

Extension of Haseman-Elston Regression Expression Studies

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Abstract:

The Haseman-Elston (HE) regression is simple robust model-free linkage analysis method. We have extended Haseman-Elston regression in following ways:

1. We modify the dependent variable of the revisited HE method that retains the simplicity and robustness properties, but increases its power. We demonstrate theoretically that the modification can be more powerful than the optimally weighted HE method when the sibship mean can be correctly specified. We then examine the properties of this modification by simulation when the sibship mean is replaced by its best linear unbiased predictor (BLUP). The simulation results indicate that this modification maintains good control over type I error and that the empirical power of this modification is similar to that of the optimally weighted Haseman-Elston method in most cases.
2. We propose a permutation procedure for HE regression, which can be applied to general pedigrees and non-random sampling. The basic idea of our procedure is that the grandmother and grandfather alleles in a parent are transmitted to a child with equal probability under the null hypothesis that there is no linkage between a susceptibility locus and a marker. Our procedure randomly permutes the transmission vectors and weights the obtained number of alleles identical by descent (IBD) matrix according to ambiguity of the transmission. This procedure can also be used any other IBD based model-free linkage analysis.
3. We also propose a two-level HE regression model in which linkage analysis and association analysis are unified into a single regression model: association and linkage are detected at the individual-level and the pedigree-level, respectively. This version of HE regression can make use of all the trait information in any general pedigree and simultaneously incorporate individual-level and pedigree-level covariates in a natural manner.