MULTIDIMENSIONAL LOCAL FALSE DISCOVERY RATE FOR MICROARRAY STUDIES

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Motivation: The false discovery rate (fdr) is a key tool for statistical assessment of differential expression (DE) in microarray studies. It is, however, well known that overall control of the fdr is not sufficient to address the problem of genes with small variance, which generally suffer from a disproportionally high rate of false positives. Graphical tools and modified test statistics have been proposed for dealing with this problem, but there is currently no procedure for controlling the fdr directly.

Methods: We generalize the local fdr as a function of multiple statistics, combining a common test statistic for assessing differential expression with standard error information. We use a nonparametric mixture model for DE and nonDE genes to describe the observed multidimensional statistic, and estimate the distribution for nonDE genes using the permutation method. We demonstrate this approach for both simulated and real microarray data.

Results: We find that the multidimensional local fdr allows an objective assessment of differential expression as a function of gene variability. We demonstrate that our fdr2d approach is more powerful than conventional fdr and that it eliminates the need for modified test statistics.

Availability: An R-package OCplus containing functions for computing fdr2d and other operating characteristics of microarray data is freely available at http://www.meb.ki.se/~yudpaw.