

ACMS Statistics Seminar



Jaihee Choi
Marquette University
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154 Hurley Hall
3:30 PM – 4:30 PM

High-Dimensional Inference for Genetic Association with Interval-Censored Data

Modern genetic repositories such as the UK Biobank provide massive amounts of data, including genotypes and tens of thousands of outcomes collected across hundreds of thousands of subjects. This information holds great promise for identifying genetic variants that perturb the risks of varied complex diseases. However, a major challenge is that such databases commonly record data in interval-censored form. That is, the event time of an outcome is not observed exactly but is only known to fall within a certain interval. There is a pronounced lack of tools for genetic association analysis that can be applied to interval-censored outcomes, as large-scale genetic studies have historically been conducted on binary and continuous outcomes. In this work, we develop a test to associate sets of genetic variants with multiple correlated interval-censored outcomes. This test leverages the pleiotropic nature of variants and the additional information provided by multiple outcomes to increase power for detecting weak genetic effects. Using a variance components framework, we construct two robust tests—one optimized for homogeneous genetic effects and another for heterogeneous genetic effects—and combine them into an omnibus test that adapts to both scenarios. Having established a powerful framework for testing the joint effects of multiple variants, we next focus on the question of pinpointing which individual variants are truly driving the association signal. Specifically, we employ Bayesian variable selection for interval-censored outcomes to fine-map variants within a risk locus. We discuss two prior specifications aimed at inducing sparsity, explain the consequences of major modeling decisions, and highlight the interpretability of the results. Additionally, we discuss extensions, such as incorporating functional annotation information as prior weights into the fine mapping framework.

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