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

KARL J. FRYXELL FALL, 2014

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. 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 Occoquan Hall, room 204. 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. Course materials such as lecture notes will be posted on Blackboard.

Introduction. The field of molecular evolution originated in the 1960s when Emile Zuckerkandl and Linus Pauling showed that biological evolution occurs primarily through gene duplication plus continuing small changes in gene sequences. 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: **For students enrolled in Biol 579** - 20% participation, 40% midterm exam, 40% final exam. **For students enrolled in BIOS 767** – 20% participation, 20% term paper, 30% midterm exam, 30% final exam.

The participation grade is based on both attendance and active participation in class discussions. The instructor will provide a few discussion questions as a starting point, but students are also encouraged to add their own questions as well. It helps to have read the papers before class!! These discussion questions will be the focus of midterm and final examinations, which will be short-essay format. Cell phone use of any kind (including texting) is not allowed during written examinations and will result in a grade of zero for the exam.

Students registered in BIOS 767 are required to write a term paper related to this class. The topic of your term paper should be proposed verbally by the student by the end of week 2 (in class or office hours), and may be modified by the instructor. These term papers 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.

August 26. Introduction
Text, chapter 3, pp. 43-63.

Sept 2. 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.
Ophir R, Graur D (1997) Patterns and rates of indel evolution in processed pseudogenes from humans and murids. *Gene* **205**, 191–202.

Sept 9. Natural selection, the neutral theory, and the nearly neutral theory
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 16. 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.

Sept 23. 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.

Sept 30. Genome size and organismal complexity.
Text, chapter 2.
Petrov D and Wendel JF (2006) Evolution of eukaryotic genome structure. pp 144-156 In: *Evolutionary Genetics: Concepts and Case Studies*, Fox CW and Wolf JB, eds. Oxford University Press, NY.
Podlaha O, Zhang J (2010 Pseudogenes and their evolution. In: *Encyclopedia of Life Sciences (ELS),* John Wiley & Sons, Chichester. DOI: 10.1002/9780470015902.a0005118.pub2

Oct 7. .. Midterm Exam (covers all lectures to date)

Oct 14 Columbus Day break (Monday classes meet on Tuesday, Tuesday classes do not meet this week).

Oct 21. Transposable elements
Text, chapter 7.
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. 28 Gene duplication and the evolution of gene families
text, chapter 8.
Thornton J (2006) New genes, new functions: gene family evolution and phylogenetics. Pp. 157-172 In: *Evolutionary Genetics: Concepts and Case Studies*, Fox CW and Wolf JB, eds. Oxford University Press, NY.

Nei M, Niimura Y, and Nozawa M (2008) The evolution of animal chemosensory receptor gene repertoires: roles of chance and necessity. *Nat. Rev. Genet.* **9**, 951-963.

Carroll SB (2008) Evo-devo and an expanding evolutionary synthesis: a genetic theory of morphological evolution. *Cell* **134**, 25-36.

November 4. RNA processing: Introns, alternative splicing, and MicroRNAs

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.

Berezikov E (2011) Evolution of microRNA diversity and regulation in animals. *Nat. Rev. Genet.* **12**, 846-860.

November 11. The adaptive evolution of proteins

Text, pp. 67.

Patthy L (2006) Evolution of multidomain proteins. pp. 211-221 In: *Evolutionary Genetics: Concepts and Case Studies*, Fox CW and Wolf JB, eds. Oxford University Press, NY.

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.

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 18. Society for Neuroscience annual meeting, class does not meet this week

November 25. Sex and sex chromosomes

text, chapter 12.

Bachtrog D (2013) Y-chromosome evolution: emerging insights into processes of Y-chromosome degeneration. *Nat. Rev. Genet.* **14**, 113-124.

Matson CK, Zarkower D (2012) Sex and the singular DM domain: insights into sexual regulation, evolution and plasticity. *Nat. Rev. Genet.* **13**, 163-174.

December 2. Human evolution (term papers due in class)

Text, chapter 3, pp. 63-68.

Stoneking M, Krause J (2011) Learning about human population history from ancient and modern genomes. Nat. Rev. Genet. 12, 603-614.

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 9. GMU Reading days (class does not meet)

December 16 – Comprehensive Final Exam (4:30 pm - 7:15 pm in Occoquan Hall, room 204)