Pitt Public Health

Department of Human Genetics

HUGEN 2022: Human Population Genetics
Fall 2019 syllabus

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Class: Monday and Wednesday, 11-11:55am, room A115 Crabtree. 2 credits.

Materials: Lecture notes and other course materials will be posted on courseweb. There is no required textbook, although recommended and optional readings will be made available on courseweb. Students sitting in on the class, but not enrolled, must e-mail me ASAP so that I can get you signed up for courseweb.

Course Description: This survey course covers the principles of population genetics as applicable to human populations, including (1) the laws of inheritance that govern the organization of the genomes in populations, (2) the evolutionary forces and phenomena that impact genetic diversity in human populations, and (3) the foundational concepts of genetic epidemiology and gene discovery.

This course is divided into three units. The first unit covers many of the fundamental principles of inheritance that govern the organization of genomes in populations. At the end of this unit, students will be able to perform simple calculations related to allele and genotype frequencies. The second unit covers the forces and phenomena that impact genetics in human populations from a relatively non-intensive mathematical perspective. At the end of this unit students will be able to describe the qualitative effects of evolutionary forces and solve simple mathematical problems in each area. The final unit of the course is a survey of other important quantitative topics in human genetics, including fundamental concepts of genetic epidemiology and methods of gene discovery. At the end of this unit students will be able to perform calculations related to each of these topics, describe the kinds of studies each method is used for and why, and interpret standard outputs from each method.

Learning Objectives: After completion of this course, students will be able to

- apply the Law of Hardy-Weinberg Equilibrium and its assumptions to calculate allele and genotype frequencies
- predict the consequences of genetic inheritance and recombination in populations including the concepts of linkage and linkage disequilibrium
- interpret the qualitative effects of violations of Hardy-Weinberg Equilibrium and solve simple quantitative problems demonstrating these effects
- express the fundamental goals and principles of genetic epidemiology by modeling genotype-phenotype relationships, quantitative traits, and heritability
- interpret results from gene discovery methods such as linkage analysis and large-scale genetic association studies, and critically evaluate the strengths, limitations, and appropriate applications of these methods.

Prerequisites: Students will find it helpful to have had introductory coursework in genetics, statistics or biostatistics, and epidemiology, but these are not absolutely required prerequisites.

Genetics refresher: Students seeking to brush up on fundamental genetics concepts may benefit from exploring the online resource "DNA from the beginning" (http://www.dnaftb.org/) which covers the prerequisite material related to genetics.

Statistics refresher: Students seeking tutorials on basic statistics may benefit from the Web Interface for Statistics Education (WISE, http://wise.cgu.edu/).

Assessments and Grades: Final grades will be determined based on students' performance on three in-class exams and two take-home exams, as well as participation during in-class discussions and demonstrated effort on homework. The breakdown is as follows:

Unit 1 Exam	20%
Unit 2 Take-home	15%
Unit 2 Exam	20%
Unit 3 Take-home	15%
Unit 3 Exam	20%
Homework/Participation	10%

There is no pre-determined numeric grading scale and students' cumulative performance across all assessments will lead to an assigned letter grade based on the following rubric. A: the student demonstrates mastery of all course objectives; B: the student demonstrates competency in all course objectives and mastery of some; C: the student demonstrates competency in all course objectives; D: the student demonstrates competency in most course objectives with significant deficiency in one or more objectives; F: the student fails to demonstrate competency in most course objectives.

Homework: Homework will be assigned regularly throughout the semester. Students are encouraged to work cooperatively on assignments, but must turn in final written work that is their own. Homework is not graded for correctness, but will be scored for effort and completeness.

Homework is one of the principal methods I use to see how you are doing. If you are having problems, I will let you know. Many homework problems are re-used from year to year, and old solutions exist. If you look at those before you do the homework, neither you nor I will know if you are having problems with the material until it is too late. The material covered in this class is not the type of content that you can learn without doing practice problems.

You may handwrite or type your homework, but if you type, please make sure that you do not leave out intermediate steps of calculations. I need to be able to tell if you are actually doing the problem correctly or if you are just getting the right (or wrong) answer by accident. Feel free to edit the layout of the homework documents to add more space for handwritten solutions, if needed.

Please make sure you read the solutions to all homework assignments. There is a lot of information in there that goes beyond simple solutions to the problems. Consider this to be a part of the course reading assignments.

In-class Exams: There will be three in-class exams during the course. All exams will be open notes and will require a calculator. Students are required to bring their own calculator and know how to use it. Students may not communicate (talk, e-mail, text, message, etc.) with anyone during the exams.

