BIOL 8006

M 11-1 Emerson 204

Instructors:
Roger Alexander: roger.alexander@biology.gatech.edu
Todd Streelman: todd.streelman@biology.gatech.edu

Integrative Approaches to Biological Systems

Understanding complexity is a central goal of science. Complex networks govern connection speed on the Internet, air traffic and highway control patterns, the flow of energy and species composition in ecological communities, and the relationships of proteins in human hearts and brains. To get a handle on complexity, engineers have begun to collaborate with biologists to study how evolution has 'engineered' complex biological designs (i.e., organisms). The upshot of this research includes a catalogue of design principles for complex systems (e.g., diversity, robustness, modularity, evolvability) and unexpected consequences for the relationship between form and function. It has been suggested that complexity is an emergent property of these design principles and that highly complex systems are qualitatively different from simple ones. Are there in fact general rules that biological systems (genes, cells, communities) follow? If so, what are they? These are the sorts of questions we will attempt to answer.

How Class Works

First 11 weeks:
1st hour: presentation of general topic, overview of focal papers (ppt is ok)
2nd hour: discussion of general topic, detailed dissection of 2-3 focal papers (presenter during first hour is the *de facto* expert for the day).

Each student (or pairs of students) will choose a topic and a day to be class expert. Lectures/presentations are meant to review what is known about complex systems from a particular perspective (e.g., genetics). Paper discussions are meant to reinforce the concepts discussed during presentations. **Everyone** should be prepared to discuss focal papers.

Week 12 and 13:
Continuation of class topics – OR – Guests with particular interest (and expertise) in complex systems will regale us with their knowledge. Format to be determined.

Last 3 weeks:
Student groups of 2-3 will deliver synthetic presentations to the class. These presentations/papers are meant to integrate the information learned during the semester, to generate something new and interesting. For instance, groups might investigate the following questions:

(i) Are Davidson and Erwin (2006, reading list) wrong?

(ii) Are prokaryote regulatory networks different from eukaryote regulatory networks?

(iii) Are prokaryote genomes limited by 'regulatory overhead? (Mattick papers, reading list)'

(iv) Are ecological and molecular networks similar or different? Are there indirect effects in molecular networks? What is the molecular analogue of the 'keystone species?'

(v) Is 'network fragility,' once usefully defined, a meaningful way to integrate studies of disease and environmental ruin?

Grading
Students will be graded based on (i) class participation, (ii) presentations of focal papers from the literature, and (iii) team presentations.

Schedule
Week of…
August 21: Syllabus, Grades, Introduction: What are biological systems? (Streelman)

August 28: Introduction continued: Diversity, robustness, modularity and evolvability (Streelman)

September 4: Labor Day

September 11: Biological systems as networks – network architecture (Alexander)

September 18: The network structure of genetic interactions

September 25: The network structure of transcriptomes and proteomes

October 2: The network structure of transcriptomes and proteomes

October 9: The network structure of metabolomes

October 16: Fall Recess

October 23: The network structure of development

October 30: The network structure of ecological systems

November 6: The network structure of ecological systems

November 13: The network structure of engineered systems

November 20: Group Presentations

November 27: Group Presentations

December 4: Group Presentations/Review

<u>Preliminary Reading list</u>

Alfaro ME, Bolnick DI and PC Wainwright (2004) Evolutionary dynamics of complex biomechanical systems: an example using the four-bar mechanism. Evolution 58:495-203.

Rutherford SL and S Lindquist (1998) Hsp90 as a capacitor for morphological evolution. Nature 396:336-342.

Croft LJ et al (ms) Is prokaryote complexity limited by accelerated growth in regulatory overhead? JTS preprint pdf.

Butland G. et al (2005) Interation network containing conserved and essential protein complexes in *E. coli*. Nature 433:531-537.

Csete ME and JC Doyle (2002) Reverse engineering of biological complexity. Science 295:1664-1669.

Lynch M and JS Conery (2003) The origins of genome complexity. Science 302:1401-1404.

Mattick, JS and MJ Gagen (2005) Accelerating complexity. Science 307:856-858.

Fargione JE, Tilman D (2005) Diversity decreases invasion via both sampling and complementarity effects. Ecology Letters 8: 604-611.

Estes JA, Tinker MT, Williams TM, Doak DF (1998) Killer whale predation on sea otters linking oceanic and nearshore ecosystems. Science 282: 473-476.

Croll DA, Maron JL, Estes JA, Danner EM, Byrd GV (2005) Introduced predators transform subarctic islands from grassland to tundra. Science 307: 1959-1961.

