

siggenes

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EBAM-class

Class EBAM

Description

This is a class representation for the Empirical Bayes Analysis of Microarrays (EBAM) proposed by Efron et al. (2001).

Objects from the Class

Objects can be created using the function `ebam`.

Slots

z: Object of class "numeric" representing the expression scores of the genes.

posterior: Object of class "numeric" representing the posterior probabilities of the genes.

p0: Object of class "numeric" specifying the prior probability that a gene is not differentially expressed.

local: Object of class "numeric" consisting of the local FDR estimates for the genes.

mat.fdr: Object of class "matrix" containing general statistics such as the number of differentially expressed genes and the estimated FDR for the specified values of `delta`.

a0: Object of class "numeric" specifying the used value of the fudge factor. If not computed, `a0` will be set to `numeric(0)`.

mat.samp: Object of class "matrix" containing the permuted group labels used in the estimation of the null distribution. Each row represents one permutation, each column one observation (pair). If no permutation procedure has been used, `mat.samp` will be set to `matrix(numeric(0))`.

vec.pos: Object of class "numeric" consisting of the number of positive permuted test scores that are absolutely larger than the test score of a particular gene for each gene. If not computed `vec.pos` is set to `numeric(0)`.

vec.neg: Object of class "numeric" consisting of the number of negative permuted test scores that are absolutely larger than the test score of a particular gene for each gene. If not computed `vec.neg` is set to `numeric(0)`.

msg: Object of class "character" containing information about, e.g., the type of analysis. `msg` is printed when the functions `print` and `summary` are called.

chip: Object of class "character" naming the microarray used in the analysis. If no information about the chip is available, `chip` will be set to "".

Methods

plot signature(object = "EBAM"): Generates a plot of the posterior probabilities of the genes for a specified value of Δ . For details, see `help.ebam(plot)`. For the arguments, see `args.ebam(plot)`.

print signature(object = "EBAM"): Prints general information such as the number of differentially expressed genes and the estimated FDR for several values of Δ . For details, see `help.ebam(print)`. Arguments can be listed by `args.ebam(print)`.

show signature(object = "EBAM"): Shows the output of an EBAM analysis.

summary signature(object = "EBAM"): Summarizes the results of an EBAM analysis for a specified value of Δ . For details, see `help.ebam(summary)`. For the arguments, see `args.ebam(summary)`.

Author(s)

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References

Efron, B., Tibshirani, R., Storey, J.D. and Tusher, V. (2001). Empirical Bayes Analysis of a Microarray Experiment, *JASA*, 96, 1151-1160.

Schwender, H., Krause, A. and Ickstadt, K. (2003). Comparison of the Empirical Bayes and the Significance Analysis of Microarrays. *Technical Report*, SFB 475, University of Dortmund, Germany.

See Also

[ebam](#), [find.a0](#), [FindA0-class](#)

Examples

```
## Not run:
# Load the data of Golub et al. (1999) contained in the package multtest.
data(golub)

# golub.cl contains the class labels.
golub.cl

# Perform an EBAM analysis for the two class unpaired case assuming
# unequal variances. Specify the fudge factor a0 by the suggested
# choice of find.a0
find.out <- find.a0(golub, golub.cl, rand = 123)
ebam.out <- ebam(find.out)
ebam.out

# Obtain the number of differentially
# expressed genes and the FDR if a gene is called differentially
# expressed if its posterior probability is larger than 0.8, 0.85,
# 0.9, 0.95.
print(ebam.out, c(0.8, 0.85, 0.9, 0.95))

# Generate a plot of the posterior probabilities for delta = 0.9.
plot(ebam.out, 0.9)

# Obtain the list of genes called differentially expressed if their
```

```

# posterior probability is larger than 0.99, and gene-specific
# statistics for these variables such as their z-value and their
# local FDR.
summary(ebam.out, 0.9)
## End(Not run)

```

FindA0class

Class FindA0

Description

This is a class representation for the specification of the fudge factor in an EBAM analysis as proposed by Efron et al. (2001).

Objects from the Class

Objects can be created using the function `find.a0`.

Slots

- mat.z:** Object of class "matrix" containing the expression scores of the genes for each of the possible values for the fudge factor, where each row corresponds to a gene, and each column to one of the values for the fudge factor a_0 .
- mat.posterior:** Object of class "matrix" consisting of the posterior probabilities of the genes for each of the possible values for the fudge factor, where each row of `mat.posterior` corresponds to a gene, and each column to one of the values for a_0 . The probabilities in `mat.posterior` are computed using the monotonically transformed test scores (see the Details section of `find.a0`)
- mat.center:** Object of class "matrix" representing the centers of the `nrow(mat.center)` intervals used in the logistic regression with repeated observations for estimating f/f_0 for each of the `ncol(mat.center)` possible values for the fudge factor.
- mat.success:** Object of class "matrix" consisting of the numbers of observed test scores in the `nrow(mat.success)` intervals used in the logistic regression with repeated observations for each of the `ncol(mat.success)` possible values for the fudge factor.
- mat.failure:** Object of class "matrix" containing the numbers of permuted test scores in the `nrow(mat.failure)` intervals used in the logistic regression with repeated observations for each of the `ncol(mat.failure)` possible values for the fudge factor.
- z.norm:** Object of class "numeric" comprising the values of the `nrow(mat.z)` quantiles of the standard normal distribution (if any `mat.z < 0`) or an F-distribution (if all `mat.z >= 0`).
- p0:** Object of class "numeric" specifying the prior probability that a gene is not differentially expressed.
- mat.a0:** Object of class "data.frame" comprising the number of differentially expressed genes and the estimated FDR for the possible choices of the fudge factor specified by `vec.a0`.
- mat.samp:** Object of class "matrix" consisting of the `nrow(mat.samp)` permutations of the class labels.
- vec.a0:** Object of class "numeric" representing the possible values of the fudge factor a_0 .
- suggested:** Object of class "numeric" revealing the suggested choice for the fudge factor, i.e. the value of `vec.a0` that leads to the largest number of differentially expressed genes.

delta: Object of class "numeric" specifying the minimum posterior probability that a gene must have to be called differentially expressed.

df.ratio: Object of class "numeric" representing the degrees of freedom of the natural cubic spline used in the logistic regression with repeated observations.

msg: Object of class "character" containing information about, e.g., the type of analysis. msg is printed when print is called.

chip: Object of class "character" naming the microarray used in the analysis. If no information about the chip is available, chip will be set to "".

Methods

plot signature(object = "FindA0"): Generates a plot of the (logit-transformed) posterior probabilities of the genes for a specified value of Δ and a set of possible values for the fudge factor. For details, see `help.finda0(plot)`. For the arguments, see `args.finda0(plot)`.

print signature(object = "FindA0"): Prints the number of differentially expressed genes and the estimated FDR for each of the possible values of the fudge factor specified by `vec.a0`. For details, see `help.finda0(print)`. For arguments, see `args.finda0(print)`.

show signature(object = "FindA0"): Shows the output of an analysis with `find.a0`.

Author(s)

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References

Efron, B., Tibshirani, R., Storey, J.D. and Tusher, V. (2001). Empirical Bayes Analysis of a Microarray Experiment, *JASA*, 96, 1151-1160.

Schwender, H., Krause, A. and Ickstadt, K. (2003). Comparison of the Empirical Bayes and the Significance Analysis of Microarrays. *Technical Report*, SFB 475, University of Dortmund, Germany.

See Also

[find.a0](#), [ebam](#), [EBAM-class](#)

SAM-class

Class SAM

Description

This is a class representation for several versions of the SAM (Significance Analysis of Microarrays) procedure proposed by Tusher et al. (2001).

Objects from the Class

Objects can be created using the functions `sam`, `sam.dstat`, `sam.wilc` and `sam.snp`.

Slots

- d:** Object of class "numeric" representing the expression scores of the genes.
- d.bar:** Object of class "numeric" representing the expected expression scores under the null hypothesis.
- vec.false:** Object of class "numeric" containing the one-sided expected number of falsely called genes
- p.value:** Object of class "numeric" consisting of the p-values of the genes
- s:** Object of class "numeric" representing the standard deviations of the genes. If the standard deviations are not computed, `s` will be set to `numeric(0)`.
- s0:** Object of class "numeric" representing the value of the fudge factor. If not computed, `s0` will be set to `numeric(0)`.
- mat.samp:** Object of class "matrix" containing the permuted group labels used in the estimation of the null distribution. Each row represents one permutation, each column one observation (pair). If no permutation procedure has been used, `mat.samp` will be set to `matrix(numeric(0))`.
- p0:** Object of class "numeric" representing the prior probability that a gene is not differentially expressed.
- mat.fdr:** Object of class "matrix" containing general information as the number of significant genes and the estimated FDR for several values of Δ . Each row represents one value of Δ , each of the 9 columns one statistic.
- q.value:** Object of class "numeric" consisting of the q-values of the genes. If not computed, `q.value` will be set to `numeric(0)`.
- fold:** Object of class "numeric" representing the fold changes of the genes. If not computed, `fold` will be set to `numeric(0)`.
- msg:** Object of class "character" containing information about, e.g., the type of analysis. `msg` is printed when the functions `print` and `summary`, respectively, are called.
- chip:** Object of class "character" naming the microarray used in the analysis. If no information about the chip is available, `chip` will be set to "".

