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 Matlab. 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.

Course structure

The course will meet twice a week for two hours. This time will be devoted to lectures, discussions and hands-on activities including Matlab exercises. Homework assignments will be given every week and will represent 75% of the final grade. Twice during the semester, each student will present on a project. These projects will represent 25% of the final grade.

For undergraduate students (MCB137L), the project will consist on carrying out an estimate on a biological phenomenon of interest following the style presented in class. Each presentation will be five minutes long.

Graduate students (MCB237L) will be assigned extra homework problems that will require domain of the research literature. In addition their project will consist on presenting a theoretical model developed in a recent paper of their choosing to the class. These presentations will be ten minutes long.

Tentative syllabus

- Lectures 1 and 2: A feeling for the numbers in biology
  - Street-Fighting Mathematics: Order-of-magnitude estimates as a tool for discovery in the living world.
  - *E. coli* by the numbers: Thinking up the bacterial census.
- Lectures 3 and 4: An obsession with dN/dt - Bacterial growth
  - The physical limits to bacterial growth.
  - Solving the exponential growth equation and testing it using image analysis.
- Lecture 5: Flies by the numbers
  - The making of a fly one cell at a time.
  - The machines of the central dogma in development.
- Lectures 6 and 7: Diffusion
  - Diffusion and axonal transport.
  - Measuring diffusion using photobleaching: FRAP.
  - A universal diffusion speed limit for enzyme catalysis and other reactions.

- Lectures 8 through 10: Regulatory biology
  - Ion channels and two-state systems.
  - The constitutive promoter.
  - The ubiquitous nature of binding problems in biology.
  - Simple repression in the *lac* operon.
  - Signaling and bacterial chemotaxis.
- Lecture 11: The French Flag model of developmental patterning.
- Lectures 12 and 13: A probabilistic view of biology
  - Coin flips and binomial distributions: Calibrating protein counts using coin flips.
  - Probability of mutations in the human genome and the Poisson distribution.
- Lecture 14 and 15: First project presentations.
- Lecture 16 and 17: Biological polymers
  - Mechanics of biological polymers.
  - Cytoskeletal filament length distributions.
- Lectures 18 and 19: A dynamical view of biology
  - Dynamics of gene expression and control of polymer length.
  - Randomness in biology: Stochastic simulations and master equations.
- Lectures 20 through 22: Evolution by the numbers
  - Order of magnitude estimates for evolution.
  - The Luria-Delbrück experiment.
  - Introduction to population genetics: Hardy-Weinberg equation, genetic drift, selection, mutations.
- Lectures 23 and 24: Biological specificity: Kinetic proofreading.
- Lectures 25 and 26: Phase transitions in biology.
- Lecture 27 and 28: Second project presentations.

Required bibliography

- Phillips, R., et al. (2013). Physical Biology of the Cell, 2nd Edition. New York, Garland Science.

Suggested reading

- Alberts, B. (2015). Molecular Biology of the Cell. New York, NY, Garland Science.
- Milo, R. and Phillips, R. (to be published in 2016, can be downloaded from `book.bionumbers.org/`). Cell Biology by the Numbers. New York, NY, Garland Science.
- Mahajan, S. (2010). Street-Fighting Mathematics: The Art of Educated Guessing and Opportunistic Problem Solving. MIT Press (2010).
- Weinstein, L. and Adam, J.A. (2008). Guesstimation: Solving the World's Problems on the Back of a Cocktail Napkin. Princeton University Press.

Course policy

- 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.
- Homeworks:
  - 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 email.
  - 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.