

QBIO 475: Statistical and Evolutionary Genetics

Syllabus

General Information

Lecture time: TTh 12:30-1:50

Lecture location: RRI 301

Instructors: Michael “Doc” Edge , Jazlyn Mooney

Instructor email:

Instructor office hours:

Discussion section time and location: T 2:00-2:50, RRI 301 (no section the first Tuesday of class)

Teaching Assistant: Dandan Peng

Teaching Assistant Office Hours:

Note: Please bring a laptop and scratch paper to class.

Welcome! We are looking forward to working with you this semester. We aim to help you have as rewarding an experience learning the subjects in this course as we have had.

Course Description

This is an upper-division course designed to introduce quantitative biologists to some central ideas in the mathematical modeling and statistical analysis of genetic variation. Topics from evolutionary genetics and medical genetics will be explored using a mix of math, simulation, and data analysis. Topics may include genetic drift, natural selection, mutation, migration, population structure, and study designs for learning about genotype-phenotype relationships, such as family-based studies, analyses of gene-expression variation, and genome-wide association studies.

Textbook

Our main reading material will be Graham Coop’s notes on population and quantitative genetics, available at <https://gcbias.org/population-genetics-notes/> . These notes are free to access. Other readings will be posted on the course website.

Other recommended (but not required) books include Gillespie’s *Population Genetics: A Primer* and Säll & Bengtsson’s *Understanding Population Genetics*. Some of the mathematical derivations we do in class will follow these books.

Course Notes

There is a great deal of excitement about using genetic information to predict risk for disease or understanding the sources of disease risk. Despite the widespread availability of genetic data, these goals are still hard to reach for most common health conditions. One reason is because of the way genetic variation is structured---most genetic variants are rare, and genotypes are correlated with each other in the population. In this course, we will take a close look at human genetic variation and learn some evolutionary reasons it looks the way it does.

Learning Goals

By course's end, our aim is that you will be able to:

- Describe the major evolutionary “forces” studied by population geneticists.
- Prove some key mathematical results used in population genetics.
- Apply some major insights of theoretical population genetics to thinking about the distribution and effects of genetic variation within populations.
- Discuss the application of population-genetic and quantitative-genetic thinking to biomedical research.
- Conduct basic data analyses in population and statistical genetics
- Explain the strengths and weaknesses of major methods for learning about connections between genetic and phenotypic variation.

Prerequisites

The only required prerequisite is a course that covers probability---either QBIO 310, MATH 307, or MATH 407 will suffice. Comfort with algebra is also a must. Statistics, and some experience with statistical programming (at the level of QBIO 310) will be helpful. For biological context, the fundamentals of genetic inheritance and evolutionary biology (at the level covered in BISC 120) and some knowledge of DNA replication and meiosis (at the level of BISC 220) will also be useful, but these courses are not required.

Some of the material in this course is covered in BISC 313. This course is intended primarily for QBIO majors, and as such it places a heavier emphasis on math and computation and a lighter emphasis on biological mechanisms and processes.

Grading Policy

Your final grade will be calculated on the basis of a weighted average, with the weights:

40% Homework

5% Participation

20% Exam 1

20% Exam 2

15% Final Project (including write-up)

Homework

Doing the homework will be your most important method for learning the material. Homework assignments will be graded on the following scale:

0: missing, more than 24 hours late, or less than 50% complete.

1: mediocre or poor effort, late by less than 24 hours, or incomplete.

2: Good effort, though some answers may be wrong.

3 (Bonus): Exceptional. Your TA is weeping with ecstasy.

All “2”s would give you a perfect homework score. Scores of “3” will not happen often and are considered bonus. If your score is somewhere between a “1” and a “2,” your TA may give you the option to turn in a corrected version of your homework to earn a “2.” The TA may also assign fractional scores (e.g., 1.5) if they choose.

You are encouraged to work collaboratively on the homework, but please write your own solutions. We will drop your lowest homework score.

Participation

Participation grades are mainly a function of attendance and in-class participation in both lecture and section. We may ask you to turn in the results of short in-class or in-section activities as components of your participation grade.

Software

We will use R, a programming language designed for statistical computing. R is available free online from the R Project website, <https://www.r-project.org/>. We recommend you also use RStudio, and interactive development environment designed for use with R. RStudio is also free. (Download the open source version of RStudio Desktop from <https://www.rstudio.com/products/rstudio>.) RStudio requires an active R installation.

Contacting the instructors

For administrative questions that apply to everyone or any questions about course content, please post to slack or the forum on blackboard, ask your TA, or come to office hours. Please email the instructors directly for questions relating to class administration issues that apply to you specifically (e.g. disability-related accommodations, scheduling an appointment, etc.). We will do our best to reply to all emails within 48 hours, but there is no guarantee we will be able to do so earlier than that. Please include the course name or number in the subject line of any emails you send the instructors.

