The Molecular Biosciences cluster administers the qualifying examination in two formats: 1) A proposal format that provides a mentored experience in developing a grant proposal, and 2) a comprehensive written format that emphasizes quantitative problem solving. Students may choose either format at the end of fall semester; depending on their choice, an appropriate preparatory seminar course must be selected for spring semester (Course IDs will be provided at a later date).

Proposal Format Exam
(Updated 10 August 2011)

Dates are preliminary and may change slightly in final schedule.

The purpose of the Molecular Biosciences Qualifier is to prepare students for writing of a grant proposal. The ability to write a cogent, persuasive research proposal will be an integral component of your future career in science, and the Molecular Biosciences qualifier will give you a mentored opportunity to learn more about this process. If you intend to take this qualifier, it is expected that you have a background in the general areas of microbiology, molecular biology and virology. The Department offers a variety of courses in these areas including BIOL 41600 (Viruses and Viral Disease) or BIOL69500 (Advanced Virology), BIOL 43800 (General Microbiology), BIOL 52900 (Microbial Physiology), BIOL 53300 (Medical Microbiology), BIOL 53700 (Immunobiology), BIOL 54100 (Molecular Genetics of Bacteria), BIOL 54200 (Bacterial Genetics Laboratory, and as preparation for the qualifier, we strongly recommend that you take relevant courses from this selection.

The faculty will select 10 recently published manuscripts that represent the breadth of molecular biosciences. These will be drawn from the broad areas of microbial physiology, genetic regulation, genomics, molecular biology, molecular and cellular virology, and bacterial/viral pathogenesis. Students will meet with the conveners at the beginning of the Spring Semester to select one of the recommended papers that they will pursue in their research proposal. The paper chosen should be outside the students’ area of thesis research. The purpose of this restriction is to ensure that your proposal represents your independent thoughts. In addition, it is our hope that this exercise will introduce you to concepts and techniques in a new topic in molecular biosciences, enabling you to think more broadly about your future thesis work. The conveners will make decisions as to the final proposal topics based on students’ research interests and appropriate balance among all students taking the qualifier.

The objective of the assignment will be to propose a set of experiment(s) based on the chosen paper that would expand the understanding of that research area. The proposed experiments should be original and make significant contributions to the field, but feasible to do in 3 years. Examples of possible projects could be experiments that test a hypothesis that you formulate from the data in the paper, or experiments that answer question raised by the paper. Students will submit a 300-word Abstract and an outline of the proposed project for approval by the faculty. They will assemble a reading list for this topic and study it in depth. After critically evaluating the existing knowledge in this area, students will develop the proposed experiments. As for a real grant proposal submitted to a funding agency, the students are strongly encouraged to solicit peer feedback on their written proposals, but no faculty (other the faculty administering the qualifier) may read or critique the document. The research plan will be reviewed by the faculty, who will provide a one-page written critique. Two weeks after receiving the critique, students will give an oral presentation of their research proposal. The clarity and effectiveness of the oral presentation will represent the first evaluation of the students; this portion of the work will comprise 25% of the qualifying examination grade. Two weeks after the oral presentation,
A final version of the grant will be submitted. This final draft will be graded and will make up 75% of the student’s final qualifying examination grade. No additional opportunities will be available for revision.

A composite grade of B (80%) or better is considered passing.

**Timeline: January 14, 2011:** Papers selected by the faculty will be available.

**February 14, 2011:** Abstract and outline of proposed research due to faculty.

**February 21, 2011:** Written comments on abstract and outline returned to students.

**April 18, 2011:** Complete written proposal due. This version should represent your completed proposal, not a draft! If the faculty deem this grant to represent a passing grade, this will be the final draft.

**May 2, 2011:** Last day that written critique of proposal by faculty returned to students. You will be notified at this time whether a revision is necessary.

**May 3 -16, 2011:** Oral proposal presentations (25% of final grade). **May 20, 2011:** Final revised proposal due (75% of final grade). **May 27, 2011:** Final grades returned to students. Composite grade of B (80%) or better is considered passing.

