Spring, 2024

Syllabus

MCB195: Foundations of Systems Biology and Biological Engineering

This class is cross-listed with ES195

Prof. Philippe Cluzel

Office Hours: Fridays 2:05-3:05pm or to be arranged by email, Northwest building, room 435.

Email: cluzel@mcb.harvard.edu

Teaching fellow: Richard Huang

Email: rhuang@g.harvard.edu

Office Hours: Mondays during 5:30-6:30pm in Jefferson 256

Topics to be covered:

Noise, stochastic processes, single-cell biology, robustness and evolvability of intracellular networks, structure-function relationships, modularity in biology, chaos, cell-to-cell variability, cell fate variability, predictive modeling.

Details about requirements will be discussed during the first class: Biweekly assignments (~5 total = 30%); two midterms (20% each); final exam (30%).

No Textbook

Relevant papers will be available from the course website

Mathematical tools that we will learn (for most of you): Fluctuations analyses with Fourier transform, Linearization, stochastic equations (Langevin formalism), solving easy differential equations, basic integration, statistical physics of dynamical behavior of large networks.

Topic 1: **From pollen to polymers**

Discovery of Brownian motion and diffusive processes

Random walk, how big is a coil of DNA?

Pipetting DNA, stretching DNA, stem-coil transition

Topic 2: **Donâ€™t filter the noise, use it! (Part 1)**

What is noise in biology?

How can I get rid of it?

Using it to measure concentration of proteins and mRNAs in living cells, application: Fluorescence correlation spectroscopy

Topic 3: **Donâ€™t filter the noise, use it! (Part 2)**

Using noise to characterize signaling pathways and gene expression;

Langevin stochastic equation

Week 5: Midterm/exam #1

Topic 4: **Can we listen to a bacterium dream?**

Inverse problem in biology: from observations of an organismâ€™s behavior, can we infer its internal states? Bacterial chemotaxis: an example.

Topic 5: **The sluggish spring**

Can we predict a cellâ€™s future response from its responses to smaller stimuli?

Coarse-graining signaling pathways using an elastic spring and a small bead.

Sluggishness of ultra-sensitive signaling cascades; Interdependence of fluctuations and cellular response. Concept of the fluctuation-dissipation theorem.

[Topic 6: From phrenology to systems biology]

Phrenology is a failed system of ideas, including the idea that personality traits are correlated with bumps on the skull, thought to be reflective of the underlying brain structure. What can systems biologists learn from phrenologists?

Introduction to structure-function relationships, correlations, causality, and prediction.

Topic 7: The power of power laws

Exploring power laws across sociology, biology, and economics.

Structure-function relationship, large intracellular networks. Understanding the role various random distribution and the deceptive effect of taking the mean.

Week 9: Midterm exam #2

Topic 8: Are there rules to the game of biology?

Reducing the collective behavior of *real* complex systems:

Using pairwise approximation and scaling for multi-drug therapies

and cancer treatments.

Topic 9: How Networks can Learning efficiently?

Introduction to Kauffman and threshold Boolean networks.

Robustness and evolvability in Boolean networks

Topic 10: Memoirs of a network

How do networks learn, remember, and forget?

Using Neural Nets to test different hypotheses about learning.

We will discuss how network topology and external perturbations can govern learning.