Systems Biology 205

Topics in Synthetic Biology

Lecture and Discussion schedule

Pam Silver and Jack Szostak, Department of Systems Biology
Matthew Mattozzi and Anna Chen, Teaching Fellows

436 Warren Alpert
TTh 4-5:30 PM

The emerging field of Synthetic Biology (Hobum, 1980; Rawls, 2000) offers some exciting new research and production opportunities, drawing on advances in biology and engineering. This course will introduce the student to some of exciting topics of the field, and students will present some of the hottest new research. Each week will consist of a lecture (on Tuesday) and a TF/faculty led discussion on Thursday.

Discussion sections will consist of a journal club-type presentation by a student or group (30 minutes) followed by discussion of that paper and other recent, relevant topics in the field (60 minutes). A recent review article is listed below for relevant background.

Students will work in groups (depending on size of class) to give a final project and associated presentation at the end of class…part proposal, part sales pitch for a project that may be pursued at the Wyss Institute for Biologically Inspired Engineering. Slides and a brief summary (1 page) of each project will be due at the end of the semester.

Grading rubric:
10% Attendance (please get absences excused in advance)
20% Journal club presentation
20% Participation in class and others' presentations
50% Final presentation and summary

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Date	Topics
Jan 25	Introduction to Synthetic Biology Pam Silver and Jack Szostak Brief presentation on course requirements, etc. Suggested reading: Presidential Commission for the Study of Bioethical Issues. 2010. "New Directions: The Ethics of Synthetic Biology and Emerging Technologies"
Jan 27	Discussion Molecular biology crash course (Matt and Anna)
Feb 1	Synthetic circuits in prokaryotes (Pam) Suggested reading: Sprinzak D and Elowitz MB. 2005. Reconstruction of genetic circuits. *Nature* **438**(7076): 443-8.
Feb 3	Discussion Required reading: Basu S, Mehreja R, Thiberge S, Chen M, and Weiss R. 2004. Spatiotemporal control of gene expression with pulse-generating networks *PNAS* **101**(17):6355-6360.

Feb 8	Logic and engineering applied to biology (Tom Knight)
Feb 10	Discussion Required reading: Norville JE, Derda R, Gupta S, Drinkwater KA, Belcher AM, Leschziner AE, Knight TF Jr. 2010. Introduction of customized inserts for streamlined assembly and optimization of BioBrick synthetic genetic circuits. *J Biol Eng*. **4**(1):17.
Feb 15	Synthetic circuits in eukaryotes (Pam) Suggested reading: Haynes KA, Silver PA. 2009. Eukaryotic systems broaden the scope of synthetic biology. *J Cell Biol*. **187**(5):589-96.
Feb 17	Discussion Required reading: Thomas DD, Donnelly CA, Wood RJ, and Alphey LS. 2000. Insect population control using a dominant, repressible, lethal genetic system *Science* **287**(5462):2474-2476.
Feb 22	Modeling biological systems (Jeremy Gunawardena)**.** Suggested reading: Lewis J. 2003. Autoinhibition with transcriptional delay: a simple mechanism for the zebrafish somitogenesis oscillator. *Current Biology* **13**:1398-408
Feb 24	Discussion Required reading: Tigges M, Marquez-Lago TT, Stelling J, and Fussenegger M 2009. A tunable synthetic mammalian oscillator *Nature* **457**(7227):309-312.
March 1	Engineering genomes (George Church) Suggested reading: Ugwumba IN et al. 2011. Improving a Natural Enzyme Activity through Incorporation of unnatural Amino Acids. J Am Chem Soc. 133(2):326-333.
March 3	Discussion Required reading: Gibson et al.Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome. *Science* **329**, 52(2010).
March 8	Biofuels (Dave Savage) Suggested reading: Ducat D, Way JC, and Silver PA. 2011. Engineering cyanobacteria to generate high-value products. *Trends Biotech* Jan 4. [Epub ahead of print] Wackett LP. 2008. Biomass to fuels via microbial transformations. Current Opinion in Chemical Biology 2008, **12**:187-193 Somerville S. 2007. Biofuels. *Current Biology* **17**(4): R115-R119.
March 10	Discussion Required reading: Schirmer A *et al.* 2010. Microbial Biosynthesis of Alkanes. *Science* **329**:559-62.
	SPRING BREAK
March 22	Metabolic Engineering (Matt Mattozzi) Suggested reading: Prather KL and Martin CH. 2008. De novo biosynthetic pathways: rational design of microbial chemical factories *Curr.Opin.Biotechnol.* **19**(5):468-474. Keasling JD. 2009. Synthetic Biology for Synthetic Chemistry. *ACS Chemical Biology* **3**(1):64-76.
March 24	Discussion Required reading: Martin VJJ, Pitera DJ, Withers ST, Newman JD, Keasling JD. 2003. Engineering a mevalonate pathway in *Escherichia coli* for production of terpenoids. *Nature Biotechnology* **21**:796-802
March 29	Lecture – Evolution or Design of Molecular Components (Jack) Seelig B, Szostak JW. 2007. Selection and evolution of enzymes from a partially randomized non-catalytic scaffold. *Nature.* **448**(7155):828-31. Alterovitz G, Muso T, Ramoni MF. 2010. The challenges of informatics in synthetic biology: from

