EEOB 711 - Winter Quarter 2006
MOLECULAR EVOLUTION

Syllabus

Instructor: Paul Fuerst - Room 884 Biological Sciences Building
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Time: 11:00 – 12:30 TR

Textbook: Dan Graur & Wen-Hsiung Li, Fundamentals of Molecular Evolution, second edition, Sinauer Press 1999

Overview

What can molecular data tell us about the history of life, about similarities of the human genome to other organisms and about how our genetic makeup has changed in the evolution from microbes to man? This course provides a review of current knowledge in molecular evolution. Attention will be placed on the role of evolutionary theory in describing molecular change. The patterns and processes of molecular change, both within and between species, will be examined. Emphasis will be placed on examining the between-species processes. Methods of evolutionary trees reconstruction from gene sequences will be presented. Evolutionary trees can be used to understand the evolution of organisms. They also provide insight into the evolution of patterns within the genome, such as the production of gene families and their functions. Finally, some consideration will be given to recent insights into the evolution of development.

Prerequisites

This is a course for undergraduates with a some background in biology. It is assumed that students will have had a course in basic genetics, and have some background in areas of molecular biology, or cell biology. No specific background in evolutionary biology is expected. Students approaching this material from a background in mathematics or statistics will be welcome and material will be provided to familiarize such students with the life science material.

Approaches to the material

There are two ways that material concerning molecular evolution can be mastered. In one approach, learning about molecular evolution involves understanding basic concepts and techniques and then seeing how they are implemented in published research papers on important subjects. To that end, a series of papers related to particular topics will be mixed with lectures and discussion. In the second approach to learning, methods must be mastered by doing. A series of problem sets, related to the topics under discussion, will be assigned and results will be discussed and subsequently evaluated as part of a students grade.

Grading criterion:
Students grades will be determined as follows: one mid-term examination (20%), a final examination (20%), six-eight graded problem sets (5-10% each; total 60%). Exams will be based on lecture material; the reading alone does not substitute for all the material taught in class.

Problem sets:
At the present time I expect that three problem sets regarding database issues will be assigned. Each will consist of an analysis exercise in which sequences will be retrieved from one of the databases (probably GENBANK). One exercise will involve retrieving sequences which are part of a multigene family, aligning sequences and performing an analysis of sequence changes and a phylogenetic analysis. A second exercise will retrieve homologous sequences from a series of species and doing a similar analysis to the first exercise. A third exercise will involve genome comparisons (details undetermined at present) using complete microbial sequences. Other exercises (probably about 3 or 4) which will be assigned periodically and will involve a set of problems and questions concerning data analysis topics in molecular evolution. These will allow all students to become familiar with techniques.

Reading

The primary textbook for the course is
D. Graur and W-H Li. *Fundamentals of Molecular Evolution*. Sinauer, 1999.
This is a very good introduction to methods and concepts in molecular evolution. It is weak on certain points, however, particularly phylogenetics, so it will be supplemented with additional readings material as listed in the syllabus. It is also beginning to become out of date on some topics.

The following books are recommended to clarify topics in the lectures that are not well covered in Graur and Li. Specific chapters are listed in the syllabus. "Highly recommended" refers to subjects on when Graur and Li do a grossly inadequate job, so these are the only useful references.

D.B. Futuyma. *Evolutionary Biology, Third Edition*. Sinauer, 1997. This is an excellent general evolution textbook. While it is expensive, it is a great reference and learning tool for anyone interested in evolution in general.

RDM Page and LC Holmes. *Molecular Evolution: A Phylogenetic Approach.* Blackwell Science, 1998. A very good introduction with an emphasis on techniques and concepts in molecular systematics, one of the major weak points in Graur and Li.

Participation: I encourage students to ask questions during class about topics being considered. I especially encourage students to visit me during office hours, or as arranged, to discuss any topic, but especially if you have question about problems. Papers from the primary literature will be regularly assigned as supplemental reading, and will be the basis of in class discussion.

