Syllabus: Modeling the Living Cell
Models and Algorithms in Biophysics**.**
AS 250.302 , co-listed with ChemBE (4 credits)

Course description. An introduction to physical and mathematical models used to represent biological systems and phenomena. Students will learn algorithms for implementing models computationally and perform basic implementations in MATLAB (or code of choice). We will discuss the types of approximations made to develop useful models of complex biological systems, and the comparison of model predictions with experiment.
THIS COURSE HAS A HEAVY COMPUTER PROGRAMMING LOAD

The course contains 5 major sections:

1) Thermodynamics and basic statistical mechanics. Here we also will go through coding best practices.
2) Dynamics of equilibrium and non-equilibrium systems, equations of motion and applications to molecular systems.
3) Fluid dynamics and continuum models (partial differential equations). Reaction diffusion and cell scale modeling.
4) Optimization and dimensionality reduction for model fitting and data analysis.
5) Additional topics studied from the book and in-class journal clubs: membranes, cytoskeletal assembly, self-assembly, action potentials, gene expression.

See Specific Lecture Topics at the end of the Syllabus. **Labs meet on Mondays.

People:

Prof: Margaret E Johnson, 121C Mergenthaler Hall
margaret.johnson@jhu.edu
Office Hours: Tuesdays, after class: 2:45-3:45P

TA: Moon Ying: yying7@jhu.edu
Moon TA'ed this class last year (2022) very successfully! Make sure you go to his lab sessions!

Lectures: Tuesday and Thursdays from 1:30-2:45PM. **Hodson 313**

Labs: Labs meet on Mondays from 5-6PM **UTL G98**

Required Text: Physical Biology of the Cell. Phillips, Kondev, Theriot, Garcia. Link to JHU bookstore copy.

Additional Reading will be selected from the following texts and made available on blackboard:

Understanding Molecular Simulation, Frenkel and Smit
Information Theory, Inference, and Learning Algorithms, MacKay
Introduction to Modern Statistical Mechanics, David Chandler
Physical Models of Living Systems, Philip Nelson
Molecular Modeling and Simulation: An Interdisciplinary Guide, Tamar Schlick
Numerical Recipes (www.nr.com)

Prerequisite: An intro computing course. Calculus 3. NOTE: This class has a heavy computer programming load in the HW assignments. Students are given 2 weeks per assignment, but experience in a high-level programming language is needed. Any language is allowed but TAs and posted solutions have used MATLAB.

Who should take this course? Sophomores or above can enroll in the course. There is a large range of material covered. Masters and graduate students welcome.

Grading: 50% of the grading will be based on bi-weekly homework sets, 22% will be based on the midterm exam, 3% will be based on journal-club participation (2 lectures), and 25% will be based on the final project.

Late Homework Policy: Submitting homework a day late costs 20% of the points, 2 days late is 50%, 3 days is zero credit. *Computer programming is very difficult to get right the first time, debugging is inevitable, start early!*

Journal Club Classes: For a few lectures a year, students read a recent paper that describes an application of the methods we are learning about to new research problems. Students will read the paper prior to the lecture, work in small groups for half the class to discuss part of the paper (assigned by me), and then present their findings, each student presents in one of the journal clubs. This contributes to the grade.

Final Project: Each group has a choice of final project.

1. **Global optimization of protein model, and structural analysis.** This final project will build off code developed throughout the homework assignments to study coarse grained modeling approaches for studying proteins *in silico*. Students will be given target protein sequences and use bead models of protein structure and energetics to sample possible folded protein structures. They will compete to identify the global minimum of the protein structure, which represents the native folded structure, using global optimization techniques. They will also analyze their equilibrium trajectories and construct a Markov state model for understanding protein folding pathways. At least one new feature must be implemented.
2. **Create your own project.** Based on material and HW developed throughout the course, your team can propose their own final project that they are most excited about. Examples from previous years: Project 1 but applied to a specific protein system, Hemoglobin cooperative binding model, SIR disease

spread model for COVID19, SIR model of COVID19 including impact of vaccinations, PAR proteins pattern forming systems, more atomic-level protein folding model, genetic repressillator model, ghrelin hormone model for dynamics of hunger and satiety, HIV immune response model, dimerization of gramicidin in the membrane.

The final project is evaluated based on a final presentation of the project (during the final exam time), as well as a submission of the code used and a brief written summary of results.
THE FINAL PROJECTS WILL OCCUR DURING THE SCHEDULED FINAL EXAM TIME FOR THE CLASS TU/TH 1:30-2:45.

Ethics:

From the undergraduate academic ethics board: "Undergraduate students enrolled in the Krieger School of Arts and Sciences or the Whiting School of Engineering at the Johns Hopkins University assume a duty to conduct themselves in a manner appropriate to the University's mission as an institution of higher learning. Students are obliged to refrain from acts which they know, or under circumstances have reason to know, violate the academic integrity of the University."

Violations include and are not limited to cheating, plagiarism, and submitting work that is not your own, and will result in a **zero** on the assignment.

