What is this course about?

Understanding any important phenomenon in biology ultimately comes down to understanding macromolecules, their structures, and how they interact with each other and with small molecules. Examples: Genes are switched on and off by the specific interactions of transcription factor proteins with DNA; cells sense and respond to their environment by producing receptors that can bind to specific target molecules; binding triggers conformational changes in the receptors that in turn trigger the cellular response; the correct reactions of metabolism occur only because protein and RNA catalysts form structures with functional groups placed with sub-Ångstrom precision in the positions needed for catalysis.

The main difficulty encountered in understanding macromolecular structures and interactions is that any given macromolecule is incredibly complex. Even a small protein has billions of possible molecular configurations. Two individual molecules in a complex somehow choose a few specific non-covalent interactions out of millions of possible ones. A macromolecule must perform its function while contacting and interacting with thousands of water molecules; these contacts are the most important factor in determining the macromolecule’s structure. Detailed enumeration and analysis of these possible structures and interactions at the level of individual atoms and bonds ranges from difficult to impossible.

Fortunately, such enumeration is not necessary. This course will cover a relatively small number of principles and techniques that have been highly successful at revealing and interpreting macromolecular structures and interactions. The ideas we will discuss will help you understand why proteins, nucleic acids, and membranes in general behave the way they do. When you are doing research and are confronted with a specific question, the same ideas will help to formulate and test hypotheses about the structures and interactions of the particular macromolecule you are studying. The power of these concepts is that they are all based on simple physical models of the molecules and the forces that act on them. A consequence of this simplicity is that, in most cases, you can get the correct answer (or at least a good approximation to it) very quickly and using only rudimentary tools (e.g., a pencil, a piece of paper, and a brain).

The course requires knowledge of basic biochemistry. This is a second-semester physical chemistry course; I will assume that you already are familiar with fundamental concepts like Gibbs free energy and chemical equilibria. The course is calculus-based; you will need to be able to differentiate and integrate with ease.
Text

Bchm 104b is a graduate-level course; much of the reading consists of articles taken from the original research literature. Most of these will be available on the Brandeis Libraries E-Res server (see "Electronic Resources" below). Photocopies of assigned readings will also be placed on reserve at the science library. The protein structure and crystallography part of the course will use a conventional text:


Electronic Resources

**E-Res server**, [http://ereserves.publib.brandeis.edu/](http://ereserves.publib.brandeis.edu/). From this Web site you can print out a copy of most of the readings (except those from the Branden and Tooze book). You will need to give the password "gibbs" and indicate that you will abide by the applicable copyright restrictions. Any readings missing from the server are absent because the copyright holder denied permission to post the material.

**Course Web page**, [http://www.bio.brandeis.edu/classes/biochem104](http://www.bio.brandeis.edu/classes/biochem104). Copies of all handouts, problem sets, and other materials handed out in class will be posted here. If you lose your copy or didn’t get one in the first place, print another copy from the Web. The course Web page will also contain various data files used in the protein structure part of the course.

**RasMol Structure Viewer**. This is an easy-to-use program for looking at macromolecular structures. It is loaded on the library computers in the Biochem 104 folder. You can also download it to your own computer by going to the course Web page and following instructions there. **I urge you to use this program frequently!**
Biochem. 104: Rules for the Course

My general attitude is to welcome questions, queries, and confusions from students. I want to help you understand the quantitative material presented in the course, and I am aware that the lectures will not at all times be crystal-clear on all points. I do not keep office hours, but rather am always available in my lab to be interrupted for help. Since I'm sometimes away, you should phone before coming to see me. In spite of the soft-and-cuddly words above, I am hard-nosed and unyielding about assigned work, so here are the rules now. You cannot credibly say later that you didn't know.

1. Homework. Along with readings, about 3 hours worth of problems per week will be assigned. These problems are essential for understanding the material covered in class; they are at least as important as the lectures. They will not be formally graded, but I will collect them, check over your work, and return them to you promptly. It will be essential to master them each week because they give you real-life experience in the concepts I'm trying to get across in the lectures. In addition, the problems give you practice in doing "word problems" using high-school algebra and first-year calculus, minimal elements of mathematical literacy with which you must be comfortable in this course (and for the rest of your lives).

2. Hour exams. There will be three hour-exams during the course. They will all be counted towards a final grade. There will not be a formal final exam, but the last hour exam will refer to issues treated throughout the course.

3. Missed work and makeups. Students are expected to perform all the work, period! There will be no makeups for missed exams, which will without exception receive a failing grade. In unusual circumstances in which an hour exam is missed for documentable reasons -- e.g., death of the student -- a makeup oral exam will be given to the corpse.

4. Grades. Final grades will be calculated as an impressionistic mix of exam grades, class participation, and outright bribes. All grading will be done by me, not by the TA.

5. Discussion sections. Each week, a discussion session will be held by the course's graduate teaching assistant, Mike Walden. These sessions are for clarifying confusions, going over problems, and correcting my mistakes. Skip them at your peril!

6. Promptness. Lectures will begin and doors will close at 11:10 AM sharp! Late arrivals are very disruptive to me (and, I suspect, to others), so make sure you arrive by 11:05. Once the door closes, it will not be opened for latecomers.

7. Background expectations. This is a second-semester course in physical chemistry. I expect that everyone will have some familiarity with basic thermodynamics, especially equilibrium constants and Gibbs free energy. You must be able to differentiate and integrate with ease, and have a good feeling for simple mathematical functions -- polynomials, exponentials, logarithms, trig functions.