Pop Gen

Department of Human Genetics | University of Pittsburgh

HUGEN 2022: Human Population Genetics
Fall 2021 syllabus

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Class: Monday and Wednesday, 11:00am-11:55am, 2 credits.
332 Cathedral of Learning

Materials: Lecture notes and other course materials will be posted on Canvas, the University's course management system. There is no required textbook, although recommended and optional readings will be made available on Canvas. Students participating in the class, but not officially enrolled, must e-mail me so that I can provide access to the course on Canvas.

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 and make inferences related to alleles, genotypes, and their frequencies in populations. The second unit covers the forces and phenomena that impact genetic variation 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: There are no firm prerequisites. Introductory coursework in genetics, biostatistics, and epidemiology may prepare students for this course, 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 five 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%
Mid-Unit 2 Exam	15%
Unit 2 Exam	20%
Mid-Unit 3 Exam	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 learning objectives; B: the student demonstrates competency in all learning objectives and mastery of some; C: the student demonstrates competency in all learning objectives; D: the student demonstrates competency in most learning objectives with significant deficiency in one or more objectives; F: the student fails to demonstrate competency in most learning 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 and serves as a low-stakes opportunity to self-assess your understanding of the material. 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.

Homework will be submitted electronically. You may handwrite and scan 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. If you handwrite and scan your homework, please use a scanner or scan app on your phone/device rather than a regular photo. 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.

Take-home Exams: There will be five 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 Canvas. 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.
- Nordsletten AE, Larsson H, Crowley JJ, et al. Patterns of nonrandom mating within and across 11 psychiatric disorder. *JAMA Pyschiatry*. 2016.

- Robinson MR, Kleinman A, Graff M. Genetic evidence of assortative mating in humans. Nature Hum Behav. 2017;1:0016.
- 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

Accommodation for Students with Disabilities: If you have a disability for which you are or may be requesting an accommodation, you are encouraged to contact both your instructor and Disability Resources and Services, 140 William Pitt Union, 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: https://www.diversity.pitt.edu/civil-rights-title-ix/make-report/report-form

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: https://www.diversity.pitt.edu/civil-rights-title-ix-compliance/make-report

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Diversity Statement: Pitt Public Health Diversity Statement | Effective Academic Year 2021-22

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 and promote social justice. 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 director or course instructor
- the Pitt Public Health Associate Dean responsible for diversity and inclusion
- the University's Office of Diversity and Inclusion at 412-648-7860
- https://www.diversity.pitt.edu/civil-rights-title-ix/make-report/report-form (anonymous reporting form)

COVID-19 Statement

I want to acknowledge the atypical nature of teaching and learning during this continuing pandemic. We will follow the plans and policies enacted by the University and School of Public Health, which may change in response to the evolving threat to our health and safety.

Zoom-optional for the first two weeks: During the first two weeks of the semester (Aug.27th to Sept. 10th) my plan is that class will be held in person with the option to participate synchronously via Zoom. This plan can be adapted based on the number of students choosing to attend in person and remotely and the quality of the hybrid learning experience.

Rules for in-person learning: The initial plan is to hold this course in person. Form-fitting masks are required. Food and beverage consumption is prohibited in the classroom. Physical distancing is not required per University policy, but 3 feet (1 meter) physical distancing is strongly encouraged by Pitt Public Health.

Back-up plan for remote learning: While the initial plan is for the class to be held in person (with optional Zoom participation until Sept. 13th), if local pandemic conditions necessitate moving this course to remote technologies, online participation in the "in-class" activities will be conducted synchronously through Zoom. This back-up plan can be adjusted as needed based on what works best for us.

Canvas: The University's course management system is Canvas, which is where course materials such as lecture notes, homework assignments, readings, and lecture recordings will be posted. In addition to distributing materials, Canvas will also be used as the portal for submitting and receiving feedback on homework assignments and exams. Canvas can be accessed via web browser or phone/portable device apps.