Mezey JG, Cheverud JM and GP Wagner (2000) Is the genotype-phenotype map modular? A statistical approach using mouse quantitative trait loci data. Genetics 156:305-311.

Wagner GP and L Altenberg (1996) Complex adaptations and the evolution of evolvability. Evolution 50:967-976.

Kennedy TA, Naeem S, Howe KM, Knops JMH, Tilman D, Reich P (2002) Biodiversity as a barrier to ecological invasion. Nature 417: 636-638.

Bellwood DR, Hoey AS, Choat JH (2003) Limited functional redundancy in high diversity systems: resilience and ecosystem function on coral reefs. Ecology Letters 6: 281-285.

Tilman D, Reich PB, Knops JMH (2006) Biodiversity and ecosystem stability in a decade-long grassland experiment. Nature 441: 629-632.

France KE, Duffy JE (2006) Consumer diversity mediates invasion dynamics at multiple trophic levels. Oikos 113: 515-529.

Straub CS, Snyder WE (2006) Species identity dominates the relationship between predator biodiversity and herbivore suppression. Ecology 87: 277-282.

Ives AR, Cardinale BJ, Snyder WE (2005) A synthesis of subdisciplines: predator-prey interactions, biodiversity and ecosystem functioning. Ecology Letters 8: 102-116.

Thebault E, Loreau M (2005) Trophic interactions and the relationship between species diversity and ecosystem stability. American Naturalist 116: E95-E114.

Paine RT (2002) Trophic control of production in a rocky intertidal community. Science 296: 736-739.

Duffy JE (2003) Biodiversity loss, trophic skew and ecosystem functioning. Ecology Letters 6: 680-687.

Worm B, Duffy JE (2003) Biodiversity, productivity and stability in real food webs. Trends in Ecology and Evolution 18: 628-632.

Lehner B et al (2006) Systematic mapping of genetic interactions in *C. elegans* identifies common modifiers of diverse signaling pathways. Nature Genetics 38:896-903.

Lenski RE et al. (2003) The evolutionary origin of complex features. Nature 423:139-144.

Chesler EJ et al (2005) Complex trait analysis of gene expression uncovers polygenic and pleiotropic networks that modulate nervous system function. Nature Genetics 37:233-242.

Sharan R et al. (2005) Conserved patterns of protein interaction in multiple species. PNAS 102:1974-1979.

Uetz P et al (2000) A comprehensive analysis of protein-protein interactions in *Saccharomyces cerevisiae*. Nature 403:623-627.

Davidson EH et al (2002) A genomic regulatory network for development. Science 295:1669-1678.

Davidson EH and DH Erwin (2006) Gene regulatory networks and the evolution of animal body plans. Science 311:796-800.

Proulx SR, Promislow DEL and PC Phillips (2005) Network thinking in ecology and evolution. Trends in Ecology and Evolution 20:…

Noble D (2002) Modeling the heart – from genes to cells to the whole organ. Science 295:1678-1682.

Bascompte J, Melián CJ, Sala E (2005) Interaction strength combinations and the overfishing of a marine food web. PNAS 102:5443-5447.

Kondoh M (2003) Foraging adaptation and the relationship between food-web complexity and stability. Science 299:1388-1391.

McCann KS (2000) The diversity-stability debate. Nature 405:228-233.

Montoya JM, Pimm SL and RV Sole (2006) Ecological networks and their fragility. Nature 442:259-264.

Lenski RE et al (1999) Genetic complexity, robustness and genetic interactions in digital organisms. Nature 400:661-664.

von Dassow G, Meir E, Munro EM and GM Odell (2000) The segment polarity network is a robust developmental module. 406:188-192.

Barkai N and Leibler S (1997) Robustness in simple biochemical networks. Nature 387:913-917.

Alon U, Surette MG, Barkai N and LeiblerS (1999) Robustness in bacterial chemotaxis. Nature 397:168-171.

Kalir S and Alon U (2004) Using a quantitative blueprint to reprogram the dynamics of the flagella gene network. Cell 117:713-720.

Kalir S, McClure J, Pabbaraju K, Southward C, Ronen M, Leibler S, Surette MG and Alon U (2001) Ordering genes in a flagella pathway by analysis of expression kinetics from living bacteria. Science 292:2080-2083.

Balazsi G, Barabasi AL, Oltvai ZN (2005) Topological units of environmental signal processing in the transcriptional regulatory network of *Escherichia coli*. PNAS 102:7841-7846.

Milo R, Shen-Orr S, Itzkovitz S, Kashtan N, Chklovskii D and Alon U (2002) Network motifs: Simple building blocks of complex networks. Science 298:824-827.