

Family-based analysis of genome-wide gene \times gene interactions

Marit Ackermann^{1,*}, Andreas Beyer¹

1. Cellular Networks & Systems Biology, Biotechnology Center, TU Dresden

* Contact author: marit.ackermann@biotec.tu-dresden.de

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Complex diseases are caused by an interplay of several genetic alterations and environmental factors such as life style [1]. Recent advances in genomics and biotechnology have opened the gate to the genome-wide genotyping of thousands of possibly related individuals. Such data can now be used for studying epistatic genetic interactions at a genomic level.

While traditional family-based association or linkage studies are restricted to either a small number of markers or very specific pedigree structures, new methods for high-throughput data often disregard the inherent population structure leading to spurious findings of gene-gene interactions [2].

We propose an approach to infer genome-wide genetic interactions by using the genotype information of parent-child trios. Our method is applicable to very large data samples and a large number of markers. Instead of using the marginal frequencies of the observed alleles at two markers, we make use of inheritance patterns to infer the expected allele frequencies. Since the approach works conditional on ancestral genotype information it drastically reduces the number of false positive findings due to population effects. Moreover, we correct for the selection pressure against certain alleles that can also confound the results.

The approach is illustrated using a pedigree of almost 2300 mice that have been genotyped at more than 10,000 SNPs. Results of our analysis and their biological significance will be discussed.

References

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