

Your training will incorporate biology, physics, computing, and engineering to enable investigation of human health and disease at the molecular, cellular, and systems levels. Your research could ultimately lead to the design of novel therapeutics for disease prevention and treatment.

GRADUATE PROGRAM IN
**PHYSIOLOGY
BIOPHYSICS &
SYSTEMS
BIOLOGY**

STRUCTURE AND FUNCTION
OF MOLECULAR ASSEMBLIES

CELLULAR AND
BIOMOLECULAR IMAGING

NETWORK ARCHITECTURE
AND FUNCTIONAL DYNAMICS

ORGANOGENESIS AND
DEVELOPMENT

COMPUTATIONAL MODELING
OF MOLECULAR AND
SIGNALING PROCESSES

BIOINFORMATICS AND
COMPLEX SYSTEMS ANALYSIS

<http://pbsb.med.cornell.edu>



Cornell University
Weill Medical College

THE GRADUATE PROGRAM IN

PHYSIOLOGY BIOPHYSICS & SYSTEMS BIOLOGY (PBSB)

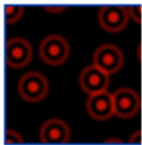
HANDBOOK 2010

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PHYSIOLOGY, BIOPHYSICS AND SYSTEMS BIOLOGY (PBSB)

OVERVIEW:



From different, but complementary perspectives, and taking advantage of advanced specialized methods, the biomedical research disciplines of ***Physiology and Biophysics*** seek to discover, analyze and explain the functions of the human body's building blocks: cells, tissues and organs. The availability of information from genomics, imaging and proteomics, combined with the power of computational methods, has enabled entirely new approaches for making these discoveries and relating them to the most basic molecular mechanisms. Most importantly, these new approaches make it possible to integrate in the research activities of the Program's faculty, the findings from genetics, structural biology, and cell and molecular biology with principles and representations from physics and engineering. Together, they create a systems-level view of function in physiological components (e.g., from the cell to the heart, and from the neuron to the nervous system). This new integrative perspective, termed ***Integrative Systems Biology***, complements and completes the study of structure and mechanisms of the body's building blocks from their embryonic development to their mature function, in both healthy and diseased states. ***The Physiology, Biophysics and Systems Biology (PBSB)*** graduate program is designed to engage the students in education through research in current and innovative aspects of these three synergistic components of modern biomedicine.

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COMPLETE PBSB FACULTY LIST

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PBSB FOCUS AREAS

- **Biophysical and Physiological Mechanisms of Membranes and Membrane Proteins:** Work in the labs of Drs. Anderson, Boudker, Christini, Palmer, and H. Weinstein has uncovered remarkable molecular properties of channels and receptors that make possible cell function and intercellular communication in the brain, and throughout the body. The discrete mechanisms of these complex molecules were revealed from creative experimental designs, as well as computational modeling and simulation. In parallel, the discovery of some previously unknown genes and their function has enabled the laboratories of Drs. Huang and Weinstein to outline the signal transduction mechanisms that connect the membrane protein signals to gene expression and regulation. All these insights enable as well the development of novel therapies and the design of targeted drugs.
- **Quantitative and Integrative Systems Biology:** With quantitative measurements of physiological processes, mathematical modeling, computational simulation, and bioinformatics, the laboratories of Drs. Aksay, Clancy, Christini, Gardner, Leibler, Nirenberg, Victor, A.M. Weinstein, and H. Weinstein have represented the components and calculated the parameters of fundamental mechanisms in neurophysiology and in the function of organs such as the heart. The approaches include construction and interpretation of gene or cell signaling networks for which a variety of questions are answered, such as the robustness and sensitivity of networks with respect to biochemical modifications of their components, the resistance of genetic networks to molecular noise, such as the noise connected with fluctuations in the number of different components, and the precision and establishment of proportions (scaling) in spatial pattern formation. The formal and quantitative models can create a new perspective on how the cellular and network properties of individual neurons, and the information they convey, give rise to the complex behavior of the brain. The mathematical models are able to integrate experimental information from basic and clinical studies to reveal the most fundamental underpinning of complex physiological mechanisms, and the mode of perturbation by disease or genetic mutations. For example, mathematical modeling of solute and water transport across the renal epithelia are developed to produce a mathematical model of the mammalian distal nephron in order to assess the extent to which known defects can account for observed solute excretion patterns. Conversely, simulations of clinical tests of distal nephron function can be used to evaluate their accuracy in defining a specific transport defect. Similarly, modeling of ion channels in heart cells where molecular defects disrupt the delicate balance of dynamic interactions between the ion channels and the cellular environment, results in simulations that reveal how the resulting altered cell function manifests itself as cardiac arrhythmia.
- **Organogenesis and Physiological Genomics:** To answer the key questions about the development of the complex functions in specialized cells of tissues and organs, the laboratories of Drs. Basson, Herzlinger and Coonrod identify both the genes that regulate differentiation, and the nature of the inductive signal that triggers multipotent organogenic progenitors to differentiate. For example, molecular genetic techniques were applied to identify novel genes that regulate cardiac differentiation and morphogenesis, in order to understand

