

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>

# THE GRADUATE PROGRAM IN PHYSIOLOGY BIOPHYSICS & SYSTEMS BIOLOGY (PBSB)

## HANDBOOK – FALL 2017



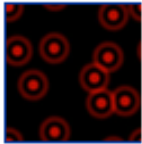
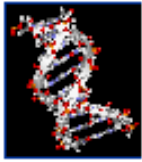
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# PHYSIOLOGY, BIOPHYSICS AND SYSTEMS BIOLOGY (PBSB)

## 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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 Weill Cornell Medical College (WCMC)

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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 2<sup>nd</sup> year, students present at the Program retreat and du Vigneaud graduate school symposium.
- During the second year, students form their Special Committee, which consists of the thesis advisor and at least two other Weill Cornell Graduate School of Medical Sciences (WCGS) 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 an examination 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 4 Core courses, 2 electives, and 3 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

- Contemporary PBSB: Cells, Systems, and Quantitative Methods – Modules 1, 2, and 3 (*core course 1*)
- Quantitative Understanding in Biology I (*core course 2*)
- PBSB Wednesday Seminar Series (*seminar course 1*)
- Faculty Research Presentations (*seminar course 2*)
- Tri-Institutional Responsible Conduct of Research (RCR) (*mandatory*)
- Begin Rotation #1 (*by mid-September*):
  - Register online at LEARN - <https://learn.weill.cornell.edu/ics>
  - Complete online Laboratory Rotation Agreement Form with Rotation Preceptor
- Meeting with Program Director (*Emre Aksay, Ph.D., October*)
- End Rotation #1 (*by late-December*):
  - Complete online Laboratory Rotation Evaluation Form with Rotation Preceptor

## FIRST YEAR, JANUARY - MARCH

- Contemporary PBSB: Cells, Systems, and Quantitative Methods – Modules 4, 5, and 6 (*core course 3*)
- Quantitative Understanding in Biology II (*core course 4*)
- Critical Dissection of Scientific Data (CDS) (*seminar course 3*)
- PBSB Wednesday Seminar Series (*seminar course 1 - continued*)
- Begin Rotation #2 (*by early-January*):

- Register online at LEARN - <https://learn.weill.cornell.edu/ics>
  - Complete online Laboratory Rotation Agreement Form with Rotation Preceptor
- Meeting with Program Director (*Emre Aksay, Ph.D., February*)
  - End Rotation #2 (*by late-March*):
    - Complete online Laboratory Rotation Evaluation Form with Rotation Preceptor

### **FIRST YEAR, APRIL - JUNE**

- Continue courses
- Begin Rotation #3 (*by early-April*):
  - Register online at LEARN - <https://learn.weill.cornell.edu/ics>
  - Complete online Laboratory Rotation Agreement Form with Rotation Preceptor
- Meeting with Program Director (*Emre Aksay, Ph.D., June*)
- End Rotation #3 (*by late-June*):
  - Complete online Laboratory Rotation Evaluation Form with Rotation Preceptor

### **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, should be equivalent to a core course in workload. See Director for options or special cases*)
- PBSB Wednesday Seminar Series
- Form and meet with your special committee to discuss thesis and ACE goals (*by December*): *Submit committee meeting report to Program Coordinator*
- ACE Tutorial (*November*)
- Critical Dissection of Scientific Data (CDS) (*February-June*)
- ACE exam (*begin preparation in January, complete by June 30<sup>th</sup>*)

## **THIRD YEAR +**

- Continue research in thesis lab
- Present at Program Retreat
- Annual special committee meetings
- 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.

Course updates can be found on the PBSB website at <http://pbsb.med.cornell.edu/courses/index.php>

### **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

Course Directors: Dr. Alessio Accardi

#### **Contemporary PBSB: Cells, Systems, and Quantitative Methods - Quarters I-IV (required):**

Course content and organization are designed to prepare students for twenty-first century research in the function, analysis, modeling, and understanding of living systems at each of several scales, from the molecular through the cellular to the organ system and organism. Multiscale and translational examples develop conceptual skills necessary to design meaningful experiments, derive insight from journal reports, work within the group structure now essential for contemporary research, and communicate new developments and related findings to today's peers and future students. Structural and developmental concepts are covered as they illuminate function.

Each module consists of multiple weeks. Typical weeks for modules CPBSB1 through 5 include two in-depth lecture-conferences that combine careful presentation of core material with student participation, and conclude with either a computational analysis and/or model, or a relevant illuminating article from the literature. The final module, CPBSB6, introduces new instructional modalities and perspectives designed to instill skills essential for researchers.



