MCB 291: Genetics, Genomics, and Evolutionary Biology

***Instructors*:** **Cassandra Extavour (CE), Andrew Murray (AM), Andrew Berry (AB)**
***Teaching Assistants*:** **Guo-Liang "Chewie" Chew (GC), Nichole Collins (NC)**
***Office Hours*:**

***Lectures*: M, W, 10:30 – Noon**

***Discussion*: F, 10 – Noon**

This is a graduate student class that will provide an integrated introduction to the interface between genetics, genomics, and evolutionary biology. Our aim is to assume a minimum of background information and progress rapidly to a sophisticated level of understanding by focusing on a few examples rather than trying to provide a comprehensive view of a very large subject. The course will begin with three lectures on applying quantitative approaches to understanding biological problems (Murray), touch on Darwin/Wallace and Mendel in their historical contexts (Berry/Murray), discuss how to find and analyze genetic elements that control traits of interest (Extavour/Murray), introduce some key concepts in population genetics (Murray), cover the evolution of developmental processes, biological regulatory networks, and proteins (Extavour), and close by discussing some unsolved problems in evolution.

The format of the course will be informal, with the expectation that lectures will be frequently interrupted by questions and discussion, and that all students will participate in each of the weekly discussion sections.

The course will be graded on three problem sets (30%), a final exam (50%), and participation in discussion sections (20%).

Books
There is no textbook that we recommend for the entire class. For population genetics, two short books may be useful, although both go well beyond the material we will present.

Maynard-Smith, J. 1997 Evolutionary Genetics. Oxford University Press.
Hartl, D. 2000. A primer of population genetics. Sinauer.

For genetics, all the standard textbooks have expanded to a point where they are more useful as doorstops than a distillation of the minimum material that a graduate student should master. There is little to choose between the contenders, although

Suzuki et al. 2004. An introduction to genetic analysis.. Freeman.

may be the least excessive, and has a website at http://www.whfreeman.com/iga/.

For comparative and evolutionary developmental issues, see the following:

Minelli, A. and Fusco, G., eds. 2008 Evolving Pathways: Key Themes in Evolutionary Developmental Biology. Cambridge University Press.

Reviews

Some things to warm up with, only if the beach has begun to seem stale, flat, and unprofitable.

Hartwell, L. H., Hopfield, J. J., Leibler, S., and Murray, A. W. (1999). From molecular to modular cell biology. Nature *402*, C47-52. *A review about modularity and levels of explanation*

Abzhanov, A., Extavour, C., Groover, A., Hodges, S. A., Hoekstra, H. E., Kramer, E. M. and Monteiro, A. (2008). Are we there yet? Tracking the development of new model systems. Trends in Genetics *652,* 353-360.

Rules and regulations

Discussion sections

You should read the paper or papers in depth and come prepared to discuss them. We don't pre-assign individual students to lead the discussion or research specific questions. We do direct questions to individual students, so each of you will need to be ready to answer questions about the fundamental question the paper sets out to tackle, the design of the experiments or calculations, the results obtained, and the extent to which you buy the authors conclusions, inferences, and speculations. Doing things this way is not a hazing ritual, but an attempt to make sure that you each get as much as you can out of each discussion and that you participate equally, rather than allowing the extroverts to dominate the introverts.

Problem sets

There will be three problem sets. Each will focus on a specific area and ask you to read and think about a topic that is related to something that we covered in class, but will require you to approach the topic in a depth that we cannot reach in a course that covers such a wide array of material. You are encouraged to collaborate with each other in thinking about and discussing the topic and the questions you ask, but each of you must write your own answers to the questions. Beware of the herd effect. The point of view that the majority of your colleagues has decided a particular is correct may be wrong, or even dead wrong! We expect that the reading, thinking, and writing associated with each problem set will occupy around 12 hours of your time.

Final

There will be a 3 hour, in-class, final, which will be designed to test your ability to use the concepts we expose you to. You may bring with you all the facts that you can fit on one side of a single piece of 8.5 x 11 inch paper.

