

Multipoint linkage disequilibrium mapping for multiple causative loci of complex disease

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Abstract

The genetic basis of complex diseases is often involved multiple linked causative loci. Consequently, it is likely to induce bias and lose efficiency in disease locus estimation if assuming one disease locus in linkage disequilibrium mapping. In the present study, we proposed a semi-parametric multipoint association mapping approach aiming to localize positions of multiple causal variants simultaneously. However, the estimating procedure may easily fail to converge because of the multiplicably increasing number of parameters coming along with the number of disease loci. To circumvent this problem, we proposed to estimate the main and gene-gene interaction effects at the disease loci through an interpolation approach separately, then plug them into the generalized estimating equation to obtain the disease loci estimates. This procedure was conducted iteratively until it converged. The proposed method provided us with the estimates and their confidence intervals for the disease loci, genetic effects of the disease loci, and interactions between these loci. Simulations and the data examples suggested the developed method performed well in terms of bias and coverage probability regardless of the underlying numbers of disease loci.