Course Title: Introduction to Systems Biology

Catalog Description: The goal of this course is to highlight elementary design principles inherent in biology. Many of the underlying principles governing biochemical reactions in a living cell can be related to network circuit motifs with multiple inputs/outputs, feedback and feedforward. This course draws on control theory and elementary biology to provide a mathematical framework to understand biological networks. The topics examined in the course are drawn from current research and include: transcription networks, stochastic gene induction, adaptation, oscillators (circadian rhythms), riboswitches, plasticity, metabolism, pattern development and cancer. The course is intended for advanced undergraduates and graduate students. There is an optional lab that focuses on transforming bacteria, stem cell biology and stochastic simulation.

Prerequisites: Elementary Chemistry and Differential Equations.

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Proposed Text(s): The notes, along with research papers and links of interest can be found on *Sakai*:

Recommended Text:
1. *Molecular Biology of the Cell* by B. Alberts, D. Bray, J. Lewis, M. Raff, K. Roberts and J. Watson (5th edition)
2. *Gene IX* by Benjamin Lewin (9th edition)
3. *The Molecules of Life: Physical and Chemical Principles* by John Kuriyan, Boyana Konforti and David Wemmer, Garland Science (2013).
4. *The Cell, a Molecular Approach* by Geoffrey Cooper and Robert Hausman, Sinauer Assoc. (6th edition, 2012).
5. *Signals, Systems and Controls* by B.P. Lathi.

Lect/Disc clock hrs./wk: 3 for undergrad, 4 with lab/ 4 for graduate credit (lab)

Lectures: Meets in 100 Stinson-Remick Hall on Tuesday/Thursday from 12:30 pm to 1:45 pm Eastern.
Laboratory: Meets in 208 Stinson-Remick Hall either on Thursday from 6:00 pm to 9:00 pm Eastern OR 9:30am to 12:30 pm Eastern on Wednesday.

Grade: The final grade is comprised of three (four) components for undergraduate (graduate) students:
1. Homework problems + peer review (20%);
2. Mid-term (20%) and Final Exams (40%)
3. Class participation generally and analysis of current research in particular (20%).

- 5-7 homework problem sets will be assigned during the course of the semester. You will be allowed to work in teams on each homework. A team will be assigned to you and the composition of your team will rotate. Each team will produce only one set of solutions to the homework. Your homework grade will be based in part on your team performance, evident in the homework write-up, and in part on the team member evaluation forms (see attached.) If the homework is not completed on-time, NO GRADE will be given for that homework and the TEAM RECEIVES A ZERO. The homework sets are due at the beginning of the class.
- The exams are 1.5 HOUR duration, administered during the regular class time. The exam usually consists of problems derived from the homework, the class work, or assigned reading. The exams score is an individual grade. Thus, you are encouraged to attend class and participate in the class discussion, and do all of the homework problems yourself. If you have an unexcused absence from the class the day an exam is

administered, you will receive a ZERO for the test. Excused absences are only given prior to the class, NOT AFTERWARD.

- There are assigned readings of about 8-10 papers. You will be asked to critically evaluate these articles as if you were reviewing them for publication against the usual criterion such as originality, relevance to the field, timeliness, scientific competence, etc. You will be graded on your comprehension of the paper as demonstrated by your ability to summarize the research ORALLY in class, and through your evaluation of it. The grade is either PASS or FAIL. Lack of participation counts as a FAIL.
- For graduate credit an additional project/paper will be required along with a 15 minute report to the class (33%) to be accomplished in conjunction with the lab. The paper will be presented in the form of a short NSF-style proposal (10 pages or less) consisting of 4 components (Scientific Foundation, Aims, Preliminary Data, and Research Design and Methods).

4. For additional credit hours (3→4 hrs) a lab component will be offered. The lab consists of 3-5 lab practicals and demands a write-up at the end of each. The grade for the lab is determined by four components:

- Lab write-up (25%)
- Participation (25%)
- Lab performance (25%)
- Safety procedures (25%)

Lecture Topics:	Hours (40 hrs total)
1. Introduction to molecular/cell biology	1.0
2. A review of network concepts: properties and modeling of feedback/feed-forward systems	1.0
3. The cell as a microreactor: metabolism and transport	1.0
4. Introduction to molecular biology (molecular recognition, proteins, DNA, repressors/promoters/ Hill functions)	1.0
5. Transcription networks (timescales, introduction to gene regulation)	1.0
6. Transcription networks revisited (multi-input functions, dynamic response in gene regulation)	1.0
7. Autoregulation(AR) (negative for fast response time and robust stable production in gene circuits)	1.0
8. Autoregulation (positive AR slows response and leads to bi-stability:	1.0
9. Cell-to-Cell variability, stochastic gene induction,stochastic simulation	1.5
10. Feed-forward Loop (FFL) Network Motif (Dynamics of coherent FFL with AND logic)	1.0
11. FFL is a sign-sensitive delay element	1.0
12. Incoherent FFL (dynamics—pulse generator; response acceleration)	1.0
13. Eukayrotic Transcription and the RNA World	1.0
14. Riboswitches, Ribozymes (natural and synthetic) and miRNA	1.5
15. Network Motifs in development transcription networks (positive feedback loops for making decisions; regulating feedback; developmental timing; interlocked feed-forward loops in *B. subtilis*)	1.0
16. Information processing using Multi-layer perceptrons.	1.0
17. Network Motifs in neuronal networks (An example: *C. elegans*)	1.0
18. Network Motifs: negative feedback and oscillator motifs	1.0
19. Conformational transitions in biomolecules (in action)	1.0
20. Protein circuits (an example: bacterial chemotaxis in *E. coli*):	1.0
21. Two models for Adaptation: 1. Robust and 2. Fine-tuned:	1.0
22. The Robust Adaptation (Barkai-Leibler) and Integral Feedback.	1.0
23. Linearization of nonlinear systems--linear system response	1.0
24. Stability— Routh criterion, Nyquist criterion, root locus techniques	1.0
25. Circadian rhythms—how to build an oscillator; repressillator	1.5
26. Buzzers, Toggles, sniffers, and oscillators	1.0
27. Kinetic Proofreading (proofreading the genetic code to reduce error rates of molecular recognition) Recognizing Self and Non-self	1.5
28. Robust Patterning in Development	1.0
29. Differentiation, development and early cell fate	1.0
30. Self-renewal, plasticity, and stem cells	1.0

31. Gene Circuit Design (optimal expression of a protein in a constant, periodic and stochastic environment)	1.5
32. The Savageau Demand Rule: e.g. the demand rule in *E. coli*	1.5
33. Rules for gene regulation (based on minimal error load or selection repression; multiregulator systems)	1.0
34. Conformational transition in biomolecules revisited (on an evolutionary scale)	1.0
35. Metabolism and Metabolic Control Analysis	1.5
36. The Systems Biology of Cancer, oncogenes, and p53 tumor suppressor	1.5