BE459/559 Multiscale Modeling of Biological Systems Spring 2009
Instructor: Ravi Radhakrishnan, Bioengineering
Tuesdays, Thursdays 1.30 to 3.00 pm

The course will be constituted by Class Lectures, In-Class Computational Lab Sessions, Running Simulations in CETS Linux Labs for homework assignments. 60% lectures, 40% computational laboratory

Pre-requisites for Graduate students: none
Pre-requisites for Undergraduate students: BE324 or equivalent advanced physical chemistry or statistical mechanics course. Others, email instructor rradhak@seas.upenn.edu for permission

Evaluation for Graduate Students:
60% Homework Assignments;
30% Course Project (Presentation required on finals day)
10% In-class presentation: Articles from literature. Articles will be assigned from the references in the course textbook.

Evaluation for Undergraduate Students:
60% Homework Assignments in teams of two;
30% Course Project in teams of two (Presentation required on finals day)
10% In-class presentation: Chapters from reference textbook on Intracellular Signaling Mechanisms.

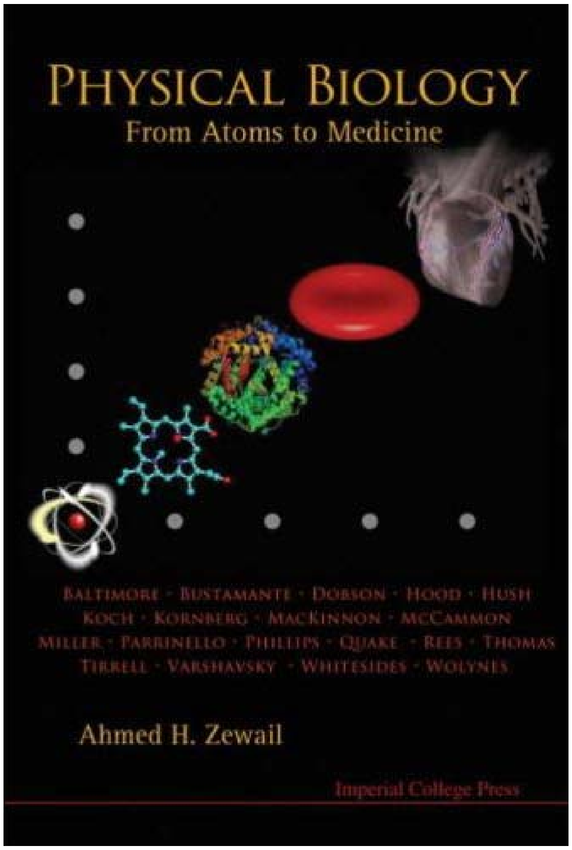
Other requisites: No programming skills required; as part of lectures and assignments, simulations will be run on Linux platforms, hence knowledge of some basic commands in Linux will be necessary (a primer will be given at the beginning of the course). Special Emphasis will be placed on cellular signal transduction

Course Textbook:
Required: Physical Biology: From Atoms to Medicine (Paperback) by Ahmed Zewail (Editor) ISBN-13: 978-1848162006

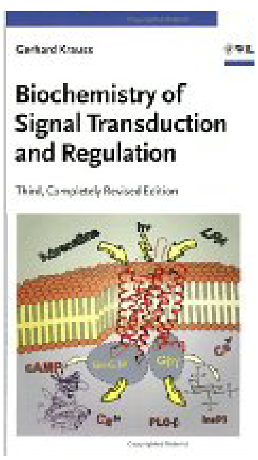
Course notes, online manuals, journal review articles, and book chapters from reference textbook will be provided electronically through blackboard.

Reference Textbooks (not required, will be provided electronically): Biochemistry Of Signal Transduction And Regulation, edited by Gerhard Krauss, Wiley-VCH

Course description: This course aims to provide theoretical, conceptual, and hands-on modeling experience on three different length and time scales that are pertinent to biochemical phenomena in cells and to nanobiotechnology applications.



