

A Latent Variable Model of Segregation Analysis for Ordinal Traits

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Abstract:

Many health conditions including cancer and psychiatric disorders are believed to have a complex genetic basis, and genes and environmental factors are likely to interact one another in the presence and severity of these conditions. Assessing familial aggregation and inheritability of disease is a classic topic of genetic epidemiology, which is commonly referred to as segregation analysis. While it is routine now to conduct such analyses for quantitative and dichotomous traits, there do not exist methods and software that accommodate ordinal traits. To this end, we propose a latent variable model by extending the work of Zhang and Merikangas (2000) who examined binary traits. The advantage of this latent variable model lies in its flexibility to include environmental factors (usually represented by covariates) and its potential to allow gene-environment interactions. The model building employs the EM algorithm for maximization and a peeling algorithm for computational efficiency. Asymptotic theory is provided for statistical inference and simulation studies are conducted to confirm that the asymptotic theory is adequate in practical applications. We also apply our model to examine the familial transmission of alcoholism, which is categorized into three ordinal levels: normal control, alcohol abuse, and alcohol dependence. Not only does our analysis confirm that alcoholism is familial, but also it suggests that the transmission may have a major gene component, which was not revealed by previous analyses using dichotomous traits. This is based on a joint work with Heping Zhang and Rui Feng.