Methods

- identify** signature(`x = "SAM"`): After generating a SAM plot, `identify` can be used to obtain information about the genes by clicking on the symbols in the SAM plot. For details, see `help.sam(identify)`. Arguments are listed by `args.sam(identify)`.
- plot** signature(`x = "SAM"`): Generates a SAM plot or the Delta plots. If the specified `delta` in `plot(object, delta)` is a numeric value, a SAM plot will be generated. If `delta` is either not specified or a numeric vector, the Delta plots will be generated. For details, see `?sam.plot2`, `?delta.plot` or `help.sam(plot)`, respectively. Arguments are listed by `args.sam(plot)`.
- print** signature(`x = "SAM"`): Prints general information such as the number of significant genes and the estimated FDR for a set of Δ . For details, see `help.sam(print)`. Arguments are listed by `args.sam(print)`.
- show** signature(`object = "SAM"`): Shows the output of the SAM analysis.
- summary** signature(`object = "SAM"`): Summarizes the results of a SAM analysis. If `delta` in `summary(object, delta)` is not specified or a numeric vector, the information shown by `print` and some additional information will be shown. If `delta` is a numeric vector, the general information for the specific Δ is shown and additionally gene-specific information about the genes called significant using this value of Δ . The output of `summary`

is an object of class `sumSAM` which has the slots `row.sig.genes`, `mat.fdr`, `mat.sig` and `list.args`. For details, see `help.sam(summary)`. All arguments are listed by `args.sam(summary)`.

Note

SAM was developed by Tusher et al. (2001).

!!! There is a patent pending for the SAM technology at Stanford University. !!!

Author(s)

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References

Schwender, H., Krause, A. and Ickstadt, K. (2003). Comparison of the Empirical Bayes and the Significance Analysis of Microarrays. *Technical Report*, SFB 475, University of Dortmund, Germany. <http://www.sfb475.uni-dortmund.de/berichte/tr44-03.pdf>.

Schwender, H. (2004). Modifying Microarray Analysis Methods for Categorical Data – SAM and PAM for SNPs. To appear in: *Proceedings of the the 28th Annual Conference of the GfKI*.

Tusher, V.G., Tibshirani, R., and Chu, G. (2001). Significance analysis of microarrays applied to the ionizing radiation response. *PNAS*, 98, 5116-5121.

See Also

[sam](#), [sam.dstat](#), [sam.wilc](#), [sam.snp](#), [args.sam](#), [sam.plot2](#), [delta.plot](#)

Examples

```
## Not run:
# Load the package multtest and the data of Golub et al. (1999)
# contained in multtest.
library(multtest)
data(golub)

# Perform a SAM analysis for the two class unpaired case assuming
# unequal variances.
sam.out<-sam(golub,golub.cl,B=100,rand=123)
sam.out

# Alternative ways to show the output of sam.
show(sam.out)
print(sam.out)

# Obtain a little bit more information.
summary(sam.out)

# Print the results of the SAM analysis for other values of Delta.
print(sam.out,seq(.2,2,.2))

# Again, the same with additional information.
summary(sam.out,seq(.2,2,.2))

# Obtain the Delta plots for the default set of Deltas.
plot(sam.out)
```

```

# Generate the Delta plots for Delta = 0.2, 0.4, 0.6, ..., 2.
plot(sam.out,seq(0.2,0.4,2))

# Obtain the SAM plot for Delta = 2.
plot(sam.out,2)

# Get information about the genes called significant using
# Delta = 3 (since neither the gene names nor the chip type
# has been specified ll is set to FALSE to avoid a warning).
sam.sum3<-summary(sam.out,3,ll=FALSE)
sam.sum3

# Obtain the rows of the Golub et al. (1999) data set containing
# the genes called differentially expressed
sam.sum3@row.sig.genes

# and their names
golub.gnames[sam.sum3@row.sig.genes,3]

# The matrix containing the d-values, q-values etc. of the
# differentially expressed genes can be obtained by
sam.sum3@mat.sig
## End(Not run)

```

buildSNPannotation *Construct Annotation for Affymetrix SNP Chips*

Description

Constructs a data frame from a metadata package containing annotations for the SNPs from the corresponding Affymetrix SNP Chip

Usage

```

buildSNPannotation(pkg, rs = TRUE, allele = TRUE, gene = TRUE,
  chromosome = FALSE, position = FALSE, strand = FALSE, cytoband = FALSE,
  max.genes = 0, lib.loc = NULL, others = NULL, subset = NULL,
  pattern = NULL, na.rm = TRUE)

```

Arguments

pkg	the name of the metadata package from which the data frame containing the annotations of the SNPs should be generated
rs	should the RefSNP-ID of the SNPs be added to the data frame?
allele	should the two alleles of each SNP be added to the data frame?
gene	should the genes associated with the SNPs be added to the data frame?
chromosome	should the chromosome to which the respective SNP belongs be added to the data frame?
position	should the physical positions of the SNPs be added to the data frame?
strand	should the strands be added to the data frame?

cytoband	logical indicating whether the cytoband of each SNP is added to the data frame
max.genes	integer specifying the maximum number of genes associated with the respective SNP that should be stored in the data frame. By default, all entries are considered. The corresponding column of the data frame can also be shortened afterwards using shortenGeneDescription . Shortened entries are marked by <code>...</code> at the end of the entries
lib.loc	the directory in which the metadata package is stored. Needs only to be specified if it is not stored in the usual directory of the packages
others	character string or vector naming other entries of the object <code>featureSet</code> saved in <code>pkg</code> that should be added to the data frame
subset	character string consisting of the probe set IDs of the SNPs for which the data frame should be generated. The data frame will contain all SNPs if <code>subset = NULL</code>
pattern	character string specifying the pattern of the probe set IDs of the SNPs for which the data frame should be generated. For example, <code>pattern = "SNP%"</code> will lead to a data frame containing all SNPs whose probe set ID start with "SNP"
na.rm	should the rows of the data frame corresponding to SNPs specified by <code>subset</code> for which no information is available in the metadata package be removed?

Value

a data frame composed of annotations for the SNPs for which information is available in the specified metadata package

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See Also

[shortenGeneDescription](#), [link.genes](#), [link.siggenes](#), [sam2html](#)

cat.ebam

EBAM Analysis for Categorical Data

Description

Generates the required statistics for an Empirical Bayes Analysis of Microarrays (EBAM) of categorical data such as SNP data.

Should not be called directly, but via `ebam(..., method = cat.ebam)`.

Usage

```
cat.ebam(data, cl, approx = FALSE, B = 100, n.split = 1,
  check.for.NN = FALSE, lev = NULL, B.more = 0.1,
  B.max = 50000, n.subset = 10, fast = FALSE,
  n.interval = NULL, df.ratio = 3, df.dens = NULL,
  knots.mode = NULL, type.nclass = "wand", rand = NA)
```


Arguments

<code>data</code>	a matrix or data frame. Each row must correspond to a variable/SNP, and each column to a sample
<code>cl</code>	a numeric vector of length <code>ncol(data)</code> indicating to which class a sample belongs. Must consist of the integers between 1 and c , where c is the number of different groups
<code>approx</code>	should the null distribution be approximated by a χ^2 -distribution?
<code>B</code>	the number of permutations used in the estimation of the null distribution, and hence, in the computation of the expected z -values.
<code>n.split</code>	number of chunks in which the variables are splitted in the computation of the values of the test statistic. Currently, only available if <code>approx = TRUE</code> . By default, the test scores of all variables are calculated simultaneously. If the number of variables or observations is large, setting <code>n.split</code> to a larger value than 1 can help to avoid memory problems
<code>check.for.NN</code>	if <code>TRUE</code> , it will be checked if any of the genotypes is equal to "NN". Can be very time-consuming when the data set is high-dimensional
<code>lev</code>	numeric or character vector specifying the codings of the levels of the variables/SNPs. Must only be specified if the variables are not coded by the integers between 1 and the number of levels. Can also be a list. In this case, each element of this list must be a numeric or character vector specifying the codings, where all elements must have the same length
<code>B.more</code>	a numeric value. If the number of all possible permutations is smaller than or equal to $(1+B.more)*B$, full permutation will be done. Otherwise, B permutations are used
<code>B.max</code>	a numeric value. If the number of all possible permutations is smaller than or equal to <code>B.max</code> , B randomly selected permutations will be used in the computation of the null distribution. Otherwise, B random draws of the group labels are used
<code>n.subset</code>	a numeric value indicating in how many subsets the B permutations are divided when computing the permuted z -values. Please note that the meaning of <code>n.subset</code> differs between the SAM and the EBAM functions
<code>fast</code>	if <code>FALSE</code> the exact number of permuted test scores that are more extreme than a particular observed test score is computed for each of the variables/SNPs. If <code>TRUE</code> , a crude estimate of this number is used
<code>n.interval</code>	the number of intervals used in the logistic regression with repeated observations for estimating the ratio f_0/f (if <code>approx = FALSE</code>), or in the Poisson regression used to estimate the density of the observed z -values (if <code>approx = TRUE</code>). If <code>NULL</code> , <code>n.interval</code> is set to 139 if <code>approx = FALSE</code> , and estimated by the method specified by <code>type.nclass</code> if <code>approx = TRUE</code>
<code>df.ratio</code>	integer specifying the degrees of freedom of the natural cubic spline used in the logistic regression with repeated observations. Ignored if <code>approx = TRUE</code>
<code>df.dens</code>	integer specifying the degrees of freedom of the natural cubic spline used in the Poisson regression to estimate the density of the observed z -values. Ignored if <code>approx = FALSE</code> . If <code>NULL</code> , <code>df.dens</code> is set to 3 if the degrees of freedom of the approximated null distribution, i.e. the χ^2 -distribution, are less than or equal to 2, and otherwise <code>df.dens</code> is set to 5
<code>knots.mode</code>	if <code>TRUE</code> the <code>df.dens - 1</code> knots are centered around the mode and not the median of the density when fitting the Poisson regression model. Ignored if

	<code>approx = FALSE</code> . If not specified, <code>knots.mode</code> is set to <code>TRUE</code> if the degrees of freedom of the approximated null distribution, i.e. the χ^2 -distribution, are larger than or equal to 3, and otherwise <code>knots.mode</code> is set to <code>FALSE</code> . For details on this density estimation, see denspr
<code>type.nclass</code>	character string specifying the procedure used to compute the number of cells of the histogram. Ignored if <code>approx = FALSE</code> or <code>n.interval</code> is specified. Can be either "wand" (default), "scott", or "FD". For details, see denspr
<code>rand</code>	numeric value. If specified, i.e. not <code>NA</code> , the random number generator will be set into a reproducible state

Details

For each variable, Pearson's Chi-Square statistic is computed to test if the distribution of the variable differs between several groups. Since only one null distribution is estimated for all variables as proposed in the original EBAM application of Efron et al. (2001), all variables must have the same number of levels/categories.

