Efficient Multi-Marker Tests for Association in Case-Control Studies

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Abstract

As case-control studies employ increasingly dense panels of genetic markers, the linkage disequilibrium (LD) between nearby markers can induce correlation between statistics that test for genotype/phenotype association. By taking advantage of this correlation structure, a more powerful test than an individual marker test or a standard Bonferroni adjustment to the minimum P-value is possible. To address this opportunity, we present and evaluate methods for forming a region-based test statistic, either through an optimal linear combination of score test z-statistics or by appropriate adjustment of the maximum of the z-statistics (minimum of P-values) over a genetic region of interest. We present results illustrating the performance of these methods under different LD structures and minor allele frequency distributions.

Keywords: Association tests; Linkage disequilibrium; Combining z-scores.

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