MOLECULAR BIOPHYSICS AND BIOCHEMISTRY

336 Bass Center, 203.432.5662
http://medicine.yale.edu/mbb
M.S., M.Phil., Ph.D.

Chair
Mark Hochstrasser

Director of Graduate Studies
Yong Xiong (336 Bass, 203.432.5662, nessie.stewart@yale.edu)

Professors Karen Anderson (Pharmacology), Susan Baserga, Ronald Breaker (Molecular, Cellular & Developmental Biology), Gary Brudvig (Chemistry), Sandy Chang (Laboratory Medicine), Enrique De La Cruz, Daniel DiMaio (Genetics; Therapeutic Radiology), Donald Engelman, Alan Garen, Mark Gerstein, Nigel Grindley (Emeritus), Mark Hochstrasser, Jonathon Howard, Anthony Koleske, William Konigsberg, Peter Lengyel (Emeritus), J. Patrick Loria (Chemistry), I. George Miller (Pediatric Infectious Diseases; Public Health), Andrew Miranker, Peter Moore (Emeritus, Chemistry), Karla Neugebauer, Thomas Pollard (Molecular, Cellular & Developmental Biology), Lynne Regan, Karin Reinisch (Cell Biology), David Schatz (Immunobiology), Robert Shulman (Emeritus), Fred Sigworth (Cellular & Molecular Physiology; Biomedical Engineering), Dieter Söll, Mark Solomon, Joan Steitz, Thomas Steitz, Scott Strobel, William Summers (Emeritus), Patrick Sung, Kenneth Williams (Adjunct; Research)

Associate Professors Titus Boggon (Pharmacology), Michael Koelle, Christian Schlieker, Charles Sindelar, Yong Xiong

Assistant Professors Julien Berro, Wendy Gilbert, Erdem Karatekin (Cellular & Molecular Physiology), Nikhil Malvankar, Matthew Simon, Sarah Slavoff (Chemistry), Seyedtaghi Takyar (Internal Medicine/Pulmonary)

FIELDS OF STUDY

The principal objective of members of the department is to understand living systems at the molecular level. Laboratories in MB&B focus on a diverse collection of problems in biology. Some specialize in the study of DNA dynamics, including replication, recombination, transposition, and/or functional genomics. Others focus on transcriptional regulation, from individual transcription factors to the control of lymphocyte activation, the interferon response, and organismal development. Other groups study RNA catalysis, RNA-protein interactions, and ribonucleoproteins including spliceosomes and the ribosome. Additionally there are those that emphasize protein folding and design, transmembrane signaling, and control of the cell cycle. Structural and computational biology is a strong component of many of these research efforts.

SPECIAL ADMISSIONS REQUIREMENTS

Courses in introductory biology, general chemistry, organic chemistry, physical chemistry, mathematics through differential equations, and one year of physics with calculus are required for admission. Biochemistry is strongly recommended. Applicants must take the GRE General Test, which is preferred, or the MCAT.

To enter the Ph.D. program, students apply to an interest-based track within the interdepartmental graduate program in Biological and Biomedical Sciences (BBS), http://bbs.yale.edu.

INTEGRATED GRADUATE PROGRAM IN PHYSICAL AND ENGINEERING BIOLOGY (PEB)

Students applying to one of four tracks of the Biological and Biomedical Sciences program may simultaneously apply to be part of the PEB program. See the description under Non-Degree-Granting Programs, Councils, and Research Institutes for course requirements, and http://peb.yale.edu for more information about the benefits of this program and application instructions.

