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QBio 110a: Numerical Modeling of Biological Systems

Contact Details

Michael Hagan
Office location: 350 Abelson Hall
Telephone: (781) 736-2845
Email: hagan@brandeis.edu

Please communicate with me by email (my office phone messages are never checked). I will respond as soon as possible, but depending on the situation a response may require 24-48 hours.

Meeting Times

Classes

Monday, Wednesday 4:00 – 5:20 PM, via Zoom link (which will be posted on Latte once it is set up)

Office Hours

Time: TBA: I will take a poll on the first day of class, and select the optimal (or least un-optimal) times. Office hours will be performed via a zoom link which will be posted on Latte once it is set up. TBD

Course Description

Course overview and philosophy

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, enhanced sampling techniques, and numerical solutions of differential equations.

Learning Goals

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.

Specific objectives include:

- Give students practical experience in building and evaluating models of biological systems

• Give students practical experience in molecular graphics, molecular dynamics, and Monte Carlo simulations

• Enhance students' understanding of how physical forces drive and control biological phenomena

• Increase students' ability in critically evaluating modeling efforts within the scientific literature

• Introduce students to the fundamental principles that underlie molecular mechanics force fields and algorithms

Prerequisites

This course is generally taken by junior/senior level undergraduates and graduate students from across the spectrum of the Physical and Life Sciences. Students should have taken Phys 11a/b, Phys 15 a/b, or equivalent-level introductory physics courses, and have at least an introductory familiarity with solving ordinary differential equations. Some familiarity with computer programming (in any language) is highly recommended. While the course will begin with a brief introduction to Python programming, it will not be possible to provide the equivalent of a semester-long course on programming. A familiarity with thermodynamics and statistical mechanics is also desirable (e.g. Phys 40) but not essential.

Credit Hours

Success in this four-credit course is based on the expectation that students will spend a minimum of nine hours of study time per week in preparation for class (readings, papers, discussion sections, preparation for exams, etc.)

Course Requirements

Academic Integrity

> The work you turn in -- problem sets, reading questions, and term paper -- must be your own. Identical problem sets will be considered as plagiarized and treated as such.

Every member of the University community is expected to maintain the highest standards of academic integrity. A student shall not submit work that is falsified or is not the result of the student's own effort. Infringement of academic honesty by a student subjects that student to serious penalties, which may include failure on the assignment, failure in the course, suspension from the University or other sanctions (see section 20 of R&R). Please consult Brandeis University Rights and Responsibilities for all policies and procedures related to academic integrity. A student who is in doubt regarding standards of academic honesty as they apply to a specific course or assignment should consult the faculty member responsible for that course or assignment before submitting the work. Allegations of alleged academic dishonesty will be forwarded to the Department of Student Rights and Community Standards. Citation and research assistance can be found at Brandeis Library Guides - Citing Sources (https://guides.library.brandeis.edu/c.php?g=301723).

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Reading
There will be extensive reading assignments, posted on Latte. I expect the students to have taken a first pass by the time of the lecture. You should read actively: take notes on the reading, consult your classmates, the course TA, me, and additional books to work through things you don't understand. We will discuss reading assignments during lecture.

Problem Sets
Problem sets will be assigned on Latte, usually a problem set every one or two weeks. Please note: problem sets will involve modifying and even writing computer programs, and typically cannot be completed in a single day. Don't procrastinate! If you have a health or family emergency, contact me as soon as you are able. If you have scheduled travel for a conference, wedding of yourself or immediate family, or visits to graduate schools, contact me a week in advance to arrange an accommodation. Absent these reasons I will accept assignments up to a week late, for 50% of full credit.

Term Project/Presentation
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. This project will allow you to test the numerical modeling skills learned in the course, to develop some of these skills further, and to obtain a "real world" understanding of the intricacies involved in applying these skills. Moreover, you will gain experience in written and oral communication of the results of a modeling study. You will begin your term project midway through the term, and you will meet with the professor and other students regularly to assess progress and overcome stumbling blocks.

