School of Molecular & Cellular Biology

MCB 493 sxn MFD, Fall 2025

Molecular Foundations in Chemical Biology and Drug Discovery

Course Description

This course is designed to teach students what makes a good chemical probe and drug by focusing on the early stage of drug discovery. Students will learn about the thermodynamic and kinetic parameters that are used to assess drug potency. We will discuss biochemical, bioanalytical, biophysical, and cell biological approaches along with best practices to determine these parameters. Several lectures will explore new modalities in drug discovery, such as covalent inhibitors, molecular glues, and bifunctional proximity inducers. Through several lectures, students will learn that drug activity especially in the early stages of drug discovery is often due to non-specific effects such as aggregation, lack of stability, redox activity, assay interference, and other factors. We will have several lectures that cover best practices for reporting non-clinical data along with statistical analysis. The course will cover modern screening methods to identify hits such as fragment-based drug design, virtual screening, DNA-encoded libraries, and high-throughput screening. We will also cover the use of artificial intelligence in the drug discovery process. The course is intended for graduate and advanced undergraduate students interested in a career in drug discovery or chemical tool development whether in academia or industry. The course is also suitable for graduate students in chemistry, chemical biology, biochemistry, chemical engineering or biology who are involved in the design and synthesis of small-molecule drug or exploring the mechanism of drug action at the biochemical or biological level.

Instructor Information

- **Name:** Samy Meroueh
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- **Office:** RAL 321
- **Office Hours:** By request

Course Information

- **Course Title:** Molecular Foundations in Chemical Biology and Drug Discovery
- **Department:** Biochemistry, School of Molecular and Cell Biology
- **Institution:** University of Illinois at Urbana-Champaign
- **Semester:** Fall 2025
- **Meeting Time:** MWF 3:00-3:50 PM
- **Location:** 106B1 Engineering Hall
- **Credits:** 3

Learning Objectives

By the end of this course, students will be able to:

1. Understand the fundamental principles of molecular recognition and binding
2. Analyze biochemical data for small-molecule binding and inhibition
3. Apply biochemical and cell biological approaches to study biological systems
4. Evaluate quality of chemical hits, leads, probes and drugs
5. Design and critique experiments in chemical biology and drug discovery
6. Understand the molecular basis of drug action and pharmacology

Grading

- Exam 1: 25%
- Exam 2: 25%
- Final Presentation: 40%
- Class Participation: 10%

Course Policies

- Attendance of 90% of classes is required to receive 10% of your grade.
- Recording of lectures either by audio or video is not permitted.
- Exam questions will be multiple choice. Only final answer counts.
- Lectures will be provided by email at least one hour before lecture.

Academic Integrity:

The Student Code will be applied in all instances of academic misconduct committed by students. This applies to all exams, presentations, assignments, and materials distributed or used in this course. You can review these policies in the Student Code, specifically (https://studentcode.illinois.edu/article1/part4/1-401/). Ignorance is not an excuse for any academic dishonesty. It is your responsibility to read this policy to avoid any misunderstanding. Do not hesitate to ask the instructor(s) if you are ever in doubt about what constitutes plagiarism, cheating, or any other breach of academic integrity.

Course Schedule

Week 1:

- **Monday, August 25** – Academic drug discovery overview
- **Wednesday, August 27** – Structural basis of molecular recognition
- **Friday, August 29** – Equilibrium binding constant

Week 2:

- **Monday, September 1** -- NO CLASS (Labor Day)

- **Wednesday, September 3** – Equilibrium binding constant
- **Friday, September 5** – Binding kinetics

Week 3

- **Monday, September 8** – Binding kinetics
- **Wednesday, September 10** – Mechanism of action for enzymes
- **Friday, September 12** – Mechanism of action for enzymes

Week 4

- **Monday, September 15** – Covalent inhibitors (mechanism)
- **Wednesday, September 17** – Covalent inhibitors (mechanism)
- **Friday, September 19** – Introduction to fluorescence for assay development

Week 5

- **Monday, September 22** – Target engagement assays PPIs
- **Wednesday, September 24** – Target engagement assays – biosensing
- **Friday, September 26** – Target engagement assays – thermal

Week 6

- **Monday, September 29** – Target engagement assays – PPIs in cells
- **Wednesday, October 1** – Exam #1
- **Friday, October 3** – Covalent inhibitors

Week 7

- **Monday, October 6** – Chemical proximity inducers 1
- **Wednesday, October 8** – Chemical proximity inducers 2
- **Friday, October 10** – Molecular glues

Week 8

- **Monday, October 13** – GPCRs and their inhibitors and assays
- **Wednesday, October 15** – Kinases and their inhibitors and assays
- **Friday, October 17** – Proteases and their inhibitors and assays

Week 9

- **Monday, October 20** – Channels and their inhibitors and assays
- **Wednesday, October 22** – PPIs and their inhibitors
- **Friday, October 24** – Assay interference – chemical reaction

Week 10

- **Monday, October 27** – Assay interference - aggregation
- **Wednesday, October 29** – Assay interference – fluorescence and luciferase
- **Friday, October 31** – DNA encoded libraries

Week 11

- **Monday, November 3** – Fragment based drug design
- **Wednesday, November 5** – Structure-based drug design
- **Friday, November 7** – High-throughput screening

Week 12

- **Monday, November 10** – Best practices for reporting Non-Clinical Data
- **Wednesday, November 12** – Best practices for reporting Non-Clinical Data
- **Friday, November 14** – In vivo studies

Week 13

- **Monday, November 17** – ADME and PK intro
- **Wednesday, November 19** – ADME and PK in vivo
- **Friday, November 21** – Exam #2

Week 14: Thanksgiving Week

- **Monday, November 24** – Presentations
- **Wednesday, November 26** - NO CLASS (Thanksgiving Break)
- **Friday, November 28** - NO CLASS (Thanksgiving Break)

Week 15

- **Monday, December 1** – Presentations
- **Wednesday, December 3** – Presentations
- **Friday, December 5** – Presentations

Week 16: Final Week

- **Monday, December 8** – Presentations
- **Wednesday, December 10** – Presentations

Important Dates Summary

- **First Day of Classes:** Monday, August 25, 2025
- **Labor Day (No Class):** Monday, September 1, 2025
- **Midterm Exam 1:** Wednesday, October 15, 2025
- **Midterm Exam 2:** Wednesday, November 19, 2025
- **Thanksgiving Break:** Wednesday-Friday, November 26-28, 2025

- **Last Day of Classes:** Wednesday, December 10, 2025
- **Final Exam:** During finals week (December 11-17, 2025)