

BE 703: Numerical Methods and Modeling in Biomedical Engineering

Fall 2008

Course Coordinator: Daniel Kamalic

Phone: (617) 358-3311

Email: kamalic@bu.edu

Office Hours: Monday/Wednesday 12:00pm-2:00pm or by appointment
Module instructors will provide their own office hours later

Office: 24 Cummington Street, room B06

Class Meeting Time: Monday and Wednesday, 2:00pm-4:00pm

Class Location: 24 Cummington Street, BME Computational Simulation Facility (LSE B03/B04)

Course Web Site: http://courseinfo.bu.edu/courses/08fallengbe703_a1/

Course description: The objective of this graduate course is to provide students with the skills and knowledge necessary for computational modeling of biological and physiological systems

Textbooks:

You do not need to purchase any textbooks for this course—they are available free online or in the lab. However, will not regret purchasing a paper copy of one or more of these, since they will be useful reference manuals for you for many years to come.

- *Numerical Recipes: The Art of Scientific Computing* by W. H. Press, Saul A. Teukolsky, William T. Vetterling, and Brian P. Flannery (Cambridge University Press)
 - C, F77, and F90 versions are available online at <http://www.nr.com/oldverswitcher.html>
- *Learning the Bash Shell* by C. Newham (O'Reilly, 2005)
 - Available online at <http://proquest.safaribooksonline.com/0596009658>
- *Visual QuickStart Guide: Unix* by D. S. Ray and E. J. Ray (Peachpit Press, 2006)
 - several copies are always on hand in the lab

Grading:

There are no midterm and final exams in this course. Your final grade will be the mean of your grades for the four lab modules.

Lab Reports: Lab reports should be ready to turn in at the end of the “catch-up” day after each module. If students have problems that have been identified on the catch-up day which they need a bit more time to fix, they may be granted an extension to fix those specific problems and hand in a revised report no later than the start of class for the first class of the next module (or finals week for the final module). No late reports beyond this date will be accepted.

Academic Conduct Code: While discussing assignments with your fellow students and getting help outside of class is both authorized and encouraged, copying solutions from any source is considered an Academic Conduct Code violation, as is sharing or re-use of a computer file. Please read the College of Engineering Academic Conduct Code at <http://www.bu.edu/eng/handbook/documents/ugrad-handbook-ch09-academic-conduct.pdf>.

COURSE SCHEDULE:

| | | |
|---------|----------|---------------------|
| [intro] | Mon 9/8, | Wed 9/3 Wed 9/10 |
|---------|----------|---------------------|

| | | |
|------------|------------------------|----------------------|
| [module 1] | Mon 9/15, Mon 9/22, | Wed 9/17 Wed 9/24 |
|------------|------------------------|----------------------|

| | | |
|------------|----------|--|
| [catch-up] | Mon 9/29 | |
|------------|----------|--|

| | | |
|--------------|--------------------------------------|--|
| [2nd module] | Mon 10/6, TUE 10/14, Mon 10/20 | Wed 10/1 Wed 10/8 Wed 10/15 MONDAY SCHEDULE ON TUESDAY |
|--------------|--------------------------------------|--|

| | | |
|------------|--|-----------|
| [catch-up] | | Wed 10/22 |
|------------|--|-----------|

| | | |
|--------------|---------------------------------------|------------------------------------|
| [3rd module] | Mon 10/27, Mon 11/3, Mon 11/10, | Wed 10/29 Wed 11/5 Wed 11/12 |
|--------------|---------------------------------------|------------------------------------|

| | | |
|------------|-----------|--|
| [catch-up] | Mon 11/17 | |
|------------|-----------|--|

| | | |
|--------------|--------------------------------------|---|
| [4th module] | Mon 11/24, Mon 12/1, Mon 12/8, | Wed 11/19 FALL RECESS Wed 12/3 Wed 12/10 |
|--------------|--------------------------------------|---|

MODULE CONTENT:

Module 1: Numerical methods in macromolecular interaction prediction

Instructor: Prof. Sandor Vajda, Dima Kosakov

The goal of protein-protein docking is to determine the structure of a complex in atomic detail, starting from the coordinates of the unbound component molecules. Based on the thermodynamic hypothesis, at fixed temperature and pressure the Gibbs free energy of the macromolecule-solvent system reaches its global minimum at the native state of the complex. Thus, docking requires a computationally feasible free energy evaluation model and an effective minimization algorithm. The goal of this module to give an overview of the minimization methods used in macromolecular modeling. This will include the entire modeling process, from the construction of an algorithm to calculate the approximate free energy of the system based on physical considerations to the development of computer programs running on multiple processors. The methods introduced will be illustrated on the real and test macromolecular systems.

