

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

KARL J. FRYXELL SPRING, 2025

Contact Information

Course meets: Wednesdays at 4:30 - 7:10 pm, Colgan Hall, room 204, SciTech campus.

Office hours: Fridays, 1:00 pm - 2:00 pm online via Zoom. Point your browser (not Zoom app) to this URL:

<https://gmu.zoom.us/j/7931936280?pwd=RWV1OC9oVmRpQUNQb3Y5czhURG91UT09#success>

You do not need an appointment or a password to enter this Zoom room.

E-mail: kfryxell@gmu.edu (*Please INCLUDE THE COURSE NUMBER in the subject line of your e-mails!*)

Telephone: 703-993-1069 (*Please leave a detailed message including your name, class number callback phone number, and dates/times when you are available for me to call you back.*)

Course web site: Information for both BIOL 579 and BIOS 767 have been merged in a single web page on Blackboard. Lecture notes and other information will be posted on the "course content" tab. Study questions will be posted on the "assignments" tab.

Readings. There is one required text for this course, "Molecular and Genome Evolution" by Dan Graur (2016). Additional assigned reading will include primary research articles in scientific journals. These are available through the GMU library through the E-journals web link (or will be posted on Blackboard). Many of these articles are also available on paper in the Fenwick and/or Mercer Libraries.

Introduction. The field of molecular evolution originated in the 1960s when Emile Zuckerkandl and Linus Pauling showed that biological evolution occurs through continuing small changes in gene sequences, punctuated by episodes of gene duplication. 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, methods of understanding the evolution of gene regulation, the neutral theory, whole-genome analysis of natural selection, genetic pathways, and human ancestry. The field of molecular evolution has become the conceptual foundation of most of biology, including gene structure and function, genomics, biotechnology, and, of course, evolution.

Molecular evolution also has applications in conservation genetics, including molecular definitions of the effective population size of a species, molecular definitions of species boundaries, and the concept of a minimal sustainable population size (which is the basis of the Endangered Species Act). It has become possible to study the molecular evolution of human ancestors, which is providing new answers to the question of who we are and where we came from.

Grading summary for BIOL 579: 45% midterm exam, 45% final exam, 10% participation. Midterm and final exams will be in-class, closed-book, short answer format (typically one sentence to one paragraph for each portion of the question). Exam material will be based primarily on the study questions that are posted each week on Blackboard. Makeup examinations are not given in this course. Excused absences from exams require the prior permission of the instructor (not just firing off an e-mail or voice mail at the last minute). Cell phone use of any kind (including texting) is not allowed during examinations.

The participation grade is a small incentive, in which students receive points for both attendance and active participation in class discussions. The first absence will be dropped for all students, but subsequent absences will count (in proportion to your participation).

Grading summary for BIOS 767: 30% midterm exam, 30% final exam, 20% term paper, 10% oral presentation, 10% participation. Exams and participation grades as above. For the term paper, one of the assigned papers should be used as a starting point for the term paper topic. The topic of your term paper must be proposed verbally by the student before the end of week 2 (in class or office hours), and may be modified by the instructor. Term papers must include at least 15 pages of text, double-spaced (not counting the title page, abstract page, figures or reference pages) and 30 technical references (not Wikipedia entries, web sites, newspaper or popular articles). These are minimal requirements. Students are encouraged to write longer papers, and will be rewarded for doing so, provided that the paper is well written. The term paper should advocate a specific point of view, hypothesis and/or conclusion on this topic, and present evidence for and against your argument. The term paper is due on the last day of class. Students are also required to make a verbal presentation of their term paper findings on the last day of class. The presentation should be ~15 min (10-15 slides, including suggested questions for class discussion) plus 5 min class discussion.

Late term papers will receive a penalty of 10% per day!

January 22 – Introduction (lecture 1)

Text, chapter 1.

January 29 - Basic rates and patterns of DNA sequence change (lecture 2)

text, pp. 107-125; pp. 130-138.

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.

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.

February 5 - Natural selection, the neutral theory, and the nearly neutral theory (lecture 3)

text, pp. 35-62; 72-77; pp. 163-164.

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. (1993) Amino acid substitution at the *Adh* locus of *Drosophila* is facilitated by small population size. *Proc. Natl. Acad. Sci. USA* **90**, 4548-4551.

February 12 - Genetic diversity – population bottlenecks vs. positive selection (lecture 4)

text, pp. 66-71; pp. 128-130.

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.

Zhai, T. *et al.* (2017) Effects of population bottleneck and balancing selection on the Chinese alligator are revealed by locus-specific characterization of MHC genes. *Sci. Rep.* **7**, 5549.

