MCB137L / MCB237L: Physical Biology of the Cell

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Introduction

Biology is being revolutionized by new experimental techniques that have made it possible to quantitatively query the inner workings of molecules, cells and multicellular organisms in ways that were previously unimaginable. The objective of this course is to respond to this deluge of quantitative data through quantitative models and the use of biological numeracy. The course will explore the description of a broad array of topics from modern biology using the language of physics and mathematics. One style of thinking we will emphasize imagines the kinds of simple calculations that one can do with a stick in the sand.

We will draw examples from broad swaths of modern biology from our department and beyond including cell biology (signaling and regulation, cell motility), physiology (metabolism, swimming), developmental biology (patterning of body plans, how size and number of organelles and tissues are controlled), neuroscience (action potentials and ion channel gating) and evolution (population genetics) in order to develop theoretical models that make precise predictions about biological phenomena. These predictions will be tested through the hands-on analysis of experimental data and by performing numerical simulations using Python. Physical biology will be introduced as an exciting new tool to complement other approaches within biology such as genetics, genomics and structural biology. The course will introduce students to the enabling power of biological numeracy in scientific discovery and make it possible for them to use these tools in their own future research.

Note that no previous coding or advanced math skills are required. The course is designed with the objective of being widely accessible.

When and where

Lecture: Tuesday and Thursday, 11:00am – 12:30pm, 251 Dwinelle
Discussion section: Friday, 12:00pm – 1:00pm, 259 Dwinelle
Course Website
Piazza

Instructor and GSI

Instructor:

- Hernan Garcia (hggarcia@berkeley.edu)
- Office hours: Wednesdays, 2:30pm – 3:30pm, 505 Weill Hall and Zoom

GSI:

- NIck Gravina (nick_gravina@berkeley.edu)
- Office hours: Fridays, 1pm – 2pm, 505 Weill Hall

NOTE: For transparency, rather than emailing Hernan or Nick, we encourage you to message us through the course's Piazza website about any questions regarding homework assignments and class logistics.

Course structure

The class as a whole (approximately 25 students) will meet twice a week for one hour and a half. This time will be devoted to lectures, discussions and hands-on activities including Python exercises. Further, the class will be split into weekly one-hour lab sessions. During these lab sessions, students will work closely with the GSIs to implement the concepts they learned in class in the context of different biological problems, to elaborate on coding exercises, and to discuss anything related to the class. Homework assignments will be given every week and will represent 70% of the final grade. Homework assignments must be submitted and will be graded on GradeScope (entry code KK7J4G). At the end of the semester, students will prepare a written project. A list of possible projects will be provided on the course website. This project will represent 20% of the final grade. Further, 10% of the grade will be based on class participation.

Tentative syllabus

- Lectures 1 – 2: A Feeling for the Numbers in Biology
  - Street-Fighting Mathematics: Order-of-magnitude estimates as a tool for discovery in the living world.
  - What sets the scale of X?
- Lectures 3 – 4: Stuff(t)
  - Time evolution in biology.
  - Control and limits to bacterial growth.
- Lectures 5 – 7: Null Hypotheses in Biology: The Poisson Distribution.
  - The Great Probability Distributions of Biology.
  - The Poisson distribution: Bombs over London, constitutive promoters and sequencing the human genome.
  - Synthetic transcriptomes and the single-cell sequencing revolution.
- Lecture 8: Null Hypotheses in Biology: The Exponential Distribution
  - Waiting times for photobleaching and ion channel dynamics.
- Lectures 9 – 11: Diffusion as Biology's Null Hypothesis for Dynamics
  - Diffusion and axonal transport.
  - The binomial distribution: Coin flips, carboxysome partitioning and calibrating fluorescent protein counts.
  - FRAP: Measuring diffusion using photobleaching.
  - A universal diffusion speed limit for enzyme catalysis and other reactions.
- Lectures 12 – 15: Entropy Rules
  - Entropy maximization and the mathematics of superlatives.
  - Entropic forces: A DNA entropic spring
  - Phase transitions in biology.

- Lectures 16 – 17: The Boltzmann Distribution and Statistical Mechanics
  - Ion channels and two-state systems.
  - The ubiquitous nature of binding problems in biology.
  - Regulatory biology: simple repression in the *lac* operon.
- Lectures 17 – 20: Defiance Is the Secret of Life: Burning Energy for Fun and Profit
  - Energy estimates in biology
  - Biological batteries
  - Defying diffusion: Paying for positional information using degradation vs. transport.
  - Biological specificity: Kinetic proofreading.
- Lectures 21 – 23: Biological Networks
  - A life-or-death decision: The Lambda switch.
  - Vertebrate development and oscillations.
  - Epidemiology and the SIR model.
  - A genome-wide view of biological networks.
- Lectures 24 – 25: Biological Patterns in Space and Time
  - Morphogen gradients and the French flag model.
  - Turing patterns and digit formation.
- Lectures 26–27: Active Matter
  - The active filament: flagellar beating.
  - Intraflagellar active transport.
- Lectures 28: Evolution by the Numbers
  - The Luria-Delbrück experiment.
  - Introduction to population genetics: Hardy-Weinberg equation, genetic drift, selection, mutations.