Value

a list containing statistics required by `ebam`

Warning

This procedure will only work correctly if all SNPs/variables have the same number of levels/categories.

Author(s)

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References

- Efron, B., Tibshirani, R., Storey, J.D. and Tusher, V. (2001). Empirical Bayes Analysis of a Microarray Experiment, *JASA*, 96, 1151-1160.
- Schwender, H. (2007). Empirical Bayes Analysis of Single Nucleotide Polymorphisms. *Technical Report*, Department of Statistics, University of Dortmund. To appear soon.
- Schwender, H., Krause, A. and Ickstadt, K. (2003). Comparison of the Empirical Bayes and the Significance Analysis of Microarrays. *Technical Report*, SFB 475, University of Dortmund, Germany.

See Also

[SAM-class,sam](#)

cat.stat *SAM Analysis for Categorical Data*

Description

Generates the required statistics for a Significance Analysis of Microarrays of categorical data such as SNP data.

Should not be called directly, but via `sam(..., method = cat.stat)`.

Usage

```
cat.stat(data, cl, B = 100, approx = FALSE, n.split = 1,
         check.for.NN = FALSE, lev = NULL, B.more = 0.1,
         B.max = 50000, n.subset = 10, rand = NA)
```

Arguments

<code>data</code>	a matrix or data frame. Each row must correspond to a variable/SNP, and each column to a sample
<code>cl</code>	a numeric vector of length <code>ncol(data)</code> indicating to which class a sample belongs. Must consist of the integers between 1 and c , where c is the number of different groups
<code>B</code>	the number of permutations used in the estimation of the null distribution, and hence, in the computation of the expected d -values
<code>approx</code>	should the null distribution be approximated by the χ^2 -distribution?
<code>n.split</code>	number of chunks in which the variables are splitted in the computation of the values of the test statistic. Currently, only available if <code>approx = TRUE</code> . By default, the test scores of all variables are calculated simultaneously. If the number of variables or observations is large, setting <code>n.split</code> to a larger value than 1 can help to avoid memory problems
<code>check.for.NN</code>	if TRUE, it will be checked if any of the genotypes is equal to "NN" or "NoCall". Might be very time-consuming when the data set is high-dimensional
<code>lev</code>	numeric or character vector specifying the codings of the levels of the variables/SNPs. Must only be specified if the variables are not coded by the integers between 1 and the number of levels. If the codings of the levels differ between variables, a list can be used to specify the different codings. In this case, each element of this list must be a numeric or character vector specifying the codings, where all elements must have the same length
<code>B.more</code>	a numeric value. If the number of all possible permutations is smaller than or equal to $(1+B.more)*B$, full permutation will be done. Otherwise, B permutations are used
<code>B.max</code>	a numeric value. If the number of all possible permutations is smaller than or equal to <code>B.max</code> , B randomly selected permutations will be used in the computation of the null distribution. Otherwise, B random draws of the group labels are used
<code>n.subset</code>	a numeric value indicating how many permutations are considered simultaneously when computing the expected d -values
<code>rand</code>	numeric value. If specified, i.e. not NA, the random number generator will be set into a reproducible state

Details

For each SNP, Pearson's Chi-Square statistic is computed to test if the distribution of the SNP differs between several groups. Since only one null distribution is estimated for all SNPs as proposed in the original SAM procedure of Tusher et al. (2001) all SNPs must have the same number of levels/categories.

Value

a list containing statistics required by `sam`

Warning

This procedure will only work correctly if all SNPs/variables have the same number of levels/categories. Therefore, it is stopped when the number of levels differ between the variables.

Author(s)

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References

Schwender, H. (2004). Modifying Microarray Analysis Methods for Categorical Data – SAM and PAM for SNPs. To appear in: *Proceedings of the the 28th Annual Conference of the GfKI*.

Tusher, V.G., Tibshirani, R., and Chu, G. (2001). Significance analysis of microarrays applied to the ionizing radiation response. *PNAS*, 98, 5116-5121.

See Also

[SAM-class,sam](#)

d.stat

SAM Analysis Using a Modified t-statistic

Description

Computes the required statistics for a Significance Analysis of Microarrays (SAM) using either a (modified) t- or F-statistic.

Should not be called directly, but via the function `sam`.

Usage

```
d.stat(data, cl, var.equal = FALSE, B = 100, med = FALSE, s0 = NA,
s.alpha = seq(0, 1, 0.05), include.zero = TRUE, n.subset = 10,
mat.samp = NULL, B.more = 0.1, B.max = 30000, gene.names = NULL,
R.fold = 1, use.dm = TRUE, R.unlog = TRUE, na.replace = TRUE,
na.method = "mean", rand = NA)
```

Arguments

<code>data</code>	a matrix, data frame or <code>ExpressionSet</code> object. Each row of <code>data</code> (or <code>exprs(data)</code> , respectively) must correspond to a gene, and each column to a sample
<code>c1</code>	a numeric vector of length <code>ncol(data)</code> containing the class labels of the samples. In the two class paired case, <code>c1</code> can also be a matrix with <code>ncol(data)</code> rows and 2 columns. If <code>data</code> is an <code>ExpressionSet</code> object, <code>c1</code> can also be a character string. For details on how <code>c1</code> should be specified, see <code>?sam</code>
<code>var.equal</code>	if <code>FALSE</code> (default), Welch's t-statistic will be computed. If <code>TRUE</code> , the pooled variance will be used in the computation of the t-statistic
<code>B</code>	numeric value indicating how many permutations should be used in the estimation of the null distribution
<code>med</code>	if <code>FALSE</code> (default), the mean number of falsely called genes will be computed. Otherwise, the median number is calculated
<code>s0</code>	a numeric value specifying the fudge factor. If <code>NA</code> (default), <code>s0</code> will be computed automatically
<code>s.alpha</code>	a numeric vector or value specifying the quantiles of the standard deviations of the genes used in the computation of <code>s0</code> . If <code>s.alpha</code> is a vector, the fudge factor is computed as proposed by Tusher et al. (2001). Otherwise, the quantile of the standard deviations specified by <code>s.alpha</code> is used as fudge factor
<code>include.zero</code>	if <code>TRUE</code> , <code>s0=0</code> will also be a possible choice for the fudge factor. Hence, the usual t-statistic or F statistic, respectively, can also be a possible choice for the expression score d . If <code>FALSE</code> , <code>s0=0</code> will not be a possible choice for the fudge factor. The latter follows Tusher et al. (2001) definition of the fudge factor in which only strictly positive values are considered
<code>n.subset</code>	a numeric value indicating how many permutations are considered simultaneously when computing the p-value and the number of falsely called genes. If <code>med = TRUE</code> , <code>n.subset</code> will be set to 1
<code>mat.samp</code>	a matrix having <code>ncol(data)</code> columns except for the two class paired case in which <code>mat.samp</code> has <code>ncol(data)/2</code> columns. Each row specifies one permutation of the group labels used in the computation of the expected expression scores \bar{d} . If not specified (<code>mat.samp=NULL</code>), a matrix having <code>B</code> rows and <code>ncol(data)</code> is generated automatically and used in the computation of \bar{d} . In the two class unpaired case and the multiclass case, each row of <code>mat.samp</code> must contain the same group labels as <code>c1</code> . In the one class and the two class paired case, each row must contain -1's and 1's. In the one class case, the expression values are multiplied by these -1's and 1's. In the two class paired case, each column corresponds to one observation pair whose difference is multiplied by either -1 or 1. For more details and examples, see the manual of <code>siggenes</code>
<code>B.more</code>	a numeric value. If the number of all possible permutations is smaller than or equal to $(1+B.more)*B$, full permutation will be done. Otherwise, <code>B</code> permutations are used. This avoids that <code>B</code> permutations will be used – and not all permutations – if the number of all possible permutations is just a little larger than <code>B</code>
<code>gene.names</code>	a character vector of length <code>nrow(data)</code> containing the names of the genes
<code>B.max</code>	a numeric value. If the number of all possible permutations is smaller than or equal to <code>B.max</code> , <code>B</code> randomly selected permutations will be used in the computation of the null distribution. Otherwise, <code>B</code> random draws of the group labels are

used. In the latter way of permuting it is possible that some of the permutations are used more than once