Course notes and supplemental readings can be accessed at:
http://www.biosci.ohio-state.edu/~pfuerst/courses/index.html

STUDENTS WITH DISABILITIES: Any student who feels he or she may need an accommodation because of a physical or learning disability should contact Dr. Fuerst privately to discuss your particular needs. Students should be registered with the Office for Disability Services (ODS, 614-292-3307) in 150 Pomerene Hall and should contact that office to arrange for specific accommodations. Please contact Dr. Fuerst for completion of ODS proctor sheets.

ACADEMIC MISCONDUCT: All instructional faculty and staff are required by Ohio State University to forward all cases of suspected cheating to the Committee on Academic Misconduct. Any form of academic misconduct, no matter how seemingly small, will not be tolerated in this course. Unless indicated on an assignment, problems sets and take-home material are expected to be the ultimate product of the student handing in the assignment. Students are expected to adhere to the university's honor code or else suffer the consequences.

COURSE SYLLABUS (tentative sequence of topics with suggested readings)

I. Foundations

1. Introduction to course business. Central concepts: evolution, natural selection, phylogeny.
   Recommended reading: Futuyma, ch. 1;
   review Graur and Li, ch. 1.

2. The Neo-Darwinian Synthesis / Evolution of genes in populations. Hardy-Weinberg equilibrium; mutation.
   Selection without life: LE Orgel. Selection in vitro. *Proc. R. Soc. Lond. B* 205:435-442, 1979.
   Graur and Li, ch. 2.
   Recommended: Futuyma, pp. 24-28, 231-239, 267-283.

3. Population genetics continued: Natural selection.
   Graur and Li, ch. 2, cont.
   Recommended: Futuyma, ch. 13.

4. Population genetics, continued: Genetic drift; population structure (inbreeding and gene flow); measures of genetic diversity.
   Graur and Li, ch. 2, cont.
   Recommended: Futuyma, ch. 11.

   Exercises on population genetics.

II. Manipulating sequences

5. Aligning DNA and protein sequences.
   Demonstration of alignment software
   Exercise on alignment
   Graur and Li, ch. 3.

6. Calculating evolutionary distances among sequences; corrections and models.
   Graur and Li, ch. 3, cont.
   Exercise on distance calculations

III. Natural Selection: rates, clocks, and the neutral theory

7. Selection at the molecular level: variations in substitution rates and their causes in nuclear, organellar, and viral DNA; tests of selection.

Graur and Li, ch. 4.

8. The neutral and nearly-neutral theories of molecular evolution.
   Graur and Li, ch. 4, cont.
   T. Ohta. The current significance and standing of neutral and nearly neutral theories. *Bioessays* 18:673, 1996.
   M. Kreitman. The neutral theory is dead; long live the neutral theory. *Bioessays* 18:678, 1996.
   Recommended: Page and Holmes, ch. 7.

9. Molecular clocks.
   Lahn BT, Page DC. Four evolution strata on the human X chromosome. Science 286:964-967, 1999.
   Ayala FJ. Molecular clock mirages. Bioessays 21:71-75, 1999.

10. Dating major evolutionary events. The Cambrian explosion and the K-T radiation.
    Hedges SB, Parker PH, Sibley CG, Kumar S. Continental breakup and the ordinal diversification of birds and mammals. *Nature* 381:226-9, 1996. (See also Benton MJ. Early origins of modern birds and mammals: molecules vs. morphology. *Bioessays* 21:1043-1051, 1999.)
    Wray GA, Levinton JS, Shapiro LH. Molecular evidence for deep precambrian divergences among metazoan phyla. *Science* 274:568-573, 1996. (See also Ayala FJ et al. *Proc. Natl Acad. Sci USA* 95:606-611, 1998.)