Classroom Climate:

I am committed to creating a classroom environment that values the diversity of experiences and perspectives that all students bring. Everyone here has the right to be treated with dignity and respect. I believe fostering an inclusive climate is important because research and my experience show that students who interact with peers who are different from themselves learn new things and experience tangible educational outcomes. Please join me in creating a welcoming and vibrant classroom climate. Note that you should expect to be challenged intellectually by me, the TAs, and your peers, and at times this may feel uncomfortable. Indeed, it can be helpful to be pushed sometimes in order to learn and grow. But at no time in this learning process should someone be singled out or treated unequally on the basis of any seen or unseen part of their identity.

If you ever have concerns in this course about harassment, discrimination, or any unequal treatment, or if you seek accommodations or resources, I invite you to share directly with me or the TAs. I promise that we will take your communication seriously and to seek mutually acceptable resolutions and accommodations. Reporting will never impact your course grade. You may also share concerns with the Director of Undergraduate Studies (Prof Sua Myong or Lise Dahuron), the Assistant Dean for Diversity and Inclusion (Darlene Saporu, dsaporu@jhu.edu), or the Office of Institutional Equity (oie@jhu.edu). In handling reports, people will protect your privacy as much as possible, but faculty and staff are required to officially report information for some cases (e.g. sexual harassment).

Family accommodation policy: You are welcome to bring a family member to class on occasional days when your responsibilities require it (for example, if emergency child care is unavailable, or for health needs of a relative). Please be sensitive to the classroom environment, and if your family member becomes uncomfortably disruptive, you may leave the classroom and return as needed.

Personal Wellbeing:

- COVID19: We will follow all university guidelines with regard to COVID, including masking, reporting, etc. For up-to-date information, see: https://covidinfo.jhu.edu
- If you are sick, in particular with an illness that may be contagious, notify me (or the TA) by email to be excused from class. Rather, visit the Health and Wellness Center: 1 East 31 Street, 410-516-8270. See also http://studentaffairs.jhu.edu/student-life/support-and-assistance/absences-from-class/illness-note-policy/
- All students with disabilities who require accommodations for this course should contact me at their earliest convenience to discuss their specific needs. If you have a documented disability, you must be registered with the JHU Office for Student Disability Services (385 Garland Hall; 410-516-4720; http://web.jhu.edu/disabilities/) to receive accommodations.
- If you are struggling with anxiety, stress, depression or other mental health related concerns, please consider visiting the JHU Counseling Center. If you are concerned about a friend, please encourage that person to seek out our services. The Counseling Center is located at 3003 North Charles Street in Suite S-200 and can be reached at 410-516-8278 and online at http://studentaffairs.jhu.edu/counselingcenter/

Date: 2022	Lecture	Topic	Extra Reading
Aug 29	1	Introduction to models and algorithms	Phys. Biol. Of Cell: Chapter 1
Aug 31	2	Dimensional analysis, length/time scales, model development	Phys. Biol. Of Cell: Chapter 2 &3
Sep 5	3	Computer programming best practices. Random numbers	Numerical Recipes: Rand
Sep 7	4	Energy, Entropy and equilibrium	PBoC Chapter 5-6. Chandler-Chapter 1, 3
Sep 12	5	Boltzmann distribution and Monte Carlo	Frenkel and Smit, Ch 3.
Sep 14	6	Monte Carlo	Frenkel and Smit, Ch 3
Sep 19	7	Rate equations, ODEs and chemical kinetics	Numerical Methods, Ch. 6, PBoC Ch 15
Sep 21	8	Stochastic simulations and Gillespie algorithm.	Van Kampen, Ch 3
Sep 26	9	Molecular Dynamics (MD): Model description	Frenkel and Smit, Ch. 4 (to section 4.4)
Sep 28	10	MD: Energy function and algorithms	Frenkel and Smit, Ch. 4.
Oct 3	11	MD & Langevin Dynamics	JOURNAL CLUB CLASS: Read the paper, Piana
Oct 5	12	Brownian dynamics and random walks	PBoC Ch. 13
Oct 10	13	Diffusion in the cell	PBoC Ch. 8, 16
Oct 12		**MIDTERM**	
Oct 17	14	Hydrodynamics, Reynolds number	PBoC Ch. 12
Oct 19		**FALL BREAK**	
Oct 24	15	Fluid dynamics, Navier-Stokes	PBoC Ch. 12
Oct 26	16	Pattern Formation and RD	PBoC Ch 20
Oct 31	17	Reaction-diffusion modeling	PBoC Ch 20
Nov 2	18	Optimization, simulated annealing	Schlick, Ch. 10
Nov 7	19	Clustering and Dimensionality reduction for analysis	MacKay Ch. 20 and 25, Schlick, Ch. 14, section 14.4
Nov 9	20	Markov models & Parameter estimation	MacKay, Ch. 22, Nelson, Ch. 6
Nov 14	21	Gene Expression and feedback	JOURNAL CLUB CLASS, Read the paper: Vilar et al
Nov 16	22	Membrane Mechanics	PBoC Ch 11
Nov 21		**THANKSGIVING WEEK**	
Nov 28	22	Electricity and Hodgkin Huxley	PBoC Ch 17
Nov 30	23	Cytoskeletal dynamics	PBoC Ch 15, (Ch 10)
Dec 5	24	Automatic differentiation for dynamical systems	Pdfs on Canvas

Dec 7	25	Control of self-assembly at the membrane	Research talk + slide rules