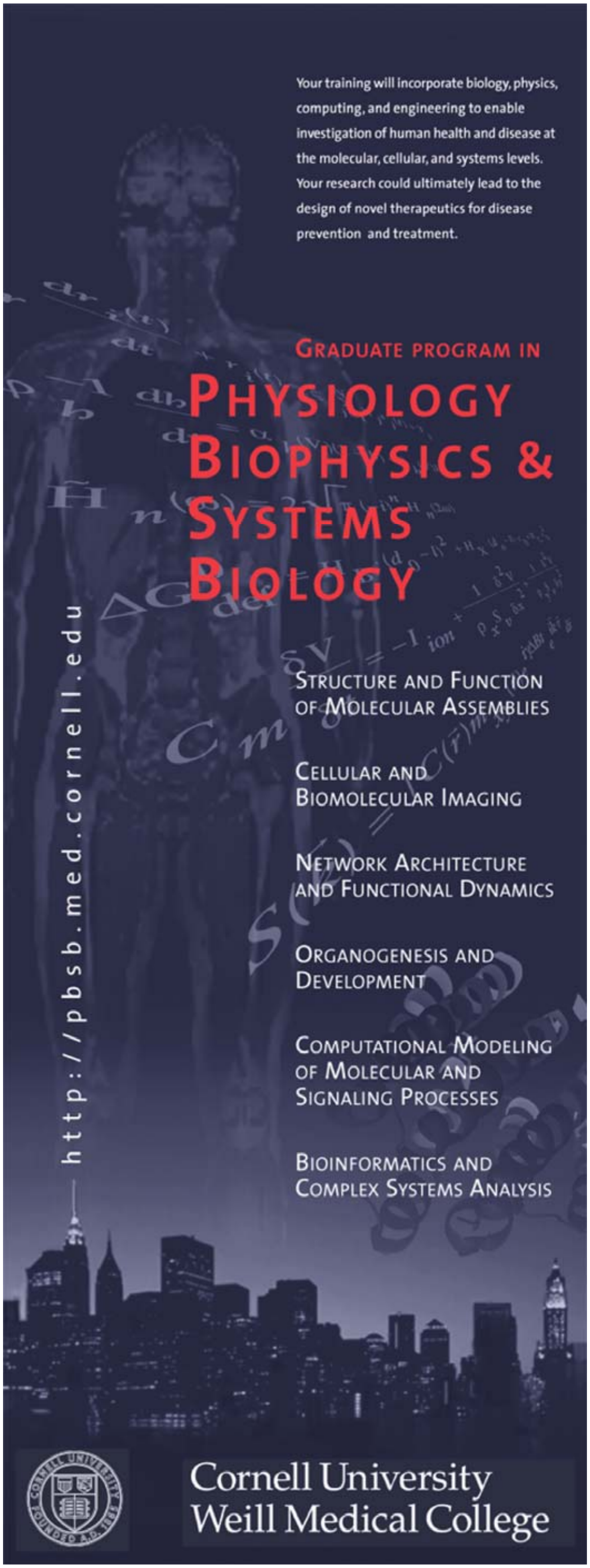

THE GRADUATE PROGRAM IN

PHYSIOLOGY BIOPHYSICS & SYSTEMS BIOLOGY (PBSB)

HANDBOOK 2009

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PHYSIOLOGY, BIOPHYSICS AND SYSTEMS BIOLOGY (PBSB)

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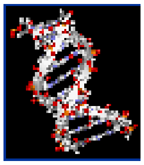

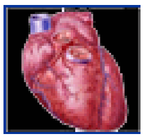

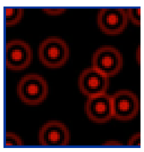

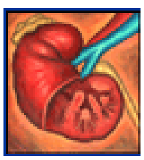

From different, but complementary perspectives, and taking advantage of advanced specialized methods, the biomedical research disciplines of ***Physiology and Biophysics*** seek to discover, analyze and explain the functions of the human body's building blocks: cells, tissues and organs. The availability 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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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.

GUIDANCE COMMITTEE OF FACULTY ADVISORS

During graduate school, and throughout your career, it will be imperative that you seek and obtain guidance and advice. This will be crucial as you search for rotations, identify a thesis lab, consider different courses to take, juggle different research projects, and look for post-graduate options. Sometimes the mentors that help you with these decisions are found informally, be they more senior students you meet at seminars, or a faculty member you get to know at a gathering. Most of the time though, advice will come from folks you have made a formal arrangement with.

During your first year, before choosing a thesis lab, you will be formally advised by the Program Director. You can seek out the Director for matters great and small, and items will be handled in few days time. He will be available before the Faculty Lunches and Scientific Presentation series held every Wednesday at noon, can be reached by email of phone for correspondence or appointments. You will also meet with the Director after the first and second semesters for a formal evaluation of progress.