**Preparation of the written proposal:** This is a written exam in the style of a typical NIH predoctoral research plan. The proposed experiments should be something a single graduate student can accomplish within about 3 years. You should assume that you are a new graduate student in the laboratory of the senior author for your manuscript, and she/he has asked you to design your thesis proposal independently.

The grant should be succinctly written to provide the examination committee with adequate background and details to understand the current state of the chosen research topic and to evaluate your proposed experiments. Too little detail will make it difficult for the committee to understand the proposal, and excessive length can indicate a lack of focus. The proposal should not exceed 20 pages, double-spaced, including figures and figure legends, but excluding References. Font should be Arial, 12 point (as used in this text), except figure labels and legends, which can use 9 point font or larger.

Margins must be 1 inch on all sides.

For a detailed description of how to organize of a research proposal, consult the NIH annotated sample grant at http://www.niaid.nih.gov/ncn/grants/app/default.htm. The format given here is for a longer proposal (an "R01 grant"), but this will give you an excellent example how to organize each section.

1. **Abstract.** Gives a brief statement of the background, specific aims, and significance of the project. Should be no more than 300 words. Should be written so that a biologist who is not a specialist in this area could understand the project.

2. **Specific Aims.** 1 - 2 pages. Provide a brief paragraph stating how the overall problem or question fits into a broader perspective, and then list your specific experimental aims in outline form. You should state the hypothesis or hypotheses to be tested. This can be one overall hypothesis for the entire proposal or several hypotheses, one associated with each Aim, as appropriate. A maximum of 3 Specific Aims is recommended for this exercise.

3. **Background and significance.** 5 - 6 pages. Provide a brief background of the field, describing the current knowledge as it relates to your proposal. Try to stick to the significant findings, but indicate issues that are controversial or unclear. You may use figures from the literature as “preliminary data” if
they are essential to the understanding of your research aims, provided you cite the source. In this section, it is advisable to say no more and no less than what a person who is knowledgeable about biology but not necessarily an expert in your field needs understand the significance and rationale of your proposal.

4. Research design and methods. 12 - 14 pages. For each of your Specific Aims, organize the text into the following subheadings: Rationale, Experimental Design, Experimental Methods, and Potential Problems and Alternative Approaches. The Rationale section should state concisely what question(s) you are attempting to answer and how your studies are expected to advance the field. This section is extremely important for your reviewers to grasp. The Experimental Design is a general overview of the approach, leaving out minute experimental details. The Experimental Methods section provides details, focusing on how the data will be collected, analyzed (including any necessary statistical treatment), and interpreted. While not every conceivable detail need be included, you should be aware of the mechanics of the experiment and instrumentation used, as well as the strengths and limitations of the method. In a real life situation, this section is needed to convince the reviewers that you have the necessary expertise with the techniques to be able to carry out the proposed experiments. You should discuss alternative approaches, should your original proposed experiment fail. You may include figures from the literature, provided you cite the source. You should include a clear description of possible outcome(s) of the experiments and what conclusions you would draw from various possible outcomes.

5. References. In the body of your proposal, you should cite references for important previous work in the field and for experimental procedures. This is essential for the reviewers to obtain supplemental information and to convince them that you are familiar with the field. In-text citations should use a standard and convenient bibliography format. In real life, it is most helpful to cite references in the text by the author(s) name, because if your reviewer is familiar with the field, this will be the most convenient way for her/him to recognize whether you cited the important papers. While there is no "correct" number of references required, you might aim for approximately 30-40 papers that include a mixture of reviews and original research articles. (To be on the safe side, in real life, it is better to err on the side of citing too many papers - remember, it is likely that your grant will be evaluated by one of the experts in the field who may become antagonistic to you if you ignore his/her contributions.)

6. Criteria for evaluation:

i. Clarity and logic of the general development and rationale of the topic.

ii. Clarity and logic of the hypotheses to be tested.

iii. Rigor with which the hypothesis will be tested (the experimental design proposed): Are proper controls employed? What are the anticipated results? Will both positive and negative results be interpretable?

iv. Are the methods the most appropriate to test your hypotheses?

v. Extent to which written comments from the faculty are addressed in the final proposal.

