GGE GENOMES AND GENE EVOLUTION

BIO 385 Spring 2009

"You can't understand the stock market by studying a single trader, or a movie by putting a DVD under a microscope. The fallacy is … in thinking that an individual gene will matter, at least in a way that is large and intelligible enough for us to care about." ___ Steven Pinker

"The vast majority of innovation in the human genome has been not in the invention of new genes at all, but more than 95% of all the major innovations have been in the controls for genes, the regulations of when to turn them on and off…It's not as if the symphony has been inventing lots of new notes; it's been figuring out what order to play them in." ___ Eric Lander

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Charles Darwin and Alfred Wallace advanced the theory of evolution through natural selection during the mid-19th century. Despite over 150 years of modification, the central theory remains as the most important organizing principle of modern biology. The genetic revolution of the 20th century provided an understanding of the conceptual and molecular basis for the heritable variation imagined by Darwin and Wallace: genes are sequences of DNA that are subject to a natural process of mutation. However, evolutionary biologists continued to focus their efforts primarily on understanding variation at the level of organismal form and function, without probing the underlying molecular mechanisms. At the same time, molecular biologists focused most of their attention on understanding the functions of the cell, without probing the implications of these mechanisms for understanding organismal change over long periods of time. The challenge of 21st century biology is to synthesize these two approaches into a cohesive picture of how change at the DNA level leads to changes in the form and function of organisms. This has been the motivation for the nascent field of "Evo-Devo," evolutionary developmental biology, which seeks to elucidate the mechanisms by which changes in genes and their regulation cause changes in the development and physiology of organisms. These central biological problems have been addressed through comparative and regulatory genomic approaches.

GGE takes an in-depth look at modern comparative and regulatory genomics primarily through the lens of the evolution of animal genes. The choice of animals reflects the greater research emphasis on animal systems, although many of the general principles are relevant to understanding all organisms. The primary technical focus of the course will be bioinformatic methodologies that allow comparisons among DNA and protein sequences and measurement of gene regulation. These technologies are applicable to a wide range of biological research and applications in the clinic and forensics. Thus we will also have the opportunity to discuss investigations of whole genome responses to differing environmental conditions or disease states.

SCHEDULE

CLASS	TOPIC	READING	ACTIVITY
	PART I: CORE CONCEPTS		
T 1/13	Evolution		
R 1/15	Animal evolution and gene evolution	*Caroll et al.* (handout)	
T 1/20	Gene regulation		
R 1/22	Case study: Hox genes I	*Carroll et al.*	
T 1/27	Case study: Hox genes II	*Averof and Patel.* (PDF)	DISCUSSION
R 1/29	Methods I (regulatory genomics)		Pre-survey
T 2/3	Methods II (genome sequencing)		
	PART 2: COMPARATIVE GENOMICS		
R 2/5	Comparative genomic projects I		
T 2/10	*No class*		
R 2/12	Comparative genomic projects II	*DeRosa et al.* (PDF)	DISCUSSION; EXAM 1
T 2/17	Sequence retrieval and analysis		Lab
R 2/19	Sequence alignment ; phylogenetic trees	*Hall, Ch. 1-5, Appendices*	Lab
T 2/24	Algorithms and bioinformatics (C. Kussmaul)	TBA	
R 2/26	Phylogenetic trees	*Hall, Ch. 1-5, 10*	Lab
	SPRING BREAK		
T 3/10	Phylogenetic trees		Lab
R 3/12	Phylogenetic trees		Lab
	PART 3: REGULATORY GENOMICS		
T 3/17	Identification of regulatory elements		PAPER 1
R 3/19	Analysis of regulatory elements	*Gompel et al.* (PDF)	DISCUSSION
T 3/24	Introduction to microarray lab; cDNA synthesis	Lab handout	Lab
R 3/26	Preparation of DNA		Lab
T 3/31	Hybridization 1	Lab handout	Lab
R 4/2	Wash; hybridization 2		Lab
T 4/7	Microarray applications I	*Abzhanov et al.* (PDF)	DISCUSSION
R 4/9	Introduction to MagicTool	Handout	Lab
T 4/14	Microarray data analysis	Handout	Lab
R 4/16	More microarray data analysis	Handout	Lab
T 4/21	Discussion of results		Lab
R 4/23	Microarray applications II	*Hughes et al.* (PDF)	DISCUSSION
	PART 4: APPLIED GENOMICS		
T 4/28	Student-led seminars		Post-survey
R 4/30	Student-led seminars		PAPER 2
TBA	Final exam period to be determined		EXAM 2