<code>R.fold</code>	a numeric value. If the fold change of a gene is smaller than or equal to <code>R.fold</code> , or larger than or equal to <code>1/R.fold</code> , respectively, then this gene will be excluded from the SAM analysis. The expression score d of excluded genes is set to NA. By default, <code>R.fold</code> is set to 1 such that all genes are included in the SAM analysis. Setting <code>R.fold</code> to 0 or a negative value will avoid the computation of the fold change. The fold change is only computed in the two-class unpaired cases
<code>use.dm</code>	if TRUE, the fold change is computed by 2 to the power of the difference between the mean log ₂ intensities of the two groups, i.e. 2 to the power of the numerator of the test statistic. If FALSE, the fold change is determined by computing 2 to the power of <code>data</code> (if <code>R.unlog = TRUE</code>) and then calculating the ratio of the mean intensity in the group coded by 1 to the mean intensity in the group coded by 0. The latter is the definition of the fold change used in Tusher et al. (2001)
<code>R.unlog</code>	if TRUE, the anti-log of <code>data</code> will be used in the computation of the fold change. Otherwise, <code>data</code> is used. This transformation should be done when <code>data</code> is log ₂ -transformed (in a SAM analysis it is highly recommended to use log ₂ -transformed expression data). Ignored if <code>use.dm = TRUE</code>
<code>na.replace</code>	if TRUE, missing values will be removed by the gene-wise/row-wise statistic specified by <code>na.method</code> . If a gene has less than 2 non-missing values, this gene will be excluded from further analysis. If <code>na.replace=FALSE</code> , all genes with one or more missing values will be excluded from further analysis. The expression score d of excluded genes is set to NA
<code>na.method</code>	a character string naming the statistic with which missing values will be replaced if <code>na.replace=TRUE</code> . Must be either "mean" (default) or <code>median</code>
<code>rand</code>	numeric value. If specified, i.e. not NA, the random number generator will be set into a reproducible state

Value

an object of class SAM

Author(s)

Holger Schwender, <holger.schw@gmx.de>

References

Schwender, H., Krause, A. and Ickstadt, K. (2003). Comparison of the Empirical Bayes and the Significance Analysis of Microarrays. *Technical Report*, SFB 475, University of Dortmund, Germany.

Tusher, V.G., Tibshirani, R., and Chu, G. (2001). Significance analysis of microarrays applied to the ionizing radiation response. *PNAS*, 98, 5116-5121.

See Also

[SAM-class,sam](#)

`delta.plot`*Delta Plots*

Description

Generates both a plot of Δ vs. the FDR and a plot of Δ vs. the number of identified genes in a SAM analysis.

Usage

```
delta.plot(object, delta = NULL, helplines = FALSE)
```

Arguments

<code>object</code>	a object of class SAM
<code>delta</code>	a vector of values for Δ . If NULL, a default set of Δ values will be used
<code>helplines</code>	if TRUE, help lines will be drawn in the Δ plots

Details

The Δ plots are a visualization of the table generated by `sam` that contains the estimated FDR and the number of identified genes for a set of Δ values.

Value

Two plots in one graphsheet: The plot of Δ vs. FDR and the plot of Δ vs. the number of identified genes

Author(s)

Holger Schwender, <holger.schw@gmx.de>

References

Tusher, V., Tibshirani, R., and Chu, G. (2001). Significance Analysis of Microarrays Applied to the Ionizing Radiation Response. *PNAS*, 98, 5116-5121.

See Also

[SAM-class,sam](#)

Examples

```
## Not run:
# Load the package multtest and the data of Golub et al. (1999)
# contained in multtest.
library(multtest)
data(golub)

# Perform a SAM analysis.
sam.out<-sam(golub,golub.cl,B=100,rand=123)
```

```

# Generate the Delta plots for the default set of Deltas computed by sam.
delta.plot(sam.out)

# Another way of generating the same plot.
plot(sam.out)

# Generate the Delta plots for Delta = 0.2, 0.4, ..., 2.
plot(sam.out, seq(0.2, 2, 0.2))
## End(Not run)

```

denspr

*Density Estimation***Description**

Estimates the density of a vector of observations by a Poisson regression fit to histogram counts.

Usage

```
denspr(x, n.interval = NULL, df = 5, knots.mode = TRUE,
       type.nclass = c("wand", "scott", "FD"))
```

Arguments

<code>x</code>	a numeric vector containing the observations for which the density should be estimated
<code>n.interval</code>	an integer specifying the number of cells for the histogram. If <code>NULL</code> , <code>n.interval</code> is estimated by the method specified by <code>type.nclass</code>
<code>df</code>	integer specifying the degrees of freedom of the natural cubic spline used in the Poisson regression fit
<code>knots.mode</code>	if <code>TRUE</code> the <code>df - 1</code> knots are centered around the mode and not the median of the density, where the mode is estimated by the midpoint of the cell of the histogram that contains the largest number of observations. If <code>FALSE</code> , the default knots are used in the function <code>ns</code> . Thus, if <code>FALSE</code> the basis matrix will be generated by <code>ns(x, df = 5)</code>
<code>type.nclass</code>	character string specifying the procedure used to compute the number of cells of the histogram. Ignored if <code>n.interval</code> is specified. By default, the method of Wand (1994) with <code>level = 1</code> (see the help page of <code>dpih</code> in the package KernSmooth) is used. For the other choices, see nclass.scott

Value

A list consisting of

<code>y</code>	a numeric vector of the same length as <code>x</code> containing the estimated density for each of the observations
<code>center</code>	a numeric vector specifying the midpoints of the cells of the histogram
<code>counts</code>	a numeric vector of the same length as <code>center</code> composed of the number of observations of the corresponding cells
<code>x.mode</code>	the estimated mode
<code>ns.out</code>	the output of <code>ns</code>
<code>type</code>	the method used to estimate the numbers of cells

Author(s)

Holger Schwender, (holger.schw@gmx.de)

References

Efron, B., and Tibshirani, R. (1996). Using specially designed exponential families for density estimation. *Annals of Statistics*, 24, 2431–2461.

Wand, M.P. (1997). Data-based choice of histogram bin width. *American Statistician*, 51, 59–64.

See Also

[cat.ebam](#)

 ebam

Empirical Bayes Analysis of Microarrays

Description

Performs an Empirical Bayes Analysis of Microarrays (EBAM). It is possible to perform one and two class analyses using either a modified t-statistic or a (standardized) Wilcoxon rank statistic, and a multiclass analysis using a modified F-statistic. Moreover, this function provides a EBAM procedure for categorical data such as SNP data and the possibility to employ an user-written score function.

Usage

```
ebam(x, cl, method = z.ebam, delta = 0.9, which.a0 = NULL, p0 = NA,
     p0.estimation = c("splines", "interval", "adhoc"), lambda = NULL,
     ncs.value = "max", use.weights = FALSE, gene.names = dimnames(x)[[1]],
     ...)
```

Arguments

- x** either a matrix, a data frame or an ExpressionSet object, or the output of find.a0, i.e. an object of class FindA0. If **x** is not a FindA0 object, then each row of data (or `exprs(data)`, respectively) must correspond to a variable (e.g. a gene), and each column to a sample.
- cl** a specification of the class labels of the samples. Ignored if **x** is a FindA0 object. Typically, **cl** is specified by a vector of length `ncol(data)`. In the two class paired case, **cl** can also be a matrix with `ncol(data)` rows and 2 columns. If **data** is an ExpressionSet object, **cl** can also be a character string naming the column of `pData(data)` that contains the class labels of the samples.
- In the one-class case, **cl** should be a vector of 1's.
- In the two class unpaired case, **cl** should be a vector containing 0's (specifying the samples of, e.g., the control group) and 1's (specifying, e.g., the case group).
- In the two class paired case, **cl** can be either a numeric vector or a numeric matrix. If it is a vector, then **cl** has to consist of the integers between -1 and $-n/2$ (e.g., before treatment group) and between 1 and $n/2$ (e.g., after treatment group), where n is the length of **cl** and k is paired with $-k$, $k = 1, \dots, n/2$. If **cl** is a matrix, one column should contain -1's and 1's specifying, e.g., the

before and the after treatment samples, respectively, and the other column should contain integer between 1 and $n/2$ specifying the $n/2$ pairs of observations.

In the multiclass case and if `method = cat.stat`, `c1` should be a vector containing integers between 1 and g , where g is the number of groups.

