ENS 222 Spring 2016

Biological Circuits and Molecular Machines

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Lectures: `Thr 10:40-11:30 FASS G056`
`Fri 12:40-14:30 FMAN G056`

Course Description: 21st century already is, and will continue to be, the century of biology. Thus, any aspiring engineer should be equipped with knowledge of biological systems and tools to model their quantitative aspects. This course offers an introduction to molecular and cellular biology from an engineering point of view. It assumes no prior knowledge of biology beyond the level of NS 101-102.

The course will start by introducing "the cell" as the smallest unit of life. In the context of cell growth, students will learn a simple strategy for solving differential equations numerically, which will be used throughout the course to model the energetic and informational aspects of life.

When discussing the energetic aspects, I will introduce some of the "voltages" that cellular energetics relies on and the "wires" needed to dissipate these voltages. We will see that many proteins (enzymes, transporters, channels) serve as wires for these voltages. In fact, because of their ability to "charge" one battery by "dissipating" another, these proteins can also be viewed as *machines* that convert energy from one form to another. We will see that, in order to work continuously, these molecular machines need to go through *cycles* of operational states. However, unlike the machines we are familiar with from everyday life, the operation of these molecular machines is *random*. We will learn how to mathematically model these random, cyclic machines.

In the second part of the course we turn from energy to *information*. We will see how other proteins (transcription factors) implement molecular *logic gates*, like the familiar AND, OR and NOT gates of digital electronics. We will consider the information (in bits) that these proteins "read" while doing their jobs. Then, we will bring several of these logic elements together and analyze the *circuits* that bacterial cells employ when making decisions about "eating" sugars other than glucose. When examining their dynamical responses, we will first model these control circuits as *Boolean networks*. This will allow us to develop intuition about the qualitative features of the responses without delving into more advanced mathematical modeling. At the end, we will perform a quantitative analysis of the dynamical responses of these information control circuits.

Evaluation:

Homework assignments	25 %
First exam	25 %
Second exam	25 %
Final exam	25 %

Course Content:

I. Cells and mathematical modeling (2 weeks)

II. Molecular energetics

   A. Batteries and wires in the cell (2 weeks)

   B. Proteins as random machines (2 weeks)

   C. Proteins are cyclic machines (2 weeks)

III. Molecular information

   A. Molecular logic gates and information (2 weeks)

   B. Information control circuits in the cell (2 weeks)

Detailed Course Content:

	Cells and mathematical modeling	
Feb 4	General information about the course	
Feb 5	Mathematical model of cell growth	Cell growth with saturation
Feb 11	Numerical solution of cell growth model	
Feb 12	What is inside a cell?	
	HW 1: Logistic growth with MATLAB	(due Feb 19)
	Batteries and wires in the cell	
Feb 18	ATP hydrolysis as a battery	
Feb 19	Equilibrium of chemical reaction	The “voltage” of the ATP battery
	HW 2: Visualizing protein structures with VMD	(due Feb 26)
Feb 25	ATP battery needs a wire (rates of reactions)	
Feb 26	Proteins as “wires” for chemical batteries	Alternative conformations of ADK
	HW 3: Adenylate kinase (ADK)	(due Mar 4)
	Proteins as random machines	
Mar 3	Membrane permeability for glucose and ions	
Mar 4	Transporters and channels as machines	Protein machines are random
	HW 4: Permeation through lipid bilayers	(due Mar 11)
Mar 10	Kinetic modeling of random transitions	
Mar 11	Transporters and channels as machines	Random association of molecules
	HW 5: Random jumps between two states	(due Mar 18)
	Proteins as cyclic machines	
Mar 17	Fast and slow processes	
Mar 18	Approximate analysis of a 3-state cycle	Operational cycle of Phosphoglucose Isomerase
	HW 6: Phosphofructokinase	(due Mar 25)
Mar 24	Independent binding of multiple ligands	
Mar 25	Glucose Transporter as a 4-state machine	Analysis of the Glucose Transporter cycle
	HW 7: Glucose transporter	(due Apr 7)
Mar 31 Apr 1	Semester Break	
Apr 7		
Apr 8	**First exam**	
	Molecular logic gates and information	
Apr 14	Eating lactose instead of glucose	
Apr 15	Regulation of transcription	Boolean logic of *lac* operon
	HW 8: Logic gates from activators and repressors	(due Apr 22)
Apr 21	Language and entropy (Claude Shannon)	
Apr 22	Information needed to find DNA binding site	Information content of DNA binding sites
	HW 9: Information content of operator sequences	(due Apr 29)
	Cellular information control circuits	
Apr 28	Molecular Boolean networks	
Apr 29	Motifs in information control circuits	Three-node, feed-forward (FF) motifs
	HW 10: Boolean analysis of feed-forward motifs	(due May 6)
May 5	Kinetics of protein production and degradation	
May 6	Mathematical analysis of coherent FF loop	...and incoherent FF loop
May 12		
May 13	**Second exam**	
May ?	**Final exam**	