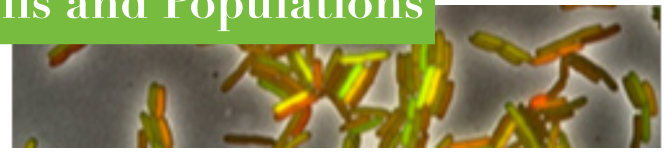
Biophysical Modeling of Cells and Populations



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Course No.: BIOL-GA 1131 and cross-listed as MATH-GA 2852 & PHYS-GA 2061
Time: Thursdays, 9:30 AM–12:15 PM
Location: To be determined

Description: The course covers modeling of biological systems at multiple levels. In the first part, we begin with some basic molecular biology, including cooperative binding and simple induction of genes. We develop a general approach to quantitative modeling of transcriptional regulation. We apply this to study small genetic circuits with feedback loops. We study pattern formation, and the mechanisms by which cells perceive spatial information from chemical signals. We investigate how biological systems can function robustly in the face of noise. In the second part, we study cellular behaviors within heterogeneous populations. We introduce population models, and relate these to the molecular/cellular models of the first part. Diverse biological examples (see Syllabus & Reading List) will be presented over the course of the semester to illustrate key concepts in modeling.

Grading: 20% Problem Sets (5 problem sets over the semester)
40% Discussions (in-class, student-led)
40% Final Project (presentation + paper)

Prerequisites: This course is geared towards a highly diverse group of students, including biologists, mathematicians, and physicists. For this reason, there are no hard prerequisites. Comfort with mathematics is the only requirement (e.g. familiarity with differential equations). Previous exposure to programming or computational software such as *Matlab* or *Mathematica* will be useful for the projects, though the ambitious student could learn these along the way. For any further questions, please contact me at elk2@nyu.edu.

Books (recommended)
Phillips, R., Kondev, J., Theriot, J., *Physical Biology of the Cell*, Garland Science, 2nd ed.
Berg, Howard, C., *Random Walks in Biology*, Princeton University Press, 1993.
Ptashne, M., *A Genetic Switch: Phage Lambda Revisited*, 3rd edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York, 2004.

Papers:
Will be available on NYU Classes.

Syllabus

Basic elements	Jan 31		Lecture:	– Introduction and some estimates – Cooperativity (7.2.4)
	Feb 7		Discussion:	Cooperativity in Hemoglobin
			Lecture:	A statistical mechanics primer (6.1)
Classic systems	Feb 14		Discussion:	The *lac* operon I
			Lecture:	Transcriptional regulation (19.2)
	Feb 21	(due: PS1)	Discussion:	The *lac* operon II
			Lecture:	Bistablity (19.3.5)
	Feb. 28		Discussion:	Phage λ
			Lecture:	Chemotaxis (19.4)
	Mar 7	(due: PS2)	Discussion:	Chemotaxis
			Lecture:	Diffusion and gradients (13.1,13.2)
	Mar 14		Discussion:	*Drosophila* development
			Lecture:	Dynamics of scale (20.2)
	Mar 21		NO CLASS – Spring Break	
Noise & Oscillations	Mar 28	(due: PS3)	Lecture:	– Stochastic Dynamics – Stability Analysis
	Apr 4		Discussion:	Circadian Clocks
			Lecture:	Pattern Formation (20.3)
	Apr 11	(due: PS4)	Discussion:	Noise in Biological Systems (19.3)
Populations			Lecture:	Introduction to Populations
	Apr 18		Discussion:	Simpson's Paradox
			Lecture:	Fitness and diversity
	Apr 25		Discussion:	Gene Surfing
			Lecture:	Phenotypic switching
	May 2		Discussion:	Antibiotic persistence
			Lecture:	Game theory I
	May 9		Discussion:	Bacterial games
			Lecture:	Game Theory II
	May 16		Presentations	

Reading Schedule

read by:

Feb 7

Read Chapters 1 & 2 in Phillips.

Changeux, JP and Edelstein, SJ. *Allosteric mechanisms of signal transduction*, Science, 308:1424 (2005).

