Population Genetics
ECOL/GENE 426, 526 (3)
Prerequisites: ECOL 181, 182, 320
Spring 2006

Lectures: TTh 2:00 – 3:15, BSW 210

Professor: Michael Nachman
Bio Sciences West Bldg., Rm 334
Phone: 626-4595
Email: nachman@u.arizona.edu
Office Hours: Friday 2-3, or by appointment

TA: Jeff Good
BioSciences West Bldg., Rm 333
Phone: 621-4747
Email: jgood@email.arizona.edu
Office Hours: Tuesday 3:15-4:15, Wednesday 3-4, or by email appointment

General Course Content

This is a general introductory course on empirical and theoretical population genetics. It will involve two weekly lectures, weekly problem sets, readings from the text, and readings from the primary literature. A major goal of this course is to make students familiar with basic models of population genetics and to acquaint students with empirical tests of these models. As much as any field of biology, population genetics has been divided into a theoretical and an empirical branch. However, these two bodies of knowledge are intimately related and this course will cover both in roughly equal amounts. We will discuss the primary forces and processes involved in shaping genetic variation in natural populations (mutation, drift, selection, migration, recombination, mating patterns, population size and population subdivision), methods of measuring genetic variation in nature, and experimental tests of important ideas in population genetics.

This class usually includes roughly equal numbers of graduate and undergraduate students. Undergraduates often find this course challenging and fairly fast-paced. A basic knowledge of algebra and calculus is assumed.

Required text:

Hedrick, P.W. 2005 *Genetics of Populations*, *Third Edition*. Jones and Bartlett Publishers, Sudbury, MA.

Errata for this text can be downloaded from: http://lsweb.la.asu.edu/phedrick/

Class Website:

http://eebweb.arizona.edu/Courses/Ecol426_526/Home.html

Course Policy and General Expectations

1. Attendance. Regular attendance in lecture is expected and necessary for learning the material. Some of the topics covered in lecture are not in the text or other readings.

2. Text. There are weekly readings from the text. You are encouraged to read slowly, take notes, and work through the math yourself to make sure you understand it. It is a good idea to read the relevant sections of the text before the corresponding lecture on that topic.

3. Primary Literature. There are also weekly readings from the primary literature. These papers are listed below and will be available on the course website. Some exam questions will derive solely from this material. The readings will include both classic papers as well as more recent papers in population genetics.

4. Written Summaries of Research Papers. Students are expected to turn in a one-page summary of each of the papers from the primary literature. These summaries are intended to help you distill the main points from each paper. The summary should be divided into four sections, addressing each of the following: (*i*) What major question is being addressed by the authors? (*ii*) What did the authors do? (*iii*) What did the authors find? (*iv*) What is the significance of the work? These sections will often correspond to the Introduction, Materials and Methods, Results and Discussion sections of research papers, although you will see that some of the readings do not follow this format.

5. Presentations (required only for graduate students). All graduate students will briefly present one of the assigned papers to the class. These presentations will be on Thursdays during the last fifteen minutes of class, or on dates specifically reserved for presentations. Graduate students must make an appointment with Nachman to go over the material at least one week in advance of their presentation.

6. Exams. Both the mid-term and the final exams will be in-class exams. Graduate students will be required to answer an additional question on each exam. The final exam will cover material from the entire course, with an emphasis on material covered in the second half.

7. Problems Sets. There will be weekly problems sets to be completed as take-home exercises. Doing the problems is an essential part of this course. Population genetics involves a fair amount of simple mathematics, and like math, cannot be learned without working through examples. Each problem set will be worth ten points and will be due at the start of class each Thursday. Points will be deducted for late assignments. You are free (and encouraged) to work with other students when doing the problems. The problems will be graded each week and returned to you. After they are returned, the solutions will be posted on the course website. These solutions will be useful study guides for the exams.

8. All students are expected to adhere to the University of Arizona student code of conduct: http://w3.arizona.edu/%7Estudpubs/policies/ppmainpg.html.

