A Graph Synchronization Model for Identifying SNP Interactions in Disease Association Studies

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Abstract. In disease association studies, identifying the interactions among single nucleotide polymorphisms (SNPs) increasingly attracts more and more interest, as SNP interactions are considered to affect for many complex diseases. In this research, we focus on detecting the interactions among multiple SNPs. Although there are several existing approaches and models, there is little consensus on optimally selecting the causal SNPs. Most of previous methods are either based on the Monte Carlo framework that have difficulties to find exact solutions, or has low statistical power caused by many factors. In our paper, we propose a graph synchronization model based on SNP-SNP interaction graph, in which each node denotes a SNP and edges build from the results of Chi-square tests of each pair of SNPs. The whole graph is used to describe the coupled relationships among the interacting SNPs by topology and edge weights. Then we introduce two kinds of probabilities as the observations of the graph and the internal state vector of all the SNPs, separately. The first one measures the posterior probability of a SNP allele when the SNP is estimated as the causal one, while the second one denotes the likelihood of a SNP associated with the phenotype. When train this graph by each haplotype data, these probabilities are modified itself and other coupled SNPs. A synchronization detection algorithm is designed to divide a sub-graph from the whole one, which consists of those candidate causal SNPs that satisfies the synchronization conditions. Finally, we show the applications of the proposed method on simulated datasets.

Keywords: Disease association studies, SNP interactions, Graph synchronization