical/bioorthogonal peptide bond formation
Solution-phase synthesis of short peptides
Solid-phase organic synthesis of peptides (e.g., protected amino acids, succinimide activators, and coupling reagents such as the carbodiimides)
Incorporation of un-natural amino acids into proteins

**M4. Small-Organic-Molecule Regulators and Inhibitors**

Interactions between organic molecules and nucleic acids. Synthetic drug molecules that work by stalling DNA replication or translation (e.g., organic / organometallic intercalators)
Interactions between organic molecules and proteins. Small-molecule inhibitors of protein enzymes

**M5. Bioconjugate Chemistry and Applications in Chemical Biology**

Chemoselective and bioorthogonal reactions used in chemical biology:
    Ligations, cycloadditions (e.g., Diels-Alder reaction, copper-mediated and copper-free click chemistry, tetrazine chemistry), and other bioorthogonal conjugation reactions (e.g., 1,4-addition of nucleophiles)

**M6. Photochemistry and Applications in Chemical Biology**

Jabłoński diagram (excitation, emission, stokes shift, quantum efficiency)
Chemical design principles of photoswitchable probes

**M7. Chemical Tools for Biomolecular Imaging**

Organic fluorophores for tracking biomolecules *in vitro* and *in vivo*
The concepts of luminescence (chemiluminescence and bioluminescence)
Green Fluorescent Protein (GFP) and its variants
Nucleic acid-derived imaging technologies
Aptamer-based imaging tools
Organic dyes: Types, synthesis, and applications in chemical biology