Computation and Control in Biological Systems

Credits: 2
Lecture hours: 32
Time: 9:50-12:15, E10-306, Week 1 to Week 11
Course website: https://chemaoxfz.github.io/ccbs/

Instructor: Fangzhou Xiao
Office hours: 1 hour / week, by email appointment.

TAs: Yihang Ding, Qinguo Liu
Office hours: 10am (Yihang), 2pm (Qinguo), at E3-111 BMAC lab 2nd floor.

Course Description:

Biological organisms exhibit many fascinating behaviors, from magical transformation of matter via thousands of steps of metabolic reactions, to robust homeostasis adapting to rapidly shifting environments, to survival and growth that balances persistence in extreme conditions and all-out ventures into opportunistic moments of rich nutrients, to dominance and terraforming of surroundings to its own advantage. Such complex behaviors involving lots of interacting components demand a rigorous and quantitative way of reasoning, like how we reason about complex engineered machines. In this course, we introduce and master tools of reasoning from three different schools of thought pondering about life: physics, system, and industry. Physics asks what life is as an object. System asks how life works as a machine. Industry asks how life could be useful as a tool. These three schools of thought have distinct origins, approaches to analysis, and goals. They shape how we think about life forms. The tools we learn from them span a wide range, from order of magnitude estimate to design of a single protein molecule, from Markov chains to control systems, from simple reasoning based on central dogma to whole-genome models. By the end of the course, you will be able to integrate these tools and perspectives into a cohesive whole and have the confidence to reason about any biological problem thrown at you, from single molecules to populations of organisms. No background needed, but an exuberant love for biology is mandatory.

Learning Objectives

- To understand and master the tools of analysis in quantitative synthetic biology
- To formulate problems encountered in synthetic biology into forms analyzable using the tools in quantitative synthetic biology
- To get familiar with the theoretical background and technical aspects underlying the tools

Grading

Assessment Criteria	Percentage
Attendance	10
Homework hand in	30
Homework presentation	40

Lecture note scribe	20

Grade	Assessment Standard
A	90-100%
B	80-89%
C	70-79%
D	60-69%
F	0-59%

Each homework has 3 points. If you hand in the homework on time, you get 3 points. That's 30 points on whether the homework is handed in.

Every week from week 2 to 11, students will be selected to present on their approach to the homework problems of the previous week. Each student is expected to give two presentations. 40 points are based on presentations, 20 points per presentation. We'll grade from 1 to 10, and take an average among the instructor and the two TAs.

The students selected to present each week will also serve as lecture note scribes for the lecture of that week. Use the latex template provided on the course website. The lecture notes should be of high quality, and serve as a useful reference during the course and for the future. The completed lecture note should be handed in two weeks after the lecture. This will count for 20 points.

Course Schedule

Roughly one homework each week. It will not be graded, but students will be asked to present on their solution to last week's homework problems in class.

The course will run for 11 weeks, 3 course hours (45 min per course hour) each week. With 2 course hours of lecture, and 1 course hour of student presentation on previous week's homework problems.

Week	Theme/Topic
1	Cell biology by the numbers, dimensional analysis, separation of time scales
2	Chemical reaction networks, rate equation, ODE and phase plane analysis and simulation, Stability analysis in general.
3	Adaptation biomachines. Basics of control (input/output), and adaptation as integral control. How biology implements integral control differently from electrical circuits. IFFL works in biology but not in traditional engineering.
4	Stochasticity, chemical master equation, noise analysis, Gillespie algorithm, gene expression burstyness, bimodal distribution, ergodicity.
5	Energy and equilibrium physics (kinetic proofreading), Markov chain
6	Computation biomachines. Biological networks as calculators, computers, artificial neural networks, and ... themselves?

7	Combinatorial regulation and promiscuous interactions in cell signaling and cell fate decisions, also ultrasensitivity in ligand-receptor binding. ROP as a way for holistic analysis, three archetypal behaviors in a binding reaction.
8	Holistic analysis solving the above problems. Behavior in ROP as trajectory through regimes. Computation of binding-catalysis networks - homotopy continuation.
9	Flux balance analysis (metabolic engineering), bioenergetics and metabolism (where does energy of ATP come from)
10	PROTEIN DESIGN! HANDS ON!!!! Nupack, Rosetta, Fold it.
11	Growth dynamics, proteome partition, diauxie, upshift/downshift

References

No background knowledge is needed, as anything necessary to understand the materials will be covered in the lectures. The following references are just for your general interest.

For general background on modeling of biological circuits, a nice (and free!) reference is Richard Murray's book "Biomolecular Feedback Systems" (most relevant are the first 3 chapters): http://www.cds.caltech.edu/~murray/BFSwiki/index.php/Main_Page

Of course another good general reference is Uri Alon's book on systems biology: https://www.amazon.com/Introduction-Systems-Biology-Mathematical-Computational/dp/1439837171/ref=pd_sbs_1?pd_rd_w=wdYPy&pf_rd_p=ed1e2146-ecfe-435e-b3b5-d79fa072fd58&pf_rd_r=JDGW416B0FACJD43JFET&pd_rd_r=bad2f030-2484-4414-bd96-e0da217b5971&pd_rd_wg=m5v3i&pd_rd_i=1439837171&psc=1

A very good course with abundant online materials: biocircuits.github.io

Cell biology by the numbers, by Rob Phillips. Available online: book.bionumbers.org

Nonlinear dynamical systems and Chaos by Steven Strogatz.