The six modules are:

CPBSB 1: Membranes and cells (MAC)

CPBSB 2: Protein function signaling and synthesis (PFSAS)

CPBSB 3: Control and communication in bodies and brains (CCBB)

CPBSB 4: Action and mechanical work from biochemical energy ( $\Delta G$ )

CPBSB 5: Introduction to Computational Systems Biology (CSB)

CPBSB 6: Physiology of Systems and Diseases

Each module consists of multiple weeks. Each week includes two in-depth lecture-conferences that combine careful presentation of core material with student participation, and concludes with either a computational analysis and/or model, or a relevant illuminating article from the literature.

Course Director: Dr. Daniel Gardner

### **Faculty Research Presentations / 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

### **Quantitative Understanding in Biology I-II, Quarters I-III:**

This course will prepare students to apply quantitative techniques to the analysis of experimental data. To emphasize both practical and theoretical skills, the course will involve several hands-on workshops, and the completion of several projects will be required. Students will be well positioned to meet the emerging requirements of funding agencies for formally planned experiments and fully reproducible and documented data analysis methods.

Specific topics include: practical aspects of data formatting and management; graphical, mathematical and verbal communication of quantitative concepts; a review of statistics, with emphasis on the selection of appropriate statistical tests, the use of modern software packages, the interpretation of results, and the design of experiments; the formulation, evaluation, and analysis of mathematical models of biological function, with an emphasis on linear and non-linear regression, determination of model parameters, and the critical comparison of alternative models with regard to over-parameterization.

Course Director: Jason R. Banfelder, MCh.E., Dr. Luce Skrabanek, and Dr. Michael LeVine

### **Critical Dissection of Scientific Data, 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. Carl Blobel, Dr. Olga Boudker, and Dr. Christopher Mason

### **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 J. Ballon

### **Principles of Medical Imaging, Quarters I-II:**

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. Yi Wang

Prerequisite: Calculus based physics is required.

*NOTE: This course is video-conferenced from Ithaca most of the time.*

### **Quantitative Genomics and Genetics, Quarter III:**

A rigorous treatment of analysis techniques used to understand complex genetic systems. This course will cover both the fundamentals and advances in statistical methodology used to identify genetic loci responsible for disease, agriculturally relevant, and evolutionarily important phenotypes. Data focus will be genome-wide data collected for association, inbred, and pedigree experimental designs. Analysis techniques will focus on the central importance of generalized linear models in quantitative genomics with an emphasis on both frequentist and Bayesian computational approaches to inference.

Course Director: Dr. Jason G. Mezey

*NOTE: Taught on both the Ithaca and Weill campus by Video-conference*

### **Molecular Mechanisms of Membrane Transport, Quarters III- IV:**

This course focuses on the biophysics, properties, and physiological roles of ion channels and transporter. We discuss the contributions to cell function in physiology and pathology of the principal ion channel and transporter families. We emphasize the mechanistic insights that have emerged from the recent explosion of structural information and how this has drastically changed our understanding of gating and selectivity of these proteins.

Course Directors: Dr. Crina Nimigean and Dr. Alessio Accardi

### **COURSES OFFERED EVERY OTHER YEAR:**

#### **Mathematical Structures in Neuroscience, Quarters III-IV:**

The course will present a range of mathematical approaches that play a central role in systems neuroscience, both for model-driven and data-driven investigations. We will take an approach beginning with the mathematical fundamentals, and emphasize concepts rather than theorems.

Typical topics include time series analysis, linear and nonlinear systems theory, point processes, dimension reduction techniques, and information theory; these can be tuned to the needs of the group. For topics, notes, and homework problems from previous years, please see

<http://www-users.med.cornell.edu/~jdvicto/mathcourse1011.html>  
and  
<http://www-users.med.cornell.edu/~jdvicto/mathcourse0809.html>

Prerequisites include familiarity with matrices and basic linear algebra, complex numbers, and calculus, preferably multivariate.

Course Director: Dr. Jonathan Victor

### **Scientific Computing in Biomedicine, Quarters I-II:**

This course will teach students the fundamental skills and knowledge required for scientific computing in the biomedical sciences. Topics include: scripting, working with large datasets, data and software management, and effective use of high-performance computing resources. Students will learn relevant theory as well as develop practical application skills using contemporary tools and technologies including R for data analysis and presentation, SQL databases for structured data management, the Ruby scripting language for practical programming tasks, git for software and data revision control, Sun Grid Engine for batch job management on large clusters, and Maestro from the Schrödinger Suite for molecular modeling and visualization.

Prerequisites: familiarity with basic UNIX/Linux environment and commands (vi/emacs, stdin/stdout/pipe, grep and regular expressions).

Expectations: In addition to two classroom hours per week, students will be expected to spend several hours per week independently learning material. Several lectures will employ a 'flipped-classroom' model, in which students will be expected to complete assigned reading and study prior to class time.

This course will require the completion of several projects, which may be tailored to the specific research interests and lab activities of each student. The course will be most practical for those that have the opportunity to integrate learned methods and skills into their current research activities, and be able to demonstrate results of these activities to the class.

Course Director: Jason R. Banfelder, MCh.E.

