BIO 304: Biological Function and Structure - Spring 2014

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Lectures: W 15:40-16:30 FENS L067
Th 10:40-12:30 FENS L055

Course Description: The aim of this course is to walk students through the main ideas and experimental techniques in structural biology following the shortest path from the significant events in the history of the field to the recent research literature. We will start by reviewing the building blocks of proteins and DNA and discussing the physical interactions responsible for their structures. Basic knowledge about X-ray crystallography as a tool for revealing the three dimensional structures of biomolecules will be provided. The motivation for this general overview will come from reading some of the classic papers that contributed to the birth of structural biology. In particular, we will read the foundational papers of Linus Pauling (Nobel Prize in Chemistry, 1954), James Watson and Francis Crick (Nobel Prize in Physiology, 1962), Max Perutz and John Kendrew (Nobel Prize in Chemistry, 1962). To establish a quantitative connection between biomolecular structure and function we will look at binding—the simplest recognition event at the molecular scale—in terms of equilibrium and rate constants. Cooperative binding will be introduced to understand how hemoglobin in the red blood cells carries oxygen. In this context, we will familiarize ourselves with the relevant aspects of the work of Jacques Monod (Nobel Prize in Physiology, 1965). Coming to the present century, we turn to the question of how ion channels embedded in the cellular membrane conduct ions in a selective and controlled way. To this end, we will read and discuss the work of Roderick MacKinnon (Nobel Prize in Chemistry, 2003) on the structural aspects of ion conduction and gating of potassium channels. Motivated by the modern view that biomolecular function is determined by structure as well as dynamics, we will then turn to nuclear magnetic resonance (NMR) spectroscopy. The basic ideas of NMR as applied to structural biology will be illustrated through the Nobel lecture of Kurt Wüthrich (Nobel Prize in Chemistry, 2002). Recent applications of NMR to elucidating the role of enzyme dynamics in catalysis and the importance of DNA dynamics for protein-DNA recognition will also be examined.

Evaluation:

In-class discussion	10 %
Quizzes and homework assignments	15 %
Midterm exam	25 %
Written report and oral presentation	25 %
Comprehensive final exam	25 %

The course will consist of lectures and in-class discussions of pre-assigned research papers, both historical and recent. Homework assignments and short quizzes will be given to make sure that the material in the lectures has been absorbed in a timely manner. Students will be expected to have read the assigned papers carefully and critically, and to actively participate in the discussion. In the second half of the semester, students will be expected to choose a biological question, which they will examine from a structural perspective using the recent research literature. In the last week, they will make an in-class presentation of their findings and submit a short written report.

Textbooks:

Kuriyan	Kuriyan, Konforti, and Wemmer, *The Molecules of Life*, Garland Science, 2012.
Petsko	Petsko and Ringe, *Protein Structure and Function*, New Science Press, 2004.
Branden & Tooze	Branden and Tooze, *Introduction to Protein Structure*, 2nd edition, Garland Science, 1999.

Detailed Course Content:

	Lecture topic (*Discussion topic*)
Feb 12	General information about the course
Feb 13	Overview of biological molecules and their functions
Feb 19	Structural chemistry
Feb 20	Interactions between molecules
Feb 26	*Helices, pleated sheets and Pauling*
Feb 27	Introduction to X-ray crystallography
Mar 5	*The double helix of Watson and Crick*
Mar 6	X-ray crystallography and biomolecular structure
Mar 12	*Kendrew and the structure of myoglobin*
Mar 13	The hydrophobic effect and protein folding
Mar 19	*Perutz and the two states of hemoglobin*
Mar 20	Cooperativity and protein quaternary structure
Mar 26	Lipid membranes and permeation of small molecules
Mar 27	Membrane potential and ion channels
Apr 2	*Structure of the potassium channel KcsA*
Apr 3	*Ion conduction in the selectivity filter of KcsA*
Apr 9	*Gating of the potassium channel MthK*
Apr 10	**Midterm Exam**
Apr 16 Apr 17	Semester Break
Apr 23	National Holiday
Apr 24	Introduction to NMR spectroscopy (and relaxation)
Apr 30	Biomolecular structure determination with NMR
May 1	Labour Day
May 7	*Interaction of the lac repressor with DNA*
May 8	Enzyme thermodynamics and kinetics
May 14	*Intrinsic dynamics coupled to catalysis in CypA*
May 15	*CypA minor state with X-ray crystallography and NMR*
May 21	**Presentations**
May 22	**Presentations**