The lectures and the labs will cover the following topics:

- 1) The physical basis of macromolecular interactions. Interactions as global optimization problem. Molecular mechanics as computational model for working with macromolecules.
- 2) General overview of multidimensional minimization methods. Line search as an important component of the minimization problem.
- 3) Minimization with and without derivatives. Powell method, steepest decent, and conjugate

- gradient algorithms.
- 4) Quasi-Newton methods - general overview.
 - 5) Stochastic global search methods derived from physical considerations. The Metropolis Monte Carlo algorithm and its implementations.

Module 2: From measurements to models: simulating the eye's input to the brain

The aim of this module is to give students experience in the practice of building computer models of biological systems from experimental measurements. The system of study for this purpose will be the horseshoe crab lateral eye, the details of operation of which are probably foreign to them. We make use of this fact to illustrate how one might go about constructing a model of an unknown process from scratch, which is often the situation in biomedical engineering. By module's end the students will have formulated a model of the crab's eye that realistically simulates its input to the crab's brain. In so doing, they will learn some systems identification techniques, numerical methods/tricks-of-trade, and how we and other animals may see.

We tackle the modeling effort by dividing it into several pieces that are completed in succession over several classes. We start by briefly delving into the horseshoe crab literature in order to provide background information about the eye that the students will utilize as we progress through the module. We then introduce non-parametric methods of model building and use published data to identify major computational elements in the eye. We formulate a parametric model of each element and link them together into an electrical equivalent circuit of a receptor unit. Finally, we couple the receptor-unit circuits together into a massively-connected neural network and simulate the network output to inputs that are behaviorally relevant to horseshoe crabs and visually interesting to us.

- L1: Overview
- L2: Optics
- L3: Membrane Biophysics/Spike Coding
- L4: Phototransduction
- L5: Inhibition
- L6: Noise

Module 3: The dynamic response of the vestibular semicircular canals

Instructor: Prof. Ed Damiano

The problem we will be analyzing concerns the dynamic response of the semicircular canals of the vestibular system. The primary function of the vestibular semicircular canals is to transduce angular motion of the head into neural signals that are sent to the brain. Afferent signals originating from the canals provide vital inputs that are necessary to maintain dynamic equilibrium and stabilize the image on the retina via the vestibulo-ocular, collic, and spinal reflexes. Transduction by the canals is achieved through mechanical activation of innervated sensory hair cells that reside on the surface of a sensory epithelium. Transduction originates with angular acceleration of the head, which induces hydrodynamic pressure and flow within the fluid-filled semicircular canals. This flow induces deformation of a viscoelastic structure (known as the cupula), which spans an entire cross section of the canal. Deformation of the cupula imparts deflections to imbedded stereocilia hair-cell bundles. Deflections of the stereocilia in turn give rise to transduction currents through gating of displacement-sensitive ion channels.

We will develop a model of the hydrodynamics within the canals and the fluid-structure interactions that arise between the fluid (known as endolymph) within the semicircular canals and the cupula in response to sinusoidal rotation of the head. A hydrodynamic boundary condition acting across the cupula will be derived and coupled to a viscoelastic model of the cupula. Numerical solutions to the deformation field of the cupula will be obtained using a weighted residuals method attributed to Galerkin. The amplitude and phase of the spatially averaged displacement field of the cupula will be computed as a function of forcing frequency and then compared with the frequency response of individual semicircular canal afferent responses measured on the vestibular nerve.

Module 4: Imaging micromechanical motion in the cochlea

Instructor: Prof. David C. Mountain

Like the vestibular system, the cochlea uses hair cells to transduce sound induced vibrations into electrical signals that are then relayed to the brain via the auditory nerve. The cochlea consists of a spiral-shaped fluid-filled tube that is separated into two longitudinal compartments by the basilar membrane. The hair cells along with several types of supporting cells are located on this membrane and collectively form what is known as the organ of Corti.

In the cochlea, there are two types of hair cells: inner (IHC) and outer hair cells (OHC). The vast majority of the auditory nerve fibers are connected to the IHCs while the OHCs receive extensive neural input from the brain. Outer hair cells also differ from inner hair cells in that they possess an unusual form of motility that can change cell length on a cycle-by-cycle basis at acoustic frequencies. The source of this motility is a transmembrane protein called prestin which changes its shape in response to changes in the electric potential across the cell membrane.

Since the anatomy of the organ of Corti is complex, and because it is acted upon by both external (acoustic) forces and internal (OHC) forces, it is not surprising that the motion of cells within the organ is complex. In this module we will explore some of the digital microscopy techniques that have been developed to study displacement down to the nanometer level and up to frequencies in the tens of kilohertz. These include stroboscopic video microscopy, signal averaging, image enhancement, and motion estimation techniques.