GRADUATE STUDIES IN

Biochemistry and Molecular Biophysics
The central focus of the Graduate Group in Biochemistry and Molecular Biophysics is the relationship between form and function. The goal of the program is to provide students with a foundation in the physical and quantitative methods necessary to explore the molecular basis of biological events. The faculty of the Graduate Group have a common theme of seeking to understand biological phenomena using an array of genetic, biochemical and biophysical approaches. Research topics are far-ranging and include the genetic, biochemical and structural basis of signal transduction; membrane biochemistry; biochemical imaging; mechanisms of transcription; replication and recombination; molecular immunology; protein structure, dynamics and folding; enzymology; regulation of metabolism; RNA biochemistry; de novo protein design; and the mechanism of action of large protein “machines.”

Overview

The curriculum is designed to provide a superior graduate level education by tailoring the program to each individual student in order to round out his or her knowledge of biochemistry or molecular biophysics. A central goal is to build on the strengths and interests of the student and prepare the student for dissertation research.

By the end of the second year of study, students should have achieved a general level of understanding of biochemistry, molecular biology, and cell biology appropriate for a contemporary biomedical scientist, through appropriate courses, semester-long laboratory rotations, and independent study with their intended dissertation advisor. After successfully passing a Candidacy Examination at the end of the second year, the student begins full-time dissertation research. Students also participate in research seminars and informal interactions with other graduate students, postdoctoral fellows and faculty members, all of which form an important part of graduate education.

Much of gene expression regulation in eukaryotes occurs post-transcriptionally and is mediated by RNA-binding proteins and small non-coding RNAs. Small nuclear RNP’s (snRNPs) are the major subunits of the splicing machinery that produces mRNAs. Each snRNP contains a small RNA ringed by 7 Sm proteins, a remarkable structure that is assembled by the SMN complex. Dissecting this process, the Dreyfuss laboratory captured a key assembly intermediate containing 5 Sm proteins, gripped by Gemin2 and part of SMN, and determined its crystal structure. Dreyfuss and co-workers (Cell 146:384-395, 2011).

Structure of the Rtt109/Vps75 histone acetyltransferase complex provides new insights into chaperone-mediated histone acetylation for maintenance of genomic stability in yeast. Marmorstein and co-workers (Structure 19:221-231, 2011)

Montage of electron micrographs of melanosomes, intracellular organelles of melanocytes that contain intralumenal amyloid fibrils of Pmel17. In increasing magnification from bottom are a thick section from a melanocyte, an early stage melanosome from this section, a three-dimensional electron tomograph, detail from a melanosome and finally an image of recombinant Pmel17 fibrils. Marks and co-workers (J. Biol. Chem. 281:35543-35555, 2009).
Conventional nucleosomes package chromosomal DNA and carry epigenetic marks. Specialized nucleosomes contain a histone variant, CENP-A, that epigenetically marks the chromosome location— the centromere (red dots)—that directs the inheritance of the entire chromosome (green) at cell division. The physical basis of how CENP-A marks centromere location and the relationship of CENP-A-containing chromatin to the recruitment of key regulatory proteins, such as the Aurora B kinase, are the subject of current investigation. Bassett (BMB student), Salimian (BMB student), Ballister (BMB student), Smoak (BMB student), Lampson, Black and co-workers (Nature 467:347-351, 2010, Cell 144:471-479, 2011, Curr. Biol. 21:1158-1165, 2011).

Faculty members of the Graduate Group oversee many of these resources. The Perelman School of Medicine also maintains a wide range of ancillary resources supporting almost any imaginable biomedical research effort. The vast array of research capabilities that are available is a true advantage to the students and faculty of the Graduate Group.

The ability to sense molecular tension is crucial for a wide array of cellular processes, including the detection of auditory stimuli, control of cell shape, and internalization and transport of membranes. The motor protein myosin I is important in powering key steps in these processes. Optical trap technology can be used to dissect the events of a working stroke of a single myosin I (blue) as it walks along an actin filament (red). The highlighted steps are force sensitive, resulting in a system where motile properties respond to tension. Laakso (BMB graduate, Ph.D. 2009), Ostap and co-workers (Science 321:133-136, 2008).
Student Activities

In addition to classes and research, students participate in many activities that enhance their education and development as scientists. These activities help students develop a network of contacts, acquire career skills, and interact with faculty in less formal environments. In addition, social activities provide a support system and, most importantly, foster long-lasting friendships.

**Friday Research Discussions:** Every Friday during the academic year, faculty, students and postdocs gather over refreshments in the Johnson Foundation Library to listen to a faculty member describe his or her research.

**Annual Retreat:** This two-day event is sponsored by the Graduate Group and the Department of Biochemistry and Biophysics. Students, faculty, and postdocs present their work in poster sessions and talks. A highlight of this event is the student-faculty softball game, followed by the annual picnic.

