MOLECULAR BIOPHYSICS AND BIOCHEMISTRY

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M.S., M.Phil., Ph.D.

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Associate Professors Julien Berro, Titus Boggon (*Pharmacology*), Wendy Gilbert, Erdem Karatekin (*Cellular and Molecular Physiology*), Christian Schlieker, Matthew Simon, Seyedtaghi Takyar (*Internal Medicine/Pulmonary*), Yongli Zhang (*Cell Biology*)

Assistant Professors Franziska Bleichert, Allison Didychuk, Lilian Kabeche, Nikhil Malvankar, Wei Mi (*Pharmacology*), Candice Paulsen, Sarah Slavoff (*Chemistry*), Kai (Jack) Zhang

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, cell cycle control, cytoskeletal dynamics, and neuroscience. Structural and computational biology is a strong component of many of these research efforts.

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

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 (encompassed by MB&B 650 and MB&B 651, Lab Rotation for BQBS First-Year Students). All students from the BQBS track who affiliate with MB&B are required to take, for credit, six one-term science courses. To obtain the desired breadth and depth of education, students coming from the BQBS track are required to take MB&B 720, MB&B 730, one course in molecular biophysics or quantitative biology, and one course in molecular biology (MB&B 743 is strongly recommended but not required). The credit in molecular biophysics or quantitative biology and the credit in molecular biology may be satisfied by taking appropriate courses from an approved list available each fall and listed in the MB&B graduate handbook. Students originating from a BBS track other than BQBS must discuss their curriculum with the MB&B DGS prior to joining the department to ensure equivalent foundational course work in MB&B topic areas; these students are strongly encouraged to take or audit MB&B 720. 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 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 during their graduate careers, usually during the second and third years. Students who require additional support from the Graduate School must teach additional terms, if needed, after they have fulfilled the academic teaching requirement.

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 MB&B faculty members. The chair of the committee will be an MB&B faculty member who is not the research adviser; this rule was established in 2020 and applies to all students matriculating in 2019 or later. 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 MB&B 651, 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 or b / MCDB 500a or b, Biochemistry Ronald Breaker and Staff
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 / MCDB 517b / PHYS 517b, Methods and Logic in Interdisciplinary Research Corey O'Hern and Emma Carley
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 graduate course requirements. ½ Course cr

MB&B 520a, Boot Camp Biology Corey O'Hern and Emma Carley
An intensive introduction to biological nomenclature, systems, processes, and techniques for graduate students with previous backgrounds in non-biological fields including physics, engineering, and computer science who wish to perform graduate research in the biological sciences. Counts as 0.5 credit toward MB&B graduate course requirements. ½ Course cr

MB&B 523a / CB&B 523a / ENAS 541a / PHYS 523a, Biological Physics Yimin Luo
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 and Julien Berro
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 / MCDB 561a / PHYS 561a, Modeling Biological Systems I Thierry Emonet
Biological systems make sophisticated decisions at many levels. This course explores the molecular and computational underpinnings of how these decisions are made, with a focus on modeling static and dynamic processes in example biological systems. This course is aimed at biology students and teaches the analytic and computational methods needed to model genetic networks and protein signaling pathways. Students present and discuss original papers in class. They learn to model using MatLab in a series of in-class hackathons that illustrate the biological examples discussed in the lectures. Biological systems and processes that are modeled include: (i) gene expression, including the kinetics of RNA and protein synthesis and degradation; (ii)

activators and repressors; (iii) the lysogeny/lysis switch of lambda phage; (iv) network motifs and how they shape response dynamics; (v) cell signaling, MAP kinase networks and cell fate decisions; and (vi) noise in gene expression. Prerequisites: MATH 115 or 116, BIOL 101–104, or with permission of instructors. This course also benefits students who have taken more advanced biology courses (e.g. MCDB 200, MCDB 310, MB&B 300/301).

MB&B 562b / AMTH 765b / CB&B 562b / ENAS 561b / INP 562b / MCDB 562b / PHYS 562b, Modeling Biological Systems II Joe 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; 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: a 200-level biology course or permission of the instructor.

MB&B 565b, Biochemistry and Our Changing Climate Karla Neugebauer

Climate change is impacting how cells and organisms grow and reproduce. Imagine the ocean spiking a fever: cold-blooded organisms of all shapes, sizes, and complexities struggle to survive when water temperatures go up two–four degrees. Some organisms adapt to extremes, while others cannot. Predicted and observed changes in temperature, pH, and salt concentration do and will affect many parameters of the living world, from the kinetics of chemical reactions and cellular signaling pathways to the accumulation of unforeseen chemicals in the environment, the appearance and dispersal of new diseases, and the development of new foods. In this course, we approach climate change from the molecular point of view, identifying how cells and organisms#from microbes to plants and animals#respond to changing environmental conditions. To embrace the concept of "one health" for all life on the planet, this course leverages biochemistry, cell biology, molecular biophysics, and genetics to develop an understanding of the impact of climate change on the living world. We consider the foundational knowledge that biochemistry can bring to the table as we meet the challenge of climate change. Prerequisites: MB&B 500, MB&B 600, and MB&B 601, or permission of the instructor.