For examples of how `c1` can be specified, see the manual of **siggenes**

<code>method</code>	a character string or name specifying the method or function that should be used in the computation of the expression score z . If <code>method = z.ebam</code> , a modified t- or F-statistic, respectively, will be computed as proposed by Efron et al. (2001). If <code>method = wilc.ebam</code> , a (standardized) Wilcoxon sum / signed rank statistic will be used as expression score. For an analysis of categorical data such as SNP data, <code>method</code> can be set to <code>cat.ebam</code> . In this case, Pearson's Chi-squared statistic is computed for each row. It is also possible to employ an user-written function for computing an user-specified expression score. For details, see the vignette of siggenes
<code>delta</code>	a numeric vector consisting of probabilities for which the number of differentially expressed genes and the FDR should be computed, where a gene is called differentially expressed if its posterior probability is larger than Δ
<code>which.a0</code>	an integer between 1 and the length of <code>quan.a0</code> of <code>find.a0</code> . If NULL, the suggested choice of <code>find.a0</code> is used. Ignored if <code>x</code> is a matrix, data frame or ExpressionSet object
<code>p0</code>	a numeric value specifying the prior probability p_0 that a gene is not differentially expressed. If NA, p_0 will be estimated automatically
<code>p0.estimation</code>	either "splines" (default), "interval", or "adhoc". If "splines", the spline based method of Storey and Tibshirani (2003) is used to estimate p_0 . If "adhoc" ("interval"), the adhoc (interval based) method proposed by Efron et al. (2001) is used to estimate p_0
<code>lambda</code>	a numeric vector or value specifying the λ values used in the estimation of p_0 . If NULL, <code>lambda</code> is set to <code>seq(0, 0.95, 0.05)</code> if <code>p0.estimation = "splines"</code> , and to 0.5 if <code>p0.estimation = "interval"</code> . Ignored if <code>p0.estimation = "adhoc"</code> . For details, see pi0.est
<code>ncs.value</code>	a character string. Only used if <code>p0.estimation = "splines"</code> and <code>lambda</code> is a vector. Either "max" or "paper". For details, see pi0.est
<code>use.weights</code>	should weights be used in the spline based estimation of p_0 ? If TRUE, $1 - \lambda$ is used as weights. For details, see pi0.est
<code>gene.names</code>	a vector of length <code>nrow(x)</code> specifying the names of the variables. By default, the row names of the matrix / data frame comprised by <code>x</code> are used
<code>...</code>	further arguments of the specific EBAM methods. If <code>method = z.ebam</code> , see z.ebam . If <code>method = wilc.ebam</code> , see wilc.ebam . If <code>method = cat.ebam</code> , see cat.ebam

Value

an object of class EBAM

Author(s)

Holger Schwender, <holger.schw@gmx.de>

References

Efron, B., Tibshirani, R., Storey, J.D. and Tusher, V. (2001). Empirical Bayes Analysis of a Microarray Experiment, *JASA*, 96, 1151–1160.

Schwender, H., Krause, A. and Ickstadt, K. (2003). Comparison of the Empirical Bayes and the Significance Analysis of Microarrays. *Technical Report*, SFB 475, University of Dortmund, Germany. <http://www.sfb475.uni-dortmund.de/berichte/tr44-03.pdf>.

Storey, J.D. and Tibshirani, R. (2003). Statistical Significance for Genome-Wide Studies. *Proceedings of the National Academy of Sciences*, 100, 9440–9445.

See Also

[EBAM-class](#), [find.a0](#), [z.ebam](#), [wilc.ebam](#), [cat.ebam](#)

Examples

```
## Not run:
# Load the data of Golub et al. (1999) contained in the package multtest.
data(golub)

# golub.cl contains the class labels.
golub.cl

# Perform an EBAM analysis for the two class unpaired case assuming
# unequal variances. Specify the fudge factor a0 by the suggested
# choice of find.a0
find.out <- find.a0(golub, golub.cl, rand = 123)
ebam.out <- ebam(find.out)
ebam.out

# Since a0 = 0 leads to the largest number of genes (i.e. the suggested
# choice of a0), the following leads to the same results as the above
# analysis (but only if the random number generator, i.e. rand, is set
# to the same number).
ebam.out2 <- ebam(golub, golub.cl, a0 = 0, fast = TRUE, rand = 123)
ebam.out2

# If fast is set to TRUE in ebam, a crude estimate of the number of
# falsely called genes is used (see the help file for z.ebam). This
# estimate is always employed in find.a0.
# The exact number is used in ebam when performing
ebam.out3 <- ebam(golub, golub.cl, a0 = 0, rand = 123)
ebam.out3

# Since this is the recommended way, we use ebam.out3 at the end of
# the Examples section for further analyses.

# Perform an EBAM analysis for the two class unpaired case assuming
# equal group variances. Set a0 = 0, and use B = 50 permutations
# of the class labels.
ebam.out4 <- ebam(golub, golub.cl, a0 = 0, var.equal = TRUE, B = 50,
  rand = 123)
ebam.out4

# Perform an EBAM analysis for the two class unpaired case assuming
```

```

# unequal group variances. Use the median (i.e. the 50% quantile)
# of the standard deviations of the genes as fudge factor a0. And
# obtain the number of genes and the FDR if a gene is called
# differentially when its posterior probability is larger than
# 0.95.
ebam.out5 <- ebam(golub, golub.cl, quan.a0 = 0.5, delta = 0.95,
  rand = 123)
ebam.out5

# For the third analysis, obtain the number of differentially
# expressed genes and the FDR if a gene is called differentially
# expressed if its posterior probability is larger than 0.8, 0.85,
# 0.9, 0.95.
print(ebam.out3, c(0.8, 0.85, 0.9, 0.95))

# Generate a plot of the posterior probabilities for delta = 0.9.
plot(ebam.out3, 0.9)

# Obtain the list of genes called differentially expressed if their
# posterior probability is larger than 0.99, and gene-specific
# statistics for these variables such as their z-value and their
# local FDR.
summary(ebam.out3, 0.99)
## End(Not run)

```

find.a0

Computation of the Fudge Factor

Description

Suggests an optimal value for the fudge factor in an EBAM analysis as proposed by Efron et al. (2001).

Usage

```

find.a0(data, cl, method = z.find, B = 100, delta = 0.9, quan.a0 = (0:5)/5,
  include.zero = TRUE, gene.names = dimnames(data)[[1]], n.chunk = 5,
  n.interval = 139, df.ratio = NULL, p0.estimation = c("splines",
  "adhoc", "interval"), lambda = NULL, ncs.value = "max",
  use.weights = FALSE, rand = NA, ...)

```

Arguments

data	a matrix, data frame or an ExpressionSet object. Each row of data (or <code>exprs(data)</code> , respectively) must correspond to a gene, and each column to a sample
cl	a numeric vector of length <code>ncol(data)</code> containing the class labels of the samples. In the two class paired case, <code>cl</code> can also be a matrix with <code>ncol(data)</code> rows and 2 columns. If <code>data</code> is an ExpressionSet object, <code>cl</code> can also be a character string naming the column of <code>pData(data)</code> that contains the class labels of the samples. In the one-class case, <code>cl</code> should be a vector of 1's. In the two class unpaired case, <code>cl</code> should be a vector containing 0's (specifying the samples of, e.g., the control group) and 1's (specifying, e.g., the case group).

In the two class paired case, `c1` can be either a numeric vector or a numeric matrix. If it is a vector, then `c1` has to consist of the integers between -1 and $-n/2$ (e.g., before treatment group) and between 1 and $n/2$ (e.g., after treatment group), where n is the length of `c1` and k is paired with $-k$, $k = 1, \dots, n/2$. If `c1` is a matrix, one column should contain -1 's and 1 's specifying, e.g., the before and the after treatment samples, respectively, and the other column should contain integer between 1 and $n/2$ specifying the $n/2$ pairs of observations.

In the multiclass case and if `method=cat.stat`, `c1` should be a vector containing integers between 1 and g , where g is the number of groups.

For examples of how `c1` can be specified, see the manual of **siggenes**

<code>method</code>	the name of a function for computing the numerator and the denominator of the test statistic of interest, and for specifying other objects required for the identification of the fudge factor. The default function <code>z.find</code> provides these objects for t- and F-statistics. It is, however, also possible to employ an user-written function. For how to write such a function, see the vignette of siggenes
<code>B</code>	the number of permutations used in the estimation of the null distribution
<code>delta</code>	a probability. All genes showing a posterior probability that is larger than or equal to <code>delta</code> are called differentially expressed
<code>quan.a0</code>	a numeric vector indicating over which quantiles of the standard deviations of the genes the fudge factor a_0 should be optimized
<code>include.zero</code>	should $a_0 = 0$, i.e. the not-modified test statistic also be a possible choice for the fudge factor?
<code>gene.names</code>	a character vector of length <code>nrow(data)</code> containing the names of the genes. By default the row names of <code>data</code> are used
<code>n.chunk</code>	an integer specifying in how many subsets the <code>B</code> permutations should be split when computing the permuted test scores
<code>n.interval</code>	the number of intervals used in the logistic regression with repeated observations for estimating the ratio f_0/f
<code>df.ratio</code>	integer specifying the degrees of freedom of the natural cubic spline used in the logistic regression with repeated observations
<code>p0.estimation</code>	either "splines" (default), "interval", or "adhoc". If "splines", the spline based method of Storey and Tibshirani (2003) is used to estimate p_0 . If "adhoc" ("interval"), the adhoc (interval based) method proposed by Efron et al. (2001) is used to estimate p_0
<code>lambda</code>	a numeric vector or value specifying the λ values used in the estimation of p_0 . If <code>NULL</code> , <code>lambda</code> is set to <code>seq(0, 0.95, 0.05)</code> if <code>p0.estimation = "splines"</code> , and to <code>0.5</code> if <code>p0.estimation = "interval"</code> . Ignored if <code>p0.estimation = "adhoc"</code> . For details, see pi0.est
<code>ncs.value</code>	a character string. Only used if <code>p0.estimation = "splines"</code> and <code>lambda</code> is a vector. Either "max" or "paper". For details, see pi0.est
<code>use.weights</code>	should weights be used in the spline based estimation of p_0 ? If <code>TRUE</code> , <code>1 - lambda</code> is used as weights. For details, see pi0.est
<code>rand</code>	integer. If specified, i.e. not <code>NA</code> , the random number generator will be set into a reproducible state
<code>...</code>	further arguments for the function specified by <code>fun</code> . For further arguments of <code>fun = z.find</code> , see z.find

Details

The suggested choice for the fudge factor is the value of a_0 that leads to the largest number of genes showing a posterior probability larger than `delta`.

