

A likelihood-based trait-model-free approach for linkage detection

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Abstract:

Trait-model-free methods provide a robust approach to linkage detection for complex traits using pedigree data. Affected related individuals have increased probability of sharing genes identical-by-descent (IBD) at trait loci and hence also at linked marker loci at which they therefore show increased similarity over that predicted under Mendelian segregation. Relatives of discordant phenotype have decreased probability of sharing genes IBD at trait loci and hence have decreased similarity at linked markers.

We have proposed a new likelihood-based approach that models the segregation of alleles at a location conditional on the affection status of individuals in a pedigree without making any assumption of the underlying trait model. The model can incorporate information on individuals of discordant phenotype. The asymptotic distribution of the likelihood-ratio statistic under the null hypothesis is derived and linkage can be inferred from the significance of the observed likelihood-ratio test statistic. For extended pedigrees, exact computation of the likelihood is infeasible. We have used a Markov chain Monte Carlo (MCMC) approximation of the likelihood. I will discuss different properties of the new model. The distribution of the likelihood-ratio statistic both in presence of complete and of incomplete IBD information in pedigrees will be discussed. The performance of the model in detecting linkage will be illustrated with different examples.

Joint with Elizabeth Thompson and Matthew Stephens.