MICHIGAN STATE UNIVERSITY
Department of Statistics and Probability

COLLOQUIUM

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A Unified Framework for Variance Component Estimation with Summary Statistics in Genetic Association Studies

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10:20 a.m. - 11:10 am
Refreshments 10:00 am
C405 Wells Hall

Abstract

Linear mixed model (LMM) is among the most commonly used tools for genetic association studies. However, the standard method for estimating variance components in LMMs -- the restricted maximum likelihood estimation method (REML) -- suffers from several important drawbacks. Specifically, REML is computationally slow, requires individual-level genotypes and phenotypes, and produces biased estimates in case control studies. To remedy these drawbacks, we present an alternative framework, which we refer to as MQS, for variance component estimation in LMMs. Our method is based on the method of moments (MoM) and the minimal norm quadratic unbiased estimation (MINQUE) criteria, and brings two seemly unrelated methods -- the renowned Haseman-Elston (HE) regression and the recent LD score regression (LDSC) -- into the same, unified framework. With the new framework, we provide an alternative but mathematically equivalent form of HE that allows for the use of summary statistics and is faster to compute. We also provide an exact estimation form of LDSC to yield both unbiased estimates and calibrated confidence intervals. A key feature of our method is that it can effectively use only a small random subset of individuals for computation while still produce estimates that are almost as accurate as if the full data were used. As a result, our method produces unbiased and accurate estimates with calibrated standard errors, while is computationally efficient for large data sets. Using simulations and applications to 33 phenotypes from 7 real data sets, we illustrate the benefits of our method for estimating and partitioning chip heritability. Our method is implemented in the GEMMA software package, freely available at www.xzlab.org/software.html.

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