Take-home Exams: There will be two take-home exams during the course. Take-home exams are open notes and will require a calculator. Students are **not** permitted to work together on take-home exams, nor seek any outside help.

Recommended and optional readings: Review articles and original research articles corresponding to class lectures will be made available on courseweb. These include the following list of readings, which are subject to change.

- Mayo O. A century of Hardy-Weinberg equilibrium. *Twin Res Hum Genet*. 2008;11(3):249-256.
- Slatkin M. Linkage disequilibrium--understanding the evolutionary past and mapping the medical future. *Nat Rev Genet*. 2008;9(6):477-485.
- Zhang Y, Syed R, Uygar C, et al. Evaluation of human leukocyte N-formylpeptide receptor (FPR1) SNPs in aggressive periodontitis patients. *Genes Immun*. 2003;4(1):22-29.
- Mitchell-Olds T, Willis JH, Goldstein DB. Which evolutionary processes influence natural

genetic variation for phenotypic traits? *Nat Rev Genet*. 2007;8(11):845-856.
- Hurst LD. Fundamental concepts in genetics: genetics and the understanding of selection. *Nat Rev Genet*. 2009;10(2):83-93.
- Soskine M, Tawfik DS. Mutational effects and the evolution of new protein functions. *Nat Rev Genet*. 2010;11(8):572-582.
- Baer CF, Miyamoto MM, Denver DR. Mutation rate variation in multicellular eukaryotes: causes and consequences. *Nat Rev Genet*. 2007;8(8):619-631.
- Barbujani G, Ghirotto S, Tassi F. Nine things to remember about human genome diversity. *Tissue Antigens*. 2013;82(3):155-164.
- Bryc K, Durand EY, Macpherson JM, Reich D, Mountain JL. The genetic ancestry of African Americans, Latinos, and European Americans across the United States. *Am J Hum Genet*. 2015;96(1):37-53.
- Holsinger KE, Weir BS. Genetics in geographically structured populations: defining, estimating and interpreting F(ST). *Nat Rev Genet*. 2009;10(9):639-650.
- Lander ES. Initial impact of the sequencing of the human genome. *Nature*. 2011;470(7333):187-197.
- Balding DJ. A tutorial on statistical methods for population association studies. *Nat Rev Genet*. 2006;5(7):781-791.
- Visscher PM, Hill WG, Wray NR. Heritability in the genomics era--concepts and misconceptions. *Nat Rev Genet*. 2008;9(4):255-266.
- Manolio TA. Bringing genome-wide association findings into clinical use. *Nat Rev Genet*. 2013;14(8):549-558.
- Kruglyak L. The road to genome-wide association studies. *Nat Rev Genet*. 2008;9(4):314-318.
- Karlsson EK, Kwiatkowski DP, Sabeti PC. Natural selection and infectious disease in human populations. *Nat Rev Genet*. 2014;15(6):379-393.
- Chaissan MJ, Wilson RK, Eichler EE. Genetic variation and the de novo assembly of human genomes. *Nat Rev Genet*. 2015;16(11):627-640.
- Seunggeung L, Abecasis GR, Boehnke M, et al. Rare-Variant Association Analysis: Study Designs and Statistical Tests. *Am J Hum Genet*;95(7)5-23.
- Metzker ML. Sequencing technologies – the next generation. *Nat Rev Genet*. 2010;11(1):31-46.
- Ott J, Wang J, Leal SM. Genetic linkage analysis in the age of whole-genome sequencing. *Nat Rev Genet*. 2015;16(5):275-284.

For students interested in a supplemental textbook, there are a number of good options available. Much of the material covered in Units 1 and 3 is described (sometimes in greater detail) in Ziegler and König. The material covered in Unit 2 is presented at a similar level in Relethford.

- Ziegler A, König IR. *A Statistical Approach to Genetic Epidemiology*. 2nd ed. 2010. Wiley-Blackwell. ISBN-13: 978-3527323890
- Relethford J.H. *Human Population Genetics*. 2012. Wiley-Blackwell. ISBN-13: 978-0470464670

Disabilities: If you have a disability that requires special accommodation, you need to notify both the instructor and the Office of Disability Resources and Services 140 William Pitt Union (Voice or TTD 412-648-7890) as early as possible in the term.

Academic Integrity Statement: All students are expected to adhere to the school's standards of academic honesty. Cheating/plagiarism will not be tolerated. The Graduate School of Public Health's policy on academic integrity, which is based on the University policy, is available online in the Pitt Public Health Academic Handbook www.publichealth.pitt.edu/home/academics/academic-requirements. The policy includes obligations for faculty and students, procedures for adjudicating violations, and other critical information. Please take the time to read this policy.