a number of congenital and inherited disorders of human cardiac growth and development. Similarly, a single gene product was shown to trigger embryonic renal cell differentiation. The life span of animals is also genetically controlled, and the rate of cellular aging can be regulated by genes that directly affect intracellular mechanisms for protection, turnover, and repair of macromolecules and cell membranes. The lab of Dr. Huang has developed a genetic screen for gene mutations that extend life-span in *Drosophila*, and has isolated a mutant methuselah (*mth*) that displays increased average life-span and enhanced resistance to various forms of stress. The *mth* gene encodes a membrane protein (G protein-coupled receptor) that signals to biochemical mechanisms regulating the aging process.

- **Aspects of Biomedical Imaging and Bioengineering:** Faculty members with laboratories at the Hospital for Special Surgery (Drs. Boskey, Torzilli) and in the Imaging Center (Ballon, Wang) complement the quantitative research aspects with perspectives on physiological processes in tissue engineering, and the biophysics of biomedical imaging. The research directions include quantitative aspects of the physiology of biomineralization, analyzed with biophysical methods from the structure of mineral and matrix in health and disease, and the engineering of soft tissues. Such approaches take advantage of and are often supported by development and application of novel techniques for imaging tissues and mechanisms, e.g., of malignancies of the bone marrow, breast and other organs. New methods are being developed to assess properties and understand mechanisms of drug delivery, so as to provide insights needed for new therapies and tissue engineered products.

STUDENT GUIDANCE

The graduate school experience is only as good as the guidance offered. The PBSB faculty take advising very seriously and dedicate a great deal of time to the mentoring effort. The guidance students receive happens in many settings, from informal discussions at the laboratory bench to formal evaluations during periodic reviews:

- During the first year students will meet with a Program Director (Aksay) a minimum of three times to discuss progress in courses, research rotations, and thesis decisions. The Director will serve as the primary mentor and is available at a snap of fingers.
- During the first year students also obtain guidance and direction from three rotation faculty.
- At the end of the first year students identify their thesis advisor, who then becomes the primary mentor.
 - Faculty critique and evaluation of research progress is offered when, at the beginning the 2nd year, students present at the Program retreat and du Vigneaud graduate school symposium.
- During the second year students form their Special Committee, consisting of the thesis advisor and two other faculty. This committee is the primary guidance body that monitors student progress until graduation.
- In advance of the ACE and Thesis examination, additional faculty are added to your special committee to form a body that in many ways is there to help prepare you as they are to test you.

PBSB REQUIREMENTS and CALENDAR

REQUIREMENTS:

Prior to the taking the ACE exam, a student must take 3 Core courses, 2 electives, and 2 Seminar course series. Students should also complete 3 research rotations.

Students start their thesis research before completing their formal course-work, but they are not admitted to Ph.D. candidacy until passing their Admission to Candidacy Exam (ACE) at the end of the second year.

