

“Adjustment of Local Ancestry in Association Analysis of Admixed Populations”

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Abstract:

Admixed populations offer a unique opportunity *for* mapping complex human diseases that have large disease allele frequency differences between ancestral populations. However, association analysis in such populations is challenging because unrecognized population stratification may lead to spurious association. This problem can be exacerbated in genome-wide association studies, which typically involve large numbers of subjects.

Here we develop a novel association test that adjusts for local ancestry difference between study subjects. Our method is based on a retrospective likelihood framework which models the conditional distribution of a test SNP given disease status of a study subject and genotypes of ancestry informative markers surrounding the test SNP. This retrospective likelihood allows us to explicitly model local ancestry difference between study subjects and thus eliminates the effect of population stratification at the test SNP. To evaluate the performance of our method, we conducted extensive simulations under various settings. Our results indicate that regardless of the mechanism of population stratification -- either due local or global ancestry difference, the type I errors of our method are always under control; however, global adjustment procedures such as EIGENSTRAT may fail to control for type I errors when population stratification is due to local ancestry difference. With the proposed likelihood framework, we can easily extend our method to the analysis of family data and quantitative traits. We believe that this novel method will provide a useful tool for association analysis in admixed populations.