## STATISTICAL STRATEGIES FOR TESTING GENE-ENVIRONMENT INTERACTION IN ASSOCIATION ANALYSES

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In the context of testing for association of genetic polymorphisms with complex diseases when gene-environment interaction may be present, we propose to construct statistical tests allowing restricted forms of interaction between a known environmental risk factor e with two levels and tested polymorphisms. The principle is equally applicable to testing of polymorphisms individually and in haplotypes. We consider the following two approaches. First, we consider restricted interaction models where the genotype at the tested polymorphism affects the risk of disease in only one of the strata defined by e. The second approach consists in maximizing the likelihood over sub-families of interaction models indexed by one parameter. Simulations and resampling methods are used to generate the null distribution of the test statistics and derive correct critical values. The power of these proposed approaches is compared to the power of tests ignoring interaction, and to the power of tests for the genetic effects in saturated models, under case-control designs. Evaluation of the power in finite samples is accomplished by sampling individual phenotype, known risk factor status and genotype, and performing the tests described above. In simulations, we show that for some relative risk scenarios, the power of tests under both approaches previously described is modestly better than the power of tests ignoring interaction and the power of tests in saturated models, especially when the relative frequency of the environmental exposure is high.