updated November 22, 2012 to reflect schedule changes after Hurrican Sandy!

BIOSCIENCES 767: MOLECULAR EVOLUTION
BIOLOGY 579: MOLECULAR EVOLUTION AND CONSERVATION GENETICS

KARL J. FRYXELL FALL, 2012

Readings. There is one required text for this course, "The Origins of Genome Architecture" by Michael Lynch (2007). Two additional recommended texts may be helpful for some students: "Reading the story in DNA: a beginner's guide to molecular evolution" by L. Bromham (2008); and "Fundamentals of Molecular Evolution" by D. Graur and W.-H. Li (2000). Additional assigned reading includes primary research articles in scientific journals. These are available through the GMU library E-journals web link, and some may also be available on paper in the Fenwick Library or Prince William library.

Dates, Times, and Contact Information. This course meets Tuesdays at 4:30 - 7:10 pm, in Bull Run Hall, room 246. My office hours this semester will be Fridays, from 3-4 pm in Discovery Hall, room 305. Phone: 703-993-1069 E-mail: kfryxell@gmu.edu Web site: http://mason.gmu.edu/~kfryxell

Introduction. The field of molecular evolution originated in the 1960s when Emile Zuckerkandl and Linus Pauling showed that biological evolution occurs primarily through the slow and steady accumulation of changes in DNA sequences and occasional gene duplications. Fundamental discoveries have followed in every subsequent decade – such as the discovery that all genes belong to gene families, statistical methods of analyzing protein functions, the development of evo/devo methods of understanding the evolution of gene regulation, the neutral theory, and whole-genome analysis of natural selection. The field of molecular evolution has become the conceptual foundation of genomics and drug discovery, and the basis of our methods of gene discovery and biotechnology.

These results give us the ability to understand the process of evolution in considerable detail. Progress is accelerating, and is helping to answer the question of who we are and where we came from. It is also having a major impact on biotechnology and the biomedical sciences, and is widely used in analyzing genetic pathways.

Molecular evolution also has applications in conservation genetics, such as molecular assays of the effective population size of a species, a molecular definition of species boundaries , and a more detailed understanding of why and when a minimal population size may be needed for the long-term survival of the species.

Grading summary: 10% presentation, 10% participation, 40% term paper, 40% final exam.

Students registered in this class will be required to write one term paper. The topic of your term paper should use your assigned article as a starting point, but should go well beyond that to a critical evaluation of recent developments in that field. These articles will be assigned on a "first come, first served" basis, one student per paper, so choose early if you wish to have a choice.

Papers labeled with an asterisk are reserved for Ph.D. students. Ph.D. student will be required to present their paper to the class (~30 min), in the week in which the paper is assigned (see below). These presentations should focus on explaining the assigned paper to the class, plus the background material that the class will need to understand it. You are encouraged to briefly mention other recent research and ideas you are developing for your term paper on this topic. Term papers written by Ph.D. students are required to include at least 15 pages of text, double-spaced (not counting the title page, abstract page, figures or reference pages) and 30 references. These are minimal requirements, and students are encouraged to write much longer papers. The paper should advocate a specific point of view, hypothesis and/or conclusion, and present evidence for and against your conclusions. The term paper is due on the last day of class (see below). Late papers will receive a penalty of 10% per day.

M.S. student will present a brief, verbal summary of their term paper (5-10 min) to the class during the last class meeting. Due to time limitations, we will not have time for PowerPoint slides, and handouts (optional) will be limited to a maximum of 3 pages. Term papers written by M.S. students are required to include at least 10 pages of text, double-spaced (not counting the title page, abstract page, figures or reference pages) and 20 references. These are minimal requirements, and students are encouraged to write much longer papers. The paper should advocate a specific point of view, hypothesis and/or conclusion, and present evidence for and against your conclusions. The term paper is due on the last day of class (see below). Late papers will receive a penalty of 10% per day.

Each week, during and following the lecture, we will have open-ended discussions as long as time allows. I will provide several discussion questions as a starting point, and students are encouraged to add additional discussion questions. You are expected to participate actively in these discussions (it helps to have read the papers) and your participation will count for 10% of your course grade.