Course Schedule (Subject to change)

Unit I: Course introduction and review

Week 1

8/26 (Edge) Course policies and introduction

8/28 (Edge) Review of basic genetics (information content in the genome, genetic code, central dogma, mitosis/meiosis)

Reading: Coop notes, ch. 1

Week 2

9/2 (Edge) Probability review (independence, conditional probability, Bayes’ theorem, expectation, variance, covariance, commonly used distribution families)

Reading: Coop notes, appendix A

9/4 (Edge) Genotypes and allele frequencies (Hardy-Weinberg, descriptions of variation, inbreeding and homozygosity)

Reading: Coop notes, ch. 2

Unit 2: Evolutionary genetics models

Week 3

9/9 (Edge) Correlations among loci, or “linkage disequilibrium” (D , D' , and r^2 , recombination and decay of LD, haplotype structure)

Reading: Coop notes, section 3.0.5

Reading: Coop notes, ch. 2

9/11 (Edge) Genetic drift I (The Wright-Fisher process, loss of diversity, θ and N_e)

Reading: Coop notes ch 4, through the end of section 4.1

Week 4

9/16 (Edge) Genetic drift II (The coalescent: time to coalescence, fixation probability, heterozygosity, SFS)

Reading: Coop notes section 4.2 until end of ch 4

9/18 (Edge) Natural Selection I (Analyzing a deterministic model of selection)

Reading: Coop notes, Ch 10 through the end of 10.1, first 3 pages of ch 11 (i.e. intro and 11.0.1)

Week 5

9/23 (Edge) Natural Selection II (The W-F diffusion: selection and drift)

Reading: Coop notes, Ch 12

9/25 (Edge) Quantitative Genetics I: Resemblance among relatives and heritability

Reading: Coop notes, ch. 7

Week 6

9/30 (Edge) Gene mapping and GWAS (Linkage studies and GWAS, LD as “tagging” causal variants, genome-wide significance)

Reading: Grady, D. (2020) Haunted by a gene. *New York Times*, March 10, 2020

<https://www.nytimes.com/2020/03/10/health/huntingtons-disease-wexler.html>

10/2 (Edge) What causes a genotype-phenotype association? (Direct and indirect effects, stratification, assortment) + Downstream GWAS analyses

Reading: Young, A. I., Benonisdottir, S., Przeworski, M., & Kong, A. (2019). Deconstructing the sources of genotype-phenotype associations in humans. *Science*, 365(6460), 1396-1400.

Week 7

10/7 (Edge) Statistical Genetics Cont.

10/9 Fall recess, no class

Unit III: Human variation and detecting selection

Week 8

10/14 (Edge) **Exam 1**

10/16 (Mooney) Human genetic variation and relatedness

Reading: Biddanda, A., Rice, D. P., & Novembre, J. (2020). Geographic patterns of human allele frequency variation: a variant-centric perspective. *eLife*.

Week 9

10/21 (Mooney) Models and summaries of population structure (F_{ST} and the Wahlund principle, split and migration models, models of admixture)

Reading: Coop notes, chapter 3 (up to 3.0.1)

10/23 (Mooney) Methods for studying structure and admixture (STRUCTURE, PCA, etc.) and in-class data analysis

Reading: Coop notes, 3.0.2-3.0.4.

Week 10

10/28 (Mooney) Natural Selection III (purifying selection, positive selection, heterozygote advantage, linked selection, balancing selection, background selection)

Reading: none

10/30 (Mooney) Natural Selection IV (Detecting selection and genetic variation: the neutral theory, Tajima's D, SFS, k_A/k_S and the MK test)

Reading: Coop notes, Ch 13 up to 13.1.2 (background selection)

Week 11

11/4 (Mooney) Data analysis for final project, converting allele counts to metrics (in-class)

11/6 Guest Lecture: Dr. Maria Akopyan

Week 12

11/11 No class: Veteran's Day

11/13 Guest Lecture: Almost (Dr.) Dandan Peng

Unit IV: Applying Population and Evolutionary Genetics**Week 13**

11/18 Exam Review

11/20 **Exam II (In-class)**

Week 14

11/25 (Mooney) Putting it all Together: A Brief History of Genetics and the Future

11/27 Thanksgiving, no class

Week 15

12/2 (Mooney) In-class applied population genetics

12/4 (Mooney) In-class applied population genetics and course wrap-up

Finals Week

12/16 project write-up due 1:00pm

Table of important dates

Date	Item
8-Sep	Problem set 1 (probability review) due 11:59 pm
15-Sep	Problem set 2 (HWE and LD) due 11:59pm
22-Sep	Problem set 3 (genetic drift) due 11:59pm
29-Sep	Problem set 4 (natural selection) due 11:59pm
6-Oct	Problem set 5 (quantitative genetics)
9-Oct	Fall recess
14-Oct	Exam 1
3-Nov	Problem set 6 (population structure) due 11:59pm
17-Nov	Problem set 7 (detecting natural selection) due 11:59pm
20-Nov	Exam 2
27-Nov	Thanksgiving break
16-Dec	Final project write-up due 1:00pm

Academic Integrity

The University of Southern California is foremost a learning community committed to fostering successful scholars and researchers dedicated to the pursuit of knowledge and the transmission of ideas. Academic misconduct is in contrast to the university's mission to educate students through a broad array of first-rank academic, professional, and extracurricular programs and includes any act of dishonesty in the submission of academic work (either in draft or final form).

