

Mixed Analysis for Genomewide Association Studies

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Abstract

Genomewide association studies are being conducted to unravel the genetic etiology of complex human diseases, in which complex epistasis may play an important role. Joint two-stage designs are efficient and powerful for genome-wide association studies. However, it can not detect the loci with complex epistasis. Thus, I address the following question: given the plausibility of interactions between genetic loci, how might we design and analyze genome-wide association studies more efficiently?

In order both to be cost-effective for genotyping and be possible to detect interacting loci across the genome with high power, I will demonstrate that a mixed two-stage analysis for genome-wide association studies always results in increased power to detect genetic association between interaction loci and the disease, despite the need to use more stringent significance levels. Further, I explore how the power of mixed analysis are affected by important genetic parameters such as mode of disease inheritance, age of trait causing mutation, frequency of associated allele and the other factors such as the proportion of markers identified for follow-up genotyping in stage 2 and the proportion of samples used in stage 1. In addition, we know that the genotyping cost of mixed analysis is less than that of the one-stage analysis/the simultaneous method.