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A nonparametric empirical Bayes framework for large-scale multiple testing

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We propose a flexible and identifiable version of the two-groups model, motivated by hierarchical Bayes considerations, that features an empirical null and a semiparametric mixture model for the non-null cases. We use a computationally efficient predictive recursion marginal likelihood procedure to estimate the model parameters, even the nonparametric mixing distribution. This leads to a nonparametric empirical Bayes testing procedure, which we call PRtest, based on thresholding the estimated local false discovery rates. Simulations and real-data examples demonstrate that, compared to existing approaches, PRtest's careful handling of the non-null density can give a much better fit in the tails of the mixture distribution which, in turn, can lead to more realistic conclusions.

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