SPECIAL REQUIREMENTS FOR THE PH.D. DEGREE

All first-year students (except M.D./Ph.D.) perform three laboratory rotations (MB&B 650, Lab Rotation for First-Year Students). All students are required to take, for credit, seven one-term science courses. To obtain the desired breadth and depth of education, students are required to take two courses in molecular biophysics (one of which must be MB&B 720), one course in critical thinking (MB&B 730), and one course in molecular biology (MB&B 743 is recommended but not required). The second credit in molecular biophysics and the molecular biology credit may be satisfied by taking appropriate courses from an approved list available each fall. Additional courses, chosen from within MB&B or from related graduate programs, should form a coherent background for the general area in which the student expects to do dissertation research. All students also attend MB&B 676, Responsible Conduct of Research. In their fourth year of study, all students must successfully complete B&BS 503, RCR Refresher for Senior BBS Students. Students with an extensive background in biochemistry or biophysics are permitted to substitute advanced courses for the introductory courses. There is no foreign language requirement. The student’s research committee (see below) makes the final decision concerning the number and selection of courses required of each student. All students are required to assist in teaching two terms at the TF-10 level during their graduate careers, usually during the second and third years. The student selects a research adviser by the end of the second term of residence. At that time two additional faculty members are chosen to form a research committee, with the total committee including at least two members of MB&B. Students are required to meet with this committee in the spring of years two and three, and in both the fall and spring of
subsequent years. The qualifying examination, usually taken in the fall of the second year, is an oral defense of a research proposal consisting of (1) thesis aims and (2) extended goals on the same topic. The extended goals should include approaches beyond those in the thesis aims, typically beyond those generally employed by the host lab. Thus, a predominantly molecular biological set of thesis aims should be accompanied by biophysical approaches in the extended goals section, and vice versa. The three-member oral examination committee usually includes at least one of the two members of the research committee excluding the thesis adviser. Requirements for admission to candidacy, which usually takes place after four terms of residence, include (1) completion of course requirements; (2) completion of the qualifying examination; (3) certification of the student’s research abilities by vote of the faculty upon recommendation from the student’s research committee; and (4) submission of a brief prospectus of the proposed thesis research. Completion of the teaching requirement is not required for admission to candidacy. Once final drafts of the thesis chapters have been approved by the research committee, the student presents a dissertation seminar to the entire department, and only afterward may the thesis be submitted. Students must have written at least one first-author paper that is submitted, in press, or published by the time of the thesis seminar.

**HONORS REQUIREMENT**

Students must meet the Graduate School’s Honors requirement by the end of the fourth term of full-time study; see Degree Requirements under Policies and Regulations. Students must also maintain an overall High Pass average. Student progress toward these goals is reviewed at the ends of the first and second terms.

**M.D./PH.D. STUDENTS**

M.D./Ph.D. students must satisfy the requirements listed above for the Ph.D. with the following modifications: Laboratory rotations are not required but are available. Assisting in teaching of one lecture course is required. Students are required to take MB&B 800 as part of their medical curriculum in addition to the two courses in molecular biophysics described above. Students with weak backgrounds in molecular biology will need to take MB&B 743.

**MASTER’S DEGREES**

M.Phil. See Degree Requirements under Policies and Regulations. Awarded only to students admitted to candidacy who are continuing for the Ph.D. Students need not have completed their teaching requirement to receive the M.Phil. Students are not admitted for this degree.

M.S. Students are not admitted for this degree. It may only be awarded to a student in the Ph.D. program who is in good standing upon completion of at least two terms of graduate study and who will not continue in the Ph.D. program. A student must receive grades of Pass or higher in at least five courses approved by the DGS as counting toward a graduate degree, exclusive of seminars or research. Students must have taken at least ten courses. A typical schedule would consist of six traditional courses, two terms of MB&B 650, and one term each of MB&B 675 and MB&B 676. A student must also meet the Graduate School’s Honors requirement for the Ph.D. program and maintain a High Pass average. Students who are eligible for or who have already received the M.Phil. will not be awarded the M.S.

More detailed program materials are available upon request to the Director of Graduate Admissions, Department of Molecular Biophysics and Biochemistry, Yale University, PO Box 208114, New Haven CT 06520-8114.

**COURSES**

**MB&B 500a / MCDB 500a, Biochemistry**

An introduction to the biochemistry of animals, plants, and microorganisms, emphasizing the relations of chemical principles and structure to the evolution and regulation of living systems.

**MB&B 517b / ENAS 517b / MCB 517b / PHYS 517b, Methods and Logic in Interdisciplinary Research**  Staff

This half-term PEB class is intended to introduce students to integrated approaches to research. Each week, the first of two sessions is student-led, while the second session is led by faculty with complementary expertise and discusses papers that use different approaches to the same topic (for example, physical and biological or experiment and theory). Counts as 0.5 credit toward MB&B graduate course requirements. ½ Course cr

**MB&B 523b / CB&B 523b / ENAS 541b / PHYS 523b, Biological Physics**  Simon Mochrie

The course has two aims: (1) to introduce students to the physics of biological systems and (2) to introduce students to the basics of scientific computing. The course focuses on studies of a broad range of biophysical phenomena including diffusion, polymer statistics, protein folding, macromolecular crowding, cell motion, and tissue development using computational tools and methods. Intensive tutorials are provided for MATLAB including basic syntax, arrays, for-loops, conditional statements, functions, plotting, and importing and exporting data.

