Instructor: Dr. Ã‰adaoin (â€œAy-Deenâ€) Harney â€“ Email: harney@g.harvard.edu

Time and Location: 9:00-10:15 am â€“ Tuesday & Thursday â€“ MCZ 539

Office Hours: Thursday 10:30-11:30am â€“ MCZ 539 â€“ and by appointment

Course Objectives: This course is intended for students who have some training in genetics, either gained through an introductory genetics course or as part of a broader biology course, and are interested in learning more about the field of human population genetics. By taking this course, students will:

- Gain a broad understanding of the fundamental concepts in the field of human population genetics, without being required to understand the specific details of the more complex mathematical concepts upon which these concepts are based (i.e. there will be some algebra, but calculus and linear algebra will be kept to a minimum).
- Learn to read and critically assess academic papers from the field of population genetics.
- Synthesize the concepts they have learned into a final research paper or project.

Course Structure: This course is primarily lecture-based, but students will be asked to participate in small in-class exercises and discussions throughout the semester. Two in class tests will be given during the semester. At the end of the course, students will share their chosen final research paper/project topics with the class through a short, in-class presentation. All problem sets, readings and article responses will be completed outside of class.

Grading:

Attendance and Participation:	5%
Problem Sets (x5):	25% (5% each)
Tests (x2):	20% (10% each)
Article Responses (x2):	20% (10% each)
Final Paper/Project Proposal:	5%
Final Paper/Project Presentation:	5%
Final Paper/Project Report:	20%

Readings

The primary textbook for this course will be â€œAn Owner's Guide to the Human Genome: an introduction to human population genetics, variation and diseaseâ€ by Jonathan Pritchard, which is freely available online: https://web.stanford.edu/group/pritchardlab/HGbook.html

While the course will largely follow the topics outlined in this book, this is a brand new textbook and currently only half of it has been released. Additional readings will be made available through canvas to complement this textbook, or to serve as the primary reading material when covering topics from the unreleased portion of the book.

Additionally, four class sessions will be dedicated to an in-depth discussion of an article from the field of population genetics, which will be made available via canvas. Students are expected to have read these articles **prior to** the class period during which they will be discussed.

Assignments

Problem Sets (5 pts each; x5): These problem sets are meant to be low stress assignments that will provide you with the opportunity to apply the techniques that we learn in class to real data. You may collaborate with other students on these problem sets, but you must be able to explain the rationale behind your answers. Grades for problem sets will be assigned based on completion (i.e., did you make an effort to complete the problem set) and accuracy.

Tests (10 pts each; x2): Twice during the semester, students will take an in class test to test their understanding of the topics that we have learned in class.

Article Responses (10 pts each; 2x): Twice during the semester, you will select a recent article (published within the last year) that relates to a topic that we have covered in the course. Read this article critically and prepare a 2-page (double-spaced, 12pm, Arial, Calibri or Times New Roman font, 0.5 inch margins) response that summarizes the main findings of the paper. Be sure to highlight how it furthers the field and what limitations it has. You may turn in the article responses as early as you wish, but they must be received before the deadline indicated in the weekly schedule. (Detailed guidelines)

Final Paper/Project Proposal (5 pts): A short (~1 page, double-spaced, 12pm, Arial, Calibri or Times New Roman font, 0.5 inch margins) proposal describing the topic that you have chosen for your final research paper or project. Students are encouraged to meet with their instructor to discuss their plan prior to submitting their proposals.

Final Paper/Project Presentation (5 pts): During the final class session, students will take turns presenting on the topic they have chosen to cover in their final paper or project. Presentation length will be determined based on course enrollment. In the presentation, students will tell us about their chosen topic, providing background about why they have chosen this topic for their final paper or project. Students are not expected to have finished their paper/project at the time of their presentation, but should describe what they have learned thus far and what they plan to address going forward.

All presentations should include accompanying slides. Be sure that your slides contain enough detail (either on the slide or in the presenter notes) so that someone who did not see your presentation can still learn about your chosen paper/project by reviewing them.

