Appendix A

Molecular Modeling Sample Syllabus

Please Note: Article numbers in the Homework column refer to items in the course reading list (Appendix B).

Class	**Subject**	Homework
1	Course and Field Overview: ● What is molecular modeling and how has it evolved? ● What are the practical applications and important questions? (**Preface** and **Chapter 1**)	**1**: Introduction to sequence and structural databases and to the early molecular modeling literature. *Read papers 1,2,3,20,33,42, 44,47,52,54,58.*
2	● Continuation of the overview on biomolecular modeling and simulation, from drug design to new materials. ● Discussion of the 1959 paper of Alder & Wainwright and 1971 work of Rahman & Stillinger: difficulties then and now. ● Introduction to interesting biomolecular modeling problems: protein folding, protein misfolding, nucleic acid/protein interactions, and RNA folding. (**Chapter 2**)	**2**: Retrieval of structural information from the Protein Data Bank (PDB), and the display, manipulation, and analysis of three-dimensional biomolecular structures with the Insight II molecular graphics package. Explore kinemage tutorials. *Read papers 5,8,30,31,34,37*
3	● Minitutorial on protein structure: amino acid repertoire, primary to quaternary structure, protein structure classification. ● Kinemage tutorial demonstration: folding motifs and major protein classes. (**Chapters 3 & 4**)	**3**: Construction and analysis of the pentapeptide Met-enkephalin with the Insight II program. *Read papers 2,4,6.*
4	● Discuss homework assignments 1 and 2. ● Minitutorial on nucleic acid structure: building blocks, backbone conformational flexibility, helical parameters, and DNA supercoiling. (**Chapters 5–7**)	**4**: Generation and analysis of Ramachandran plots for proteins and introduction to the NDB. *Read papers 23,29,47,50.*
5	Guest Lecturer: *The Nucleic Acid Database and the 'New Protein Databank' (RCSB)*, Prof. Helen Berman (Rutgers University, Department of Chemistry), Director of NDB and RCSB.	**5**: Analysis of Protein/DNA Complexes with Insight and NDB. *Read papers 7, 21.*
6	● Discuss homework assignment 4. ● Computational and theoretical approaches to structure prediction (from the quantum-mechanical to the molecular mechanical description). (**Chapters 8 & 9**)	**6** (**MIDTERM**): Sequence/Structure/Function Relationships in Proteins, A Contest! *Read papers 22,36,38,56.*

Table A.1: (continued)

Week	**Subject**	Homework
7	Guest Lecturer: *Protein Structure Modeling*, Dr. Andrej Sali, expert in protein modeling.	**7**: Molecular mechanics force fields: approximations, variations, and the assessment of results with respect to experiment and other simulations (*papers 10,11,15,16*). *Read papers 13,14,17,24.*
8	Amer. Chem. Soc. 1990 videotapes: *Molecular Modeling in Biological Systems*: 1 – Peter Kollman, "Methods in Molecular Modeling", 4 – Panel Discussion.	
9	Guest Lecturer: *Ab Initio Calculation of Protein Structure by Global Optimization of Potential Energy*, Prof. Harold Scheraga (Cornell University, Department of Chemistry), pioneer of protein force fields and computation of protein structure.	**8**: A bit of programming: nonbonded versus bonded energy computations.
10	MIDTERM class presentations	
11	• Continue MIDTERM presentations. • Force Field Debate!	**9 (TERM PROJECT)**: The Successes (Failures?) of Molecular Modeling. *Read papers 9,18,19.*
12	• Molecular mechanics force fields — origin, variations, and parameterization. • Special topics — molecular topology: bookkeeping and data structures, potential energy differentiation. • Special issues in nonbonded energy computations — spherical cutoffs, fast electrostatics by the multipole method, periodic boundary conditions, and the Ewald summation. (**Chapter 10**)	**10**: Experiments in Geometry Structure Optimization: Minimization of Biphenyl with Insight II/Discover. *Read paper 12.*
13	• Go over Assignment 8, including general discussion of programming and timing strategies. • Optimization techniques for multivariate functions in computational chemistry. (**Chapter 11**)	**11**: A global optimization contest for a pentapeptide! *Read papers 25,26.*
14	Monte Carlo Simulations. (**Chapter 12**)	**12**: An exercise in Monte Carlo. **13** (Optional): Advanced exercises in minimization and MC. *Read papers 27,28,32,41, 53,57,59.*
15	Molecular dynamics simulations — theory and practice. (**Chapters 13 & 14**)	**14** (Optional): Advanced exercises in molecular dynamics. **15** (Optional): Scaling of protein conformations and folding simulations.