	biomolecular networks to artificial organisms. *Brief Bioinform*. **11**(1):80-95.
March 31	Discussion Required reading: Lincoln TA, Joyce GF. 2009. Self-sustained replication of an RNA enzyme. *Science* **323**(5918):1229-32.
April 5	Lecture – DNA Origami (William Shih) Suggested reading: Seeman NC. 2010. Nanomaterials based on DNA. *Annu Rev Biochem* **79**:65-87.
April 7	Discussion Required reading: Gu H, Chao J, Xiao SJ, Seeman NC. 2010. A proximity-based programmable DNA nanoscale assembly line. *Nature* **465**(7295):202-5. Lund K, Manzo AJ, Dabby N, Michelotti N, Johnson-Buck A, Nangreave J, Taylor S, Pei R, Stojanovic MN, Walter NG, Winfree E, Yan H. 2010. Molecular robots guided by prescriptive landscapes. *Nature* **465**(7295):206-10.
April 12	Lecture – Protocells (Jack) Suggested Reading: Schrum JP, Zhu TF, Szostak JW. 2010. The origins of cellular life. *Cold Spring Harb Perspect Biol*. **2**(9):a002212. Noireaux V, Libchaber A. 2004. A vesicle bioreactor as a step toward an artificial cell assembly. *Proc Natl Acad Sci USA* **101**(51):17669-74.
April 14	Discussion Required reading: Merkle D, Kahya N, Schwille P. 2008. Reconstitution and anchoring of cytoskeleton inside giant unilamellar vesicles. *Chembiochem* **9**(16):2673-81.
April 19	Lecture – Protein engineering (Jeff Way) Suggested reading: Taylor N, Way JC, Silver PA, Cironi P. 2010. Anti-glycophorin single-chain Fv fusion to low-affinity mutant erythropoietin improves red blood cell-lineage specificity. *Protein Engineering, Design & Selection* **23**(4):251-60.
April 21	Discussion Required reading: Cironi P, Swinburne IA, Silver PA. 2008. Enhancement of cell type specificity by quantitative modulation of a chimeric ligand. *J Biol Chem* **283**(13): 8469 –76.
April 26	Lecture – Stem cell engineering (Alex Meissner) Suggested reading: Hanna JH, Saha K, Jaenisch R. 2010. Pluripotency and cellular reprogramming: facts, hypotheses, unresolved issues. *Cell*. **143**(4):508-25. Review. Jaenisch R, Young R. 2008. Stem cells, the molecular circuitry of pluripotency and nuclear reprogramming. *Cell*. **132**(4):567-82. Review.
April 28	Discussion Required reading: Koche RP, Smith ZD, Adli M, Gu H, Ku M, Gnirke A, Bernstein BE, Meissner A. 2011. Reprograming factor expression initiates widespread targeted chromatin remodeling. *Cell Stem Cell.* **8**(1):96-105. Smith ZD, Nachman I, Regev A, Meissner A. 2010. Dynamic single-cell imaging of direct reprogramming reveals an early specifying event. *Nat Biotechnol* **28**(5):521-6. Mikkelsen TS, Hanna J, Zhang X, Ku M, Wernig M, Schorderet P, Bernstein BE, Jaenisch R, Lander ES, Meissner A. 2008. Dissecting direct reprogramming through integrative genomic analysis. *Nature.* **454**(7200):49-55.
May 3	Project Presentations
May 5	Project Presentations