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Quantitative Trait Linkage Analysis
in the Presence of Temporal Trends in Genetic Effects

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Abstract: Linkage analysis has been one of the most widely used methods for identifying regions of the human genome which contain genes responsible for human diseases. Evidence suggests that the effects of some of the trait-causing genes may vary with the age of an individual, giving rise to temporal trends in genetic effects. Linkage analysis routinely tends to ignore such gene-by-age interactions. While linkage analysis methods have been proposed for analysis of longitudinal family data for exploring temporal trends, there are no models to characterize such trends nor methods for analysis of cross-sectional family data. We extend variance component linkage analysis methodology by modeling the variance components due to the quantitative trait locus (QTL) and that due to the polygenic effect to be age-dependent. With this model, we investigate the power of linkage analysis in the presence of temporal trends. We show that modeling true temporal trends in QTL effects can substantially increase the power of linkage analysis even when the average locus-specific heritabilities (when trends are ignored) are quite low, thereby demonstrating that, ignoring the gene-by-age interactions, when present, could jeopardize gene discovery.

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Short Bio: Gang Shi received the B.E. degree in automatic control engineering in 1996 and the M.E. degree in pattern recognition and intelligence system in 1999, both from the Xi’an Jiaotong University, China. From 1999 to 2000, he worked as a teaching associate in the Xi’an Jiaotong University. In 2006, he received the D.Sc. degree in electrical engineering from Washington University in St. Louis under Dr. Arye Nehorai. He is now a postdoctoral researcher at the Biostatistics Division, Washington University School of Medicine.