Grading:	Mid term exam	100 pts
	Final Exam	200 pts
	Problem Sets	140 pts
	Written summaries	40 pts
	Participation and attendance	20 pts

Lecture Schedule - Spring 2006

	Date		Topic	Reading	Problems
1.	Jan.	12	Intro, models, probability and distributions	Ch 1	
2.		17	More on distributions		
3.		19	Genetic and phenotypic variation	Ch 2	p. 58, 1-7
4.		24	Hardy Weinberg, basic and complex models, neutral theory		
5.		26	Selection - basic diploid model	Ch 3	p. 110, 1-15
6.		31	Selection - dominance		
7.	Feb	2	Selection - heterosis and underdominance		p. 169, 1-3
8.		7	Selection - X linked, haplodiploid, multiple alleles (Good)		
9.		9	Selection - viability, sexual, and gametic (Good)	Ch 4	p. 169, 4-7, 13-14
10.		14	Selection - estimation from natural populations		
11.		16	Selection - ecological genetics and natural examples		p. 235, 2, 5
12.		21	Non-random mating	Ch 5	
13.		23	Non-random mating		p. 235, 9, 13, 14
14.		28	Genetic Drift: binomial sampling	Ch 6	
15.	Mar	2	Genetic Drift and effective population size		p. 296, 1-12
16.		7	Open		
17.		9	Mid Term Exam		p. 354, 1-9
		14	Spring Break		
		16	Spring Break		
18.		21	Mutation - basic ideas, mutation-selection balance	Ch 7	
19.		23	Mutation - balance between mutation and drift		p. 405, 2-7
20.		28	Mutation - estimation of rates		
21.		30	Population Structure - models of migration	Ch 9	p. 405, 8-10, 12-15
22.	April	4	Population Structure - estimation of gene flow		
23.		6	Linkage disequilibrium	Ch 10	p. 522, 1-8
24.		11	Molecular population genetics - neutral theory	Ch 8	
25.		13	Molecular population genetics - the coalescent process		p. 594, 1-5
26.		18	Molecular population genetics - tests of selection		
27.		20	Molecular population genetics - tests of selection (Good)		p. 467, 1-6
28.		25	Human molecular variation		
29.		27	Quantitative traits and association studies	Ch 11	p. 467, 8-12
30.	May	2	Open		

FINAL EXAM: Tuesday, May 9, 2-4 pm, BSW 210

Weekly Readings

(Some of these assignments may change during the semester – consult the website for the latest information.)

These papers will be available on the course website (http://eebweb.arizona.edu/Courses/Ecol426_526/Home.htm). The date listed is the due date for the written summary of each paper. *You are not required to write a summary for these papers.

January 19

Hubby, J.L. and R.C. Lewontin, 1966 A molecular approach to the study of genic heterozygosity in natural populations. I. The number of alleles at different loci in *Drosophila pseudoobscura*. Genetics 54: 577-594.*

Lewontin, R.C. and J.L. Hubby, 1966 A molecular approach to the study of genic heterozygosity in natural populations. II. Amount of variation and degree of heterozygosity in natural populations of *Drosophila pseudoobscura*. Genetics 54: 595-609.

January 26

Kreitman, M., 1983 Nucleotide polymorphism at the alcohol dehydrogenase locus of *Drosophila melanogaster*. Nature 304: 412-417.

Li, W.-H. and L.A. Sadler, 1991 Low nucleotide diversity in man. Genetics 129: 513-523.*

Aquadro, C.F., V. Bauer DuMont, and F.A. Reed, 2001 Genome-wide variation in the human and fruitfly: a comparison. Curr. Op. Genet. Develop. 11: 627-634.*

February 2

Evans, P.D. et al. 2005. *Microcephalin*, a gene regulating brain size, continues to evolve adaptively in humans. Science 309: 1717-1720

February 9

Palumbi, S.R., 2001. Humans as the world's greatest evolutionary force. Science 293: 1786-1790.

Bamshad, M. and S.P. Wooding, 2003. Signatures of natural selection in the human genome. Nat. Rev. Genet. 4: 99-111.*

February 16

Bustamante, C. et al. 2005. Natural selection on protein coding genes in the human genome. Nature 437: 1153-1157.