**MB&B 545b, Methods and Logic in Molecular Biology**  Wendy Gilbert, Donald Engelman, Mark Hochstrasser, and Christian Schlieker

An examination of fundamental concepts in molecular biology through analysis of landmark papers. Development of skills in reading the primary scientific literature and in critical thinking. Open only to MB&B students pursuing the B.S./M.S. degree.
MB&B 561a / CB&B 561a / MCDB 561a / PHYS 561a, Introduction to Dynamical Systems in Biology Thierry Emonet and Kathryn Miller-Jensen
Study of the analytic and computational skills needed to model genetic networks and protein signaling pathways. Review of basic biochemical concepts including chemical reactions, ligand binding to receptors, cooperativity, and Michaelis-Menten enzyme kinetics. Deep exploration of biological systems including: kinetics of RNA and protein synthesis and degradation; transcription activators and repressors; lyosogeny/lysis switch of lambda phage and the roles of cooperativity and feedback; network motifs such as feed-forward networks and how they shape response dynamics; cell signaling, MAP kinase networks and cell fate decisions; bacterial chemotaxis; and noise in gene expression and phenotypic variability. Students learn to model using MATLAB in a series of in-class hackathons that illustrate biological examples discussed in lectures.

MB&B 562b / AMTH 765b / CB&B 562b / ENAS 562b / INP 562b / MCDB 562b / PHYS 562b, Dynamical Systems in Biology Damon Clark, Thierry Emonet, and Jonathan Howard
This course covers advanced topics in computational biology. How do cells compute, how do they count and tell time, how do they oscillate and generate spatial patterns? Topics include time-dependent dynamics in regulatory, signal-transduction, and neuronal networks; fluctuations, growth, and form; mechanics of cell shape and motion; spatially heterogeneous processes; and diffusion. This year, the course spends roughly half its time on mechanical systems at the cellular and tissue level, and half on models of neurons and neural systems in computational neuroscience. Prerequisite: MB&B 561 or equivalent, or a 200-level biology course, or permission of the instructor.

MB&B 570a, Intensive Research for B.S./M.S. Candidates Staff
Required of students in the joint B.S./M.S. program with Yale College. 2 Course cr per term

MB&B 571b, Intensive Research for B.S./M.S. Candidates Staff
For students in the joint B.S./M.S. program with Yale College. 2 Course cr

MB&B 591a / ENAS 991a / MCDB 591a / PHYS 991a, Integrated Workshop Corey O’Hern, Lynne Regan, Simon Mochrie, Christine Jacobs-Wagner, Scott Holley, and Megan King
This required course for students in PEB involves hands-on laboratory modules with students working in pairs. A biology student is paired with a physics or engineering student; a computation/theory student is paired with an experimental student. The modules are devised so that a range of skills is acquired, and students learn from each other. Modules are hosted in faculty laboratories. Receives no course credit toward MB&B graduate course requirements. With permission of the DGS, can be used by PEB students to replace the third rotation of MB&B 650 but will receive no separate course credit toward MB&B course requirements.

MB&B 600a, Principles of Biochemistry I Matthew Simon and Michael Koelle
Discussion of the physical, structural, and functional properties of proteins, lipids, and carbohydrates, three major classes of molecules in living organisms. Energy metabolism, hormone signaling, and muscle contraction as examples of complex biological processes whose underlying mechanisms can be understood by identifying and analyzing the molecules responsible for these phenomena.

MB&B 601b, Principles of Biochemistry II Christian Schlieker and Joan Steitz
A continuation of MB&B 600a that considers the chemistry and metabolism of nucleic acids, the mechanism and regulation of protein and nucleic acid synthesis, and selected topics in macromolecular biochemistry.

MB&B 602a / CBIO 602a / MCDB 602a, Molecular Cell Biology Charles Lusk, Michael Caplan, Pietro De Camilli, Thomas Pollard, Peter Takizawa, David Calderwood, James Rothman, Valerie Horsley, Thomas Melia, Megan King, and Josephina van Wolfswinkel
A comprehensive introduction to the molecular and mechanistic aspects of cell biology for graduate students in all programs. Emphasizes fundamental issues of cellular organization, regulation, biogenesis, and function at the molecular level.

