

University of Wisconsin-Madison
2023 Spring
BMI 826 – Statistics in Human Genetics

1. Basic Information

Time and Location

Tue/Thu 1:00 – 2:15pm

Instructor

Qiongshi Lu

Email: glu@biostat.wisc.edu

Office Hour: TBD

Teaching Assistant

Jiacheng Miao

Email: jmiao24@wisc.edu

Office Hour: TBD

Textbook

Laird, N. M. and Lange, C. *The Fundamentals of Modern Statistical Genetics*.

Laird and Lange will be useful for the first 3 weeks. Lectures in later modules will focus on frontier research topics. Reading materials (mostly research articles) will be assigned for each lecture.

2. Course Description

This 3-credit course provides a comprehensive survey of statistical methods in human genetics research. Topics include linkage analysis, genome-wide association study, rare variant association analysis, meta-analysis, genome and variant annotation, heritability estimation, multi-trait modeling techniques, multi-omic data integration, and genetic risk prediction. Lectures will cover a variety of state-of-the-art methods and will discuss both the biological motivation and the statistical justification of these methods. Students will also learn to apply these methods to real genetic data through homework assignments and final project.

This course is primarily designed for students who are pursuing degrees in statistics and biomedical data sciences. Undergraduate students who are interested in inter-disciplinary topics of statistics and genetics are also encouraged to take the course.

Prerequisites: Stat 309-310 or equivalent. Prior knowledge of genetics is not required. Ability to carry out analyses using R is assumed.

3. Grading

Homework Assignments (60%)

A 0.7x penalty will be applied to late submissions. Submissions will not be graded after 48 hours past due.

Final Project (30%)

The final exam will be in the form of a project presentation (~10 min) in the last week of the semester (10%) and a written report (20%). The written report should include a short abstract (<150 words), main texts (<1,500 words), at least one table and one figure, and references.

Attendance and Participation (10%)

Students are expected to attend all lectures and finish the reading materials.

4. Lectures

Module 1. Basic concepts in human genetics

- Lecture 1 Review of molecular genetics, Mendel's Laws, and genetic models for disease
- Lecture 2 Mendelian inheritance and gene mapping

Module 2. Fantastic associations and where to find them

- Lecture 3 Linkage and association
- Lecture 4 The basics of genetic association analysis
- Lecture 5 Population stratification
- Lecture 6 Meta-analysis

Module 3. Beyond GWAS

- Lecture 7 Genetic risk prediction I – basic methods
- Lecture 8 Functional annotation I – coding variants
- Lecture 9 SNP-set association tests
- Lecture 10 Analysis of ultra-rare and *de novo* variants
- Lecture 11 Functional annotation II – noncoding variants
- Lecture 12 eQTL and transcriptome-wide association study
- Lecture 13 GxG interaction

Module 4. What we talk about when we talk about genetic architecture

- Lecture 14 Heritability I – statistical concept and study design
- Lecture 15 Heritability II – partitioning heritability by functional annotation
- Lecture 16 Multi-trait modeling I – genetic correlation
- Lecture 17 Multi-trait modeling II – local genetic correlation
- Lecture 18 Multi-trait modeling III – advanced topics
- Lecture 19 Omnigenicity is the new black
- Lecture 20 GxE interaction
- Lecture 21 Genetic basis of educational attainment

Module 5. Mirror, mirror on the wall, who's the "smartest" of them all

- Lecture 22 Genetic risk prediction II – advanced methods
- Lecture 23 Genetic risk prediction III – model evaluation and fine-tuning
- Lecture 24 Genetic risk prediction IV – portability
- Lecture 25 Nature of nurture I – empirical evidence and implications
- Lecture 26 Nature of nurture II – estimating indirect genetic effects

Module 6. Final project presentation

- Lecture 27 Student presentation I
- Lecture 28 Student presentation II