2021 Syllabus for BIOC 675: Fundamentals of cryo-electron microscopy

Instructors: Richard Baker (baker@med.unc.edu, GMB 3046)
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Target audience: Graduate students conducting research in the fields of molecular biology, biochemistry, or biophysics with an emphasis on structural biology. The primary emphasis of the course will be on the use of cryo-electron microscopy (cryo-EM) to determine high-resolution reconstructions of macromolecules.

Course Description: cryo-electron microscopy (cryo-EM) is fast becoming a dominant technique in structural biology, with applications ranging from high-resolution single particle reconstruction to tomography of *in situ* cellular structures. This course will provide a survey of biological applications of cryo-EM, with a particular emphasis on single particle techniques used to determine high-resolution structures of macromolecules. At the end of the course, students will have a basic understanding of cryo-EM theory, the methodology for creating samples and collecting data, and strategies for reconstructing 3D models of macromolecules. The course will primarily consist of lectures, with a 1-week lab component in the UNC cryo-EM core facility.

Prerequisites: Must be in good standing as a graduate student at UNC. If the course is over-subscribed, preference will be giving to students enrolled in the Biophysics Training Program.

Course requirements: Graduate student status

Grades: Students are expected to complete all assigned readings, attend all lectures, complete all homework assignments, and participate in a hands-on module in the UNC cryo-EM core facility. One homework assignment will be given each week. Grades will be determined by attendance, participation, homework assignments, and a final exam.

Time Table/ Schedule
Lectures on TTH at TBD
Ten 75-minute classes
Four weeks of class instruction, one week of lab instruction

Course Topics

Week 1 – Fundamentals of cryo-EM
Lecturer: Baker
Topics: Anatomy of a microscope; applications of cryo-EM to biological problems; Historical perspective of cryo-EM

Week 2 – Image formation, aberrations, and beam-induced motion
Lecturer: Baker
Topics: Theory of image formation; contrast transfer function (CTF); spherical aberration; beam-induced motion and motion correction

Week 3 – Classification, refinement, and reconstruction of 3D models
Lecturer: Baker

Topics: 2D and 3D classification; high-resolution refinement; central slice theorem; statistical methods in cryo-EM

Week 4 – Sample preparation and practical considerations in cryo-EM
Lecturer: Baker
Topics: cryo grid making; air-water interface problem; strategies for high-resolution data collection and 3D model refinement

Week 5 – Hands-on workshop for single-particle cryo-EM
Lecturer: Baker and Strauss
Topics: Workshop for preparation of cryo grids, collection of data, and determination of a high-resolution structure. Students will collect data with the supervision of Dr. Joshua Strauss in the cryo-EM core facility and will process the data under the supervision of Dr. Baker. Students will determine a high-resolution cryo-EM structure at the end of Week 5.

Final Exam (take-home)

Course resources: Outside readings will consist of peer-reviewed literature and hand-outs prepared by the instructor. All documents will be provided by web (e.g. Sakai) or by email as PDF documents or web links.

Honor Code: Students are expected to follow the UNC honor code. The final exam will be a take-home exam with a deadline of one week; students will be expected to work independently and not discuss the exam with others.

Accommodations: accommodations for students with disabilities, chronic medical conditions, a temporary disability, or other concerns will be handled according to university guidelines.