Structural Biophysics:
Advanced Methods for 3-D Structure Determination of Biomolecules
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Offered: Spring Semester

Credits: 3

Enrollment: 15 students

Classroom: Online and Institute for Quantitative Biomedicine, Rooms 206, 174 Frelinghuysen Road, Piscataway, NJ 08854

Prerequisites: Biochemistry

Course Coordinator: Arek Kulczyk

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Course Description: This course is a survey of advanced techniques for structure determination of biomolecules. We will discuss: (i) physical basis of cryo-EM, NMR and X-ray crystallography. Special emphasis will be put on cryo-EM, (ii) other emerging methods including: CLEM, cryo-ET and FIB –SEM, (ii) advantages and disadvantages of each technique (iii) specific examples of bio-molecular complexes whose 3-D structures have been determined using one of the above methods. Except of learning theory, students will have the opportunity to visit state-of the-art cryo-EM and NMR facilities, and determine a high-resolution cryo-EM structure using a high-performance computing Linux cluster.

Instructors: Arek Kulczyk & Invited speakers

Textbook and Readings: There will be no specific textbook for the course. Students will be provided with handouts or referred to resources available online or through Rutgers Libraries.

Course URL: Course materials will be posted on Canvas.

Course-specific Learning Goals: Upon completion of this course, students will be able to: (i) Understand the theory and practice of modern methods for 3-D structure determination of biomolecules. (ii) Calculate a high-resolution cryo-EM structure using high-performance computing. (iii) Deliver a scientific presentation in front of the class.

Exams, Assignments, and Grading Policy: The exam covering a theoretical part of the course will count for 30% of the grade. The ability to calculate a cryo-EM structure will count for 30% of the grade. The student presentation will count for 30% of the grade. We will also take into account class participation, especially in the structure calculation and student presentation part of the course (10%). There will be no final exam.

Draft Schedule

Week	Class	Topic	Reading
1 Jan 18	1	Overview of methods for structure determination of biomolecules.	Prof. Arek Kulczyk, Rutgers
Jan 20		Basic concepts in EM: electron waves, field emission guns, lenses, energy filters and direct detectors.	Online resources: http://cryo-em-course.caltech.edu/videos Prof. Arek Kulczyk, Rutgers
2 Jan 25	3	Processing of cryo-EM data in Scipion.	Online resources: http://scipion.i2pc.es/ Prof. Carlos Oscar Sorzano, NCB, Spain
Jan 27	4	Fourier transforms, Contrast Transfer Function (CTF), phase and amplitude contrast, defocus.	Handout Online resources: http://cryo-em-course.caltech.edu/videos Megan DiIorio, Ph.D. Student in Kulczyk lab, Rutgers
3 Feb 1	5	EM data collection, image processing and structure calculations.	Handout Online resources: http://cryo-em-course.caltech.edu/videos Prof. Craig Yioshioka, Director of PNCC, OHSU
Feb 3	6	Algorithms for cryo-EM structure calculation.	Handout Prof. Hans Elmlund, NIH
4 Feb 8	7	Correlative Light and Electron Microscopy (CLEM), cryo-Electron Tomography (cryo-ET) and Focus Ion Beam Scanning Electron Microscopy (FIB-SEM).	Handout Online resources: http://cryo-em-course.caltech.edu/videos Prof. Wei Dai, Rutgers
Feb 10	8	Tour of the cryo-EM and NMR facilities in the IQB.	Zoom or in-person, Prof. Arek Kulczyk, Rutgers
5 Feb 15	9	Basic Concepts in NMR: energy levels, the vector model, chemical shifts, spin-spin coupling, chemical exchange, spin relaxation.	Handout Online resources: http://www-keeler.ch.cam.ac.uk/lectures/

			Book: "Nuclear Magnetic Resonance" by P.J. Hore, Oxford University Press Prof. David Case, Rutgers
Feb 17	10	Application of NMR for structure determination of biomolecules.	Handout Prof. Haribabu Arthanari, Harvard
6 Feb 22	11	Multidimensional NMR.	Handout Prof. Guy Montelione, Rensselaer Polytechnic
Feb 24	12	Basic concepts in X-ray crystallography: crystal growth, X-ray generators and synchrotrons, Bragg's law, diffraction.	Handout Dr. Gregg Crichlow, PDB
7 Mar 1	13	Phasing methods and structure determination in X-ray crystallography.	Handout Dr. Ezra Peisach, PDB
Mar 3	14	X-ray crystallography- Protein Data Bank.	Handout Prof. Stephen Burley, Director of PDB and IQB, Rutgers
8 Mar 8	15	Theoretical exam.	Prof. Arek Kulczyk, Rutgers
Mar 10	16	Discussion of exam's Q&As.	Prof. Arek Kulczyk, Rutgers
9 Mar 22	17	Cryo-EM structure calculation: importing movies, motion and CTF corrections.	Practical, Handout Prof. Arek Kulczyk, Rutgers
Mar 24	18	Cryo-EM structure calculation: particle picking, extraction, screening and 2-D classification.	Practical, Handout Prof. Arek Kulczyk, Rutgers
10 Mar 29	19	Cryo-EM structure calculation: 2-D classification, creating an initial model.	Practical, Handout Prof. Arek Kulczyk, Rutgers
Mar 31	20	Cryo-EM structure calculation: 3-D classification	Practical, Handout Prof. Arek Kulczyk, Rutgers
11 Apr 5	21	Cryo-EM structure calculation: 3-D refinements.	Practical, Handout Prof. Arek Kulczyk, Rutgers
Apr 7	22	Fitting atomic coordinates to cryo-EM map in UCSF Chimera.	Handout Dr. Brian Hudson, PDB
12 Apr 12	23	Scientific storytelling and preparing a scientific presentation.	Handout Maria Voigt, PDB

		Selection of articles for student presentations.	
Apr 14	24	Student presentations & Q&As #1.	Prof. Arek Kulczyk, Rutgers
13 Apr 19	25	Student presentations & Q&As #2.	Prof. Arek Kulczyk, Rutgers
Apr 21	26	Student presentations & Q&As #3.	Prof. Arek Kulczyk, Rutgers
14 Apr 26	27	Student presentations & Q&As #4.	Prof. Arek Kulczyk, Rutgers
Apr 28	28	Wrap-up & farewells	Prof. Arek Kulczyk, Rutgers