A structural mixed model to shrink covariance matrices for time-course differential gene expression studies

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Time-course microarray studies require a particular modelling of covariance matrices when measures are repeated on the same individuals. Taking into account the within-subject correlation in the test statistics for differential gene expression involves, however, a large number of parameters when a gene-specific approach is used, which often results in a lack of power due to the small number of individuals usually considered in microarray experiments. Shrinkage approaches can improve this detection power in differential gene expression studies by reducing the number of parameters, while offering a good flexibility and a small rate of false positives. The aim of this presentation is to propose several other F-type statistics for time-course microarray studies based on an extension of the structural mixed model presented by [1] to the multivariate case. We will focus on two main decompositions of the empirical gene-by-gene covariance matrices: eigenvalue/eigenvector and Cholesky decomposition. A structural mixed model will be used in three configurations to shrink i) the eigenvalues, ii) the innovation variances, iii) both the innovation variances and antedependence parameters. The F-statistics based on these shrunk covariance matrices were compared to a gene-by-gene analysis, an homogeneous covariance model and the modified Limma F-test both on simulated and real data sets. The proposed methods were found to perform well compared to other empirical Bayesian approaches, and outperformed the gene-specific or common-covariance methods in many cases. Computing the denominator degrees of freedom of these F-statistics under H0 still remains, however, an open question.

References

[1] Jaffrézic F, Marot G, Degrelle S, Hue I, Foulley J-L (2007) A structural mixed model for variances in differential gene expression studies. Genetical Research 89:19-25.