FIRST YEAR, SEPTEMBER - DECEMBER

- Cell Physiology (*core course 1*)
- Logic and Experimental Design (*core course 2*)
- Faculty research lunches. (*seminar course 1*)
- PBSB Monday seminars (*seminar course 2*)
- Tri-Institutional Responsible Conduct of Research Course (*mandatory*)
- Begin Rotation #1 (*by mid-September*): *Submit laboratory rotation agreement to Program Coordinator*
- Meeting with Program Director (*Aksay, October*)
- End Rotation #1 (*by late-December*): *Submit rotation report and faculty evaluation to Program Coordinator, present to classmates.*

FIRST YEAR, JANUARY - MARCH

- Essentials of Human Systems Physiology (*core course 3*)
- Quantitative Understanding in Physiology (*core course 4*)
- Scientific Presentation and Critique (*seminar course 1*)
- PBSB Monday seminars (*seminar course 2*)
- Begin Rotation #2 (*by early-January*): *Submit laboratory rotation agreement to Program Coordinator*
- Meeting with Program Director (*Aksay, February*)
- End Rotation #2 (*by late-March*): *Submit rotation report and faculty evaluation to Program Coordinator, present to classmates.*

FIRST YEAR, APRIL - JUNE

- Continue courses
- Begin Rotation #3 (*by early-April*): *Submit laboratory rotation agreement to Program Coordinator*
- Meeting with Program Director (*Aksay, June*)
- End Rotation #3 (*by late-June*): *Submit rotation report and faculty evaluation to Program Coordinator, present to classmates.*

FIRST YEAR, SUMMER

- Students join their thesis laboratory and begin research
or
- complete a fourth rotation and decide on a thesis lab (*by early September.*)

SECOND YEAR

- Continue research in thesis lab
- Present thesis ideas and early data at Program Retreat (*October*)
- Complete 2 electives (*can be chosen from any of the tri-institutional offerings*)
- PBSB Monday seminars (Seminar Course 2)
- Form and meet with your special committee to discuss thesis and ACE goals (*by December*): *Submit committee meeting report to Program Coordinator*
- ACE Tutorial (*January*)
- Scientific Presentation and Critique (*March-June*)
- ACE exam (*by July 1st*)

THIRD YEAR +

- Continue research in thesis lab
- Present at Program Retreat
- Annual special committee meetings
- Annual meetings with a Program Director (X-Y Huang)
- Present in student research seminars (X-Y Huang)
- Present at du Vigneaud Symposium
- Present at national research meetings
- Publish!

FORMAL COURSES OFFERED BY PBSB:

The course of study in the PBSB Program is organized into modular courses and seminars offering education at the conceptual level, as well as in the experimental and computational tools of the component disciplines (Physiology, Biophysics, & Systems Biology), and offers immersion in specific research topics.

COURSES OFFERED ANNUALLY:

Physiology, Biophysics and Systems Biology Research Seminar Series, Quarters I-IV (required)

This required course exposes students to recent research developments in PBSB faculty focus areas including:

- Biophysical and Physiological Mechanisms of Membrane and Membrane Protein Function
- Quantitative and Integrative Biology
- Organogenesis and Physiological Genomics
- Biological and Biomedical Imaging

Essentials of Human Systems Physiology, Quarters II-IV (required):

This course consists of three parts. Assigned independent readings from a textbook of human physiology (Medical Physiology by R.A. Rhodes and G.A. Tanner, 2nd Edition, Lippincott Williams & Wilkins) followed by presentations and discussion of the readings led by an instructor. Assignments of Special Topics, Journal Articles, and/or Physiological Problems for student presentation and discussion in class. Physiology laboratories, including laboratories with mannequin simulators of physiological functions.

