MCB137L: Physical Biology of the Cell

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1 Introduction

Biology is being revolutionized by new experimental techniques that have made it possible to measure the inner workings of molecules, cells and multicellular organisms with unprecedented precision. The objective of this course is to explore this deluge of quantitative data through the use of biological numeracy. We will survey exciting research examples from our department and beyond 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 module 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.

2 Course structure

The course will meet twice a week for two hours. The first hour will be devoted to lecturing and hands-on exercises using Matlab. The second hour will be a GSI-led discussion section aimed at cementing the knowledge acquired during lecture.

Homework assignments will be given every week and will represent 70% of the final grade. In the last weeks of the course, student groups will work on a final project, which will be presented the last week of classes. This final project will represent 20% of the final grade. Finally, 10% of the final grade will be assigned according to class participation.

3 Tentative syllabus

- Week 1: 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.
- Week 2: Embryonic development by the numbers
  - The making of a fly one cell at a time.
  - How to tell your head from your tail: The French Flag Model.
- Week 3: An obsession with dN/dt: Bacterial growth
  - Simulating exponential growth.
  - Measuring bacterial growth using image analysis.
- Week 4: The machines of the central dogma in development
  - Making DNA and RNA at the right time and place in the embryo.
  - Measuring the rate of transcript elongation in living flies.
- Week 5: 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.
- Week 6: Diffusion and biological polymer
  - The Gaussian distribution: Diffusion and models of biological polymers.
- Week 7 and 8: The ubiquitous nature of binding problems in biology
  - Two state models: Gating of ion channels.
  - Binding everywhere you look: Antigen-antibody, ligand gated ion channels, GPCRs, gene regulation.
  - A statistical approach to binding in biology: Ligand-receptor binding and cooperativity.

- Weeks 9 and 10: Regulatory biology
  - Transcriptional regulation: How bacteria decide what to eat and how flies make stripes.
  - The MWC concept and cooperativity in biology: Oxygen transport by hemoglobin, bacterial chemotaxis, quorum sensing, and nucleosomal occupancy and transcriptional regulation.
- Week 11 and 12: A dynamical view of biology
  - Dynamics of gene expression and control of polymer length.
  - Randomness in biology: Stochastic simulations and master equations.
- Week 13: 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.
- Week 14: Project presentations

4 Bibliography

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