7. Oral Presentation.

The primary purpose of the oral presentation is to demonstrate the depth and breadth of your understanding of the biological problem in your proposal. Questions from the faculty during the oral presentation will be largely focused on the proposal. You should include the following components related to the system you are proposing to study: background information in the literature with emphasis on controversies or glaring deficiencies in our understanding, your rationale for choosing the specific experimental direction you proposed, the experimental methods and their strengths and
weaknesses, and the potential interpretations of your anticipated results. In your talk, you should be prepared to answer questions from the faculty or students in the audience on the above issues.

Oral presentations will be scheduled for 2 hours with the understanding that the oral will take 1.5-2.0 hr. You should be prepared to present approximately 45 minutes worth of information, but expect frequent interruption from the faculty or the rest of the audience.

All the students taking the qualifier are expected to attend each of the presentations and are expected to ask questions.
Molecular Biosciences Qualifier Guidelines  2011- 2011
Written Comprehensive Format Exam
(Updated 10 August 2011)

Dates are preliminary and may change slightly in final schedule.

The purpose of the Molecular Biosciences written comprehensive qualifier is to assess knowledge and scientific reasoning at the 1st year graduate level. It is primarily intended for students pursuing training in structural and computational biology, but is appropriate for students with a background in quantitative biology. General understanding of a broad range of topics such as chemistry, genetics, basic bioinformatics, cell biology, evolutionary principles, etc. at the undergraduate level are also assumed. The Molecular Biosciences written comprehensive qualifying examination is specialized for students specializing in either Biophysics and Structural Biology (SB) or Computational Biology (CB). The exam is given in two parts, SB and CB students take the same written exam in the morning session; in the afternoon session, SB and CB students take separate exams emphasizing their respective areas.

Morning Session (3hr): both SB and CB

Short answer questions that focus on basic knowledge at the advanced undergraduate/beginning graduate level. Typically, students select approximately 60% of the questions to answer from a list of 20-25. The main topics covered on the exam are shown below with courses and texts that exemplify the level of understanding represented on the qualifying exam. The exam emphasizes quantitative aspects and problem solving over simple recall of information.

- Molecular biology/molecular genetics: BIOL41500, Introduction to Molecular Biology; text: Essential Genes, B. Lewin
- Protein Structure: BIOL41700, Protein Structure and Function, G.A. Petsko and D. Ringe
- Physical chemistry/biophysics: BIOL59500, Biophysical Methods; Principles of Physical Biochemistry, K.E. van Holde, W.C. Johnson and P. S. Ho

In addition, a selection of specialized areas are represented on the exam. Students are not expected to be proficient in all of the following areas, but should have sufficient background in several from their coursework and/or lab experience. The exam allows a choice of questions so that students may select questions from the specialized areas that they are familiar with. The specialized areas are shown below.

- Bioinformatics: BIOL47800/59500, bioinformatics; text: Introduction to Bioinformatics, 2nd edition, D. Mount or Understanding Bioinformatics, Zvelebil and Baum
- Cryo-EM, BIOL59500 TEM theory; BIOL59500, Reconstruction of Macromolecules; text: Chapter 1 and 2 (exclude chapter 2.3.3 - 2.3.10) of Three-Dimensional Electron Microscopy of

- Membranes and Membrane Proteins: BIOL64700, Membrane Protein Structural Biology; no text available

**SB Afternoon Session (3hr)**

The Structural Biology afternoon session covers the same topics as the morning session, but at a more advanced level, i.e., at the introductory graduate level. Questions in the afternoon session are typically longer and require more advanced problem solving abilities or understanding. Typically students will select 40% of the questions to answer out of 10 - 15 questions.

**CB Afternoon Session (3hr)**

Students opting for the Computational Biology exam will respond to a set of short and long questions based on readings from current computational biology literature. A list of 2-4 papers will be handed out two weeks before the exam; questions may require calculations, analysis of computational methods and algorithms, and judgments as to the correctness of conclusions presented in the papers. Typically students choose one (if three papers are given) or two (if four papers are given) papers on which to answer questions.

**Passing Grade:** The morning and afternoon sessions count equally toward the grade. A minimum passing grade requires 65% of the possible points - this level may be adjusted downwards by up to 5% if, after grading, the selection or wording of questions is deemed to have made the exam more difficult than intended.