

Genome-wide data-driven weighted association testing boosted by founder information

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Abstract:

For pedigree-based genome-wide association studies, we propose a data-driven weighting scheme accommodating general pedigrees. The scheme remarkably outperforms optimal top R and optimal exponential weighting approaches in that it integrates their strong advantages with data-driven weighting and uses all available genotypic and phenotypic information. The association information conveyed by the children is partitioned into between- and within-pedigree components. In the screening stage, an accurate relative ranking of all markers is created using both the between-pedigree component and the founder information. In the testing stage, all the markers are group-wise tested using the weighted within-pedigree component which is scaled by the marker ranking from the screening stage. This scheme controls the family-wise error rate at the desired level regardless of linkage disequilibrium structure and population stratification and is robust in terms of power to population stratification up to a reasonable level.