# Molecular Simulations in Computational Biology
# BioMaPS 513 and Chemistry 544

Spring 2005

BioMaPS Institute and Department of Chemistry & Chemical Biology

**Time & Location:**
Tuesdays and Thursdays, 2:50-4:10 PM, Protein Data Bank/BioMaPS Laboratory, Doolittle Hall

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**Part I. Protein folding and binding** (January 17, 2005 – February 28, 2005)

Lecturers: Michael Andrec, Anthony Felts, Emilio Gallicchio, Jennifer Knight, Ronald Levy, and Yang Su

This series of 12 lectures and "lab exercise" classes has evolved from courses in statistical mechanics, molecular modeling, and protein physics which we have been teaching. They are meant to provide the background needed to read the current literature in the field as well as to provide "hands on" experience with molecular simulation techniques. Illustrative examples will be covered in class. Lectures will be given twice a week for six weeks. There will be two computer laboratory exercises incorporated into the schedule. The first will focus on protein folding, and the second on protein-ligand binding. The computer simulations and exercises are an integral part of the course.

1. **An overview of current research** – a overview of current research in our laboratory and an introduction to the concepts of "effective potentials", advanced simulation methods, and connections between microscopic simulations and macroscopic observables. (1.5 lectures, RL)

2. **Potential energy functions used in computer simulations** – theoretical basis, form of potential functions, parameter determination. (1 lecture, RL)

3. **Solvation** – explicit and implicit solvation models, the potential of mean force, the Poisson equation, the Generalized Born model, parameter optimization (1.5 lectures, RL)

4. **Molecular dynamics simulations and the replica exchange method** – General features of molecular dynamics and replica exchange methods. (1 lecture, EG)

5. **Protein folding laboratory** – Folding the GB1 peptide beta hairpin. Replica exchange

simulations of the GB1 peptide. Analysis of the simulations, including the potential of mean force as a function of structural order parameters, and temperature. Use of Maestro software (2 laboratory/lecture sessions, EG and TF)

6. **Protein folding kinetics** – A kinetic model for folding the GB1 peptide using the GB1 replica exchange ensemble and a kinetic network model. Introduction to the Gillespie algorithm. (1 lecture, MA)

7. **Protein-ligand binding** – statistical mechanics of binding, FEP, LIE and approximate methods, docking , z-scores (2 lectures, TF)

8. **Protein-ligand docking and binding laboratory** – Use of Maestro and GLIDE software, LIE simulations (2 lectures, TF, JK, YS)

**Part II. DNA structure, and multi-scale molecular modeling** (March 8, 2005 – April 28, 2005)

Lecturers: Wilma Olson and A.R. Srinivasan

1. **Model building at the chemical level:** Cartesian coordinates, coordinate frames, internal chemical parameters, polymeric constructs (WKO & ARS)

2. **Electronic characterization of biomolecules:** Model chemistries, fragment optimization, partial atomic charges) (WKO & ARS)

3. **Alternative representations of biomolecular structure:** virtual bonds, lattices, rigid-body parameters, helices, superhelices (WKO & ARS)

4. **Knowledge-based models and scoring functions:** elastic treatments, sequence-dependent structures and deformability, side-group profiles, ligand interaction profiles, molecular threading (WKO)

5. **Knowledge-based simulations of DNA and DNA-protein complexes:** equilibrium structures, global structural fluctuations, ring closure (WKO)

6. **Differential geometry and topological considerations** (WKO)

7. **Multi-scale molecular modeling** (WKO)

**Part III. Related BioMaPS Institute seminars**

**February 3:** BioMaPS Enrichment Seminar (12:30 - 2:00 PM, Hill Center, Room 260):
**Ruth Nussinov** (Tel Aviv University and National Cancer Institute)
"Protein Binding and Protein Folding"

**February 10:** BioMaPS Enrichment Seminar (12:30 - 2:00 PM, Hill Center, Room 260):
**Annabel Todd** (D.E. Shaw & Co.)
"Progress of Structural Genomics Initiatives: An Analysis of Solved Target Structures"

**April 7:** BioMaPS Enrichment Seminar (12:30 - 2:00 PM, Hill Center, Room 260):
**Devarajan Thirumalai** (University of Maryland, College Park)
"Dynamics of Protein Folding"

**April 14:** BioMaPS Enrichment Seminar (12:30 - 2:00 PM, Hill Center, Room 260):
**Mona Singh** (Princeton University)
'Genome-level Analysis of Protein Structure, Function, and Interactions"