Course Help

You're not alone in this course; the instructor and GSI are here to support you as you learn the material. We are committed to you succeeding and getting the most out of this course. It's expected that some aspects of this course will take time to grasp, and the best way to grasp challenging material is to ask questions. To ask a question, use Piazza, or attend office hours. **In fact, we strongly encourage you to make time in your schedule to attend at least one of the two office hours we offer.** The instructor and GSIs will monitor this discussion forum, but you should also feel free to answer questions posted by other students.

Students with Disabilities

If you require course accommodations due to a physical, emotional, or learning disability, contact UC Berkeley's Disabled Students' Program (DSP). Notify the instructor and GSI through course email of the accommodations you would like to use. You must have a Letter of Accommodation on file with UC Berkeley to have accommodations made in the course.

Course Policies and Suggestions for Success

- **Attending class and office hours:**
  - If you miss class, it is your responsibility to get notes from one of your classmates. You cannot expect the instructor or GSI to redo the lecture during office hours.
  - Being able to attend office hours are a key to success. If you cannot attend any of the three offered office hours, you might want to reconsider taking this course.
  - Please notify us in writing by the second week of the term about any known or potential academic or extracurricular conflicts. We will try our best to help you with making accommodations, but cannot promise them in all cases.
- **Homework assignments:**
  - Homeworks are due at the beginning of class one week after they are posted.

- Homeworks should be submitted through GradeScope using entry code KK7J4G as described in the course website. Any other form of homework submission will not be accepted.
- No late homeworks. Time management is key. Start to work on your homework assignments early and make use of office hours and our availability over Piazza.
- It is important to describe your reasoning. Just writing an equation or drawing a plot does not constitute a satisfactory answer to a homework problem.
- All plots in the homeworks need to have labeled axes.
- All code used needs to be submitted through GradeScope by the homework due date.
- You can work in groups, but the answers should be your own. This includes the code!

- **Grading:**
  - Regrading is done only until a week after the homework solutions are posted.
  - If you ask us to regrade an answer in a homework assignment, we reserve the right to regrade all the answers it that homework assignment.
  - Your two worst scoring homeworks will not be considered for the final grade.
  - We do not grade on a curve or anything like that. The grading scale we will used is shown below.

Letter	Percentage
A	94 – 100
A-	90 – 93
B+	87 – 89
B	84 – 86
B-	80 – 83
C+	77 – 79
C	74 – 76
C-	70 – 73
D+	67 – 69
D	64 – 66
D-	60 – 63
F	0 – 65

Academic Integrity

You're a member of an academic community at one of the world's leading research universities. Berkeley creates knowledge that has a lasting impact in the world of ideas and on the lives of others; such knowledge can come from an undergraduate paper as well as the lab of an internationally known professor. One of the most important values of an academic community is the balance between the free flow of ideas and the respect for the intellectual property of others. Scholars and students always use proper citations in papers; professors may not circulate or publish student papers without the writer's permission; and students may not circulate or post materials (handouts, exams, syllabi—any class materials) from their classes without the written permission of the instructor. Any test, paper or report submitted by you and that bears your name is presumed to be your own original work that has not previously been submitted for credit in another course unless you obtain prior written approval to do so from your instructor. In all of your assignments, including your homework or drafts of papers, you may use words or ideas written by other individuals in publications, websites, or other sources, but only with proper attribution. If you're unclear about the expectations for completing an assignment or taking a test or examination, be sure to seek clarification from your instructor or GSI beforehand. For additional information on plagiarism and how to avoid it, read the UC Berkeley Library Citation Page, Plagiarism Section. As a member of the campus community, you're expected to demonstrate integrity in all of your academic endeavors and will be evaluated on your own merits. The consequences of cheating and academic dishonesty—including a formal discipline file, possible loss of future internship, scholarship, or employment opportunities, and denial of admission to graduate school—are simply not worth it. Read more about Berkeley's Honor Code.

Suggested reading

- Phillips, R. *et al.* (2012). Physical Biology of the Cell, 2nd Edition. Garland Science.
  - Our course will be loosely based on this textbook. Many of the assigned problems will come from it. Note that we are actively working on the 3rd edition and I might hand out some chapters as we visit their topics in lecture.

- Kinder, J. and Nelson P. (2018). A Student's Guide to Python for Physical Modeling: Updated Edition. Princeton University Press.
  - This book is a great introduction to programming in Python. It could be useful reference material throughout the semester.
- Alberts, B. *et al.* (2014). Molecular Biology of the Cell. W. W. Norton & Company.
  - This book will be particularly useful for those needing a refresher of biology.
- Milo, R. and Phillips, R. (2015). Cell Biology by the Numbers. Garland Science.
  - This book, together with its companion BioNumbers website, has become the reference source for biological numeracy. The book can also be downloaded from `book.bionumbers.org`.
- Mahajan, S. (2010). Street-Fighting Mathematics: The Art of Educated Guessing and Opportunistic Problem Solving. MIT Press.
- Weinstein, L. and Adam, J.A. (2008). Guesstimation: Solving the World's Problems on the Back of a Cocktail Napkin. Princeton University Press.
  - These two books are fantastic resources for those wanting to learn more about estimation writ large.