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Correcting for pedigree structure improves the identification of differentially expressed genes in multiplex families

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Many complex diseases stem from the interaction of genetic, epigenetic and environmental factors. Integrating diverse datasets at the scale of the whole genome is a promising approach to understanding their aetiology. Multiplex families, in which several related individuals are affected by the same disease, provide a powerful opportunity for these investigations. However the relatedness of the individuals poses specific challenges to the analysis of data. Here we tackle the problem of identifying genes whose expression is altered by the disease while taking into account the pedigree structure of a multiplex family. Methods borrowed from evolutionary biology, originally developed to study the evolution of quantitative traits on phylogenetic trees, can be adapted to the study of multiplex families. Focusing on gene expression profiling, we adapt the Hansen model of quantitative trait evolution to the problem of identifying genes whose expression is altered by the disease. Using simulated data, we show that the model performs better than statistical tests which do not take into account the pedigree structure. Moreover, when we apply our method to a gene expression profiling dataset of a family with multiple members affected by multiple sclerosis, the method reveals the differential expression of additional genes relevant to the disease.

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