Background

The reductionist approach to molecular biology has given us detailed descriptions for many biochemical constituents of complex biological systems. For some of the simpler systems nearly the entire "parts catalog" has been assembled. These developments have set the stage for a new generation of questions -- questions of integration that deal with the relation between behavior of intact systems and their elemental determinants, questions of unifying design principles that will give meaning to the bewildering diversity of alternative molecular designs, questions of higher-level theory and quantitative prediction, which currently are not available in most of biology.

The motivation to develop this new perspective comes from the study of complex biochemical pathways, intricate circuits of gene regulation, network interactions within the immune system, plasticity of neural networks, and pattern formation by cellular networks. All these are cellular and molecular networks whose elemental constituents find their meaning within the context of the intact system.

Objectives

The integrative perspective requires new language and methodology. The objective of this course is to systematically develop these and to apply them to specific metabolic pathways and biochemical regulatory mechanisms, thereby demonstrating the power of this approach to formulate and answer fundamental questions concerning network function, design and evolution that currently can not be addressed by other methods.

Prerequisites

Math through calculus and introductory biology, or permission of instructor
COURSE INFORMATION

**Credits:** 4 units

**Time:** TR 10-11:50 AM

**Place:** 3202 Genome and Biomedical Sciences Facility (GBSF)

**Instructor:** Prof. Michael A. Savageau

**Office:** 3312 GBSF
(Office hours by arrangement)

**Course Pack:** "Biochemical Systems Theory", to be distributed

**Grading:**

Homework problems, approximately every week, solutions will be provided, approximately 1/6 of course grade

Midterm (Tuesday, Oct. 27), one hour, in class, closed book, closed notes, approximately 1/3 of course grade, but discounted if score is lower than that on the final exam

Final (Thursday, Dec. 10) two hours scheduled (but open ended), open book, open notes, approximately 1/2 of course grade
PART I. ANALYSIS OF INTEGRATED BIOCHEMICAL SYSTEMS

A. Conventions

Sept.  24  Molecular and Integrative Biology
        Graphical Representation of Networks (H1)
        29  Mathematical Representation of Processes
            Power-Law Formalism as a Fundamental Representation

Oct.  1   Mathematical Representation of Systems
          Alternative Mathematical Representations of Systems (H2)

B. Mathematical Tools

6     Steady State Existence
     Steady State Solutions
8     Network Theory
     Sensitivity Theory (H3)
13    Local Dynamics
     Routh Criteria
15    Global Dynamics
     Dynamic Diseases (H4)
20*   A Comparative Approach to Alternative Design
     Pathway without Feedback Control
22*   Pathway with End-Product Inhibition
     Mathematically Controlled Comparison (H5)
27    MIDTERM EXAM
PART II. ELUCIDATION OF SYSTEM DESIGN PRINCIPLES

A. Pathways

Oct. 29 Irreversible Pathways
Patterns of Feedback Control
Nov. 3 Amphibolic pathways
Regulation of Bidirectional flux (H6)

B. Branch Points

5 Distribution of Flux and Self-Starvation
Anticipatory Control: Feedforward and Feedback Control
10 Patterns of Regulatory Interactions in Branched Pathways
Regulatory Role of Enzyme-Enzyme Complexes (H7)

C. Cycles

12 Two-Component Systems
Sensing and Communication
17 Partner-Switching Systems
Stress Responses and Differentiation (H8)

D. Cascades

19 Inducible Gene Circuits
Perfectly Coupled Expression
23 Completely Uncoupled Expression
Role of Natural Inducer’s Position in Pathway (H9)
26 Thanksgiving
(no class)

E. Synthetic Circuits

Dec. 1* Generic Positive and Negative Feedback Circuitry
Input and Output Devices
3* Switches
Clocks (H10)

Dec. 10 FINAL EXAM

(H): Homework assigned and due one week later