After choosing a thesis lab, you will be primarily advised by the lab Principal Investigator. The thesis advisor assumes an absolutely crucial role in your career, and often the relationship is one sustained throughout your life. To provide this intense relationship some broad guidance, a Special Committee consisting of the thesis advisor and two other faculty members will be constituted to guide the student in his/her research preparation. The Special Committee should be formed soon after joining the lab and yearly progress meeting should be held around the beginning of the calendar year. This committee will serve as your core advising body through your thesis years, expanding with specifications from the Director and/or Dean for the Admission-to-Candidacy and Thesis examinations.

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.

FIRST YEAR, FIRST SEMESTER (QUARTERS 1-2)

Cell Physiology and Molecular Biophysics (Core Course 1)
Tues. and Thurs. 4:15 - 5:15.

Essentials of Human Systems Physiology (Core Course 2)
Mondays and Wednesdays from 1.30-3.30 pm.

"Faculty research" lunches. (Seminar Course 1)
Wednesdays, 12:00 - 1:00 pm

PBSB Monday seminars (Seminar Course 2)
Every other Monday, 4-6 pm.

(Monday after Labor Day) Submit laboratory rotation agreement to Program Director and begin laboratory rotation #1
(12/20) End Laboratory rotation #1

12/20 Laboratory rotation #1 report due
12/30 Faculty evaluation of rotating students due

1/15 Meeting with director

FIRST YEAR, SECOND SEMESTER (QUARTERS 3-4)

Elective Course(s)

"Scientific Presentation and Critique" (Seminar Course 1)
(1st year students will present 1st paper in journal club format)

PBSB Monday seminars (Seminar Course 2)
Every other Monday, 4-6 pm.

(First two weeks of January) Submit laboratory rotation agreement to Program Director and begin laboratory rotation #2

(Last day of March) End Laboratory rotation #2

4/1 Laboratory rotation #2 report due
4/30 Faculty evaluation of rotating students due

(First two weeks of April) Submit laboratory rotation agreement to program Director Begin laboratory rotation #3
(Last day of June) End Laboratory rotation #3

7/1 Laboratory rotation #3 report due
7/30 Faculty evaluation of rotating students due

7/30 Meeting with director

FIRST YEAR, SUMMER

Students may choose to enter lab chosen for thesis work or;

(First two weeks of July) Begin laboratory rotation #4
(Last day of August) End Laboratory rotation #4

8/31 Laboratory rotation #4 report due
9/5 Faculty evaluation of rotating students due

SECOND YEAR, FIRST SEMESTER (QUARTERS 1-2)

Logic and Experimental Design (Core Course 3)

Elective Course

PBSB Monday seminars (Seminar Course 2)
Every other Monday, 4-6 pm.

Work in thesis lab has begun.

Tri-Institutional RCR (Responsible Conduct of Research - required)

Meeting with Special Committee to discuss thesis and ACE

SECOND YEAR, SECOND SEMESTER (QUARTERS 3-4)

(January/February) Intro to the ACE Exam.
(mini-course by Emre Aksay).

Elective Course(s)

"Scientific Presentation and Critique" (Seminar Course 1)
(2nd year students will present second paper in journal club format)

PBSB Monday seminars (Seminar Course 2)
Every other Monday, 4-6 pm.

ACE exam. Form committee, research and write proposal.

Elective courses can be chosen from any of the existing graduate school offerings.

All students must complete at least three laboratory rotations; one of these is usually in the Thesis Advisor's laboratory.

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.

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 I-III (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: Nervous System Physiology Dr. Thomas Maack: Organ and System Physiology

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: 2006-09-20

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.

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

- The written proposal must address a significant research problem identified by the student. The proposal should be relevant to the student's intended thesis research *but may not be the student's thesis project*. The ACE project may not be based on any project initiated by the student's intended mentor.

- The oral component features a presentation by the student describing the salient features of the written proposal. The examining committee will ask the student to defend any aspect of the proposal and will probe the student's knowledge of the relevant scientific areas.

Committee: The ACE committee, which must be approved by the PBSB Director, will be comprised of 4 examiners, one of whom will serve as the ACE Committee Chairperson. All members of the committee must be WGSMS faculty. They might include the student's two PBSB faculty advisors and/or the student's thesis advisor (if the student has chosen a thesis laboratory). The student's thesis advisor cannot serve as Chairperson. It is the obligation of the ACE Committee to provide guidance; committee members may not write or be otherwise responsible for any part of the proposal.

Written exam Outline: As the first step of the written exam, the student must present a one-page outline of the intended proposal to her/his ACE Committee. The Committee members should meet with the student to discuss any amendments to the outline. Once the committee has approved the outline, the student should commence with writing the written ACE exam.

Written exam: Students will have access to template proposals selected from accepted, PBSB ACE documents. 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 an NIH research grant proposal:

a. Title page

b. 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. (suggested length: 1 page)
c. Background and Significance, including a review of the pertinent literature.
d. Research Plan describing 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.
e. Discussion of expected or possible results and their interpretation.
f. References should be comprehensive and cited in full at the end of the entire proposal.

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 2 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 2 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.

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.

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.