Lecture recordings: Live class sessions will be recorded and made available on Canvas after class for asynchronous viewing. Students are not required to be recorded. If you have questions but do not want to be recorded, please request that I pause the recording, or meet with me or the TA during office hours. Please do not make your own recordings. Please do not distribute class recordings, such as reposting them elsewhere online. Per University policy recorded lectures cannot be retained after the end of the semester.

Pre-recorded material: While the majority of the course material will be covered in class, some material may be also be pre-recorded and posted online. For example, some refresher material will be posted online. Likewise, if we do not get through the lecture material in allotted class time, the remainder may be posted online for asynchronous viewing. Further, if we find that we would prefer to reserve more in-class time for discussion, working out practice problems, or answering questions, some of the lecture material may be pre-recorded and posted online.

Homework: Homework is a key component of this course. For most lectures there will be a corresponding homework assignment, which will be provided on Canvas as a document in Word and PDF formats. The nature of the course material often lends itself best to solving homework problems by hand. Therefore, I would encourage you to write out your homework solutions for math problems either on printouts or notebook paper. Free phone/device apps are available for scanning handwritten homework. I recommend Evernote Scannable, which will yield a far better electronic version than a regular photo. The Apple iOS Notes app and the Android Google Drive app also have

scan features. All completed homework will be submitted electronically through Canvas. You can upload PDF scans of handwritten work, typed PDF files or Word documents.

Exams: All exams will be take-home, meaning that they will be completed outside of the regular class time. Exams are open note and will require a calculator. I will either: (1) post each exam as a PDF on Canvas and have students submit answers as a single file upload, the same process as the homework, or (2) use the built-in Quiz feature within Canvas.

Engagement and participation: Meaningful engagement in a course benefits student learning. Completing the homework assignments and attending lectures are two of the major ways that students will participate in this course. Lectures will include some practice problems and discussions, providing opportunities for students to engage with the material.

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. The exact date of any particular lecture or exam is subject to change with advanced notice.

Date	Class	Exam
	Unit 1: Inheritance & Hardy-Weinberg Equilibrium	
M 8-30	course introduction	
W 9-1	1.1: pedigrees and relationships	
M 9-6	**Labor Day (University closed)**	
W 9-8	1.2: probability and statistics review	
M 9-13	1.3: single-locus inheritance and Hardy-Weinberg equilibrium	
W 9-15	1.4: multi-locus inheritance	
M 9-20	1.5: statistical tests for HWE and LD	
W 9-22	review and catch-up	Assigned
	Unit 2: Evolution and Population Structure	
M 9-27	2.1: evolution 1: genetic drift	Due
W 9-29	2.2: evolution 2: natural selection	
M 10-4	2.3: evolution 3: mutation	
W 10-6	2.4: population structure 1: introduction	Assigned
M 10-11	2.5: population structure 2: migration	Due
W 10-13	2.6: population structure 3: assortative mating	
M 10-18	2.7: population structure 4: inbreeding | 2.8 unit 2 self-study	
W 10-20	2.9: real world examples	
M 10-25	review and catch up	
W 10-27	guest lecture	Assigned
	Unit 3: Genetic epidemiology	
M 11-1	3.1: genotype-phenotype relationships 1: quantitative traits	Due
W 11-3	3.2: genotype-phenotype relationships 2: model extensions	
M 11-8	3.3: genotype-phenotype relationships 3: heritability	
W 11-10	3.4: genetic epidemiology 1: measuring and testing genetic association	
M 11-15	3.5: genetic epidemiology 2: real world examples	
W 11-17	3.6: gene-mapping 1: introduction	Assigned
F 11-19	**No class; mid-unit 3 exam due**	Due
M 11-22	**Thanksgiving recess (no classes)**	
W 11-24	**Thanksgiving recess (no classes)**	
M 11-29	3.7: gene-mapping 2: GWAS (part 1)	
W 12-1	3.7: gene-mapping 2: GWAS (part 2)	
M 12-6	3.8: gene-mapping 3: sequencing	
W 12-8	3.9: gene-mapping 4: linkage analysis	
M 12-13	3.10: gene-mapping 5: copy number variation	
W 12-15	review and catch up	Assigned
F 12-18	**No class; final exam due**	Due