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, 219 Dwinelle
Discussion section I: Friday, 12:00pm – 1:00pm, 2030 Valley Life Sciences
Discussion section II: Friday, 1:00pm – 2:00pm, 2030 Valley Life Sciences
Course Website
Piazza

Instructor and GSI

Instructor:

- Hernan Garcia (hggarcia@berkeley.edu)
- Office hours: Wednesdays, 3pm – 4pm, 505 Weill Hall

GSI:

- Yasemin Kiriscioglu (ykiriscioglu@berkeley.edu)
- Office hours: TBD

GSI:

- Yovan Badal (ybadal@berkeley.edu)
- Office hours: TBD

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

Course structure

The class as a whole (approximately 50 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 75% of the final grade. Homeworks must be submitted and will be graded on GradeScope (entry code 4PE35G). Twice during the semester, students will prepare a written project. A list of possible projects will be provided on the course website. These projects will represent 25% of the final grade.

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 things?
  - Cellular size limits.
- Lectures 3 – 4: The Great Probability Distributions of Biology
  - The binomial distribution: Coin flips, carboxysome partitioning and calibrating fluorescent protein counts.
  - The Poisson distribution: Bombs over London and sequencing the human genome.
  - The exponential distribution: Waiting times for photobleaching and ion channel dynamics.
- Lectures 5 – 6: Diffusion as Biology's Null Hypothesis for Dynamics
  - Diffusion and axonal transport.
  - FRAP: Measuring diffusion using photobleaching.
  - A universal diffusion speed limit for enzyme catalysis and other reactions.
- Lectures 7 – 8: Life is Flux: The Equations of Biological Dynamics
  - Exponential growth.
  - The constitutive promoter.
  - Dynamical systems and epidemiology.

- Lectures 9 – 10: Entropy Rules
  - Entropy maximization and the mathematics of superlatives.
  - Phase transitions in biology.
- Lectures 11 – 12: 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 13 – 16: Burning Energy for Fun and Profit
  - Defying diffusion: Paying for positional information.
  - Biological specificity: Kinetic proofreading.
- Lectures 17 – 19: Active Matter
  - Diffusion and hydrodynamics from the classic field theory perspective
  - Cytoplasmic streaming in *Chara*
  - Flow and polarity establishment in *C. elegans* embryos
  - The Toner-Tu theory of flocking
- Lectures 20 – 21: Compartmentalization in Space and Time
  - Organelle size control.
  - Enzyme rates and compartmentalization.
- Lectures 22 – 23: Biological Patterns in Space and Time
  - Morphogen gradients and the French flag model.
  - Turing patterns and digit formation.
- Lectures 24 – 25: Biological Networks
  - A life-or-death decision: The Lambda switch.
  - Vertebrate development and oscillations.
- Lectures 26 – 28: Evolution by the Numbers
  - The Luria-Delbrück experiment.
  - Introduction to population genetics: Hardy-Weinberg equation, genetic drift, selection, mutations.

Required bibliography

- 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.

Suggested reading

- 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.

Course policy and suggestions

- **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.
- **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 4PE35G 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