Course Directors: [Dr. Lawrence Palmer](#): Cell Physiology , [Dr. Bernice Grafstein](#):

Cell Physiology, Quarters I-II (required):

This course will focus on important aspects of cell physiology that are required for normal cell functioning and disease processes. The contributions of specific organelles and molecular pathways in these processes will be discussed in the context of proper cell function. Topics in theories of biophysics and bioelectricity will also be covered. The course is divided into 5 modules to address each of the following areas:

Biomolecules; Cell structure
Cell and protein structure/function
Membrane proteins
Cell Biophysics
Cell signaling

Course Director: [Dr. Crina Nimigean](#)

Faculty Research Lunches, Quarters I-II (required):

This course is required for all 1st year PBSB graduate students, but is open to all WGSMS students. Come for lunch and listen to your program faculty describe their research. Make informed decisions about your laboratory rotations!

Course Director: [Dr. Emre Aksay](#)

Scientific Presentation and Critic, Quarters III-IV: (Required)

This course is required for all 1st and 2nd year PBSB graduate students, but is open to all WGSMS students. It is designed to train students in scientific presentation and critique. The structure is a formalized, in depth "journal club". Each 1st year student will choose a paper from a list provided by the Course Directors. Each 2nd year student will select a paper in their thesis field, subject to approval of the Course Directors. Each session will consist of a student formally presenting their selected paper to the class, which is expected to serve as a critical audience. The presentation should consist of an introduction of the relevant background literature, an objective presentation of the study, a subjective analysis/critique of the work, and suggestions for future work. Presentations by 2nd year students will be scheduled first, giving the 1st year students the opportunity to learn from their more senior colleagues. Grading will be based on presentation quality and contribution to constructive feedback.

Course Directors: [Dr. Emre Aksay](#) and [Dr. David Christini](#)

Quantitative Physiology, Quarters III-IV:

This course will enable students to be able to formulate, evaluate, and analyze the results of mathematical models important to understanding biological function. Developing the ability to communicate quantitative data and concepts verbally and graphically as well as mathematically is also stressed. This course will emphasize practical as well as theoretical skills; many lectures will be given in a 'hands-on' workshop style, and completion of several projects will be required. Topics in algebraic systems, statistical models, differential equations, non-linear dynamics, and numerical methods are introduced to enable quantitative modeling in arenas such as neural function, enzyme kinetics, cardiac dynamics, and signaling pathways.

Course Director: Jason Banfelder

Introduction to Bioengineering, Quarters III-IV

The objective of this one semester course is to prepare graduate students at the Weill Medical College for thesis research in fields that encompass bioengineering. The course will be team taught by Weill and Ithaca faculty using video conferencing facilities. Examples will be chosen from musculoskeletal and cardiovascular fields.

Course Director: [Dr. Boskey](#)

Principles of Biomedical Imaging, Quarters III-IV:

This survey course will cover the basic physical, biochemical, computational, and engineering principles underlying current medical imaging techniques, including magnetic resonance imaging, positron emission tomography, radionuclide production and radiochemistry, optical imaging, x-ray computed tomography, and ultrasound. The goal of the course will be to provide students with a broad knowledge of the concepts and implementation strategies of various imaging methods relevant in current research and clinical practice. Practical applications will be used to illustrate the main themes of the course. Tours of the Biomedical Imaging Core Facility and other imaging laboratories will augment the formal course material. At the end of the course students will be able to identify appropriate imaging strategies for clinical research and have a working knowledge of the major techniques available to the investigator.

Course Director: Dr. Douglas Ballon

Physiological Genomics of the Cardiovascular System, Quarter IV:

A journal club and discussion seminar approach will be used to study the process of gene regulation of cardiovascular organogenesis and function. The course will focus on fundamental advances in our knowledge in genomics and how genes regulate the structure, organization, and activity of the heart and vasculature. Weekly sessions will address topics that range from molecular to cellular to tissue to organ to organismal events.

Course Director: Dr. Cathy Hatcher

COURSES OFFERED EVERY OTHER YEAR:

Bioinformatics, Quarters III-IV

This course begins with a discussion of the history, techniques and statistical analyses used in bioinformatics today. Students will begin to analyze how these tools can be used to predict RNA, gene and protein structure. The final two weeks of the course will be focused on systems biology including current techniques used to model of protein-protein interactions, protein networks and cell signaling.

