# Differences to earlier versions of twilight

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#### 1 Changes in version 1.5.1 and 1.5.2

Minor cosmetic changes. The jump in version numbers is due to Bioconductor's version bumping regime for packages in the release and in the developmental repository.

## 2 Changes in version 1.2.3

We updated the bootstrapping procedure in twilight.getlambda to get a reliable value for the regularization parameter when  $\pi_0$  is small and many genes are truly differentially expressed.

### 3 Changes in version 1.2.2

Changes in the C code which do not effect the results.

### 4 Changes in version 1.2.1

Bug fixed on the calculation of Hamming distances.

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#### 5 Changes in version 1.2.0

We added the argument filtering = FALSE to function twilight.pval which (if set to TRUE) invokes the filtering for class label permutations that produce uniform p-value distributions. The set of admissible permutations is found using function twilight.filtering which is called internally in function twilight.pval. However, it can also be used directly.

We changed the local FDR estimation in function twilight slightly. Instead of estimating both densities  $f_0$  and f from the output of SEP, we rely on the uniform assumption such that  $f_0(p) = 1$  for all  $p \in [0, 1]$ . Hence, the 10 runs of SEP lead to 10 estimates  $\widehat{\pi_0}$ . The average of these is taken as the final value which is multiplied with the density estimate of the mixture density f.

The mixture density estimation of f also changed slightly. Still, the estimates are based on smoothed histogram counts. To improve the estimation for very small p-values, the histogram bins were changed from equidistant to quantile bins.

#### 6 Changes in version 1.1.0

The computation of p-values in twilight.pval changed from gene-wise to pooled p-values. For the computation of a gene-wise p-value for gene i, only the permutation scores of gene i are taken into account. For pooled p-values, all permutation scores of all genes are taken as null distribution. This change has several advantages: First, gene-wise p-values were not monotonically increasing with scores because each gene had its own null distribution. Thus, two genes with almost equal scores might get quite different p-values. Now, the null distribution is the same for all genes, that is the union set of all permutation scores. Second, pooled p-values are less granular than genewise p-values. Gene-wise p-values are computed from B permutation scores whereas pooled p-values are computed from B permutation scores.

These two important features gave rise to further changes: The ordering of the result table is now more intuitive because the most significant genes on top have the highest scores, the lowest p- and q-values and are candidates (if there are any). In addition, the default value of the number of permutations B is lowered to 1000 permutations. Computation of pooled p-values is slower than for gene-wise p-values. On the other hand, changing to pooled p-values increases the number of values in the null distribution by the factor of number of genes. Hence, even with less permutations, the number of null values is larger than before.

We integrated Pearson and Spearman correlation coefficients into twilight.pval.

Each gene is correlated to an numerical input vector. Expected scores are computed from random permutations of the input vector.

The result table contains an additional index column with genes indices which comes in handy for sorting back to original ordering.

All output matrices of the permutation functions twilight.combi, twilight.permute.pair and twilight.permute.unpair have the original labeling vector as first row. This is also the case if balanced permutations are wanted, although the input vector is not balanced. Hence, the permutation matrix within twilight.pval now includes the original labeling even for balanced permutations implying that the smallest possible p-value is 1/(number of permutations).

#### 7 Changes in version 1.0.3

A print.twilight function was added which produces a short information about the contents stored in the twilight object.

#### 8 Changes in version 1.0.2

The which argument of the plot command changed from plot1 style to more intuitive labels like scores or fdr.