# 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:** 2014-12-16

### Document relevance

This document details the Admissions-to-Candidacy Examination Guidelines of the Physiology, Biophysics, and Systems Biology (PBSB) graduate program. The guidelines in this document summarize and expand upon those detailed in Section X.C of the Weill Graduate School Code of Legislation and the form entitled *Regulations for the Admission-to-Candidacy Examination*. Clarification should be sought from the PBSB Program Coordinator about any perceived conflict between these three documents. Tri-I students under the umbrella of the PBSB program should also follow these guidelines, except where noted by their respective Tri-I program.

### Prerequisites

Prior to taking the ACE, the student must have satisfied all course requirements established by the PBSB Program. Any exceptions must be approved by the Program.

### Timing

There are three key dates for progressing through the ACE:

- By January 31st of the student's second year in graduate school, the student must have
  - a) formed their ACE committee
  - b) received approval from their committee on the ACE topic and the Specific Aims page of their ACE.
- By April 30th of the same year, the student must have received approval from the ACE committee on the Written portion of the ACE.
- By June 30th of the same year, the student must have taken the Oral component of the ACE examination.

Failure to meet any of these deadlines results in the student being placed on probation for a period of three months, except in extenuating circumstances as approved by the Dean. Probation is lifted, and "good-standing" is restored, by proceeding to the next stage of the ACE process. If the student does not meet requirements at the end of the three-month period, the student will be dismissed from the graduate school unless the Dean chooses to extend the probationary period.

### 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 student. Tri-I students should consult with their respective programs for specific guidance.

- 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 will be comprised of one ACE Committee Chairperson, to be selected by the Program, and at least three examiners to be selected by the student. Additional examiners are permitted and may be requested by the student, the committee, the Program, or the graduate school. Typically, one of the examiners will be the student's thesis advisor (note that the thesis advisor may not also serve as the Chairperson). Every member of the ACE committee must be a member of the Weill Graduate School faculty, unless otherwise allowed by the Dean's office. Exceptions for Tri-I students are automatically approved as detailed in the *Regulations for the Admission-to-Candidacy Examination*.

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 ideally 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 timeframe, the student should seek similar guidance through individual meetings with each committee member. As specified above, this first step must be completed by January 31st of the student's second year in graduate school.

### **Written exam**

The student should take ~2 months to complete the written portion of the examination. The proposal must follow the format of a NIH R01 research grant proposal. The written research proposal should be no more than 12 pages in length (excluding the title page, 12 pt. font, single spaced, 1" margins), including figures, but not counting references. The proposal will consist of:

- 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 the primary literature.

See [www.niaid.nih.gov/researchfunding/grant/pages/appsamples.aspx](http://www.niaid.nih.gov/researchfunding/grant/pages/appsamples.aspx) for sample R01s.

The student should consult with the members of the ACE Committee while preparing drafts of the proposal. Once the committee receives the proposal, members are obligated to read and evaluate the proposal within two weeks. Committee members can approve the proposal as written or request revisions and resubmission. Before the oral component can be scheduled, all committee members must approve the written proposal through communication with the Program Coordinator. Each member of the committee is encouraged to provide the student with a short written critique of the proposal.

Note that if the student is seeking a terminal Master's degree, they should alert the committee of this intention by the time they have submitted their written proposal. In such cases, once the committee gives the student a "Pass for Master's" designation, the Oral examination may be scheduled.

### **Oral exam**

After the written proposal has been approved by the committee, the oral examination should be formally scheduled with the Graduate School office. The formal scheduling must occur at least two weeks in advance of the oral examination date.

At the start of the Oral exam, after all members are convened, the student will be excused from the room. During this time, the committee will discuss the student's academic process, the written ACE exam, and any other pertinent issues.

The oral examination will then continue with a presentation by the student describing the salient features of the written proposal. The prepared presentation should be 45 to 60 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 the 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. At a later date, the student will receive a comment of the committee's written comments (but not the voting).

### **Grading**

*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, the student must attempt to correct deficiencies as specified by the committee within one year, or according to a time frame established by the Committee.

*Pass for Master of Science:* The PBSB ACE rules for Master's degrees are as defined by the Graduate School. If the student has already indicated during the written stage that they are seeking a terminal Master's degree, the committee's evaluation of a successful Oral examination will be that of "Pass for Master of Science." Alternatively, if the committee, before or during the examination, comes to the conclusion that the student is not a suitable candidate for the PhD, the Master's degree may also be granted.

*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, then the student will be dismissed from the graduate school. Appeals may be filed with the Dean's office.

### **Formal Feedback**

After the examination, the Chairperson will provide written feedback to the student and the Program summarizing the Committee's evaluation of the strengths and weaknesses of the student's proposal, presentation, and overall preparedness for proceeding with full-time thesis research. Where possible, the Chairperson should summarize specific suggestions and resources available for improvement.