We will also have a written final examination. The final exam questions will be similar (or identical) to the discussion questions. The final exam will consist of five 1-page essay questions (closed book). You will choose four of the five questions to answer.

August 28. Introduction
Text, chapter 3, pp. 43-63.

Sept 4. Natural selection vs. the neutral and nearly neutral theories
text, chapter 4, pp. 69-78.
Gojobori, T., E. N. Moriyama and M. Kimura (1990) Molecular clock of viral evolution, and the neutral theory. *Proc. Natl. Acad. Sci. USA* **87**, 10015-10018.
McDonald, J. and M. Kreitman (1991) Adaptive protein evolution at the *Adh* locus in *Drosophila*. *Nature* **351**, 652-654.
Ohta, T. (1995) Synonymous and nonsynonymous substitutions in mammalian genes and the nearly neutral theory. *J. Mol. Evol.* **40**, 56-63.

Sept 11. Basic rates and patterns of DNA sequence change
text, chapter 6.
Petrov, D. A., and D. L. Hartl (1999) Patterns of nucleotide substitution in *Drosophila* and mammalian genomes. *Proc. Natl. Acad. Sci. USA* **96**, 1475-1479.
*Ran, W., and P. G. Higgs (2010) The influence of anticodon-codon interactions and modified bases on codon usage bias in bacteria. *Mol. Biol. Evol.* **27**, 2129-2140.

Sept 18. Population bottlenecks, positive selection, and genetic diversity.
text, chapter 4, pp. 78-100.
Ohta, T. (1993) Amino acid substitution at the *Adh* locus of *Drosophila* is facilitated by small population size. *Proc. Natl. Acad. Sci. USA* **90**, 4548-4551.
Glenn, T. C., W. Stephan, and M. J. Braun (1999) Effects of a population bottleneck on whooping crane mitochondrial DNA variation. *Conservation Biol.* **13**, 1097-1107.
Lynd A, Weetman D, Barbosa S, Egyir Yawson A, Mitchell S, Pinto J *et al* (2010) Field, genetic, and modeling approaches show strong positive selection acting upon an insecticide resistance mutation in Anopheles gambiae s.s. *Mol. Biol. Evol.* **27**, 1117-1125.
Meer MV, Kondrashov AS, Artzy-Randrup Y, Kondrashov FA (2010) Compensatory evolution in mitochondrial tRNAs navigates valleys of low fitness. *Nature* **464**, 279-282.

Sept 25. Phylogenetic trees, speciation, gene coalescence, and the molecular clock.
text, chapter 1, pp. 9-16.
Palumbi, S. R., F. Cipriano and M. P. Hare (2001) Predicting nuclear gene coalescence from mitochondrial data: the three-times rule. *Evolution* **55**, 859-868.
Venditti, C., A. Meade and M. Pagel (2010) Phylogenies reveal new interpretation of speciation and the Red Queen. Nature **463**, 349-352.
Fournier, G. P., and J. P. Gogarten (2010) Rooting the ribosomal tree of life. Mol Biol Evol **27**, 1792-1801.

Oct 2. Genome size and organismal complexity.
Text, chapter 2.
Petrov DA, Sangster TA, Johnston JS, Hartl DL, Shaw KL (2000) Evidence for DNA loss as a determinant of genome size. *Science* **287**, 1060-1062.
Gonzalez J, Petrov DA (2012) Evolution of genome content: population dynamics of transposable elements in flies and humans. *Methods Mol. Biol.* **855**, 361-383.

Oct 9. Columbus Day break (Monday classes meet on Tuesday, Tuesday classes do not meet this week).

Oct 16 – class does not meet (work on term paper).

Oct. 23 Gene duplication and the evolution of gene families
text, chapter 8.
Hiwatashi, T., Y. Okabe, T. Tsutsui, C. Hiramatsu, A. D. Melin *et al.* (2010) An explicit signature of balancing selection for color-vision variation in new world monkeys. *Mol. Biol. Evol.* **27**, 453-464.
Yuan F, Bernard GD, Le J, Briscoe AD (2010) Contrasting modes of evolution of the visual pigments in Heliconius butterflies. *Mol. Biol. Evol.* **27**, 2392-2405.
*Martin A, Reed RD (2010). Wingless and aristaless2 define a developmental ground plan for moth and butterfly wing pattern evolution. *Mol Biol Evol* **27**, 2864-2878.