Day	Date	Notes	Lecture/Discussion	Title/Topic	Lecturer	Content Guide
W	**8/31/11**	Class Start	**Lecture 1**	**Numbers matter**	**GC + NC**	*Probabilities*
F	9/2/11		Discussion 1	Probabilities		*Problem-solving using statistics*
M	9/5/11	Labor Day	*no class*			
W	**9/7/11**		**Lecture 2**	**Why questions matter**	**AM + CE**	*Course overview, diagnostic quiz (20 min)*
F	9/9/11		Discussion 2	Luria and Delbruck		*Using statistics to make discoveries*
M	**9/12/11**		**Lecture 3**	**The Lac operon**	**AM**	*Reaching a sophisticated understanding of a classic problem*
W	**9/14/11**	**PS 1 Out**	**Lecture 4**	**Darwin in context**	**AB**	*Thought pre-Darwin, Darwin on Evolution, what's missing*
F	9/16/11		Discussion 3	Novick and Weiner, Van O		*Sophisticated analysis of Lac in 1957 and again in 2004*
M	**9/19/11**		**Lecture 5**	**Mendel in context**	**AM**	*Thought pre-Mendel, rediscovery, macro vs micro mutation*
W	**9/21/11**		**Lecture 6**	**Tree of Life**	**CE**	*Model system relationships, evolution of major morphologies*
F	9/23/11		Discussion 4	Mendel		*The pea experiments as an example of reductionism*
M	**9/26/11**	PS 1 Due	**Lecture 7**	**Homology**	**CE**	*Definitions, history, criteria, hierarchical levels of selection*
W	**9/28/11**		**Lecture 8**	**Homoplasy**	**CE**	*Convergence, parallelism, morphological & molecular levels*
F	9/30/11		Discussion 5	Lahn, Domazet		*chromosomal evolution (or genomic hourglass)??*
M	**10/3/11**		**Lecture 9**	**Genetics I**	**AM**	*How to do and exploit genetic screens & selections*
W	**10/5/11**		**Lecture 10**	**Genetics II**	**AM**	*Chromosome behavior: centromeres, origins, mitosis/meiosis*
F	10/7/11		Discussion 6	Ellis and Horvitz		*How to do a genetic screen*
M	10/10/11	Columbus Day	*no class*			
W	**10/12/11**	**PS 2 Out**	**Lecture 11**	**Genetics III**	**CE**	*Genetics in diploid organisms?*
F	10/14/11		Discussion 7	Andersen		*Genome based genetic screens*
M	**10/17/11**		**Lecture 12**	**Genomics**	**AM**	*Genome structure, high throughput analysis*
W	**10/19/11**		**Lecture 13**	**Pop Gen I**	**AM**	*Asexual issues: drift, selection, speed; Sex*
F	10/21/11		Discussion 8	Cairns and Foster		*Is Lamarck alive or dead? Adaptive mutation*
M	**10/24/11**	PS 2 Due	**Lecture 14**	**Pop Gen II**	**AM**	*Speed of evolution, mutators, regulatory networks*
W	**10/26/11**		**Lecture 15**	**Pop Gen III**	**AM**	*Detecting selection: linkage disequilibrium, drift, QTLs*
F	10/28/11		Discussion 9	Sabeti, Kingsley		*Detecting selection in the human genome*
M	**10/31/11**		**Lecture 16**	**Phylogenetics**	**AM**	*An introduction to trees, construction & interpretation*
W	**11/2/11**		**Lecture 17**	**Modularity/Co-option**	**CE**	*Definitions, implications, modification mechanisms*

F	11/4/11		Discussion 10	Seo, HIV		*Hox cluster disintegration, HIV tree analysis*
M	**11/7/11**		**Lecture 18**	**Protein Evolution**	**CE**	*Logic, support, implications, functional mechanisms*
W	**11/9/11**	**PS 3 Out**	**Lecture 19**	**Bioinformatics**	**AM**	*How to infer biological function from sequence data*
F	11/11/11		Discussion 11	Halabi, Milo		*protein sectors, constraints on the evolution of hemoglobin*
M	**11/14/11**		**Lecture 20**	**Constraint**	**CE**	*Definitions, concept evolution; evolvability*
W	**11/16/11**		**Lecture 21**	**Cis-Reg Evolution**	**CE**	*Interpretation of heterologous expression, gene duplication*
F	11/18/11		Discussion 12	Chan, McGinnis		*sticklebacks, Hox genes, Hoekstra & Coyne review*
M	**11/21/11**	PS 3 Due	**Lecture 22**	**Species, Speciation**	**AM**	*Formation, definition, immutability*
W	**11/23/11**	pre-Thanksgiving	*no class*			
F	11/25/11	Thanksgiving	*no class*			
M	11/28/11		**Lecture 23**	**Prediction/Evolution**	**AM**	*Bet-hedging: specialized kin-selection, role in disease*
W	11/30/11		Review			
F	**12/2/11**	**Class End**	**FINAL EXAM**			