

# adaptest: Data-Adaptive Statistics for High-Dimensional Testing in R

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## Summary

The `adaptest` R package contains an implementation of a methodology based on using *data-adaptive statistics* for estimating effect sizes, complete with appropriate inference, in high-dimensional settings while avoiding the inferential burdens of multiple testing corrections. To address the issue of multiple testing in situations where the dimensionality is high but sample size comparatively small (*e.g.*, analysis of RNA-seq data), we expose an implementation of a method for statistical inference on data-adaptive target parameters (Hubbard, Kherad-Pajouh, and van der Laan 2016) in the form of a software package for the R language and environment for statistical computing (R Core Team 2018).

Data-adaptive test statistics for multiple testing are motivated by efforts to address the limitations of existing multiple testing methods such as the popular Benjamini-Hochberg procedure to control the False Discovery Rate (FDR) (Benjamini and Hochberg 1995) or the Bonferroni method to control the Family-Wise Error Rate (FWER) (Dunn 1961). Such methods have been well studied in the literature on multiple testing, and it was been well establish that, for a fixed targeted effect size and fixed sample size, power decreases as the number of tests and corresponding critical values increase (Lazzeroni and Ray 2010). Further, Lazzeroni and Ray (2010) show that if the power for a single test is 80%, the power is approximately 50% for 10; 10% for 1000; and 1% for 100,000 Bonferroni-adjusted tests, a classic method to correct for Type-I error when facing multiple testing issues. This simple example demonstrates that data analysts and other practitioners must invest, at a prohibitively high rate, additional resources to collect samples in order to obtain meaningful results under high-dimensional multiple testing constraints.

Utilizing this recently developed data-adaptive statistical framework, information loss induced by standard multiple testing procedures can be avoided by reducing the dimensionality of problems via data-adaptive variable reduction. This recent methodological advance, a data-adaptive multiple testing technique (Cai, Hejazi,

and Hubbard, n.d.), is a natural extension of the data-adaptive target parameter framework introduced in Hubbard, Kherad-Pajouh, and van der Laan (2016) and Hubbard and van der Laan (2016), which present a new class of inference procedures that introduce more rigorous statistical inference into problems being increasingly addressed by clever yet *ad hoc* algorithms for data mining.

The approach of data-adaptive test statistics improves on current approaches to multiple testing by applying a set of estimation algorithms (specified by the user) across splits of a particular sample of data, allowing for parameters of interest to be discovered from the data. Such methods uncover associations that are stable across the full sample and restrict multiple testing to a smaller subset of covariates by allowing for variable importance to be measured via the data-adaptive procedure. Test statistics formulated in this framework are expected to both outperform pre-specified test statistics and provide improved power as well as Type I error control, all while simultaneously allowing for appropriate statistical inference to be performed.

We illustrate the use of data-adaptive test statistics for parameter discovery by considering a simulated data set with 100 observations in 1000 dimensions, with a “true” signal constrained to just 10 covariates/dimensions. By applying the approach discussed above, using cross-validation to rank features, we obtain a ranking of the most important covariates – that is, those dimensions most closely associated with the “true” signal. A ranking of features across folds of cross-validation is displayed below:

From the plot displayed above, it is clear to see that there is a rather sharp divide in the ranking of covariates associated with the “true” signal – that is, these are those covariates that consistently rank highly in the importance measure employed across the many rounds of cross-validation performed. The plot of p-values displayed below shows these same features with low p-values, with a clearly strong divide consistent with that displayed in the previous plot:

The **adapttest** R package provides utilities for performing the estimation and hypothesis testing procedures discussed above, and detailed in Cai, Hejazi, and Hubbard (n.d.), alongside utilities for easily producing data visualizations based on the results. The software introduces new classes and methods, based on R’s S4 class system, to facilitate its integration into the Bioconductor ecosystem (Huber et al. 2015), making it well-suited for applications in computational biology, where high-dimensional data structures very often arise. The R package includes documentation and detailed vignettes that will allow for both (bio)statisticians and computational biologists to easily make use of this new tool in such data analytic problem settings.