COURSE MATERIALS AND DESIGN

In this course, lecture and discussion will be supplemented by review of primary literature, use of bioinformatics tools (*in silico* labs) and a wet-lab experience centered on microarray technology. We will utilize one practical text for the comparative genomics and gene evolution segment of the course: *Phylogenetic Trees Made Easy: A How-to Manual* by Barry G. Hall, available for purchase at the bookstore. Supplemental readings and questions for discussion will also be assigned throughout the semester. Blackboard, the on-line course utility supported by the College, will also serve as a source for course information; please plan to check our Blackboard course site regularly.

COURSE ASSIGNMENTS

In addition to your daily participation in class, you will prepare a presentation for the class on a specific application of genomic technologies in the final week of the course. There will also be two papers developed from your work in the *in silico* labs centered on comparative and regulatory genomics. Two exams will also be given to help assess your understanding of course material. Exam 1 will cover core concepts presented in Part 1 and Exam 2 will cover the remainder of the course. More detailed information about all of these course components will be provided in class.

COURSE GRADES

The final course grade will be determined as follows:

Component	Total
Participation	100 points
Exam 1	50 points
Exam 2	100 points
Papers, 2 @ 100 points each	200 points
Presentation	100 points
	550 points total

A decile grading scale as follows will be used for the determination of final letter grades: A, 90% and above; B, 80-89%; C, 70-79%; D, 60-69%; F, 59% and below. Pluses (+) and minuses (-) may be used to denote the higher and lower end of each range.

We will assess participation as follows: A range- daily oral participation or less frequent but especially insightful participation; B range- weekly oral participation or occasional but especially insightful participation; C range- very infrequent participation. Missing more than two classes for any reason will lower the grade.

COURSE POLICIES

All course requirements are to be performed under the bounds of the Academic Behavior Code. Please familiarize yourself with this document and understand that a student who violates the Code will likely receive a failing grade for the course. Cheating will not be tolerated in any form. Keep in mind that all written work handed in for this course ***must*** be your own. You may discuss assignments with your peers or your instructors, but the written work submitted must be your work alone. Plagiarism takes many forms, including a failure to cite other work properly, and will be taken VERY seriously.

All assignments are due on the date indicated. Late assignments will result in a significant penalty. Each exam must be taken at the scheduled time. Exceptions to these policies will be allowed only in the case of serious illness or family emergency. All exceptions ***must be pre-approved*** by one of the instructors and documented by a physician or other official.

Attendance is expected at every class. If you cannot attend a particular class, it is ***your*** responsibility to obtain notes from a classmate. While we understand that you might have to miss a class due to an interview or other compelling reason, you will need to let us know ahead of time. If you expect to miss more than one or two classes, you should discuss with us whether this class is appropriate for you to take this semester.

It is important that students with documented disabilities discuss appropriate accommodations with the course instructors as soon as possible.

OFFICE HOURS

As you are probably well aware at this point, Drs. Hark and Wightman are generally fairly easy to find M-F during regular work hours, except when we are teaching this or our other class. If you want to meet with either of us for any reason, stop by during office hours or email us for an appointment.

Dr. Hark's office hours: M 2-3:30pm, R 11am-12:30pm, or by appointment.
Dr. Wightman's office hours: MW 9:30-10:30am, T 11-11:30am and R 11:30am-12:30pm, or by appointment.

We look forward to working with you in this new course and encourage you to come see us if you have any questions, comments, or concerns at any time. –BW & ATH