Participation
Class participation will be based on presence and involvement in class meetings, as well as during the question and answer session of class presentations. It includes activities such as: completing the readings each week before coming to class and preparing for class discussions, raising questions as soon as ideas become unclear (either in class or via online communications between classes), listening actively and attentively, responding thoughtfully and constructively to the comments made by other class members, reading and responding to course-related e-mails and posts, etc.

I will keep an open forum on Latte for questions based on the reading and lectures. You are encouraged to post them at any time. I usually will need 1-2 days to develop a response. *I expect each student to post at least six nontrivial, specific questions by the end of the semester.* You may also ask me additional questions privately by email, or during office hours/scheduled appointments.

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Evaluation

Class Element	Grade Percentage	Learning Goals	Due date
In-class participation	10%	Scientific communication	weekly
Problem sets	50%	Numerical modeling skills and model building	Every one or two weeks
Term Project Report	25%	Numerical modeling skills, model building, and written communication of modeling results, assessment of model validity and relevance	Last day of instruction
Term Project Presentation	15%	Oral communication of modeling results	Presentations will be given during the last two class meetings

Essential Resources

Accommodations
Brandeis seeks to welcome and include all students. If you are a student who needs accommodations as outlined in an accommodations letter, I want to support you. I want to provide your accommodations, but cannot do so retroactively. If you have questions about documenting a disability of requesting accommodations, please contact Student Accessibility Support (SAS https://www.brandeis.edu/accessibility/) at 781.736.3470 or access@brandeis.edu.

Course Materials
If you are having difficulty purchasing course materials, please make an appointment with your Student Financial Services or Academic Services advisor to discuss possible funding options and/or textbook alternatives.
However, all of the required and most optional reading materials will be available through course reserves and/or on Latte.

The primary reading assignments will come from the following five texts:

- T. Schlick, Molecular modeling and simulation: an interdisciplinary guide, (Springer, 2002)

2nd edition ISBN: ISBN-13: 978-1441963505
An excellent overview of biomolecular structure, dynamics, and simulations. (Available on course reserves)

• Jesse M. Kinder and Philip Nelson, A Student's Guide to Python for Physical Modeling: Updated Edition, ISBN: 9780691180571.
An excellent introduction to using Python for scientific computing. (Available on course reserves; also, the e-book copy is only $10 and very well worth it.)

• D. Frankel, B. Smit, Understanding Molecular Simulation: From Algorithms to Applications, (Academic Pr., 2001) 2nd Edition, ISBN: 0122673514
An excellent introduction to and reference guide for scientific computing methods. (Available on course reserves. Also some of the chapters will be provided on Latte.)

• R. Phillips, J. Kondev and J. Theriot, Physical Biology of the Cell (Garland Science, 2013, 2nd ed.).
A fantastic book that gives an introduction to cell biology, describes the physics that underlie cellular structures and processes, and how to build models to understand quantitative data. (Available on course reserves)

• Matt J. Keeling and Pejman Rohani, Modeling Infectious Diseases in Humans and Animals (Princeton University Press, 2008). (Some chapters will be posted on Latte.)

The following are some recommended textbooks for helpful background reading:

Cell Biology

• B. Alberts et al., Essential Cell Biology, 3rd Ed. (Garland Science, 2012).
This book will be a great complement, as it provides detail about the biological systems we study which goes well beyond what can be presented within an hour and a half lecture.

Thermodynamics and statistical mechanics
In an accessible manner, with an emphasis on biological systems:

- P. Nelson, Physical Models of Living Systems, (Freeman and Co., 2015) ISBN-13: 978-1464140297 ISBN-10: 1464140294

- K. Dill and S. Bromberg, Molecular Driving Forces, 2nd Ed. (Garland Science, 2012).

