Normalization for cDNA Microarray Experiments Having Many Differentially Expressed Genes

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Abstract

This talk discusses two normalization methods for cDNA microarray data in which a substantial proportion of genes differ in expression between the two mRNA samples, or there is no symmetry in the expression levels of up/down-regulated genes. The first method concerns the situation that there are no control DNA sequences on the slide. The first step of this approach is to perform global normalization based on dye-swap experiments, and then use a statistical criterion to select a set of (almost) constantly expressed genes. Based on this set, intensity dependent normalization is carried out using local regression method. The usefulness of this method is clearly demonstrated in simulation studies and in the analysis of real data sets. In particular, it is shown in the simulation studies that this method identifies genes with a lower false positive rate and a lower false negative rate than a commonly used method, when a large number of genes are turned up or down. The second method concerns the situation that there are control sequences on the slide. Calibration curves relating fluorescence signal intensities to gene expressional levels are considered in the context of Bayesian isotonic regression, which makes use of smooth priors on Bernstein polynomials and Markov Chain Monte Carlo methods to study the isotonic regression problem. The second method is applied to identify early onset genes in the study of transcriptional profiling of Autographa Californica multiple polyhedrosis virus