

# QB110a: Numerical Modeling of Biological Systems

## Spring 2009

**Instructor:** Michael Hagan, Abelson 347; E-mail: [hagan@brandeis.edu](mailto:hagan@brandeis.edu)

**Office Hours:** 3-5PM, Monday, or by appointment.

**Meeting Time and Place:** Abelson 229, TF, 1:40 – 3:00.

### **Required course work:**

Homework will be handed out in class, usually one every two weeks. Expect fairly extensive reading assignments. A term paper will be due at the last day of classes. There will be no written exams, but you will be asked to prepare a short presentation on your term paper topic at the end of the semester.

### **Grading Procedure:**

50% – Homework. 30% – Term paper. 20% – Presentation.

### **Course Description:**

Currently biology is undergoing a revolution whereby quantitative experimentation is providing remarkable molecular details of the basic processes of life. In particular, recent advances in imaging methods enable the visualization of collective interactions, while single molecule techniques can probe specific molecular species. These experimental advances afford the perfect opportunity for synergy between theory and experiments. This course will present an introduction to numerical methods that are appropriate for modeling biological systems at various length and time scales. The aim will be to provide experimentalists and theorists with an appreciation of both the possibilities and limitations of these techniques. Our modeling efforts will range in resolution from examining enzyme motions at the atomistic level to organismal development at the cellular level to large-scale population dynamics. To develop and solve these models we will develop and use techniques such as molecular dynamics, Monte Carlo simulations, and numerical solutions of differential equations.

### **Course Outline**

- 1. Introduction and motivation for numerical modeling of biological systems (1)**
- 2. Biomolecular structure at the atomic level (2-4)**
  - Classification of protein structures and the forces that stabilize them
  - Introduction to VMD, a powerful software application for visualizing biomolecules
- 3. Molecular interactions and dynamics (5-8)**
  - The origin of forces and motions that make biology work
  - Newton's Laws and the equations of motion
  - Introduction to MATLAB
  - Molecular dynamics simulation of neutral atoms
  - Measurements, averages, ensembles, and ergodicity

#### **4. Biomolecular motions at the atomic level (9-11)**

- introduction to NAMD, a biomolecular simulation package
- Molecular dynamics simulations of biomolecules: unfolding a small protein

#### **5. Coarse graining: from atoms to cells (12-15)**

- Equilibrium calculations and Boltzmann's formula
- The statistical mechanics of protein-protein interactions
- Introduction to Monte Carlo simulations
- From the Ising model to bacterial chemotaxis the propagation of allosteric states in protein complexes and signaling networks

#### **5. Genetics and cell regulation (16-21)**

- The central dogma
- Statistical mechanics of gene regulation
- Introduction to nonlinear dynamics
- Numerical solution of ODEs in MATLAB
- Genetic switches and oscillators: The  $\lambda$  phage switch and the repressilator
- Development of Drosophila

#### **6. Biased sampling techniques (22-25)**

- Calculating free energies with umbrella sampling and free energy perturbation theory
- From free energies to reaction rates and determining the reaction coordinate
- Sampling reactive trajectories with transition path sampling
- Simulating the folding of a peptide

#### **7. The future of biomolecular modeling (26)**

#### **Suggested reading**

1. T. Schlick, Molecular modeling and simulation: an interdisciplinary guide, (Springer, 2002) ISBN: 038795404X
2. Stephen P. Ellner & John Guckenheimer, Dynamic models in biology, (Princeton University press, 2006) ISBN 9780691118437
3. D. Frankel, B. Smit, Understanding Molecular Simulation: From Algorithms to Applications, (Academic Pr., 2001) ISBN: 0122673514
4. B. Alberts et. al., Essential Cell Biology (Garland Science, 2003) ISBN 081533480X
5. C. P. Fall et. al., Computational Cell Biology (Springer, 2002) ISBN 0-387-95369-8
6. K. Dill and S. Bromberg, Molecular Driving Forces,(Garland Science, 2003) ISBN 0815320515
7. P. Nelson, Biological Physics, (Freeman and Co., 2004) ISBN 0-7167-4372-8.
8. V. Ambegaokar, Reasoning about luck, (Cambridge, 1996) ISBN 0521447372