Computational modeling
• Harvey Gould, Jan Tobochnik, Wolfgang Christian, Introduction to Computer Simulation Methods : Applications to Physical Systems, (Addison – Wesley, 2005) ISBN 9780805377583
An extensive introduction to and reference guide for computer simulation techniques

LATTE
LATTE is the Brandeis learning management system: http://latte.brandeis.edu. Login using your UNET ID and password.

Library
The Brandeis Library collections and staff offer resources and services to support Brandeis students, faculty and staff. These include workshops, consultations, collaboration, materials and instruction on emerging trends in technologies such as machine learning, emerging trends in research such as data visualization, and emerging trends in scholarship such as open access. Librarians at the Circulation Desk, Research Help Desk, Archives & Special Collections, Sound & Image Media Studios, MakerLab, AutomationLab, and Digital Scholarship Lab are available to help you.
https://www.brandeis.edu/library/about/index.html

Student Support
Brandeis University is committed to supporting all our students so they can thrive. The following resources are available to help with the many academic and non-academic factors that contribute to student success (finances, health, food supply, housing, mental health counseling, academic advising, physical and social activities, etc.). Please explore the many links on this Support at Brandeis page (https://www.brandeis.edu/support/undergraduate-students/browse.html) to find out more about the resources that Brandeis provides to help you and your classmates to achieve success.

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Tentative Course Schedule

Please note: the timetable below is aspirational, and only a first-order estimate (i.e. a guess). Even in previous years when this course was taught in person, the amount of material that we covered in a semester varied widely depending on the background knowledge and interests of the course participants. It is not possible to know the timing with the new online format, until we try it.

As of now, my plan is to start lectures with approximately 20 minutes of presentations and questions from the course participants on the course material. Then, we will use the rest of the time for you to work on the in class exercises and problem sets, with the TA and me online to answer questions and help with stumbling blocks. This is essentially a lab course, and much of your effort will involve working on your own and with other students in the course to develop code, debug it, and, most importantly, analyze the results and then communicate them. We will also have opportunities out of the scheduled class time to meet one-on-one or in smaller groups with the TA and me, which we will schedule based on polling once the course starts.

The following schedule is designed to give a very rough (as noted above) estimate of the topics that we will cover and when.

Notation for reading assignments:
KN = Kinder and Nelson, A Student's Guide to Python for Physical Modeling
KR = Matt J. Keeling and Pejman Rohani, Modeling Infectious Diseases in Humans and Animals
TS = T. Schlick, Molecular Modeling and Simulation
FS = Frenkel and Smit, Understanding Molecular Simulation
PBOC = Physical Biology of the Cell, by Kondev, Theriot, and Phillips

I. Introduction to Python and scientific computing (1-5).

Reading: KN, p. 1-66;
KR, pg. 1-28 and pg. 308-310 (will be on Latte)

1. W 8/26:

-Introduction to course and course participants.

-Introduction to the concept of scientific computing.

-Tutorial on using Python for scientific computing
  -introduction to JupyterLab and Jupyter Notebooks.
  -overview of basic Python data structures,syntax, and modules, as well as packages for scientific computing: NumPy, SciPy, matplotlib

2. M 8/31
-Tutorial part 2.
-Introduce epidemiology.
-Introduce Problem set 1, modeling epidemiology

3. W 9/2
-Continue Tutorial
-Continue Problem set 1
-Continue epidemiology

% M 9/7 (Labor Day)

4. W 9/9
-Continue Tutorial
-Introduce random walks.

5. T 9/10 (Br Monday)
-Finish random walk model.

II. Molecular interactions and dynamics (6-9)

Reading: TS Chapter 1,
FS Chapters 1,4; Appendix D (all will be on Latte)

6. M 9/14 Introduce molecular interactions + molecular dynamics.
-The origin of forces and motions that make biology work
-Newton's Laws and the equations of motion
-Molecular dynamics simulation of neutral atoms
-Begin development of molecular dynamics code

7. W 9/16
-Continue development of molecular dynamics code.
-Introduce Problem set 3: MD simulations.

8. M 9/21

-First results on MD code. Visualizing output
-Measurements, averages, ensembles, and ergodocity
-Discuss FS Appendix D (on assessing statistical error)
- Problem set 3 continued: measuring correlation functions.