February 23

Hori, M., 1993 Frequency dependent natural selection in the handedness of scale-eating cichlid fish. Science 260: 216-219.

Nachman, M.W., Hoekstra, H.E., and S.L. D'Agostino, 2003. The genetic basis of adaptive melanism in pocket mice. Proc. Nat. Acad. Sci. USA 100: 5268-5273.*

March 2

Meagher, S., D.J. Penn, and W.K. Potts, 2000 Male-male competition magnifies inbreeding depression in wild house mice. Proc. Nat. Acad. Sci. USA 97: 3324-3329.

March 9

Hoelzel, A.R., J. Halley, S.J. O'Brien, C. Campagna, T. Arnbom, B. LeBoeuf, K. Ralls, and G.A. Dover, 1993. Elephant seal genetic variation and the use of simulation models to investigate historical population bottlenecks. J. Heredity 84: 443-449.

March 16
Spring Break

March 23
Makova, K.D., and W.H. Li. 2002. Strong male-driven evolution of DNA sequences in humans and apes. Nature 416: 624-626.
Haldane, J.B.S., 1935 The rate of spontaneous mutation of a human gene. J. Genetics 31: 317-326.*
Nachman, M.W., and S.L. Crowell, 2000. Estimate of the mutation rate per nucleotide in humans. Genetics 156: 297-304.*

March 30
Turner, T.L., M.W. Hahn, and S.V. Nuzhdin, 2005. Genomic islands of speciation in Anopheles gambiae. PLoS Biology 3: 1572-1578.
Hey, J. and C.A. Machado, 2003 The study of structured populations – new hope for a difficult and divided science. Nat. Rev. Genet.4: 535-543.*

April 6
Reich, D.E. M. Cargill, S. Bolk et al., 2001 Linkage disequilibrium in the human genome. Nature 411: 199-204.
McVean G.A.T., et al. 2004. The fine-scale structure of recombination rate variation in the human genome. Science 304: 581-584.
Jeffries, A.J., L. Kauppi, R. Neumann. 2001. Intensely punctate meitoic recombination in the class II region of the major histocompatibility complex. Nature Genet. 29: 217-222.*
Wall, J.D. and J.K. Pritchard, 2003. Haplotype blocks and linkage disequilibrium in the human genome. Nat. Rev. Genet. 4: 587-597.*

April 13
Kimura, M., 1968 Evolutionary rate at the molecular level. Nature 217: 624-626.
Hudson, R.R., M. Kreitman and M. Aguade, 1987 A test of neutral molecular evolution based on nucleotide data. Genetics 116: 153-159.

April 20
McDonald, J.H. and M. Kreitman, 1991 Adaptive evolution at the *Adh* locus in Drosophila. Nature 351: 652-654.
Andolfatto, P. 2005. Adaptive evolution of non-coding DNA in Drosophila. Nature 437: 1149-1152.

April 27
Begun, D.J. and C.F. Aquadro, 1992 Levels of naturally occurring DNA polymorphism correlate with recombination rates in *D. melanogaster*. Nature 356: 519-520.
Sabeti, P.C. D.E. Reich, J.M. Higgins et al., 2002 Detecting recent positive selection in the human genome from haplotype structure. Nature 419: 832-837

General Texts and Useful References

Avise, J.C. 2004. *Molecular markers, natural history and evolution. 2nd Edition*

Avise, J.C. and J.L. Hamrick, 1996. *Conservation genetics: case histories from nature.*

Baxevanis, AD and B.F. Francis Ouellette, eds. 2001. *Bioinformatics 2nd Edition*. John Wiley Publishers.

Carroll, S.B., J.K. Grenier, and S.D. Weatherbee, 2005. *From DNA to diversity: Molecular genetics and the evolution of animal design. 2nd Edition.* Blackwell Publishers.

Crow, J.F., 1986. *Basic concepts in population, quantitative, and evolutionary genetics.*

Crow, J.F. and M. Kimura, 1970. *An introduction to population genetics theory.*

Dobzhansky, T., 1970 *Genetics of the Evolutionary Process*, Columbia University Press, New York.

Falconer, D.S. and T.F.C. Mackay, 1996. *Introduction to Quantitative Genetics*, 4th Edition.