Sexual Misconduct, Required Reporting, and Title IX Statement: The University is committed to combatting sexual misconduct. As a result, you should know that University faculty and staff members are required to report any instances of sexual misconduct, including harassment and sexual violence, to the University's Title IX office so that the victim may be provided appropriate resources and support options. What this means is that as your professor, I am required to report any incidents of sexual misconduct that are directly reported to me, or of which I am somehow made aware.

There are two important exceptions to this requirement about which you should be aware: A list of the designated University employees who, as counselors and medical professionals, do not have this reporting responsibility and can maintain confidentiality, can be found here: www.titleix.pitt.edu/report/confidentiality

An important exception to the reporting requirement exists for academic work. Disclosures about sexual misconduct that are shared as part of an academic project, classroom discussion, or course assignment, are not required to be disclosed to the University's Title IX office.

If you are the victim of sexual misconduct, Pitt encourages you to reach out to these resources:

- Title IX Office: 412-648-7860
- SHARE @ the University Counseling Center: 412-648-7930 (8:30 A.M. TO 5 P.M. M-F) and 412-648-7856 (AFTER BUSINESS HOURS)

If you have a safety concern, please contact the University of Pittsburgh Police, 412-624-2121. Other reporting information is available here: www.titleix.pitt.edu/report

Statement from the Department of Gender, Sexuality, and Women's Studies
[This statement was developed by Katie Pope, Title IX Coordinator, in conjunction with GSWS instructors.]

Diversity Statement: The University of Pittsburgh Graduate School of Public Health considers the diversity of its students, faculty, and staff to be a strength and critical to its educational mission. Pitt Public Health is committed to creating and fostering inclusive learning environments that value human dignity and equity. Every member of our community is expected to be respectful of the individual perspectives, experiences, behaviors, worldviews, and backgrounds of others. While intellectual disagreement may be constructive, no derogatory statements, or demeaning or discriminatory behavior will be permitted.
If you feel uncomfortable or would like to discuss a situation, please contact any of the following:

- the course instructor;
- the Pitt Public Health Associate Dean for Diversity at 412-624-3506 or nam137@pitt.edu;
- the University's Office of Diversity and Inclusion at 412-648-7860 or https://www.diversity.pitt.edu/make-report/report-form (anonymous reporting form).

Tentative Schedule

The sequence of topics laid out below is unlikely to change, but the amount of time spent on each topic may be adjusted as we go along.

Date	Class	Take-home Exam
	Unit 1: Inheritance & Hardy-Weinberg Equilibrium	
M 8-26	1.1: single-locus inheritance and Hardy-Weinberg equilibrium	
W 8-28	1.2: multi-locus inheritance	
M 9-2	**No class (Labor Day)**	
W 9-4	1.3: pedigrees and relationships	
M 9-9	1.4: probability and statistics review	
W 9-11	1.5: statistical tests for HWE and LD	
M 9-16	review and catch-up	
W 9-18	Exam 1: covers unit 1	
	Unit 2: Evolution and Population Structure	
M 9-23	2.1: evolution 1: genetic drift	
W 9-25	2.2: evolution 2: natural selection	
M 9-30	2.3: evolution 3: mutation	
W 10-2	2.4: population structure 1: introduction	Assigned
M 10-7	2.5: population structure 2: migration	Due
W 10-9	2.6: population structure 3: assortative mating	
M 10-14	2.7: population structure 4: inbreeding	
W 10-16	TBD (ASHG)	
M 10-21	2.8: real world examples	
W 10-23	Exam 2: covers unit 2	
	Unit 3: Genetic epidemiology	
M 10-28	3.1: genotype-phenotype relationships 1: quantitative traits	
W 10-30	3.2: genotype-phenotype relationships 2: model extensions	
M 11-4	3.3: genotype-phenotype relationships 3: heritability	
W 11-6	3.4: genetic epidemiology 1: measuring and testing genetic association	
M 11-11	3.5: genetic epidemiology 2: real world examples	
W 11-13	3.6: gene-mapping 1: introduction	Assigned
M 11-18	3.7: gene-mapping 2: GWAS (part 1)	Due
W 11-20	GWAS (part 2)	
M 11-25	**No class (Fall break)**	
W 11-27	**No class (Fall break)**	
M 12-2	3.8: gene-mapping 3: sequencing	
W 12-4	3.9: gene-mapping 4: linkage analysis	
M 12-9	3.10: gene-mapping 5: copy number variation	
W 12-11	Exam 3: covers unit 3	