Title:
**Microarrays, Empirical Bayes, and the Two-Groups Model**

Author(s):
**Bradley Efron**

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**Abstract:**

The classic frequentist theory of hypothesis testing developed by Neyman, Pearson, and Fisher has a claim to being the Twentieth Century's most influential piece of applied mathematics. Something new is happening in the Twenty-First Century: high throughput devices, such as microarrays, routinely require simultaneous hypothesis tests for thousands of individual cases, not at all what the classical theory had in mind. In these situations empirical Bayes information begins to force itself upon frequentists and Bayesians alike. The two-groups model is a simple Bayesian construction that facilitates empirical Bayes analysis. This article concerns the interplay of Bayesian and frequentist ideas in the two-groups setting, with particular attention focussed on Benjamini and Hochberg's False Discovery Rate method. Topics include the choice and meaning of the null hypothesis in large-scale testing situations, power considerations, the limitations of permutation methods, significance testing for groups of cases (such as pathways in microarray studies), correlation effects, multiple confidence intervals, and Bayesian competitors to the two-groups model.