Fisher, R.A., 1958 *The Genetical Theory of Natural Selection*, Dover Publications, Inc. New York.

Gibson, G., and S.V. Muse, 2004. *A primer of genome science. 2nd Edition.* Sinauer Associates.

Gillespie, J.H, 1991. *The causes of molecular evoluton.*

Gillespie, J.H., 1998. *Population genetics. A concise guide.*

Graur, D. and W.-H. Li, 2000. *Fundamentals of Molecular Evolution*, 2nd Edition.

Haldane, J.B.S., 1924-1932, A mathematical theory of natural and artificial selection. (9 papers) Transactions and Proceedings of the Cambridge Philosophical Society. (First paper is vol 23: 19-41).

Haldane, J.B.S., 1932 *The Causes of Evolution*, Longmans and Green, London.

Halliburton, R. 2004. *Introduction to population genetics.*

Hartl, D.L., 1988 *A primer of population genetics*, 2nd edition (1988)

Hartl, D.L. and A.G. Clark, 1989. *Princeiples of population genetics* , 2nd Edition.

Hartl, D.L. and A.G. Clark, 1997 *Princeiples of population genetics* , 3rd Edition.

Hedrick, P.W. 2005 *Genetics of Populations*. 3rd Edition.

Hoelzel, A.R., 1992 *Molecular genetic analysis of populations.*

Kimura, M., 1983 *The Neutral Theory of Molecular Evolution*, Cambridge University Press, Cambridge.

Kimura, M. and T. Ohta, 1971. Theoretical Aspects of Population Genetics. Monographs in Population Biology. Princeton Univ. Press.

Lewontin, R.C., 1974 *The Genetic Basis of Evolutionary Change*, Columbia University Press, New York.

Li, C.C., 1955. *Population Genetics.*

Li, W.-H., ed., 1977 *Stochastic Models in Population Genetics*, Dowden, Hutchinson & Ross, Inc., Stroudsburg, PA.

Li, W.-H., 1997. *Molecular evolution.*

Lynch, M. and B. Walsh, 1998. *Genetics and Analysis of Quantitative Traits.*

Malecot, G., 1969 *The Mathematics of Heredity*, Freeman, San Fransisco.

Maynard Smith, J., 1989. *Evolutionary genetics.*

Nei, M., 1975. *Molecular population genetics and evolution.*

Nei, M., 1987. *Molecular evolutionary genetics.*

Nei, M. and S. Kumar, 2000. *Molecular Evolution and Phylogenetics.*

Provine, W.B., 1971 *The Origins of Theoretical Population Genetics*, Chicago University Press, Chicago.

Roughgarden, J. 1996. *Theory of Population Genetics and Evolutionary Ecology, An Introduction.*

Spiess, E.B., 1977. *Genes in populations.*

Wallace, B., 1981. *Basic population genetics.*

Wallace, B., 1991 *Fifty Years of Genetic Load: An Odyssey*, Cornell University Press, Ithaca, NY.

Wright, S, 1968. *Evolution and the Genetics of Populations, Volumes 1-4.*

Collections of Papers:

Kimura, M. 1994 *Population Genetics, Molecular Evolution, and the Neutral Theory, Selected Papers of Motoo Kimura*, Takahata, N., ed., The University of Chicago Press, Chicago.

Ohta, T. 1997. *Selected Papers on Theoretical Population Genetics and Molecular Evolution.* National Institute of Genetics, Mishima, Japan.

Wright, S. 1986 *Evolution: Selected Papers of Sewall Wright*, Provine, W.B., ed., The University of Chicago Press, Chicago.

Some key journals that publish papers in population genetics

American Journal of Human Genetics
Annual Review of Genetics
Annual Review of Genomics and Human Genetics
Biological Journal of the Linnean Society
Evolution
Genetics
Genome Research
Heredity
Journal of Heredity
Journal of Molecular Evolution
Molecular Biology and Evolution
Molecular Ecology
Nature
Nature Genetics
Nature Reviews Genetics
PLoS Biology
PLoS Genetics
Proceddings of the National Academy of Sciences, USA
Science
Trends in Genetics