Actually, only the genes having a posterior probability larger than `delta` are called differentially expressed that do not exhibit a test score less extreme than the score of a gene whose posterior probability is less than `delta`. So, let's say, we have done an EBAM analysis with a t-test and we have ordered the genes by their t-statistic. Let's further assume that Gene 1 to Gene 5 (i.e. the five genes with the lowest t-statistics), Gene 7 and 8, Gene 3012 to 3020, and Gene 3040 to 3051 are the only genes that show a posterior probability larger than `delta`. Then, Gene 1 to 5, and 3040 to 3051 are called differentially expressed, but Gene 7 and 8, and 3012 to 3020 are not called differentially expressed, since Gene 6 and Gene 3021 to 3039 show a posterior probability less than `delta`.

Value

an object of class `FindA0`

Note

The numbers of differentially expressed genes can differ between `find.a0` and `ebam`, even though the same value of the fudge factor is used, since in `find.a0` the observed and permuted test scores are monotonically transformed such that the observed scores follow a standard normal distribution (if the test statistic can take both positive and negative values) and an F-distribution (if the test statistic can only take positive values) for each possible choice of the fudge factor.

Author(s)

Holger Schwender, <holger.schw@gmx.de>

References

Efron, B., Tibshirani, R., Storey, J.D. and Tusher, V. (2001). Empirical Bayes Analysis of a Microarray Experiment, *JASA*, 96, 1151-1160.

See Also

[ebam](#), [FindA0-class](#)

Examples

```
## Not run:
# Load the data of Golub et al. (1999) contained in the package multtest.
data(golub)

# golub.cl contains the class labels.
golub.cl

# Obtain the number of differentially expressed genes and the FDR for the
# default set of values for the fudge factor.
find.out <- find.a0(golub, golub.cl, rand = 123)
find.out

# Obtain the number of differentially expressed genes and the FDR when using
# the t-statistic assuming equal group variances
```

```

find.out2 <- find.a0(golub, golub.cl, var.equal = TRUE, rand = 123)

# Using the Output of the first analysis with find.a0, the number of
# differentially expressed genes and the FDR for other values of
# delta, e.g., 0.95, can be obtained by
print(find.out, 0.95)

# The logit-transformed posterior probabilities can be plotted by
plot(find.out)

# To avoid the logit-transformation, set logit = FALSE.
plot(find.out, logit = FALSE)
## End(Not run)

```

findDelta

Finding the Threshold Delta

Description

Computes the value of the threshold Delta for a given FDR or number of genes/variables in a SAM or EBAM analysis.

Usage

```

findDelta(object, fdr = NULL, genes = NULL, prec = 6, initial = NULL,
          verbose = FALSE)

```

Arguments

object	either a SAM or an EBAM object
fdr	numeric value between 0 and 1 for which the threshold Delta and thus the number of genes/variables should be obtained. Only one of fdr and genes can be specified
genes	integer specifying the number of genes/variables for which the threshold Delta and thus the estimated FDR should be obtained. Only one of fdr and genes can be specified
prec	integer indicating the precision of the considered Delta values
initial	a numeric vector of length two containing the minimum and the maximum value of Delta that is initially used in the search for Delta. Both values must be larger than 0. If object is an EBAM object, both values must also be smaller than or equal to 1. If not specified, the minimum is set to 0.1, and the maximum to either the maximum posterior (EBAM) or the maximum absolute distance between the observed and the corresponding expected values of the test statistic (SAM)
verbose	should more information about the search process be shown?

Value

If a value of Delta is found for the exact value of fdr or genes, then a vector of length 3 consisting of Delta and the corresponding number of genes and the estimated FDR. If such a value is not found, then a matrix with two rows and three columns, where the two rows contain the number of genes/variables and the estimated FDR for the two considered values of Delta that provide the closest upper and lower bounds to the desired FDR (if fdr is specified) or number of genes/variables (if genes is specified)

Author(s)

Holger Schwender, <holger.schwender@udo.edu>

See Also

[sam](#), [ebam](#)

fudge2

Fudge Factor

Description

Computes the fudge factor as described by Tusher et al. (2001).

Usage

```
fudge2(r, s, alpha = seq(0, 1, 0.05), include.zero = TRUE)
```

Arguments

<code>r</code>	a numeric vector. The numerator of the test statistic computed for each gene is represented by one component of this vector
<code>s</code>	a numeric vector. Each component of this vector corresponds to the denominator of the test statistic of a gene
<code>alpha</code>	a numeric value or vector specifying quantiles of the <code>s</code> values. If <code>alpha</code> is numeric, this quantile of <code>s</code> will be used as fudge factor. Otherwise, the <code>alpha</code> quantile of the <code>s</code> values is computed that is optimal following the criterion of Tusher et al. (2001)
<code>include.zero</code>	If <code>TRUE</code> , $s_0 = 0$ is also a possible choice for the fudge factor

Value

<code>s.zero</code>	the value of the fudge factor s_0
<code>alpha.hat</code>	the optimal quantile of the <code>s</code> values. If $s_0 = 0$, <code>alpha.hat</code> will not be returned
<code>vec.cv</code>	the vector of the coefficients of variations. Following Tusher et al. (2001), the optimal <code>alpha</code> quantile is given by the quantile that leads to the smallest CV of the modified test statistics
<code>msg</code>	a character string summarizing the most important information about the fudge factor

Author(s)

Holger Schwender, <holger.schw@gmx.de>

References

Tusher, V., Tibshirani, R., and Chu, G. (2001). Significance Analysis of Microarrays Applied to the Ionizing Radiation Response. *PNAS*, 98, 5116-5121.

See Also

[SAM-class](#), [sam](#), [sam.dstat](#)

`help.ebam`*Help files or argument list for EBAM-specific methods*

Description

Displays the help page or the argument list, respectively, for a EBAM-specific method.

Usage

```
help.ebam(method)
args.ebam(method)
```

Arguments

<code>method</code>	a name or a character string specifying the method for which the arguments or the help page, respectively, should be shown. Currently available are <code>print</code> , <code>plot</code> , and <code>summary</code>
---------------------	---

Value

The arguments of the specified `method` are displayed or a html page containing the help for the specified `method` is opened, respectively.

Author(s)

Holger Schwender, <holger.schw@gmx.de>

See Also

[EBAM-class](#), [ebam](#)

Examples

```
## Not run:
# Displays the arguments of the function summary
args.ebam(summary)

# Opens the help page in the browser
help.ebam(summary)
## End(Not run)
```

`help.finda0`*Help files or argument list for FindA0-specific methods*

Description

Displays the help page or the argument list, respectively, for a FindA0-specific method.

Usage

```
help.finda0 (method)
args.finda0 (method)
```

Arguments

<code>method</code>	a name or a character string specifying the method for which the arguments or the help page, respectively, should be shown. Currently available are <code>print</code> and <code>plot</code>
---------------------	--

Value

The arguments of the specified `method` are displayed or a html page containing the help for the specified `method` is opened, respectively.

Author(s)

Holger Schwender, <holger.schw@gmx.de>

See Also

[FindA0-class](#), [find.a0](#)

Examples

```
## Not run:
# Displays the arguments of the function summary
args.finda0(summary)

# Opens the help page in the browser
help.finda0(summary)
## End(Not run)
```

`help.sam`*Help files or argument list for SAM-specific methods*

Description

Displays the help page or the argument list, respectively, for a SAM-specific method.

Usage

```
help.sam(method)
args.sam(method)
```

Arguments

<code>method</code>	a name or a character string specifying the method for which the arguments or the help page, respectively, should be shown. Currently available are <code>print</code> , <code>plot</code> , <code>summary</code> and <code>identify</code>
---------------------	---

Value

The arguments of the specified `method` are displayed or a html page containing the help for the specified `method` is opened, respectively.

Author(s)

Holger Schwender, <holger.schw@gmx.de>

See Also

[SAM-class,sam,sam.dstat,sam.wilc,sam.snp](#)

Examples

```
## Not run:
# Displays the arguments of the function summary
args.sam(summary)

# Opens the help page in the browser
help.sam(summary)
## End(Not run)
```

link.genes *Links for a list of genes*

Description

Generates a webpage with links to several public repositories for a list of genes.