Final Paper/Project Report (20 pts): You will have a choice to either write an original research paper (~10 pages, double-spaced, 12pm, Arial, Calibri or Times New Roman font, 0.5 inch margins) or perform an independent research project inspired by a topic of your choice covered in the course and prepare a written report. There is no grading benefit to choosing either the research paper or project option, so you are encouraged to choose whichever option you prefer. However, if you choose to perform an original research project, it is up to you to ensure that you have the computational background necessary to complete this project and access to any necessary computational resources needed to perform your proposed analyses, as no specific project support will be offered during the course. This option is therefore primarily recommended for upper level undergraduates or graduate students who already have the necessary computational and/or research experience.

Policies

Attendance and Participation: Regular attendance and active participation are critical to your success in this course. If a situation arises that prevents you from attending class, please check in with your instructor at the earliest opportunity to discuss how to prepare for your absence or to catch up on any missed work. In recognition that unavoidable or unpredictable situations may arise that disrupt your schedule, all students will be permitted one â€œunexplainedâ€ absence for you which you do not need to provide a justification (although you are still strongly encouraged to contact your instructor to discuss what content will be covered on the day that you miss). Beyond this, you must contact your instructor to discuss whether your absence can be considered excused due to a valid reason (e.g. illness, family emergency, religious holidays, or a meeting that is critical to your academic success). Extenuating circumstances that result in repeated absences will be considered on a case-by-case basis.

Deadlines and Late Assignments: Unless otherwise noted, assignments are due at the beginning of class on the day listed and should be uploaded to the class Canvas site (problem sets may also be handed directly to the instructor). Except in the case of exceptional circumstances, problem sets must be turned in by the deadline, as an answer key will be made available shortly after the submission deadline. For all other assignments, in most cases, short extensions (1-3 days) that are requested at least 24 hours in advance will be granted, while longer extensions may be considered on a case-by-case basis. Late submissions that did not receive prior approval may be penalized.

Collaboration and use of Generative Artificial Intelligence (AI): Students are encouraged to work with their classmates to complete problem sets and other assignments. However, all of the written content included in assignments must have been written by students on their own. Students may not use generative AI tools, such as ChatGPT, to assist with problem sets or writing assignments. This policy is in place as the purpose of these assignments is for students to demonstrate that they fully understand the subject matter covered each week. If a circumstance arises where a student believes that the use of generative AI tools would enhance their learning, they are encouraged to speak to the instructor about this possible use case.

Accessibility (from the Disability Access Office): Harvard University values inclusive excellence and providing equal educational opportunities for all students. Our goal is to remove barriers for disabled students related to inaccessible elements of instruction or design in this course. If reasonable accommodations are necessary to provide access, please contact the Disability Access Office (DAO) (https://dao.fas.harvard.edu/). Accommodations do not alter fundamental requirements of the course and are not retroactive. Students should request accommodations as early as possible, since they may take time to implement. Students should notify DAO at any time during the semester if adjustments to their communicated accommodation plan are needed.

Schedule

Week	Day	Date	Topic	Deadlines	Readings*
1	Tu	23-Jan	Course Introduction + Genetics 101 Part 1 (slides)		
	Th	25-Jan	Genetics 101 Part 2 (slides)		Chapter 1.1-1.2
2	Tu	30-Jan	Human Genetic Variation (slides)		Chapter 1.3
	Th	1-Feb	DNA Sequencing Technologies (slides)		Chapter 1.4
3	Tu	6-Feb	Mutation (class is virtual - zoom link) (slides)		Chapter 1.5
	Th	8-Feb	**Paper 1 Discussion** & Article Response Overview (class is virtual - zoom link) (slides) Anastasiadou, K., Silva, M., Booth, T. *et al.* Detection of chromosomal aneuploidy in ancient genomes. *Commun Biol* **7**, 14 (2024). https://doi.org/10.1038/s42003-023-05642-z		Discussion Paper 1 (Main Text) (Supplementary Notes) (Tables) Recommended readings: Raff - How to read and understand a scientific article (or you can read the longer blog post online) Carey et al - Ten simple rules for reading a scientific paper
4	Tu	13-Feb	No class		
	Th	15-Feb	Genetic Drift (slides)	Problem Set 1 (answer key)	Chapter 2.1
5	Tu	20-Feb	The Coalescent (slides)		Chapter 2.2
		22-	Linkage, Recombination and LD + Population		