Required Text



Reference Text (will be provided as e-book through blackboard)

Course Syllabus

<u>Theory and Simulations:</u>

* Motivation for Computational Biology (1 lecture)

* Interactions, Master Equation, Markov Models, Monte Carlo, Kinetic Monte Carlo (2 lectures)

* Biomolecular Structure, Forcefields, long-range interactions (1-2 lectures)

* Molecular Dynamics (1-2 lectures)

* Linear response and Fluctuation Theorems (1 lecture)

* Chapter 11: Rare-events in biomolecules (1 lecture+1lab+1assignment)

* Free Energy Methods; Transition Path Sampling

<u>Computational Laboratory:</u>

* Biomolecular Dynamics: VMD and NAMD software (2 in-class class lab sessions + 1 assignment)

* Coarse-graining: Principal Component Analysis (2 in-class class lab sessions + 1 assignment)

* Computer-Aided Drug Discovery: Molecular Docking using Autodock
(1 in-class lab + 1 assignment)

* Rare-events: 2-state and other model systems (1 lab + 1 assignment)

* Systems Biology Lab: SBML and Genesis (1 lab + 1 assignment)

<u>Applications:</u>

* Chapter 1: The Preoccupations of Twenty-First-Century Biology (reading assignment);

* Chapter 2: The World as Physics, Mathematics and Nothing Else (reading assignment)

* Chapter 7: The Future of Biological X-Ray Analysis (1 lecture)

* Chapter 5: Physical Biology at the Crossroads: single molecule force spectroscopy-theory and challenges (1-lecture)

* Chapter 12: Protein Folding: Energy Landscapes and the Organization of Living Matter in Time and Space (1-lecture)

* Chapter 9: Designing Ligands to Bind Tightly to Proteins (2-lectures)

* Chapter 14: A Systems Approach to Medicine (1 lecture)

* Spatial and Stochastic Effects in Signaling: endocytosis, biological adhesion (1-lecture)

Student In-class Presentations:

Graduate Students (10% of final grade):

* References from Chapter 3: Physical Biology: 4D Visualization of Complexity

* References from Chapter 18: Potassium Channels and the Atomic Basis of Selective Ion Conduction

* References from Chapter 10: Biology of Numbers

* References from Chapter 17: Precision measurements in Biology

* References from Chapter 8: Macromolecular design

Undergraduate Students (10% of final grade):

Chapter from Krauss: Protein and Nucleic Acid Interaction
Chapter from Krauss: Cellular Signals, Second Messengers
Chapter from Krauss: Receptor Signaling, Nuclear Signaling
Chapter from Krauss: Cell Cycle
Chapter from Krauss: Cell Cycle Deregulation and Cancer

Graduate and Undergraduate Students (30% of final grade):

* **Final Project Presentation** due on finals day (2 hrs during the period scheduled for the finals; unhealthy breakfast from Dunkin Donuts included and sponsored by Provost faculty-student interaction fund!)

Final Project:

The scope of the final project is given a topic, can you pose the right question, and can you suggest a viable answer. Students are expected to finalize their topics before spring break and are expected to spend ~20-25 hours in the reminder of the semester toward the final project. The course project can be open-ended and intellectually demanding, however it is expected that the student provides preliminary calculations or theoretical formulations to illustrate the approach and provide proof-of-principle.

For Undergraduate Students: the project can be an extension of or similar to a home-work problem.

For Graduate Students: it is expected that you show more depth, originality, and creativity commensurate with your advanced standing.

Thinking for yourself, thinking outside the box, and original propositions will be rewarded; in an engineering course, here is your chance to be the artist.

For your reference here are some completed final projects sampled from 2006-2007:

Graduate Student Projects:
- Theory and modeling of binding of nanocarriers to endothelial cells
- Modeling the structural effects of αL I domain mutants through atomistic simulations
- The best of both worlds: bridging the gap between deterministic and stochastic modeling of intracellular signaling networks
- Approaches for Multi-Scale Coupling of Platelet Deposition under Flow

Undergraduate Student Projects:
- Constant Pressure Molecular Dynamics Simulations of Troponin C(1-90)
- An Application of Monte Carlo Simulations in Neurotransmission at a Neuronal Synapse
- A Hybrid Model for Decision Making in Neural Circuits
- Scorpion Venom: The Next Frontier- Molecular docking of chlorotoxin isolated from death-stalker scorpion venom to the His-Ctlx receptor.