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“Assessment of Fast-ADELLE, an efficient global testing method, with application to gene-level association analysis”

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Abstract

Large-scale hypothesis testing is an ongoing topic in statistical genetics. Many applications require testing whether a set of related hypotheses contains any signal, such as assessing whether a set of variants within a gene is associated with a phenotype. These are challenging because the individual effects are often relatively weak and the test statistics are correlated.

Fast-ADELLE is a new general global testing tool that is based on summary statistics and accommodates dependent data. The method is based on the ADELLE and ELL framework and introduces an approximation based on the Ord distribution to increase power. This approximation allows fast-ADELLE to scale to large studies while preserving the statistical properties that make ADELLE effective for detecting sparse and weak signals. We evaluate the performance of fast-ADELLE through simulation studies and SCZ gene-level association analysis. The results show that fast-ADELLE achieves high power in settings where signals are sparse and correlations are non-negligible. Overall, it is an efficient and powerful approach for global testing in large-scale inference problems with dependence.