MB&B 625a / GENE 625a / MCDB 625a, Basic Concepts of Genetic Analysis Jun Lu
The universal principles of genetic analysis in eukaryotes are discussed in lectures. Students also read a small selection of primary papers illustrating the very best of genetic analysis and dissect them in detail in the discussion sections. While other Yale graduate molecular genetics courses emphasize molecular biology, this course focuses on the concepts and logic underlying modern genetic analysis.

MB&B 630a / MCDB 630b, Biochemical and Biophysical Approaches in Molecular and Cellular Biology Thomas Pollard and Karin Reinisch
This course introduces the theory and application of biochemical and biophysical methods to study the structure and function of biological macromolecules. The course considers the basic physical chemistry required in cellular and molecular biology but does not require a previous course in physical chemistry. One class per week is a lecture introducing a topic. The second class is a discussion of one or two research papers utilizing those methods. Does not count for graduate course credit for BBSB graduate students.

MB&B 635a / ENAS 518a, Quantitative Approaches in Biophysics and Biochemistry Nikhil Malvankar and Yong Xiong
The course offers an introduction to quantitative methods relevant to analysis and interpretation of biophysical and biochemical data. Topics covered include statistical testing, data presentation, and error analysis; introduction to dynamical systems; analysis of large datasets; and Fourier analysis in signal/image processing and macromolecular structural studies. The course also includes an introduction to basic programming skills and data analysis using MATLAB. Real data from research groups in MB&B are used for practice. Prerequisites: MATH 120 and MB&B 600 or equivalents, or permission of the instructors.
MB&B 650a and MB&B 651b, Lab Rotation for First-Year Students  Yong Xiong
Required of all first-year BBSB graduate students. Credit for full year only.

MB&B 675a, Seminar for First-Year Students  Staff
Required of all first-year BBSB graduate students.

MB&B 710b / C/MP 710b, Electron Cryo-Microscopy for Protein Structure Determination  Frederick Sigworth
Understanding cellular function requires structural and biochemical studies at an ever-increasing level of complexity. The course is an introduction to the concepts and applications of high-resolution electron cryo-microscopy. This rapidly emerging new technique is the only method that allows biological macromolecules to be studied at all levels of resolution from cellular organization to near atomic detail. Counts as 0.5 credit toward MB&B graduate course requirements. ½ Course cr

MB&B 720a, Macromolecular Structure and Biophysical Analysis  Andrew Miranker, Yong Xiong, Jonathon Howard, Nikhil Malvankar, and Wendy Gilbert
An in-depth analysis of macromolecular structure and its elucidation using modern methods of structural biology and biochemistry. Topics include architectural arrangements of proteins, RNA, and DNA; practical methods in structural analysis; and an introduction to diffraction and NMR. Prerequisites: physical chemistry (may be taken concurrently) and biochemistry.

MB&B 730a, Methods and Logic in Molecular Biology  Mark Solomon, Lynne Regan, Matthew Simon, Anthony Koleske, Scott Holley, and Christian Schlieker
The course examines fundamental concepts in molecular biology through intense critical analysis of the primary literature. The objective is to develop primary literature reading and critical thinking skills. Required of and open only to first-year graduate students in BBSB.

Lecture course with emphasis on mechanisms of viral replication, oncogenic transformation, and virus-host cell interactions.

MB&B 743b / GENE 743b / MCB 743b, Advanced Eukaryotic Molecular Biology  Mark Hochstrasser, Matthew Simon, Patrick Sung, Seyedtaghi Takyar, and Wendy Gilbert
Selected topics in transcriptional control, regulation of chromatin structure, mRNA processing, mRNA stability, RNA interference, translation, protein degradation, DNA replication, DNA repair, site-specific DNA recombination, somatic hypermutation. Prerequisite: biochemistry or permission of the instructor.

