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A Summary-Statistics-based Random Effect Model (SSREM) to estimate heritability and co-heritability in GWAS data analysis

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In the presence of individual-level data, Linear Mixed Model (LMM) is a commonly used powerful tool to conduct variance component analysis in Genome-Wide Association Studies (GWAS). Over the past few years, the methods to analyze summary statistics from GWAS become popular as (1) it is very difficult to fully access individual-level data, (2) the sample sizes are usually very large in meta-analysis across different studies, and (3) 1000 Genome Project data provides additional information to delineate linkage Disequilibrium (LD) over distinct populations. To maintain the estimation accuracy and efficiency of LMM, we proposed a unified approach, SSREM (Summary Statistics-based Random Effect Model), to explore genetic architecture of complex phenotypes using summary statistics, including both characterization of the overall genetic contribution to a phenotype (heritability estimation) and quantification of co-heritability, i.e. the genetic correlation between two phenotypes. The proposed method is based on the approximated likelihood of summary statistics uses samples from 1,000 genome project as the reference panel and implements an efficient parallel Gibbs sampling algorithm to ensure computational scalability for genome-wide data analysis. Results from empirical studies including both simulations and real data analysis (seven phenotypes from WTCCC and 25 more complex phenotypes) suggest that SSREM can be nearly as efficient as LMM that require the individual-level data and thus it outperforms other methods to estimate heritability and co-heritability using summary statistics. Majority of the findings are from real data analysis which is consistent with the results from previous studies.

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