Preassigned Reading:
Text: Creighton -2nd Edition: Chapter 1 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. – available on the course site.

Macromolecular Interactions and Assemblies is a 1 (Fall), and a 2 quarter course that focuses on the molecular basis of biological function. 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 based on a choice of papers as the basis for a new proposal. The second quarter 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 16th-20 for 65% of the total 2 quarter grade.

Format: Each week is a different titled module.
Monday 90 mins lecture.
Wednesday 45 min lecture and 45 min discussion of a paper.
Friday 90 min discussion of a seminal paper, led in parallel sessions.

Discussion papers: Please read the next focus paper before each. Each person will be asked to comment on the issues. A list of papers, their pdfs, and a general questions will be available on the web site for the course.

Graphics: We will use the computer graphics program CHIMERA to address structural questions in proteins. There will be tutorial in this and use of the Protein Data Base (PDB) early in the first quarter.

The 1-quarter Final will be ~2-3 page proposal on one of three alternative ‘Specific Aims’ that will be made available. (50% of the Q1 grade). It should include a brief introduction to the problem with background, the specific aim, 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 2-Quarter Final: 65% of the quarter grade. You should begin preparing for this final early in the second quarter. Your Q2 topic must be approved by February 1st, handed in by March 15th examined orally Mar 16th-20th 2015. Q1 counts for 25% of the combined 2 Quarter grade. The topic should be drawn from materials covered in the entire two-quarter course. The goal is to foster the
principles of scientific inquiry, encouraging creativity, and culminating in an oral defense of a research proposal. This is one of the most valuable preparations for science. 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 Rebecca Brown before February 3rd 2015. This is most important as many proposals turn out to be not viable. You can completely avoid this ahead of time.

**Hints:** 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 ~two page proposal in by **Friday Mar 13th 2015** - 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 **Mar 18-22nd**. The oral (50 mins with two faculty and yourself and a whiteboard) is an oral presentation of 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 summary of your proposal- then questions and reasoning will follow.