Course Director: [Dr. Lucy Skrabanek](#)

Mathematical Structures in Neuroscience, Quarters I-II

Introduction to the tools of computational and theoretical neuroscience, with a focus on principles and mathematical foundations. Students should be familiar with complex numbers, matrices, and univariate differential and integral calculus.

[The specific topics may be adjusted based on class interest]

Course Director: [Dr. Jonathan Victor](#)

LABORATORY ROTATIONS

Laboratory rotations are an important part of the graduate program at Cornell, giving students the opportunity to experience different research projects and allowing the faculty to assess the interests and aptitude of the students. Each student is required to rotate through 3 laboratories, each rotation lasts approximately 9-12 weeks.

At minimum, two laboratory rotations will be undertaken with PBSB program faculty.

To facilitate and optimize the rotation experience for both the student and faculty, it is important that they meet prior to the start of the rotations to discuss expectations, goals, requirements and laboratory guidelines.

PBSB ADMISSION TO CANDIDACY EXAM (ACE)

Requirements and Procedures

Document version: 2010-03-17 (EA)

Document relevance: Guidelines in this document expand upon those detailed in the Weill graduate school Code of Legislation Section X.B and the form entitled Regulations for the Admission-to-Candidacy Examination (ACE). Where there is conflict, the guidelines herein should be followed. Tri-I and Linkage students should follow the guidelines of their governing program if they conflict with the PBSB program guidelines.

Prerequisites: Prior to taking the ACE, the student must have passed all coursework designated by the student's Faculty Advisors and the Program Director.

Timing: Preparation for the ACE should begin before or during the third quarter of year 2. The exam must be completed by the end of the fourth quarter of year 2. Delays need to be approved by the Director.

Structure: The ACE consists of a tutorial study program resulting in a written research proposal and an oral component.

- The purpose of the ACE exam is to demonstrate that the student has attained a breadth of knowledge and depth of understanding commensurate with the high standards of the Doctor of Philosophy, and that the student is prepared to undertake full time thesis research. Accordingly, this examination should be a rigorous and meaningful determination of the student's ability to employ and interpret information in an area of specialization and in a more general context.
- The proposal to be defended can either be 'on thesis' or 'thesis related'. On thesis proposals will cover the student's progressing and planned thesis work. Thesis related proposals will present and defend a research plan that is on a subject related to the student's thesis project. The determination of which ACE examination format will be completed is made by the Principal Investigator.
- For 'on thesis' examinations, recognize that although preliminary data is not required, proposals with technical novelty will need to defend feasibility.

Committee: The ACE committee, which must be approved by the PBSB Director, will be comprised of 4 examiners: One examiner will be the student's thesis advisor, two others will be selected by the student and PI, and an ACE Committee Chairperson will be selected by the Director. All members of the committee must be WGSMS faculty. The student's thesis advisor cannot serve as Chairperson.

During the written process, committee members are expected to provide some guidance; however, committee members may not write or be directly responsible for any part of the proposal. It is expected that the committee members be available for discussion and feedback on the proposal details. The committee members are encouraged to provide feedback and critique at the level that they would when writing summaries for R01 reviews.

During the oral process, committee members are free to pose any question commensurate with the aims of the ACE, but are not free to provide answers or direct guidance. The thesis advisor is also free to ask questions. The Chairperson is responsible for ensuring the fairness of the questioning.

Exam Introduction: As the first step of the examination, the student should discuss with their advisor the format of the ACE to be followed and the topic to be defended. The student should then formulate a one-page, specific-aims summary of their proposal. The student should then use this aims page as an introduction to their project as they seek to identify committee members. Once the committee is defined, the student should organize a pre-meeting with their committee to formally introduce the project and discuss any amendments to the plan. The purpose of this meeting is largely to determine if the scope of the ACE proposal is appropriate. Once the committee agrees that the aims and plan are well chosen, the student should commence with writing the ACE exam. If a full committee meeting cannot be scheduled in a reasonable time the student should seek similar guidance through individual meetings with each committee member.

