MOLECULAR EVOLUTION (BIOL./CHEM. 445-645)

COURSE OUTLINE, FALL 1996

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Lecture - Tuesday and Thursday, 9:45-11:15 a.m., room 204 Natural Science Building. Laboratory-Arctic Health Research Building Room 253, the Shields Lab. (individual times to be arranged, see below).

COURSE CONTENT

This course focuses on the history of comparative molecular evolution and its contributions to knowledge of the evolutionary process. It stresses macromolecular views about genealogical relationships within and among major groups of organisms. It will demonstrate that we are finally capable of defining genetic change at the DNA level and thus, can now understand, more fully, the affect of various types of mutational change at the level of the molecule, cell, tissue, organism, population, species, and phylogeny. Additionally, the course will show how phylogenies and time scales being deduced from macromolecular comparisons are providing the basis for quantitatively reexamining the evolutionary process at various levels of biological organization and thereby testing ideas regarding the factors that determine the direction and rate of evolution.

COURSE PHILOSOPHY

Based on my 25 years of teaching experience, I am convinced students must take an active role in their own education. This means the student is the primary seeker of his or her own knowledge rather than relying on someone else to tell them what is true and important. Accordingly, you should prepare for lectures in advance by reading the assigned literature before class and come to lecture prepared to participate in the exchange of ideas. By interacting with one another on issues of science, by questioning the validity of "established" knowledge and by actively becoming involved in real research a great deal of learning and appreciation for the scientific
process can take place. This class may be unlike other classes you have taken because I will require prior preparation and very active participation from you. The last thing I want in lecture is a student whose mind is in neutral and whose thoughts are elsewhere.

SCIENTIFIC TRAINING

In my opinion, biology faculty at most U. S. universities have generally done an inadequate job of training students in the practice of science. Usually the scientific method leading to new knowledge is avoided and is replaced by "canned" demonstrations or timed observations which give the student the impression that research can be completed in a specified time without any hassles; neither is true. Moreover, the assumption is made that most of the important facts are already known and all the student has to do is listen to the "all knowing" professor who will indicate what's important. This is a travesty of our responsibilities as teachers of science. The body of scientific knowledge as we know it is based on past searches involving the scientific method. New additions to scientific knowledge occur through re-search which is literally re-searching the old knowledge base in order to more firmly understand principles. Students of science should practice the scientific method which leads directly to new research. Specifically, one should become familiar with the knowledge base in an area of science, recognize errors and gaps in our knowledge, propose hypotheses to test, recommend specific and relevant methods, carry out the methodology, analyze the data and either support or refute the initial knowledge. Students should be given the opportunity to experience the scientific method through: reading the literature, questioning "established" fact, testing hypotheses, writing research proposals, conducting careful unbiased observation, rigorously analyzing data, arriving at conclusions, promulgating conclusions (seminars, public lectures and formal publications) and continuing the search for knowledge. Whether you become a research scientist or not, it is important that you understand both the scientific method and consequently how complex life forms and ecosystems really are. Many everyday issues in society require a basic understanding of science and an appreciation for the complexity of life. A citizenry ignorant of scientific method and knowledge but having biased unfounded opinions is a dangerous citizenry indeed.
THE RESEARCH LABORATORY

Because I maintain an established research laboratory, it is easier to conduct the laboratory portion of this class in that setting rather than "rebuilding" a new student research laboratory somewhere else. Therefore, the research experience associated with this course will be conducted in room 253 of the Arctic Health Research Building and will be a major undertaking. I believe this exposure to real research can be a rewarding and exciting experience. I am committed to working with you to the extent that you gain the confidence to launch a research career, should you decide to do so. I am most interested in conveying an understanding of what it means to be a practicing scientist rather than having you become somewhat familiar with present day "facts" which might be disproven as time passes. Each student will choose a specific block of time (4-5 hours) during the week for laboratory research. This time is designated as "exclusive time" during which appropriate equipment in the laboratory is available for use by individual students. Students will also have unlimited access to the laboratory during the week in order to carry out short-term duties such as starting amplifications, termination of electrophoretic runs, etc.