This course will follow the expectations for academic integrity as stated in the [USC Student Handbook](#). All students are expected to submit assignments that are original work and prepared specifically for the course/section in this academic term. You may not submit work written by others or "recycle" work prepared for other courses without obtaining written permission from the instructor(s). Students suspected of engaging in academic misconduct will be reported to the Office of Academic Integrity.

Other violations of academic misconduct include, but are not limited to, cheating, plagiarism, fabrication (e.g., falsifying data), knowingly assisting others in acts of academic dishonesty, and any act that gains or is intended to gain an unfair academic advantage.

Academic dishonesty has a far-reaching impact and is considered a serious offense against the university. Violations will result in a grade penalty, such as a failing grade on the assignment or in the course, and disciplinary action from the university itself, such as suspension or even expulsion.

For more information about academic integrity see the [student handbook](#) or the [Office of Academic Integrity's website](#), and university policies on [Research and Scholarship Misconduct](#).

Please ask your instructor if you are unsure what constitutes unauthorized assistance on an exam or assignment or what information requires citation and/or attribution.

Statement on University Academic and Support Systems

Students and Disability Accommodations:

USC welcomes students with disabilities into all of the University's educational programs. [The Office of Student Accessibility Services](#) (OSAS) is responsible for the determination of appropriate accommodations for students who encounter disability-related barriers. Once a student has completed the OSAS process (registration, initial appointment, and submitted documentation) and accommodations are determined to be reasonable and appropriate, a Letter of Accommodation (LOA) will be available to generate for each course. The LOA must be given to each course instructor by the student and followed up with a discussion. This should be done as early in the semester as possible as accommodations are not retroactive. More information can be found at osas.usc.edu. You may contact OSAS at (213) 740-0776 or via email at osasfrontdesk@usc.edu.

Student Financial Aid and Satisfactory Academic Progress:

To be eligible for certain kinds of financial aid, students are required to maintain Satisfactory Academic Progress (SAP) toward their degree objectives. Visit the [Financial Aid Office webpage](#) for [undergraduate-](#) and [graduate-level](#) SAP eligibility requirements and the appeals process.

Support Systems:

[Counseling and Mental Health](#) - (213) 740-9355 – 24/7 on call

Free and confidential mental health treatment for students, including short-term psychotherapy, group counseling, stress fitness workshops, and crisis intervention.

[988 Suicide and Crisis Lifeline](#) - 988 for both calls and text messages – 24/7 on call

The 988 Suicide and Crisis Lifeline (formerly known as the National Suicide Prevention Lifeline) provides free and confidential emotional support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week, across the United States. The Lifeline consists of a national network of over 200 local crisis centers, combining custom local care and resources with national standards and best practices. The new, shorter phone number makes it easier for people to remember and access mental health crisis services (though the previous 1 (800) 273-8255 number will continue to function indefinitely) and represents a continued commitment to those in crisis.

[Relationship and Sexual Violence Prevention Services \(RSVP\)](#) - (213) 740-9355(WELL) – 24/7 on call

Free and confidential therapy services, workshops, and training for situations related to gender- and power-based harm (including sexual assault, intimate partner violence, and stalking).

[Office for Equity, Equal Opportunity, and Title IX \(EEO-TIX\)](#) - (213) 740-5086

Information about how to get help or help someone affected by harassment or discrimination, rights of protected classes, reporting options, and additional resources for students, faculty, staff, visitors, and applicants.

[Reporting Incidents of Bias or Harassment](#) - (213) 740-2500

Avenue to report incidents of bias, hate crimes, and microaggressions to the Office for Equity, Equal Opportunity, and Title for appropriate investigation, supportive measures, and response.

[The Office of Student Accessibility Services \(OSAS\)](#) - (213) 740-0776

OSAS ensures equal access for students with disabilities through providing academic accommodations and auxiliary aids in accordance with federal laws and university policy.

[USC Campus Support and Intervention](#) - (213) 740-0411

Assists students and families in resolving complex personal, financial, and academic issues adversely affecting their success as a student.

[Diversity, Equity and Inclusion](#) - (213) 740-2101

Information on events, programs and training, the Provost's Diversity and Inclusion Council, Diversity Liaisons for each academic school, chronology, participation, and various resources for students.

[USC Emergency](#) - UPC: (213) 740-4321, HSC: (323) 442-1000 – 24/7 on call

Emergency assistance and avenue to report a crime. Latest updates regarding safety, including ways in which instruction will be continued if an officially declared emergency makes travel to campus infeasible.

[USC Department of Public Safety](#) - UPC: (213) 740-6000, HSC: (323) 442-1200 – 24/7 on call

Non-emergency assistance or information.

[Office of the Ombuds](#) - (213) 821-9556 (UPC) / (323-442-0382 (HSC)

A safe and confidential place to share your USC-related issues with a University Ombuds who will work with you to explore options or paths to manage your concern.

[Occupational Therapy Faculty Practice](#) - (323) 442-2850 or otfp@med.usc.edu

Confidential Lifestyle Redesign services for USC students to support health promoting habits and routines that enhance quality of life and academic performance.