Spielman D., B. W. Brook and R. Frankham (2004) Most species are not driven to extinction before genetic factors impact them. *Proc. Natl. Acad. Sci. USA* **101**, 15261-15264.

Tishkoff, S. A. *et al.* (2007) Convergent adaptation of human lactase persistence in Africa and Europe. *Nat. Genet.* **39**, 31-40.

February 19 - Phylogenetic trees, speciation, gene coalescence, and the molecular clock (lecture 5)

text, pp. 149-162; pp. 165-197; pp. 205-220.

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.

Mather, N., S. M. Traves, and S. Y. W. Ho (2019) A practical introduction to sequentially Markovian coalescent methods for estimating demographic history from genomic data. *Ecol. Evol.* **10**, 579-589.

February 26 - Gene duplication, pseudogenes, and the evolution of gene families (lecture 6)

text, chapter 7.

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.

Meredith, R. W., G. Zhang, M. T. P. Gilbert, E. D. Jarvis, and M. S. Springer (2014) Evidence for a single loss of mineralized teeth in the common avian ancestor. *Science* **346** (6215), 1254390.

March 5 - Midterm Exam (covers lectures 1-6), in class 4:30 pm - 7:10 pm

March 12 – Spring Break

March 19 – Protein evolution, multidomain proteins, and alternative splicing (lecture 7)

Text, pp. 232-235; chapter 8; pp. 427-428.

Kawashima, T. et al. (2009) Domain shuffling and the evolution of vertebrates. *Genome Res.* **19**, 1393-1403.

Barbosa-Morais, N. L. et al. (2012) The evolutionary landscape of alternative splicing in vertebrate species. *Science* **338**, 1587-1593.

Park, E. et al. (2018) The expanding landscape of alternative splicing variation in human populations. *Am. J. Hum. Genet.* **102**, 11-26.

March 26 – The evolution of gene regulation and development (lecture 8)

Text, chapter 12.

Necsulea, A. and H. Kaessmann (2014) Evolutionary dynamics of coding and noncoding transcriptomes. *Nat. Rev. Genet.* **15**, 734-748.

Zhang, L. et al. (2017) Single master regulatory gene coordinates the evolution and development of butterfly color and iridescence. *Proc. Natl. Acad. Sci. USA* **114**, 10707-10712.

April 2 – The origin of life and the evolution of prokaryotic genomes (lecture 9)

Text, pp. 432-438; chapter 10.

Higgs PG and Lehman N (2014) The RNA World: molecular cooperation at the origins of life. *Nat. Rev. Genet.* **16**, 7-17.

Martinez-Cano, D. J. (2015) Evolution of small prokaryotic genomes. *Front. Microbiol.* **5**, 742.

Filloi-Salom, A. et al. (2018) Phage-inducible chromosomal islands are ubiquitous within the bacterial universe. *ISME J.* **12**, 2114-2128.

April 9 – The evolution of eukaryotic genomes and sex chromosomes (lecture 10)

Text, pp. 522-573.

Veyrunes, F. et al. (2008) Bird-like sex chromosomes of platypus imply recent origin of mammal sex chromosomes. *Genome Res.* **18**, 965-973.

Duret, L. et al. (2006) The *Xist* RNA gene evolved in eutherians by pseudogenization of a protein-coding gene. *Science* **312**, 1653-1655.

Murat, F. et al. (2023) The molecular evolution of spermatogenesis across mammals. *Nature* **613**, 308-316.

April 16 – Early humans, Neanderthals, and Denisovans (lecture 11)

Tishkoff, S. A. et al. (1996) Global patterns of linkage disequilibrium at the CD4 locus and modern human origins. *Science* **271**, 1380-1387.

Moorjani, P. et al. (2016) A genetic method for dating ancient genomes provides a direct estimate of human generation interval in the last 45,000 years. *Proc. Natl. Acad. Sci. USA* **113** (20), 5652-5657.

Iasi, L. N. M. et al. (2024) Neanderthal ancestry through time: insights from genomes of ancient and present-day humans. *Science* **386**, eadq3010.

April 23 – Genetic consequences of the Neolithic revolution (lecture 12)

Karmin M et al. (2015) A recent bottleneck of Y chromosome diversity coincides with a global change in culture. *Genome Res.* **25**, 459-466.

Haak, W. et al. (2015) Massive migration from the steppe was a source for Indo-European languages in Europe. *Nature* **522**, 207-211.

Allentoft, M. E. et al. (2015) Population genomics of Bronze Age Eurasia. *Nature* **522**, 167-172.

April 30 – Presentations by BIOS 767 students (term papers are due today)

May 7 – Final Exam (covers lectures 7-12), in class 4:30 pm - 7:10 pm.