Molecular Biosciences Qualifier Guidelines 2015-2016 (Updated 15 June 2015)

The Molecular Biosciences cluster administers the qualifying examination in two formats:

1) Proposal format that provides a mentored experience in developing a grant proposal, and
2) Comprehensive written format that emphasizes quantitative problem solving.

Students may choose either format at the end of fall semester, but should consult with their prospective thesis advisor. For those selecting the written qualifying exam, a series of short preparatory sessions are provided in fall semester; this is not a course, it is simply intended to provide insight into the range and type of questions typically asked in the exam.

Proposal Format Exam

Dates are preliminary and may change slightly in the final schedule.

The purpose of the Molecular Biosciences Proposal Format Qualifier is to prepare students to write research grant proposals. The ability to write a cogent, persuasive research proposal will be an integral component of your future career in science, and the proposal format 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, Spring) or BIOL69500 (Advanced Molecular Virology, Spring), BIOL 43800 (General Microbiology, Fall), BIOL 52900 (Bacterial Physiology, Spring), BIOL 53300 (Medical Microbiology, Fall), BIOL 53700 (Immunobiology, Spring), BIOL 54100 (Molecular Genetics of Bacteria, Fall), BIOL 54200 (Lab in Neurophysiology, Fall), and as preparation for the qualifier, we strongly recommend that you take relevant courses from this selection.

The faculty will select approximately 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, structural 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 or several of the recommended papers that they will pursue in their research proposal. The paper chosen should be outside the student’s 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.

**Approximate Timeline: Final update winter semester**

18 January 2016: Papers selected by the faculty will be available.

15 February 2016: Abstract and outline of proposed research due to faculty.

22 February 2016: Written comments on abstract and outline returned to students.

11 April 2016: 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.

22 April 2016: Last day that written critique of proposal by faculty returned to students. You will be notified at this time whether a revision is necessary.

9 May – 13 May 2016: Oral proposal presentations (25% of final grade). 20 May 2016: Final revised proposal due (75% of final grade). 27 May 2016: Final grades returned to students. Composite grade of B (80%) or better is considered passing.

**Preparation of the written proposal:** Complete information will be provided at the beginning of fall semester to students opting for this exam. The following is a brief synopsis. The proposal qualifier 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.

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 15 pages, double-spaced, including figures and figure legends, but excluding references.

Synopsis of the sections of the proposal:

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. 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. **Introduction, background and significance.** –2-4 pages. This section provides 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. 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. 9 - 12 pages. The research and design sections gives a detailed explanation of how each specific aim will be achieved: what experiments will be done, how they will be interpreted, backup strategies if approaches do not succeed, etc.. 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.

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.

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.

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 form 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.
Written Comprehensive Format Exam

The exam usually takes place 1-2 weeks after spring final exams (tentatively the week of May 9-13, 2016). This date may change slightly due to scheduling conflicts.

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.

The material on the exam is presented at the level of the following courses and readings. If you plan to take the written comprehensive qualifier, it is assumed that you will take a selection of the following courses during your first year. **You should especially note that problems emphasizing thermodynamics and energetics are a significant component of the qualifier.**

- Introduction to Molecular Biology: BIOL41500 (Fall); text: Essential Genes, B. Lewin
- Exploration of Protein Structure: BIOL4207 (Fall), G.A. Petsko and D. Ringe
- Physical chemistry/biophysics: BIOL59500, Methods and Measurments in Physical Biochemistry (Fall) and MCMP51400 (Spring); 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.

- Membrane Proteins: BIOL64700 (Spring), Membrane Protein Structural Biology; no text available
• Bioinformatics: BIOL47800/59500 (Gribskov, fall), bioinformatics; text: Introduction to Bioinformatics, 2nd edition, D. Mount or Understanding Bioinformatics, Zvelebil and Baum


• X-ray crystallography: BIOL51100 (Bolin, Spring), Introduction to X-Ray Crystallography; text: Structure Determination by X-ray Crystallography, M.F.C Ladd and R.A. Palmer

• Cryo-EM 3D Reconstruction, BIOL59500 (Spring); text: Chapter 1 and 2 (exclude chapter 2.3.3 - 2.3.10) of Three-Dimensional Electron Microscopy of Macromolecular Assemblies: Visualization of Biological Molecules in Their Native State, J Frank, 2006., and Henderson R. Realizing the potential of electron cryo-microscopy. Quarterly Reviews of Biophysics. 37(1):3-13, 2004.

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.