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Genome Scans With Gene-Covariate Interaction

Abstract: Genetic models for gene-covariate interaction are described. Methods of linkage analysis that utilize special features of these models and the corresponding score statistics are derived. Their power is compared with that of simple genome scans that ignore these special feature, and substantial gains in power are observed when the gene-covariate interaction is strong. Quantitative trait mapping in randomly ascertained sibships and affected sibpair mapping are discussed. For the latter case, a simpler statistic is proposed that has similar performance to the score statistic, but does not require the estimation of nuisance parameters. Since the nuisance parameters are not estimable solely from affected sibpair data, this statistic would be much easier to apply in practice. Similarities with linkage analysis of models for longitudinal data and multivariate phenotypes are also briefly discussed. Approximations for the p-value and power are derived under the framework of local alternatives.