Since materials are expensive and since molecular methods are labor-intensive, very careful planning must accompany the choice of your research topic as well as the specific way you approach it. Jeff and I are here to help you, so ask us about anything. Your questions will never be interpreted as naive or stupid; we might begin to think of you as an irresponsible person, however, if you don't ask questions yet continue to make costly mistakes.

RESEARCH PROJECTS

I would prefer you choose your own research projects, but my experience has shown this approach seldom works. Rather, I provide you with brief explanations of potential research projects from which you may choose your research for the semester. If you want to choose your own project and I have determined it appropriate, so be it. However, the projects I have suggested are attractive because they are doable, scientifically interesting and meaningful. Moreover, since we usually have tissues of DNA extracts already available, you won't have to delay the start of you project waiting for tissues to
arrive. We have established workable methods for most of these projects. In most cases relevant comparative data are already available. Finally, some are extensions of our earlier work and, therefore, will help our laboratory pursue an increased understanding of important topics.

Once you have chosen an appropriate research topic, immediately pursue the relevant literature and write a five page typed proposal which includes: 1) a justification of why this work should be done including the testing of alternative hypotheses, 2) the specific methods which you will use including sources of tissue, genes or DNA segments, the specific analytical methods to be used, 3) anticipated results and conclusions, and 4) a list of literature you have cited in your proposal write-up. You are required to meet with me as often as required during the preparation of your proposal. Ultimately, I will evaluate your proposal and return it to you for improvement, if necessary. The semester is short for such a project and we will have to order the necessary molecular supplies specific to each project as soon as possible.

Contrary to some opinions, comparative molecular evolution is not immune to hypothesis testing and in no case should the methodology chosen be the sole justification of the project. Important biological questions justify research not the methodology used. Therefore, each project must test a well-reasoned hypothesis while indicating alternative outcomes. It is not enough to state "that it will be interesting to apply this technique to this group of animals because this has never been done before." Once you have been given formal direction concerning your project by me and Jeff, you are expected to progress on your own initiative. The progress of student research will be summarized by both the write-up of a research paper in publishable form and by the presentation of a research seminar at the end of the semester. You are encouraged to eventually publish your results. Already parts of four publications (Shields, Hecker and Reed, 1991; Shields, Reed et al. 1993; Mouchaty, Cook and Shields, 1995; Cotter, Linberg, Sturgeon and Shields, 1996; Derenko, Malyarchuk and Shields, 1996) have resulted from research done for this class. So, it is not unlikely that you too could produce a study which results in publication. If the data and analysis warrant submission for publication, I will work with you through the publication process however long that takes.
TEACHING PHILOSOPHY

My teaching philosophy at this level of instruction (445/645) is that I will serve as a motivator and clarifier of material rather than as one who simply "summarizes what the students need to know." Consequently, a major responsibility is placed on the student in terms of approaching the material on your own, attempting to understand it and then sharing your views with me and with the rest of the class. Readings from the primary literature will be given to you on the first day of class so you can come to lecture prepared to contribute to the discussion. I will draw material for discussions from my own academic and research experience as well as from the published literature. I have organized the coverage into topics which we will address in an historical, progressive manner. Much of the progress of molecular evolution is based on the development of methodological breakthroughs which have provided new and more specific ways to look at the evolution of genes. Therefore, descriptions of methods, the data generated by them, their statistical analyses and the limitations of their application constitute a major portion of the beginning of the course.

RELEVANT LITERATURE:

In my opinion, there is no appropriate textbook for this course. No one has accepted the challenge to write an authoritative text. However, the following are good sources of relevant information.


* Important resource literature.

IMPORTANT RESEARCH JOURNALS:


Ancient Biomolecules. New journal


*Journal of Molecular Evolution. Springer International. Monthly BSL.