Usage

```
link.genes(genenames, filename, entrez = TRUE, refseq = TRUE, symbol = TRUE,
           omim = FALSE, ug = FALSE, fullname = FALSE, which.refseq = "NM",
           chipname = "", cdfname = NULL, refsnp = NULL, max.associated = 2,
           dataframe = NULL, title = NULL, bg.col = "white", text.col = "black",
           link.col = "blue", tableborder = 1, new.window = TRUE, load = TRUE)
```

Arguments

genenames	a character vector containing the names of the interesting genes
filename	a character string naming the file in which the output should be stored. Must have the suffix ".html"
entrez	logical indicating if Entrez links should be added to the output
refseq	logical indicating if RefSeq links should be added to the output
symbol	logical indicating if the gene symbols should be added to the output
omim	logical indicating if OMIM links should be added to the output
ug	logical indicating if UniGene links should be added to the output
fullname	logical indicating whether the full gene names should be added to the output
which.refseq	character string or vector naming the first two letters of the RefSeq links that should be displayed in the html file
chipname	character string specifying the chip type used in the analysis. Must be specified as in the metadata section of Bioconductor (e.g., "hgu133a" for the Affymetrix HG-U133A chip). Needs not to be specified if cdfname is specified. For Affymetrix SNP chips (starting with the 500k array set), chipname can be specified by the metadata package name, i.e. either by "pd.genomewidesnp.5", by "pd.genomewidesnp.6", by "pd.mapping250k.nsp", or by "pd.mapping250k.st" to add links to the Affymetrix webpage of the SNPs to the html output
cdfname	character string specifying the cdf name of the used chip. Must exactly follow the nomenclatur of the Affymetrix chips (e.g., "HG-U133A" for the Affymetrix HG-U133A chip). If specified, links to the Affymetrix webpage for the interesting genes will be added to the output. If SNP chips are considered, chipname instead of cdfname must be specified for obtaining these links
refsnp	either a character vector or a data frame. If the former, refsnp contains the RefSNP IDs of the SNPs used in the SAM/EBAM analysis, where names(refsnp) specifies the names of these SNPs, i.e. their probe set IDs. If a data frame, then one column of refsnp must contain the RefSNP IDs of the SNPs, and the name of this column must be RefSNP. The other columns can contain additional annotations such as the chromosome or the physical position of each SNPs. The row names of refsnp must specify the SNPs, i.e. must be the probe set IDs of the SNPs. See buildSNPannotation for an automatical way to construct such a data frame given the corresponding metadata package

max.associated	integer specifying the maximum number of genes associated with the respective SNP displayed in the html output. If all entries should be shown, set <code>max.associated = 0</code> . This however might result in a very large html output. For details, see shortenGeneDescription
dataframe	data frame having one row for each interesting gene, i.e. <code>nrow(dataframe)</code> must be equal to <code>length(genenames)</code> . The row names of dataframe must be equal to <code>genenames</code> . This matrix contains additional information on the list of genes that should be added to the output. If NULL (default) no information will be added to the link list
title	character string naming the title that should be used in the html page
bg.col	specification of the background color of the html page. See <code>?par</code> for how colors can be specified
text.col	specification of the color of the text used in the html page. See <code>?par</code> for how colors can be specified
link.col	specification of the color of the links used in the html file. See <code>?par</code> for how colors can be specified
tableborder	integer specifying the thickness of the border of the table
new.window	logical indicating if the links should be opened in a new window
load	logical value indicating whether to attempt to load the required annotation data package if it is not already loaded. For details, see the man page of <code>lookUp</code> in the package annotate

Author(s)

Holger Schwender, <holger.schw@gmx.de>

See Also

[SAM-class](#), [sam](#), [link.siggenes](#), [sam2html](#)

link.siggenes

Links for a SAM or an EBAM object

Description

Generates a html page with links to several public repositories for a list of genes called differentially expressed when using a specific Delta value in a SAM or an EBAM analysis.

Usage

```
link.siggenes(object, delta, filename, gene.names = NULL, addDataFrame = TRUE,
  entrez = TRUE, refseq = TRUE, symbol = TRUE, omim = FALSE, ug = FALSE,
  fullname = FALSE, which.refseq = "NM", chipname = "", cdfname = NULL,
  refsnp = NULL, max.associated = 2, n.digits = 3, title = NULL,
  bg.col = "white", text.col = "black", link.col = "blue", tableborder = 1,
  new.window = TRUE, load = TRUE)
```

Arguments

<code>object</code>	a SAM or an EBAM object
<code>delta</code>	a numerical value specifying the Delta value
<code>filename</code>	character string naming the file in which the output should be stored. Must have the suffix ".html"
<code>gene.names</code>	a character vector of the same length as <code>object@d</code> containing the names of the genes. Must only be specified if it is not specified in <code>object</code> , i.e. if it has not been specified in <code>sam(data, cl, ...)</code>
<code>addDataFrame</code>	logical indicating if gene-specific information on the differentially expressed genes should be added to the output
<code>entrez</code>	logical indicating if Entrez links should be added to the output
<code>refseq</code>	logical indicating if RefSeq links should be added to the output
<code>symbol</code>	logical indicating if the gene symbols should be added to the output
<code>omim</code>	logical indicating if OMIM links should be added to the output
<code>ug</code>	logical indicating if UniGene links should be added to the output
<code>fullname</code>	logical indicating whether the full gene names should be added to the output
<code>which.refseq</code>	character string or vector naming the first two letters of the RefSeq links that should be displayed in the html file
<code>chipname</code>	character string specifying the chip type used in the analysis. Must be specified as in the meta-data section of Bioconductor (e.g., "hgu133a" for the Affymetrix HG-U133A chip). Needs not to be specified if <code>cdfname</code> is specified. For Affymetrix SNP chips (starting with the 500k array set), <code>chipname</code> can be specified by the metadata package name, i.e. either by "pd.genomewidesnp.5", by "pd.genomewidesnp.6", by "pd.mapping250k.nsp", or by "pd.mapping250k.st" to add links to the Affymetrix webpage of the SNPs to the html output
<code>cdfname</code>	character string specifying the cdf name of the used chip. Must exactly follow the nomenclatur of the Affymetrix chips (e.g., "HG-U133A" for the Affymetrix HG-U133A chip). If specified, links to the Affymetrix webpage for the interesting genes will be added to the output. If SNP chips are considered, <code>chipname</code> instead of <code>cdfname</code> must be specified for obtaining these links
<code>refsnp</code>	either a character vector or a data frame. If the former, <code>refsnp</code> contains the RefSNP IDs of the SNPs used in the SAM/EBAM analysis, where <code>names(refsnp)</code> specifies the names of these SNPs, i.e. their probe set IDs. If a data frame, then one column of <code>refsnp</code> must contain the RefSNP IDs of the SNPs, and the name of this column must be <code>RefSNP</code> . The other columns can contain additional annotations such as the chromosome or the physical position of each SNPs. The row names of <code>refsnp</code> must specify the SNPs, i.e. must be the probe set IDs of the SNPs. See buildSNPannotation for an automatical way to construct such a data frame given the corresponding metadata package
<code>max.associated</code>	integer specifying the maximum number of genes associated with the respective SNP displayed in the html output. If all entries should be shown, set <code>max.associated = 0</code> . This however might result in a very large html output. For details, see shortenGeneDescription
<code>n.digits</code>	integer specifying the number of decimal places used in the output
<code>title</code>	character string naming the title that should be used in the html page

bg.col	specification of the background color of the html page. See ?par for how colors can be specified
text.col	specification of the color of the text used in the html page. See ?par for how colors can be specified
link.col	specification of the color of the links used in the html file. See ?par for how colors can be specified
tableborder	integer specifying the thickness of the border of the table
new.window	logical indicating if the links should be opened in a new window
load	logical value indicating whether to attempt to load the required annotation data package if it is not already loaded. For details, see the man page of lookUp in the package annotate

Author(s)

Holger Schwender, <holger.schw@gmx.de>

See Also

[sam](#), [ebam](#), [link.genes](#), [sam2html](#), [ebam2html](#)

list.siggenes *List of the significant genes*

Description

Lists the genes called differentially expressed by the SAM or the EBAM analysis for a specified value of the threshold Δ .

Usage

```
list.siggenes(object, delta, file = "", gene.names = NULL, order = TRUE,
              text = NULL, append = FALSE)
```

Arguments

object	either a SAM- or an EBAM-object
delta	a numeric value specifying the threshold Δ in the SAM or EBAM analysis. Note that the meaning of Δ differs between SAM and EBAM: In SAM, it is a strictly positive value, whereas in EBAM it is a probability
file	a character string naming a file in which the output is stored. If "", the significant genes will be shown in the console
gene.names	a character vector containing the names of the genes. Needs only to be specified, if the gene names were not specified in <code>sam</code> or <code>ebam</code> , respectively
order	if TRUE, the gene names will be ordered by their "significance"
text	a character string specifying the heading of the gene list. By default, the header specifies the type of analysis and the used value of Δ . To avoid a header, set <code>text=""</code>
append	If TRUE, the output will be appended to <code>file</code> . If FALSE, any existing file having the name <code>file</code> will be destroyed

Value

A list of significant genes either shown in the console or stored in a file.

Author(s)

Holger Schwender, <holger.schw@gmx.de>

See Also

[sam](#), [ebam](#)

Examples

```
## Not run:
# Load the package multtest and the data of Golub et al. (1999)
# contained in \pkg{multtest}.
library(multtest)
data(golub)

# Perform a SAM analysis.
sam.out<-sam(golub,golub.cl,B=100,rand=123)

# List the genes called significant by SAM using Delta = 3.1.
list.siggenes(sam.out,3.1, gene.names=golub.gnames[,2])
## End(Not run)
```

nclass.wand

Number of cells in a histogram

Description

Computes the number of cells in a histogram using the method of Wand (1994).

Usage

```
nclass.wand(x, level = 1)
```

Arguments

x	numeric vector of observations
level	integer specifying the number of levels of functional estimation used in the estimation. For details, see the help page of <code>dpih</code> from the package KernSmooth

Details

`nclass.wand` calls `dpih`, and then computes the number of cells corresponding to the optimal bin width returned by `dpih`

Value

a numeric value specifying the number of cells for the histogram of `x`

References

Wand, M.P. (1997). Data-based choice of histogram bin width. *American Statistician*, 51, 59–64.

See Also

[denspr](#)

pi0.est

Estimation of the prior probability

Description

Estimates the prior probability that a gene is not differentially expressed by the natural cubic splines based method of Storey and Tibshirani (2003).

