Physical Biology of the Cell

CSHL Topics in Biology Course

Hernan G. Garcia and Rob Phillips

3/8/26 – 3/14/26
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Course Philosophy

Biology has been revolutionized by 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 short, intensive 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, mathematics and computation. One style of thinking we will emphasize imagines the kinds of simple calculations that one can do with a stick in the sand.

The course draws examples from across modern biology, including cell biology (signaling, regulation, and motility), physiology and metabolism, developmental biology (patterning of body plans and the control of organelle and tissue size and number), neuroscience (action potentials and ion channel gating), and all the way to biology at the planetary scale. These examples are used to develop theoretical models that make precise, testable predictions about living systems. Those predictions are then tested through hands-on analysis of experimental data and through numerical simulations performed using Python.

Quantitative 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 enable 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: Sunday 3/8/26 through Saturday 3/14/26, Location TBD.

Instructors

Faculty:

- Hernan Garcia (hggarcia@berkeley.edu)
- Rob Phillips (phillips@pboc.caltech.edu)

Teaching Assistant:

- Sara Mahdavi (smahdavi@caltech.edu)

Course project

During the course, we will do many estimates about each biological phenomenon we address. To cement these skills, throughout the week, you will work on a short estimate individually or in groups. The idea is to present an interesting calculation about a biological phenomenon in the style of a vignette of Cell Biology by the Numbers. Some examples of interesting estimates are:

- How many proteins are in a viral capsid?
- What is the energy cost to a host cell in order to create a new virus after it has been infected?
- What is the cell-to-cell variability in the number of copies of the *lacZ* gene?
- What is the largest osmotic shock a cell can suffer without bursting?

Alternatively, you can write an estimate outside of biology. Some of our favorite examples are "MythBusters: Rapunzel", where the student estimated how much weight Rapunzel's hair could support and whether it could grow long enough, and "Cry me a River", where the student estimated the total volume he had cried due to breakups over his life.

Each evening, you will have 30 minutes to work on your estimate during our "study hall". You will then present your estimate in a short talk at the end of the course.

Tentatively Daily Rhythm

A typical day in the course looks like this:

- 9:00am-9:30am: Breakfast
- 9:30am-12:00pm: Lectures, hands-on activities and copious amounts of coffee.
- 12:00pm-1:00pm: Lunch
- 1:00pm-2:00pm: Research talk from course faculty and invited guests on their research in quantitative biology. We aim for these talks to be of high pedagogical value, so interruptions and questions are encouraged!
- 2:00pm-2:30pm: Breakout session between the students and the speaker. These sessions are perfect venues to ask follow up questions about the talk, but to also learn about the speaker's career path.
- 1:00pm-5:30pm: More lectures, hands-on activities and copious amounts of coffee.
- 5:30pm-6:00pm: Time to work on estimates for final presentation.

Tentative syllabus

- Sunday 3/8: **Bootcamp Introduction + A Feeling for the Numbers in Biology**
  - Student lightning talks
  - Course introduction
  - Street-Fighting Mathematics: Order-of-magnitude estimates as a tool for discovery in the living world
  - What sets the scale of X?
  - The cell as a bag of X
  - Speaker: Alexander Grosberg (New York University)
- Monday 3/9: **Stuff(t) and The Protocol of Biological Dynamics**
  - Update rules for dynamical systems

  - Gene expression dynamics
  - Exploratory dynamics
  - Speaker: Amy Shyer (Rockefeller University)

- Tuesday 3/10: **Quantifying Prejudice — The Great Probability Distributions of Biology**
  - Constitutive promoters: the Poisson distribution
  - Diffusion as the null model for biological dynamics: bionomial and Gaussian distributions
  - Molecular steps: The exponential distribution
  - Speaker: Jasna Brujic (New York University)

- Wednesday 3/11: **Vectors and Representations**
  - Representations: Everything is a vector
  - Finding the right coordinate system: The dance of the eigenworm
  - The theory of the transcriptome
  - Speaker: Avi Flamholz (Rockefeller University)

- Thursday 3/12: **Defiance is the Secret of Life: Burning Energy for Fun and Profit**
  - Entropy maximization and the mathematics of superlatives
  - Biological batteries
  - Defying diffusion: Paying for positional information, the cost of gradients.
  - Biological specificity: Kinetic proofreading.

- Friday 3/13: **Physical Biology of the Embryo**
  - Positional Information
  - Turing patterns
  - Morphogenesis: Shape and gut buckling

- Saturday 3/14: **Physical Biology of the Cell**
  - Dimensionless parameters
  - The protocols of Physical Biology
  - Presentations of students' projects
  - End of course party

Online Resources

- Physical Biology of the Cell @ Caltech
- Physical Biology of the Cell @ Berkeley YouTube Channel
  - Compilation of recorded lectures on Physical Biology.
- Introduction to Data Analysis in the Biological Sciences @ Caltech
  - This is an excellent and comprehensive course on Python and data analysis in the biological sciences by Justin Bois at Caltech.
- W3 Python Tutorial.
  - While we will not expect any prior Python knowledge, this online tutorial could come handy for those that want to start delving into Python or who need a refresher.

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. 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.