Mammalian Evolution. New Journal.

*Molecular Biology and Evolution. Soc. of Molecular Biology and Evolution. Univ. of Chicago Press. Monthly. (Shields lab.)

*Molecular Ecology. New Journal. (Shields lab.)

*Molecular Phylogenetics and Evolution. Academic Press. Monthly. (Shields lab.)

Nature. Weekly. RL

Proceedings of the National Academy of Sciences. Monthly. RL.

Science. Weekly. RL.

* Journals focused almost entirely on molecular evolutionary genetics.

LECTURE SEQUENCE

Sept. 5. Introduction to the course: my philosophy regarding coverage, relevant literature, discussion of research projects, requirements of the student and testing.

Sept. 10. The research proposal. The research publication.

Sept. 12. The Beginnings of Molecular Evolution as a discipline.


Sept. 24. Comparative Methodologies III - the polymerase chain reaction, sequencing of DNA, single-copy nuclear DNA, minisatellites, microsatellites DNA fingerprinting.


Other suggested readings:


Sept. 26. Shields at Carroll College of Montana for Academic Achievement Award.
Oct. 1 Interpretive Tools - molecular clocks, phylogenetic reconstruction (distance approaches - UPGMA, F-M, neighbor-joining, distance Wagner),

Required Reading: Chapter 4, Avise; on reserve Bio. Sciences Library

Oct. 3.) Interpretive Tools II - character state approaches (maximum parsimony, the bootstrap, gene trees vs. species trees).

Required Reading: Hillis et al. 1996. Chapter 11, Phylogenetic Inference

Oct. 8.) Human Molecular Evolution: "The African Eve" hypothesis

Suggested Readings:


Oct. 10.) Critique of the African Eve Hypothesis

Suggested Readings:


Oct. 15.) Molecular Clocks

Suggested Readings For Discussion:


Oct. 17.) Jurassic Park: Theory and Analysis of Ancient DNAs

Suggested Readings:


Oct. 22. First Lecture Examination

Oct. 24.) Ancient DNA II

Suggested Readings:


Oct. 29.) Conservation Genetics

Suggested Readings:


Suggested Readings:


Nov. 5. ) Human Radiation into the Western Hemisphere

*Required Readings


Nov. 7.) Intraspecific Phylogeography: The Brown Bear mtDNA Data Set

Suggested Readings:


Nov. 12.) Controversial Relationships: The True Ursids


Nov. 14). The Suggested Slow-down in the Rate of Molecular Evolution in Birds

Suggested Readings:


Nov. 19.) Second Lecture Examination

Nov. 21.) Additional Topics as Time Permits

Selection at the Molecular Level

Suggested Reading:


Nov. 26.) Metabolic Rate and the Molecular Clock


Dec. 3.) Molecular Evolution During Speciation
Suggested Readings:


Molecular Evolutionary Genetics of Nuclear Genes

Panda Phylogenetics

Dec. 5, 10, 12.) Research Seminars (to be arranged).

Dec. 12.) Deadline for Write-up of Final Research Report

Deadlines for all course associated work are listed below.

Sept. 24 Literature review of research topic, proposal write-up. Proposals are due in class (Sept. 24).

Sept. 27 Last day for student-initiated withdrawals

Oct. 22 First Lecture Exam.

Nov. 19 Second lecture Exam.

Dec. 5, 10 and 12.) Research project seminars

Dec. 12.) Deadline for Research Reports

Dec. 17 Final examination (8:00-10:00 a.m.).
Evaluation Criteria:

Class participation 10%
Laboratory work effort and participation 10%
Research Proposal 10%
Examinations 30%
(Graduate students will be asked two additional essay questions)
Final examination 20%
(Graduate students will be asked two additional essay questions)
Research Write-up and Seminar 20%
(Projects of graduate students will be expected to be more detailed and of higher quality)