9. W 9/23
-Further analysis of molecular dynamics results, and assessment of their accuracy

III. Biomolecular structure at the atomic level (10-11)

Reading: TS Chapters 3,4

% M 9/28 (Yom Kippur)

10. W 9/30 (Brandeis Monday)
-Classification of protein structures and the forces that stabilize them
-Introduction to VMD, a powerful software application for visualizing biomolecules
-start VMD tutorial
-Start problem set 4.

11. M 10/5
    -Finish VMD tutorial.
    -Continue Problem Set 4

IV. Biomolecular dynamics at the atomic level (12-15)

Reading: TS Chapters 8,9

12. W 10/7
-Biomolecular force fields
-Introduction to NAMD, a biomolecular simulation package
    -Start NAMD tutorial

13. M 10/12 (Indigenous Peoples Day)

-Finish NAMD tutorial
-Start problem set 5

14. W 10/14
-Analysis of biomolecular simulations 1
-Continue problem set 5

15. M 10/19
-Analysis of biomolecular simulations 2

16. W 10/21
-Begin Term Projects

V. Coarse graining: from atoms to cells (17-21)

A. Statistical Mechanics and Ligand Binding
Reading: FS Chapter 2 (on Latte); PBOC Chapters 5 and 6, Ch 7.2.4 (pages 298-305)

17. M 10/26
- Equilibrium calculations and Boltzmann's formula
-The statistical mechanics of ligand binding
-Modeling ligand binding
-Introduce problem set 6: modeling conformational spreading in signaling networks

B. Monte Carlo Simulations
Reading: FS Chapter 3 (on Latte); TS Chapter 12

18. W 10/28
-The Ising model
-Introduction to Monte Carlo simulations
-Start Monte Carlo simulations
-Start Ising model simulations

19. M 11/2
-Lecture: Phase transitions and the critical point
-Discuss lectures
-Measure correlation functions in the Ising model

20. W 11/4
-Find the critical point in the Ising model
- From the Ising model to bacterial chemotaxis: the propagation of allosteric states in protein complexes and signaling networks
-Continue Problem Set 6

VI. Further coarse-graining: using ODE's and PDE's to model Genetics and cell regulation, and virus self-assembly (21-24)

Reading: PBOC Ch 19, up to the end of 19.2 (pgs 801-832); Articles on virus assembly (on Latte)

21. M 11/9
-The central dogma and gene regulation
-Numerical solution of ODE's

-Getting started with numerical solution of ODE's in python
-model the genetic switch
-model the genetic oscillator

22. W 11/11 (Vet. Day)
-Finish modeling the genetic switch and genetic oscillator
-Virus self-assembly
-Introduce problem set 7: modeling viral capsid self-assembly

23. M 11/16
-Introduction to nonlinear dynamics
-Work on problem set 7

24. W 11/18
-analysis of dynamical systems
-assess accuracy of numerical solutions to differential equations
-Continue problem set 7

% Thanksgiving
%

VII. Term Project Presentations (25-26)

25. M 11/30
Term Project Presentations 1

26. W 12/2
Term Project Presentations 2

Additional topics (if time permits, or included by substitution for one of the other topics)

VIII. Biased sampling techniques

-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
-Constructing Markov State Models and using them to overcome timescale limitations in simulations

VIII. Pattern formation

Reading: PBoC Chapter 20

-How an E.coli cell finds it's middle.
-The diffusion equation
-Reaction diffusion equations and Turing patterns
-Mammalian pattern formation--How a leopard gets its spots
-Numerical solution of PDE's using finite differences (Python)