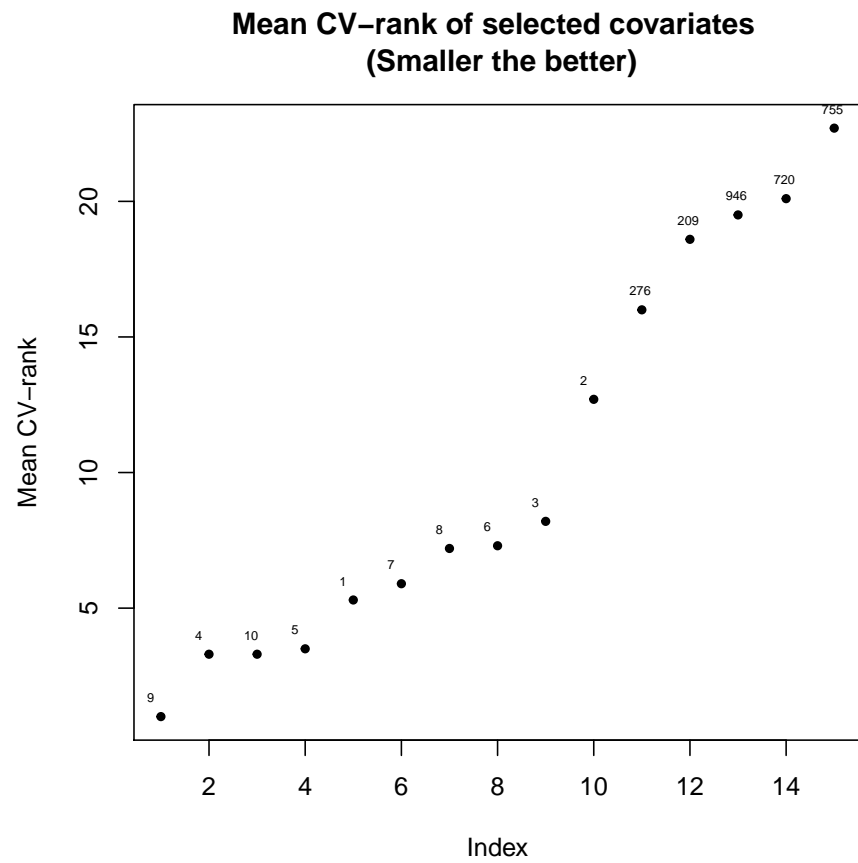


Figure 1: Average Rank of Top Covariates: here, the top ten covariates have CV-rank aligning linearly, indicating a stable ranking pattern.

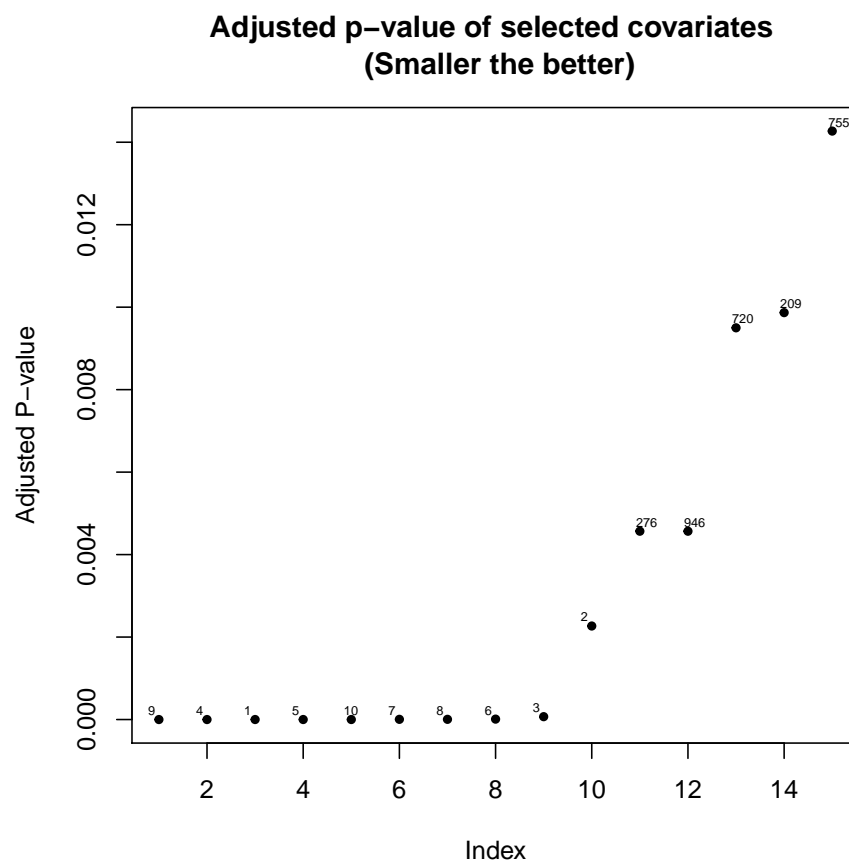


Figure 2: Adjusted P-values for the Reduced Set of Hypotheses

## References

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