MB&B 749a, Medical Impact of Basic Science  Joan Steitz, Thomas Steitz, I. George Miller, Andrew Miranker, David Schatz, Karla Neugebauer, and Seyedtaghi Takyar
Consideration of examples of recent discoveries in basic science that have elucidated the molecular origins of disease or that have suggested new therapies for disease. Emphasis is placed on the fundamental principles on which these advances rely. Reading is from the primary scientific and medical literature, with emphasis on developing the ability to read this literature critically. Aimed primarily at undergraduates. May not be taken by MB&B B.S./MS. students for graduate course credit. Prerequisite: biochemistry or permission of the instructor.

MB&B 750b, Biological Membranes  Donald Engelman
Biological membranes and their resident proteins are essential for cellular function; yet comparatively little is known about their structure and dynamics. This class provides an introduction to the biochemistry and biophysics of lipids, lipid bilayers, and lipid-derived second messengers. In addition, structural as well as functional aspects of the different classes of membrane proteins are discussed along with an outline of experimental approaches used to achieve an understanding of membrane protein structure and function at a molecular level. Counts as 0.5 credit toward MB&B graduate course requirements. Prerequisite: biochemistry.

MB&B 752b / CB&B 752b / CPSC 752b / MCB 752b, Biomedical Data Science: Mining and Modeling  Mark Gerstein
Biomedical data science encompasses the analysis of gene sequences, macromolecular structures, and functional genomics data on a large scale. It represents a major practical application for modern techniques in data mining and simulation. Specific topics to be covered include sequence alignment, large-scale processing, next-generation sequencing data, comparative genomics, phylogenetics, biological database design, geometric analysis of protein structure, molecular-dynamics simulation, biological networks, normalization of microarray data, mining of functional genomics data sets, and machine-learning approaches to data integration. Prerequisites: biochemistry and calculus, or permission of the instructor.

MB&B 753b, Biomedical Data Science: Mining  Mark Gerstein
Biomedical data science encompasses the analysis of gene sequences, macromolecular structures, and functional genomics data on a large scale. It represents a major practical application for modern techniques in data mining and simulation. This module of the full-term course MB&B 752 focuses on the first of these techniques, data mining. Specific topics include sequence alignment, comparative genomics and phylogenetics, biological databases, microarray normalization, and machine-learning approaches to data integration. Counts as 0.5 credit toward MB&B graduate course requirements. Prerequisites: biochemistry and calculus, or permission of the instructor.

MB&B 754b, Biomedical Data Science: Modeling  Mark Gerstein
Biomedical data science encompasses the analysis of gene sequences, macromolecular structures, and functional genomics data on a large scale. It represents a major practical application for modern techniques in data mining and simulation. This module of the full-term course MB&B 752 focuses on the second of these techniques, simulation. Specific topics to be covered include geometric analysis
of protein structure, molecular-dynamics simulation, and biological networks. Counts as 0.5 credit toward MB&B graduate course requirements. Prerequisites: biochemistry and calculus, or permission of the instructor.

**MB&B 760b, Principles of Macromolecular Crystallography**  Thomas Steitz and Yong Xiong
Rigorous introduction to the principles of macromolecular crystallography, aimed at students who are planning to carry out structural studies involving X-ray crystallography or who want to obtain in-depth knowledge for critical analysis of published crystal structures. Counts as 0.5 credit toward MB&B graduate course requirements. Prerequisites: physical chemistry and biochemistry.  ½ Course cr

**MB&B 800a, Advanced Topics in Molecular Medicine**  Susan Baserga and William Konigsberg
The seminar, which covers topics in the molecular mechanisms of disease, illustrates timely issues in areas such as protein chemistry and enzymology, intermediary metabolism, nucleic acid biochemistry, gene expression, and virology. M.D. and M.D./Ph.D. students only. Prerequisite: biochemistry (may be taken concurrently).

**MB&B 900a and MB&B 901b, Reading Course in Biophysics**  Yong Xiong
Directed reading course in biophysics. Term paper required. By arrangement with faculty. Open only to graduate students in MB&B. Please see syllabus for additional requirements.

**MB&B 902a and MB&B 903b, Reading Course in Molecular Genetics**  Yong Xiong
Directed reading course in molecular genetics. Term paper required. By arrangement with faculty. Open only to graduate students in MB&B. Please see syllabus for additional requirements.

**MB&B 904a and MB&B 905b, Reading Course in Biochemistry**  Yong Xiong
Directed reading course in biochemistry. Term paper required. By arrangement with faculty. Open only to graduate students in MB&B. Please see syllabus for additional requirements.