GENETIC ASSOCIATION IN CASE-CONTROL STUDIES - A LATENT VARIABLE METHOD

T. Wang[†1], H.J. Jacob[1], Z.B. Zeng[2]

[1] *Medical College of Wisconsin, Milwaukee, USA*
[2] *North Carolina State University, Raleigh, USA*

[†] E-mail: *taowang@mcw.edu*

There is a growing utilization of high-resolution polymorphic genetic markers such as single nucleotide polymorphisms (SNPs) in characterization of sequence variants in candidate regions harboring disease genes. A comprehensive test for association between a set of genetic markers and a disease phenotype requires a series of tests for marker alleles, genotypes, haplotypes or sub-haplotypes that often leads to severe multiple testing problems. In this study, we present a latent variable method for genetic association analysis in population-based case-control studies. By treating coding variables for disease susceptible genes as latent variables, we establish a logistic regression model for disease phenotype with missing data on genotypes of the disease genes. Under a general likelihood framework, we develop an EM-based algorithm to estimate genetic effects of disease mutant and haplotype frequencies of the disease gene and markers jointly. This latent variable method has flexibility to characterize either a mutant allele at a putative trait locus or a potential risk haplotype or sub-haplotype of the markers. Maximum likelihood estimates of association measures between the disease mutant and marker alleles provide helpful information for inferring positions of the disease genes. The likelihood ratio statistic also provides a joint test for association between marker genotypes and the disease phenotype without requiring an adjustment for the multiple testing.