	Th	Feb	structure (slides)		Chapter 2.3 - 2.4
6	Tu	27-Feb	Natural Selection I (slides)	Problem Set 2 (answer key)	Chapter 2.5-2.6
	Th	29-Feb	Natural Selection II (slides)		Chapter 2.6-2.7
7	Tu	5-Mar	**Paper 2 Discussion** & Test 1 Review (slides) Evershed, R.P., Davey Smith, G., Roffet-Salque, M. et al. Dairying, diseases and the evolution of lactase persistence in Europe. Nature 608, 336â€“345 (2022). https://doi.org/10.1038/s41586-022-05010-7	Problem Set 3 (answer key)	Discussion Paper 2 (Main Text) (Supplementary Notes)
	Th	7-Mar	**Test 1** (test) (key)		
	Tu	12-Mar	No Class - Spring Break		
	Th	14-Mar	No Class - Spring Break		
8	Tu	19-Mar	Ancestry (slides)		Chapter 3.1 Recommended readings: • Mathieson and Scally. "What is ancestry?." PLoS genetics 16.3 (2020): e1008624 • Using Population Descriptors in Genetics and Genomics Research. Guidelines from the National Academies of Science [News Summary] [Interactive Website] [Video Understanding Genetic Ancestry]
					Chapter 3.2

	Th	21-Mar	Admixture (slides)	Article Response 1	Recommended Readings: Patterson et al 2012 (the classic f-stat paper) Peter 2016 (a coalescent approach to fstats)
9	Tu	26-Mar	Human Prehistory (slides)		Chapter 3.3
	Th	28-Mar	Ancient DNA (slides)		Chapter 3.4 Recommended Readings: Orlando et al (2021) Ancient DNA Primer
10	Tu	2-Apr	**Paper 3 Discussion** & Final Paper/Project Overview (slides) Harris, Kelley, and Rasmus Nielsen. "The genetic cost of Neanderthal introgression." Genetics 203.2 (2016): 881-891.	Problem Set 4 (answer key)	Discussion Paper 3
	Th	4-Apr	Major effect mutations (slides)		Nature Education has some great online resources on Mendelian Genetics, including: • Mendelian Genetics • Mitochondrial Inheritance • Penetrance & Expressivity • Gene Mapping Here's a link to the full collection of topics
					Recommended Readings: • Estimating Trait Heritability • The case of the missing heritability • Chapters 7 of Graham Coop's "Population and

11	Tu	9-Apr	Complex Traits I (slides)	Final Paper/Project Proposal	Quantitative Genetics" notes, You can find his full set of notes here. • Chapter 1 of Alexander Gusev's "A molecular genetics perspective on the heritability of human behavior and group differences". You can find the full textbook here.
	Th	11-Apr	Complex Traits II (slides)		Recommended Readings: • Uffelmann, Emil, et al. "Genome-wide association studies." Nature Reviews Methods Primers 1.1 (2021): 59.
12	Tu	16-Apr	**Paper 4 Discussion** - Test 2 Review Begg, Tristan James Alexander, et al. "Genomic analyses of hair from Ludwig van Beethoven." Current Biology 33.8 (2023): 1431-1447. Wesseldijk, Laura W., et al. "Notes from Beethovenâ€™s genome." Current Biology 34.6 (2024): R233-R234.	Problem Set 5 (key)	Discussion Paper 4 (Paper 1, SM) (Paper 2, SM) Note that we are reading two related papers. Paper 2 is a short follow up note responding to Paper 1.
	Th	18-Apr	**Test 2** (key)		
13	Tu	23-Apr	**Final Paper/Project Presentations**	Article Response 2	
	W	1-May	No Class	Final Paper / Project - Due at 11:59pm	

*Chapter numbers refer to the course textbook: "An Owner's Guide to the Human Genome". Parts 1-2 are currently publicly available and Part 3 will be added later in the semester.