Pick L, Heffer A (2012) Hox gene evolution: multiple mechanisms contributing to evolutionary novelties. *Ann. N. Y. Acad. Sci.* **1256**, 15-32.

Oct 30. Hurricane Sandy!

November 6. Transposable elements

Text, chapter 7.

Osborne, P. W., and D. E. Ferrier (2010) Chordate Hox and ParaHox gene clusters differ dramatically in their repetitive element content. *Mol. Biol. Evol.* **27**, 217-220.

Petrov DA, Fiston-Lavier AS, Lipatov M, Lenkov K, Gonzalez J (2011) Population genomics of transposable elements in *Drosophila melanogaster*. *Mol. Biol. Evol.* **28**, 1633-1644.

November 13. Introns and alternative splicing

Text, chapter 9.

Keren H, Lev-Maor G, Ast G (2010) Alternative splicing and evolution: diversification, exon definition and function. *Nat. Rev. Genet.* **11**, 345-355.

*Shoval Y, Berissi H, Kimchi A, Pietrokovski S (2011) New modularity of DAP-kinases: alternative splicing of the DRP-1 gene produces a ZIPk-like isoform. *PLoS One* **6**, e17344.

November 20. The adaptive evolution of proteins

Text, pp. 67.

Jermann, T. M., J. G. Opitz, J. Stackhouse, and S. A. Benner (1995) Reconstructing the evolutionary history of the artiodactyl ribonuclease superfamily. *Nature* **374**, 57-59.

Bustamante CD, Fledel-Alon A, Williamson S, Nielsen R, Hubisz MT, Glanowski S *et al* (2005) Natural selection on protein-coding genes in the human genome. *Nature* **437**, 1153-1157.

Rodriguez GJ, Yao R, Lichtarge O, Wensel TG (2010) Evolution-guided discovery and recoding of allosteric pathway specificity determinants in psychoactive bioamine receptors. *Proc. Natl. Acad. Sci. USA* **107**, 7787-7792.

Schlinkmann KM, Honegger A, Tureci E, Robison KE, Lipovsek D, Pluckthun A (2012) Critical features for biosynthesis, stability, and functionality of a G protein-coupled receptor uncovered by all-versus-all mutations. *Proc. Natl. Acad. Sci. USA* **109**, 9810-9815.

November 27. Sex and sex chromosomes

text, chapter 12.

Skaletsky H, Kuroda-Kawaguchi T, Minx PJ, Cordum HS, Hillier L, Brown LG *et al* (2003) The male-specific region of the human Y chromosome is a mosaic of discrete sequence classes. *Nature* **423**, 825-837.

Ellegren H (2011) Sex-chromosome evolution: recent progress and the influence of male and female heterogamety. *Nat. Rev. Genet.* **12**, 157-66.

*Sin HS, Ichijima Y, Koh E, Namiki M, Namekawa SH (2012) Human postmeiotic sex chromatin and its impact on sex chromosome evolution. *Genome Res.* **22**, 827-836.

December 4. Human evolution

Text, chapter 3, pp. 63-68.

Evans PD, Anderson JR, Vallender EJ, Choi SS, Lahn BT (2004) Reconstructing the evolutionary history of microcephalin, a gene controlling human brain size. *Hum. Mol. Genet.* **13**, 1139-1145.

Green RE, Krause J, Briggs AW, Maricic T, Stenzel U, Kircher M *et al* (2010) A draft sequence of the Neandertal genome. *Science* **328**, 710-722.

*Scharff C, Petri J (2011) Evo-devo, deep homology and FoxP2: implications for the evolution of speech and language. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **366**, 2124-2140.

December 11. M.S. student verbal presentations of term papers

All written term papers are due today!

Tuesday, December 18 - FINAL EXAM (4:30 pm - 7:15 pm in Bull Run Hall, room 246)