IV. Molecular phylogenetics

11. Concepts: kinds of trees, rooting, clades, reconstructing character evolution, consensus trees, phylogeny as hypothesis.
    Graur and Li, ch. 5
    Highly recommended: Page and Holmes, ch. 2

12. Phylogenetic methods: parsimony.
    Highly recommended: Page and Holmes, ch. 6, Futuyma, ch. 5.

13. Methods, distance and likelihood-based phylogenetics.
    Exercise on phylogenetic inference

14. Examples of phylogenetic studies; Relationship of humans and African apes:
    Miyamoto MM et al. Molecular systematics of higher primates: genealogical relations and classification. *Proc. Natl. Acad. Sci. USA* 85:7627-7631, 1988.
    Two major superphyla of animals: Aguinaldo AMA et al. Evidence for a clade of nematodes, arthropods, and other moulting animals. *Nature* 387:489-493, 1997.

15. Review and overflow

16. MIDTERM EXAM

V. Mechanisms of genomic evolution

17. Endosymbiosis and lateral gene transfer.
    Graur and Li, pp. 245-246, 359-365,
    Nelson KE et al. Evidence for lateral gene transfer between Archae and Bacteria from genome sequence of *Thermotoga maritima*. *Nature* 399:323-330, 1999.
    Doolittle WF. Phylogenetic classification and the universal tree. *Science* 284:2124-2128, 1999.

18. Transposition, retroposition, and junk DNA.
    Lahn BT, Page DC. Retroposition of autosomal mRNA yielded testis-specific gene family on human Y chromosome. *Nature Genetics* 21:429-433, 1999.
    Graur and Li, ch. 7.

19. Chromosomal evolution: genome projects and comparative mapping.
    Graur and Li, pp. 402-411.

20. Genome duplications.
    Postlethwait JH, et al. Vertebrate genome evolution and the zebrafish gene map. *Nature Genetics* 18(4):345-9, 1998 (see also Smith NGC, Knight R, Hurst LD. Vertebrate genome evolution: a slow shuffle or a big bang? *Bioessays* 21:697-703, 1999.)
    Graur and Li, pp. 375-384.

21. The origin of introns.
    Gilbert W, Glynias M. On the ancient nature of introns. Gene 135:137-144, 1994.(See also Hurst LD, McVean GT. A difficult phase for introns early. *Current Biology* 6:533-536, 1996.)

VI. Evolution of gene families

22. Orthology and paralogy. Embedded trees. Inferring gene duplication and losses. Rooting the tree of life with gene families. Reconstructing the evolution of function.
    Exercise on gene family phylogeny.
    Highly recommended: Page and Holmes, pp. 286-293.

23. Domain shuffling and concerted evolution.
    Graur and Li, ch. 6.

24. The evolution of gene function. Neofunctionalization and subfunctionalization; role of gene family evolution in morphological innovations.
    Swanson WJ, Vacquier VD. Concerted evolution in an egg receptor a rapidly evolving abalone sperm protein. *Science* 281:710-712, 1998.
    Fryxell KJ. The coevolution of gene family trees. *Trends in Genetics* 12:364-369, 1996.

25. The evolution of function: examples.

Reconstructing the evolution of function: Yokoyama S, Radlwimmer FBH. The molecular genetics of red and green color vision in mammals. *Genetics* 153:919-932, 1999.

Reconstructing the evolution of function: Fitch WM, Upper K. The phylogeny of tRNA sequences provides evidence for ambiguity reduction in the origin of the genetic code. *Cold Spring Harbor Sym. Quant. Biol*. 52:759-67, 1987.

VII. Evolution of development

26. Changes in expression of developmental control genes as the cause of morphological change; homology concepts.

Cohn MJ, Tickle C. Developmental basis of limblessness and axial patterning in snakes. *Nature* 399:474-479, 1999.

Tomarev SL, Callaerts P, Kos L, Zinovieva R, Halder G, Gehring W, Piatigorsky J. Squid Pax-6 and eye development. *Proceedings of the National Academy of Sciences USA* 94:2421-2426, 1997.

Wray GA, Abouheif E. When is homology not homology. *Current Opinion in Genetics and Development* 8:6750680, 1998.

Recommended: Futuyma, ch. 23.

27. Complexity and canalization in development.

Rutherford SL, Lindquist S. Hsp90 as a capacitor for morphological evolution. *Nature* 396:336-342, 1998.

28. Review.