Biometrics-2013
OMICS Group Conferences
Accelerating Scientific Discovery
2nd International Conference and Exhibition on
Biometrics & Biostatistics
June 10-12, 2013 Hilton Chicago/Northbrook, USA

Modeling the onset of a longitudinal data with association to genetic information using a mixture model

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Abstract

Exploring the influence of genetic or environmental factors in longitudinal data has been challenging genetic studies. While some researchers have modeled sequenced data with a few data points as repeated measurements in which covariance is incorporated with certain time series structures, to date, not much research has been done to address the issue of how genetic factors or environmental factors affect the underlying behavior of the data with multiple measurements. In this study, we aim to build a statistical framework to model the anticipated association between the development of a disease and hypothesized genetic or environmental factors.

The longitudinal phenotype data we modeled consists of three parts – the incubation period, the onset, and the disease appearing period. Assuming the disease onset is missing, we propose a mixture model to model the longitudinal phenotype such as blood pressure with association to the genotype or environmental factors. An EM based approach is used to estimate the distribution of the onset, which might be related to either genotype or environmental factors. To estimate the onset distribution, a solution for a weighed logistic regression under which weights on the outcome variables are proposed. A log likelihood ratio test is used to judge the significance of the association between the distribution of the onset and the genotype or environmental factors. We conducted extensive simulation studies to evaluate the model performance and gave desirable Type I error rates and the power of the proposed test.