BMB students also participate in many other activities across the University campus, including the Chemistry and Biology Interface Training Program, which holds student-organized mini-symposia in chemical biophysics, discussion groups, and an annual retreat.

Finally, another unique aspect of the Graduate Group in Biochemistry and Molecular Biophysics is that students play an active role in shaping the program. Student representatives sit on most major committees within the Graduate Group. The faculty seriously considers student input; in fact, many features of the current program are the direct result of student suggestions.

The Johnson Research Foundation is a significant resource for the Graduate Group. Established in 1929 as the world’s first institute dedicated to biophysical research, this pioneering research foundation motivates and supports investigation of the fundamentals of biological design and function, focusing on protein structure and engineering in three dimensions from angstroms to microns. It continues its tradition of bringing advanced chemistry and physics to biology and medicine.
Molecular-mechanical modeling of a Dam1 ring on a depolymerizing microtubule. Grishchuk and co-workers (PNAS 104:19017-19022, 2007; PNAS 105:15423-15428, 2008.)

Above: Molecular chaperones in the endoplasmic reticulum govern proper protein folding and assembly. The ATPase activity of the chaperone GRP94 is required to support the production of the insulin-like growth factor. Shown is live cell imaging of a GRP94 red fluorescence protein fusion that facilitates mechanistic study of GRP94. It is expressed properly in the ER, as shown by co-localization with an ER marker (GFP-KDEL), and is an active chaperone. Argon and co-workers (PNAS 106:11600-11605, 2009).

At right: A designed and engineered artificial oxygen transport protein maquette offers not only a fresh approach to the long sought-after substitute blood, but represents the first critical step in a broad spectrum of enzymatic oxidative transformations; in respiratory energy conversion, metabolism and drug dissimulation. When reproduced in simple maquette protein scaffolds, these activities will on the one hand elucidate the minimal requirements for biological function, and on the other yield working proteins that may one day provide useful technology. Solomon (BMB student), Dutton and co-workers (Nature 458:305-309, 2009).
University of Pennsylvania

Penn is a national leader in higher education and enrolls about 20,000 full time students in its 12 graduate and professional schools. Located across the river from Center City Philadelphia, the Penn campus provides students with easy access via public transportation to a great variety of attractions: numerous museums and art galleries, opera, symphony, ballet, concert and film houses, all major professional sports, renowned gourmet and ethnic restaurants and food markets, the world’s largest city park system, and a wealth of historic landmarks and architectural treasures. Students choose among a variety of affordable housing options on campus and throughout the surrounding neighborhoods.

Penn is unique among its Ivy League peers in having all of its schools located on a single campus, facilitating interdisciplinary discourse and research. As home to the nation’s first medical school and first teaching hospital, Penn has a strong tradition in biomedical research and training. Penn ranks third in the nation in funding from the National Institutes of Health, and its Perelman School of Medicine is ranked second in NIH training grant funding. Additional information is available at http://www.upenn.edu.

Biomedical Graduate Studies

Biomedical Graduate Studies (BGS) serves as the academic home for more than 700 graduate students pursuing a Ph.D. in the basic biomedical sciences. The program is organized into seven graduate groups: Biochemistry and Molecular Biophysics, Cell and Molecular Biology, Epidemiology and Biostatistics, Genomics and Computational Biology, Immunology, Neuroscience, and Pharmacological Sciences. Over 600 faculty members representing more than thirty academic departments and seven schools throughout the University participate in BGS and cooperate in admitting, funding, advising, training, and providing career development information to BGS students. The program's structure provides for exceptionally broad-based, flexible, and interdisciplinary training. Graduate groups in BGS also participate in combined degree programs with the Perelman School of Medicine (M.D.), the School of Veterinary Medicine (V.M.D.), and the School of Dental Medicine (D.M.D.). BGS students may also enroll in certificate programs in medicine (HHMI Med into Grad Scholars Program), public health (PHCP), and environmental health issues (EHS). Each program has its own application process. More information about BGS, the combined degree programs, and the certificate programs can be found at www.med.upenn.edu/bgs.

Application and Financial Aid

Admission for Ph.D. study is offered to students having good undergraduate training in biochemistry, physics, organic chemistry, physical chemistry, biology and mathematics. The Graduate Record Examination (GRE) General Test is required; GRE Subject Tests in biology, biochemistry, chemistry, physics, or mathematics are recommended but not required. Completed applications are screened by the Admissions Committee and decisions on admission are based on undergraduate record, GRE scores, letters of recommendation and personal interviews. TOEFL scores are required for international students whose native language is not English.

All students who are admitted receive a fully funded fellowship, including tuition, fees, health insurance, and a competitive stipend. The deadline for applications for entrance in the following fall term is December 8. Applications are accepted online via the BGS website: www.med.upenn.edu/bgs.

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