

## **BP 204A Macromolecular Interactions: Organizer: Robert Stroud**

Lecture Notes/Materials <http://www.msg.ucsf.edu/macro>

**Macromolecular Interactions A/B** is a 2 quarter course that focuses on the molecular basis of biological interactions. **The first quarter can be considered as a separate core course that focuses on the key principles of protein structure, folding, interactions with ligands and enzymatic catalysis. It ends with a short written proposal. You may register for BP204A for the fall quarter segment alone.** The second quarter (BP204B) focuses on more specialized expansion to protein—protein and nucleic acid interactions, trans membrane proteins and protein assemblies. It ends with a written proposal examined orally Mar 17<sup>th</sup>-21<sup>st</sup> for 65% of the total 2 quarter grade.

**Organization:** Outlines of the lectures, Lecture notes and support materials are available on the course web site. A research proposal and 1 hour oral defense are the most important part of the course. This will take a time and will comprise **65% of the 2 quarter grade**. Your topic must be approved by February 1st, **handed in by March 14<sup>th</sup>**. The 1<sup>st</sup> quarter proposal accounts for **10%, the homework, 12.5% + 12.5%**

**Topics:** The major topic areas for the course are most fundamental elements in understanding of macromolecular interactions, that are the basis for understanding biology at the level of molecular structure and dynamics. Each topic will be introduced over a ~3 week blocks of ~9 1.5 hr. class room lecture/discussions. Each lecture after the first will be ~50% lecture, and ~50% discussion focused on a ‘focus research paper’ – these are handed out at the beginning of each section. Please **read the next focus paper before each lecture. Each person will be asked to comment on issues as assigned by groups.** A list of questions will accompany the paper. You should each be prepared to discuss these issues and any others that arise in the course of the discussion, however the class will be organized into four groups, and each group assigned specific items of major responsibility in each paper.

**Graphics:** We will use the computer graphics program PYMOL (available at [delanoscientific.com](http://delanoscientific.com)) –or Rasmol to address structural questions in proteins. This is accessible for Macs from the web site.

### **Preassigned Reading:**

Course Text: Creighton -2<sup>nd</sup> Edition: Chapter1 p1-31, 4 p139-167, 5 5 p171-199, Ch 8.2.1-Binding affinities 8,2,2 Accounting for affinities. Folded secondary structures of proteins: Kd --- DeltaG (This text was cheapest acquired from Amazon.com when I last checked)

**The final for the first quarter (MacroA)** should be ~2-3 pages and should include an introduction to the problem with background, specific aims, the methods to resolve the aims, analysis of the possible outcomes and its impact. This proposal should be something that will yield an advance in

understanding an important issue, and should not be of the kind where a negative result could lead to a dead end. This proposal should build from topics covered in the first quarter.

**The Final:** You **should begin preparing for the final early in each quarter**. The topic should be drawn from materials covered in the entire two-quarter course. They can be similar to the first quarter objectives, but the proposal should address new questions. Our goal here is to expose the principles of scientific inquiry, encouraging creativity, and culminating (**Macro B** winter quarter) in an **oral defense of a research proposal**. This is one of the most valuable preparations for science.

Throughout the first quarter you should first think of an area close to the major topic areas of the course, and an outstanding scientific question of some significance. Comments will help guide the real final. To do the final proposal you should talk directly to one or more of the course faculty **as soon as possible**. This can be a tremendous resource, and one that most scientists rely on all the time; Dialog and criticism to refine a viable concept. Use the current literature.

Obtain a signature from two faculty members of the course for written approval on your goal, summarized in a one or two paragraph pre-proposal with at least 2 references. Obtain 2 faculty signatures as to viability of the idea, and then register this with Julie Ransom **before February 1st**.

This is most important as **many proposals turn out to be not viable**. You can completely avoid this ahead of time.

Here are some some general suggestions, and clues as to what to avoid:

1. You do not need to wait until a topic has been covered in class. Your topic should generally lie within the broad scope of the course. Take note of the outstanding issues faced in the course 'focus papers'. These are good indicators of important areas.

2. Try to propose an experimental means of advancing knowledge about an important issue. The answer should be instructive. – It should not end as –'if it works great, if it doesn't work- well we have to try something else' –i.e. it should cover a viable route highly likely to come up with new insight and understanding.

3. Be sure that the 'ruler' you use is capable of making the measurements you seek with enough resolution, or accuracy to draw a conclusion.

4. Then ultimately prepare, and refine with faculty, a 1 page proposal. The proposal should include the hypothesis you propose to test, the experimental means of testing it, and the means of analyzing the results to draw definitive conclusions, and how they would address the initial questions you set out to address. This should **not** be a scientific problem that you have worked on previously, or a rotation project, but should be original, and therefore reflect your own as opposed to any previously published or colleagues insight into a chosen problem and how to resolve it.

You should hand your one/two page proposal in by **Thursday Mar 9th** - These will be read and any potential problems with each proposal identified as rapidly as possible, in a few days. The proposals will be returned for reworking in discussion with the faculty of the course to optimize the proposal. This may happen multiple times if necessary. The final oral schedule will take place on

**March 17th -21st.** The oral (1 hour with two faculty and yourself and a whiteboard) is on your proposal. This is a mini-analog of the thesis oral. The oral will anticipate that you know the material of the course, and are aware of all the relevant readings and papers that were assigned - all of which will be within range. You should plan to begin with a 5 minute verbal presentation of your proposal- then questions and reasoning will follow.