

Reassessing Design and Analysis of Two Color Microarray Experiments Using Mixed Effects Models

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Abstract:

Gene expression microarray studies have led to interesting experimental design and statistical analysis challenges. The comparison of expression profiles across groups or populations (within experimental or observational settings) is one of the most common objectives of microarray experiments. In this presentation we will discuss some issues regarding design and statistical analysis for two color microarray platforms using mixed linear models, with special attention directed towards a distinction of the different hierarchical levels of replication and the consequent effect on the use of appropriate error terms for comparing experimental groups. We will review the traditional analysis of variance (ANOVA) models proposed for microarray data with their extensions to hierarchically replicated experiments. We will also suggest and compare linear mixed models suitable for the analysis of either log ratios or log intensity values, denoting the similarity between both approaches in the presence of multiple sources of variability. In addition, we discuss power and efficiency of different experimental designs within a hierarchical replication context. Our results show that increasing the number of biological samples is the only effective design strategy to improve the statistical power of a microarray experiment whereas increasing technical replication generally yields only marginal improvement in power.