Written exam: The student should take ~2 months to complete the written portion of the examination. The written research proposal should be no more than 15 pages in length (12 pt font, single-spaced, 1" margins), including figures, but not counting references. The proposal must follow the format of a NIH R01 research grant proposal (note 15 pages are allowed as opposed to the 12 page limit of the NIH):

- 1) Title page (Title, Advisor, Committee)
- 2) Specific Aims - State the problem to be addressed and the specific aims of the proposed research. The importance of the problem at the molecular, cellular and organismal levels should be discussed. If pertinent, it is important to address the possible clinical relevance. (required length: 1 page)
- 3) Research Strategy - Significance: General background, significance in terms of basic science and disease relevance.
- 4) Research Strategy – Innovation: Explain how your proposal differs from what others have tried.
- 5) Research Strategy – Approach: More specific background information. Describe in detail the experimental design and research methods to be used. Technical hurdles to be overcome should be mentioned. Alternative approaches should be given for experiments that may not be feasible. Discussion of expected or possible results and their interpretation. Best format for each specific aim: a) rationale, b) methods, c) expected results, d) alternatives. Theory aims should follow a similar structure where possible.
- 6) References should be comprehensive and cited in full at the end of the entire proposal. Avoid leaning too much on review articles, expect to get questions on primary literature.

The student should consult with the members of the ACE Committee while preparing drafts of the proposal. The student's final draft of the proposal must be submitted to all four committee members. The committee is obligated to read and evaluate the proposal within two weeks. Committee members can approve the proposal as written or request revisions and resubmission. All four committee members must approve the written proposal and sign the "ACE written-exam approval form", which is to be submitted to the Program Director before the oral component can be scheduled. Each member of the committee is encouraged to provide the student with a short written critique of the proposal.

Oral exam: The oral component can be scheduled as early as three weeks after the written proposal is approved. The oral component must be scheduled officially with the Graduate School office.

After all members are convened, the student will be excused. During this time, the committee will discuss the student's academic process, the written ACE exam, and any other pertinent issues.

The oral component will then continue with a presentation by the student describing the salient features of the written proposal. The prepared presentation should be 20 to 30 minutes, but it may last longer if the committee chooses to ask extensive questions during the presentation. During and/or after the presentation, the committee will question the student. The committee's questions will likely focus primarily on the significance of the problem addressed, the basic biological principles governing the problem, and the logic of the experimental approach used. Furthermore, the committee will probe the student's knowledge of the relevant scientific areas (thus, any question is "fair game"), thereby ensuring that the student is an appropriate doctoral candidate in PBSB.

When the discussion has concluded, the student will again be excused from the room. The committee will discuss and vote on the exam according to the rules of the Graduate School. The committee will make a written evaluation of the student, which will be forwarded to the Graduate School by the committee chairperson. The committee will convey the assessment to the student before the committee disperses.

Passed exam: Handshakes, hugs, kisses... now get to work!

Tabled exam: If, according to the voting rules of the Graduate School, the ACE committee tables the student's ACE exam (i.e., for the written and/or oral components), the student must attempt to correct deficiencies as specified by the committee (remedies may include retaking the ACE exam) within 2 months. Final disposition of the ACE exam must be no later than 3 months from the date of the original ACE exam. Exceptions need to be approved by the Director.

Failed exam: If, according to the voting rules of the Graduate School, the ACE committee determines that a student has failed her/his ACE exam (i.e., failure to pass both the written and oral components) an academic review by the Academic Oversight Committee will occur. The Academic Oversight Committee will consider the student's global academic performance and can recommend that the student be allowed to reattempt the ACE exam or that the student be asked to leave the Program. If the

student is allowed to reattempt the ACE exam, the Academic Oversight Committee will set an appropriate timetable.

Pass for Master of Science Only: The PBSB ACE rules for “Pass for Master of Science Only” are as defined by the Graduate School. Critically, note that the student must request before the oral examination begins that they would like to be considered for a Master of Science instead of continuing for the Doctorate.