Abstract: The conventional approach to two-sample multiple testing is to first reduce the data matrix to a single vector of test statistics such as p-values and then choose a cutoff along the rankings to adjust for multiplicity. However, this inference framework often leads to suboptimal multiple testing procedures due to the loss of information in the data reduction step.

We introduce a new framework for two-sample multiple testing by incorporating a carefully constructed auxiliary variable in inference to improve the power. A data-driven multiple testing procedure is developed by employing a covariate-assisted ranking and screening (CARS) approach that optimally combines the information from both the primary and auxiliary variables. This integrative framework is then extended to handle a range of dependence structures such as those arise in multiple testing for high-dimensional linear regression, differential correlation analysis, and differential networks.

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