Extra reading (optional): Monod, J, Wyman, J, Changeux, JP. *On the nature of allosteric transitions - a plausible model*, J Mol Biol, 12:88 (1965).

Discussion:
1. Milo, R, Hou JH, Springer, M, Brenner, MP, and Kirschner, MW. *The relationship between evolutionary and physiological variation in hemoglobin*, PNAS, 104:16998-17003 (2007).

Feb 14

Read Chapters 3 & 4 in Phillips.

Discussion:
1. Novick A and Weiner, M. *Enzyme induction as an all-or-none phenomenon*, PNAS 43:553 (1957).

Feb 21

Discussion:
1. Vilar JMG, Guet CC, and Leibler S. *Modeling network dynamics: the lac operon, a case study*, Journal of Cell Biology 161:471-479(2003).

2. Choi PJ, Cai L, Frieda K, and Xie XS. *A stochastic single-molecule event triggers phenotype switching of a bacterial cell*, Science 322:442-446 (2008).

Feb 28

Read "A Genetic Switch" (Chapters 1 – 3) by Mark Ptashne.

Discussion:

1. Santillan, M and Mackey, MC. *Why the lysogenic state of phage lambda is so stable: a mathematical modeling approach*, Biophys J, 86:75 (2004).

2. Zeng L et al. *Decision making at a subcellular level determines the out come of bacteriophage infection*, Cell 141:682-691 (2010).

Mar 7

Read "Random Walks in Biology" (Chapter 6) by Howard Berg.
Discussion:
1. Sourjik V and Berg HC. *Receptor sensitivity in bacterial chemotaxis*, PNAS, 99:123-127 (2002).
2. Endres, RG and Wingreen, NS, *Precise adaptation in bacterial chemotaxis through "assistance neighborhoods."* PNAS, 103:13040 (2006).

Mar 14 **Discussion:**
1. Gregor, T., et al., *Stability and nuclear dynamics of the bicoid morphogen gradient*, Cell, 130:141-152 (2007).
2. Gregor, T., et al., *Probing the limits to positional information*, Cell, 130:153-164 (2007).

Apr 4 **Discussion:**
1. Vilar, JMG, Kueh, HY, Barkai, N and Leibler S. *Mechanisms of noise-resistance in genetic oscillators*, PNAS, 99:5988-5992 (2002).
2. Rust, JM et al. *Ordered phosphorylation governs oscillation of a three-protein circadian clock*, Science, 318:809-812 (2007).

Apr 11 **Discussion:**
1. Elowitz, MB, Levin, AJ, Siggia, ED and Swain PS. *Stochastic gene expression in a single cell*, Science, 297:1183-1186 (2002).
2. Elf, J, Li, G and Xie, XS. *Probing transcription factor dynamics at the single-molecule level in a living cell*, Science, 316:1191-1194 (2007).

Apr 18 **Discussion:**
1. Chuang, JS, Rivoire, O and Leibler S. *Simpson's paradox in a synthetic microbial system*. Science, 323:272-275 (2009).
2. Dai L, Vorselen D, Korolev KS, and Gore J. *Generic indicators for loss of resilience before a tipping point leading to population collapse*. Science, 336:1175 (2012).

Apr 25 **Discussion:**
1. Hallatschek O and Nelson DR. *Life at the front of an expanding population*, Evolution, 64:193–206 (2009).

May 2 **Discussion:**
1. Balaban NQ, Merrin, J, Chait, R, Kowalik L, and Leibler S. *Bacterial persistence as a phenotypic switch*, Science, 305: 1622-1625 (2004).
2. Rotem E, et al. *Regulation of phenotypic variability by a threshold-based mechanism underlies bacterial persistence*, PNAS, 107:12541-6 (2010).

May 9 **Discussion:**
1. Gore J, Youk H, van Oudenaarden A. *Snowdrift game dynamics and facultative cheating in yeast*. Science, 459:253 (2009).
2. Xavier JB, Kim W, and Foster KR. *A molecular mechanism that stabilizes cooperative secretions in Pseudomonas aeruginosa*. Molecular Microbiology, 79:166 (2011).