MB&B 570a or b, Intensive Research for B.S./M.S. Candidates Michael Koelle

Required of 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

This required course for students in the PEB graduate program involves a series of modules, co-taught by faculty, in which students from different academic backgrounds and research skills collaborate on projects at the interface of physics, engineering, and biology. The modules cover a broad range of PEB research areas and skills. The course starts with an introduction to MATLAB, which is used throughout the course for analysis, simulations, and modeling.

MB&B 600a, Principles of Biochemistry I Matthew Simon, Michael Koelle, and Candie Paulsen

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. o Course cr

MB&B 601b, Principles of Biochemistry II Christian Schlieker and Franziska Bleichert
A continuation of MB&B 600 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 / MBIO TBD-2 / MCDB 602a, Molecular Cell Biology Thomas Melia, Martin Schwartz, Shawn Ferguson, Malaiyalam Mariappan, Nadya Dimitrova, Xiaolei Su, Valerie Horsley, Megan King, Patrick Lusk, Christopher Burd, David Breslow, Shaul Yogev, and Min Wu
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. Graduate Prerequisites: Some knowledge of basic cell biology and biochemistry is assumed. Students who have not taken courses in these areas can prepare by reading relevant sections in basic molecular cell biology texts. We recommend Pollard et al., *Cell Biology* (3rd ed., 2016), Alberts et al., *Molecular Biology of the Cell* (6th ed., 2014), or Lodish et al., *Molecular Cell Biology* (8th edition, 2016). Undergraduate Prerequisites: This is a graduate-level cell biology class. Any undergraduates wishing to enroll must have already taken MCDB 205. In addition, undergraduates are strongly encouraged to reach out to the course directors prior to enrollment.

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 630b / MCDB 630b, Biochemical and Biophysical Approaches in Molecular and Cellular Biology Jing Yan and Sigrid Nachtergaele
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 BQBS graduate students.

MB&B 635a / ENAS 518a, Quantitative Approaches in Biophysics and Biochemistry Julien Berro 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 BQBS First-Year Students Christian Schlieker

Required of all first-year BQBS graduate students. Credit for full year only.

MB&B 675a, Seminar for First-Year Students Christian Schlieker, Thierry Emonet, and Karen Anderson

Required of all first-year BQBS graduate students.

MB&B 676b, Responsible Conduct of Research Susan Baserga, Christian Schlieker, Erdem Karatekin, Wendy Gilbert, Candie Paulsen, Gary Brudvig, Mark Solomon, Yongli Zhang, Enrique De La Cruz, and Mark Hochstrasser

Designed for students who are beginning to do scientific research. The course seeks to describe some of the basic features of life in contemporary research and some of the personal and professional issues that researchers encounter in their work. Approximately six sessions, run in a seminar/discussion format. Required of and open only to first-year graduate students in BQBS.

MB&B 710b / C&MP 710b, Electron Cryo-Microscopy for Protein Structure Determination Jack Zhang

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. ½ Course cr

MB&B 711b / C&MP 711b, Practical cryo-EM Workshop Jack Zhang, Yong Xiong, and Franziska Bleichert

This laboratory course provides hands-on training in the practical aspects of macromolecular structure determination by cryo-electron microscopy (cryo-EM). Topics include cryo-EM data collection, image preparation and correction, single-particle picking and 2-D classification, 3-D classification, refinement and post-processing, model building, refinement and evaluation. The course includes training in the use of computer programs used to perform these calculations. Prerequisite: MB&B 710/C&MP 710. ½ Course cr

MB&B 720a, Macromolecular Structure and Biophysical Analysis Yong Xiong and Joe Howard

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, Candie Paulsen, Matthew Simon, and Tony Koleske

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 BQBS.

MB&B 734b / GENE 734b / MBIO 734b, Molecular Biology of Animal Viruses Brett Lindenbach

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

MB&B 743b / GENE 743b / MCDB 743b, Advanced Eukaryotic Molecular Biology Mark Hochstrasser, Wendy Gilbert, Matthew Simon, and Franziska Bleichert

Selected topics in transcriptional control, regulation of chromatin structure, mRNA processing including spliceosomal splicing, mRNA turnover, RNA interference, translational regulation, protein modification, and protein degradation. Emphasis is placed on how these processes are regulated and the experiments that led to their discovery and understanding. Prerequisite: biochemistry or permission of the instructor.

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 Molecular Biophysics and Biochemistry Mark Solomon

Directed reading course in molecular biophysics and biochemistry. Term paper required. By arrangement with faculty. Open only to graduate students in MB&B. Please see the syllabus for additional requirements.