Usage

```
pi0.est(p, lambda = seq(0, 0.95, 0.05), ncs.value = "max",
        ncs.weights = NULL)
```

Arguments

<code>p</code>	a numeric vector containing the p-values of the genes
<code>lambda</code>	a numeric vector or value specifying the λ values used in the estimation of the prior probability
<code>ncs.value</code>	a character string. Only used if <code>lambda</code> is a vector. Either "max" or "paper". For details, see <code>Details</code>
<code>ncs.weights</code>	a numerical vector of the same length as <code>lambda</code> containing the weights used in the natural cubic spline fit. By default no weights are used

Details

For each value of `lambda`, $\pi_0(\lambda)$ is computed by the number of p-values `p` larger than λ divided by $(1 - \lambda)/m$, where m is the length of `p`.

If `lambda` is a value, $\pi_0(\lambda)$ is the estimate for the prior probability π_0 that a gene is not differentially expressed.

If `lambda` is a vector, a natural cubic spline h with 3 degrees of freedom is fitted through the data points $(\lambda, \pi_0(\lambda))$, where each point is weighed by `ncs.weights`. π_0 is estimated by $h(v)$, where $v = \max\{\lambda\}$ if `ncs.value="max"`, and $v = 1$ if `ncs.value="paper"`.

Value

<code>p0</code>	the estimate of the prior probability that a gene is not differentially expressed
<code>spline.out</code>	the output of <code>smooth.spline</code> used in this function

Author(s)

Holger Schwender, <holger.schw@gmx.de>

References

Storey, J.D., and Tibshirani, R. (2003). Statistical Significance for Genome-wide Studies. *PNAS*, 100, 9440-9445.

See Also

[SAM-class,sam,qvalue.cal](#)

Examples

```
## Not run:
# Load the package multtest and the data of Golub et al. (1999)
# contained in multtest.
library(multtest)
data(golub)

# Perform a SAM analysis.
sam.out<-sam(golub,golub.cl,B=100,rand=123)

# Estimate the prior probability that a gene is not significant
pi0.est(sam.out@p.value)
## End(Not run)
```

plotArguments

Plot Arguments

Description

Utility function for generating a plot of a SAM or an EBAM object in an html output.

Usage

```
plotArguments(pos.stats = NULL, sig.col = 3, xlim = NULL, ylim = NULL,
             main = NULL, xlab = NULL, ylab = NULL, pty = "s", lab = c(10, 10, 7),
             pch = NULL, sig.cex = 1, stats.cex = 0.8, y.intersp = 1.3)
```

Arguments

<code>pos.stats</code>	an integer between 0 and 2 for a SAM plot, and between 0 and 4 for an EBAM plot. See <code>help.sam(plot)</code> or <code>help.ebam(plot)</code> , respectively, for how <code>pos.stats</code> can be specified, and for its default
<code>sig.col</code>	a specification of the color of the significant genes. If <code>sig.col</code> has length 1, all the points corresponding to significant genes are marked in the color specified by <code>sig.col</code> . Only for a SAM plot: If <code>length(sig.col) == 2</code> , the down-regulated genes, i.e. the genes with negative expression score d , are marked in the color specified by <code>sig.col[1]</code> , and the up-regulated genes, i.e. the genes with positive d , are marked in the color specified by <code>sig.col[2]</code> . For a description of how colors are specified, see par
<code>xlim</code>	a numeric vector of length 2 specifying the x limits (minimum and maximum) of the plot
<code>ylim</code>	a numeric vector of length 2 specifying the y limits of the plot

main	a character string naming the main title of the plot
xlab	a character string naming the label of the x axis
ylab	a character string naming the label of the y axis
pty	a character specifying the type of plot region to be used. "s" (default for a SAM plot) generates a square plotting region, and "m" (default for an EBAM plot) the maximal plotting region
lab	a numeric vector of length 3 specifying the approximate number of tickmarks on the x axis and on the y axis and the label size
pch	either an integer specifying a symbol or a single character to be used as the default in plotting points. For a description of how pch can be specified, see par
sig.cex	a numerical value giving the amount by which the symbols of the significant genes should be scaled relative to the default
stats.cex	the size of the statistics printed in the plot relative to the default size. Only available for an EBAM plot
y.intersp	a numeric value specifying the space between the rows in which the statistics are plotted. Only available for an EBAM plot

Value

a list required by `sam2html` or `ebam2html` if `addPlot = TRUE`

Author(s)

Holger Schwender, <holger.schw@gmx.de>

See Also

[sam2html](#), [ebam2html](#)

`plotFindArguments` *Plot Arguments*

Description

Utility function for generating a plot of the posterior probabilities in an html file when searching for the optimal value of the fudge factor in an EBAM analysis.

Usage

```
plotFindArguments(onlyTab = FALSE, logit = TRUE, pos.legend = NULL,
  legend.cex = 0.8, col = NULL, main = NULL, xlab = NULL, ylab = NULL,
  only.a0 = FALSE, lty = 1, lwd = 1, y.intersp = 1.1)
```

Arguments

onlyTab	if TRUE, then this plot is not generated and only the table of the number of differentially expressed genes and the estimated FDR for the different values of the fudge factor is shown
logit	should the posterior probabilities be logit-transformed before they are plotted?
pos.legend	an integer between 0 and 4. See <code>help.finda0(plot)</code> for how <code>pos.legend</code> can be specified, and for its default
legend.cex	the size of the text in the legend relative to the default size
col	a vector specifying the colors of the lines for the different values of the fudge factor. For a description of how colors can be specified, see par
main	a character string naming the main title of the plot
xlab	a character string naming the label of the x axis
ylab	a character string naming the label of the y axis
only.a0	if TRUE, only the values of a_0 are shown in the legend. If FALSE, both the values of a_0 and the corresponding number of differentially expressed genes are shown
lty	a value or vector specifying the line type of the curves. For details, see par
lwd	a numeric value specifying the width of the plotted lines. For details, see par
y.intersp	a numeric value specifying the space between the rows of the legend

Value

a list required by `ebam2html` if `findA0` is specified

Author(s)

Holger Schwender, holger.schw@gmx.de

See Also

[ebam2html](#)

qvalue.cal

Computation of the q-value

Description

Computes the q-values of a given set of p-values.

Usage

```
qvalue.cal(p, p0, version = 1)
```

Arguments

p	a numeric vector containing the p-values
p0	a numeric value specifying the prior probability that a gene is not differentially expressed
version	If <code>version=2</code> , the original version of the q-value, i.e. $\min\{pFDR\}$, will be computed. if <code>version=1</code> , $\min\{FDR\}$ will be used in the computation of the q-value

Details

Using `version=1` in `qvalue.cal` corresponds to setting `robust=FALSE` in the function `qvalue` of John Storey's R package **qvalue**, while `version=2` corresponds to `robust=TRUE`.

Value

a vector of the same length as `p` containing the q-values corresponding to the p-values in `p`

Author(s)

Holger Schwender, <holger.schw@gmx.de>

References

Storey, J.D. (2003). The positive False Discovery Rate: A Bayesian Interpretation and the q-value. *Annals of Statistics*, 31, 2013-2035.

Storey, J.D., and Tibshirani, R. (2003). Statistical Significance for Genome-wide Studies. *PNAS*, 100, 9440-9445.

See Also

[pi0.est](#), [SAM-class](#), [sam](#)

Examples

```
## Not run:
# Load the package multtest and the data of Golub et al. (1999)
# contained in multtest.
library(multtest)
data(golub)

# Perform a SAM analysis.
sam.out<-sam(golub,golub.cl,B=100,rand=123)

# Estimate the prior probability that a gene is not significant.
pi0<-pi0.est(sam.out@p.value)$p0

# Compute the q-values of the genes.
q.value<-qvalue.cal(sam.out@p.value,pi0)
## End(Not run)
```

rowWilcoxon	<i>Rowwise Wilcoxon Rank Sum Statistics</i>
-------------	---

Description

Computes either the Wilcoxon Rank Sum or Signed Rank Statistics for all rows of a matrix simultaneously.

Usage

```
rowWilcoxon(X, cl, rand = NA)
```

Arguments

X	a matrix in which each row corresponds to a variable, and each column to an observation/sample
cl	a numeric vector consisting of ones and zeros. The length of cl must be equal to the number of observations. If cl consists of zeros and ones, Wilcoxon Rank Sums are computed. If cl contains only ones, Wilcoxon Signed Rank Statistics are calculated
rand	Sets the random number generator into a reproducible state. Ignored if Wilcoxon rank sums are computed, or X contains no Zeros

Details

If there are ties, then the ranks of the observations belonging to the same group of tied observations will be set to the maximum rank available for the corresponding group.

Value

a numeric vector containing Wilcoxon rank statistics for each row of X

Author(s)

Holger Schwender, <holger.schw@gmx.de>

See Also

[wilc.stat](#), [wilc.ebam](#)

sam

*Significance Analysis of Microarray***Description**

Performs a Significance Analysis of Microarrays (SAM). It is possible to perform one and two class analyses using either a modified t-statistic or a (standardized) Wilcoxon rank statistic, and a multiclass analysis using a modified F-statistic. Moreover, this function provides a SAM procedure for categorical data such as SNP data and the possibility to employ an user-written score function.

Usage

```
sam(data, cl, method = d.stat, delta = NULL, n.delta = 10, p0 = NA,
     lambda = seq(0, 0.95, 0.05), ncs.value = "max", ncs.weights = NULL,
     gene.names = dimnames(data)[[1]], q.version = 1, ...)
```

Arguments

- data** a matrix, a data frame, or an ExpressionSet object. Each row of data (or `exprs(data)`, respectively) must correspond to a gene, and each column to a sample
- cl** a vector of length `ncol(data)` containing the class labels of the samples. In the two class paired case, `cl` can also be a matrix with `ncol(data)` rows and 2 columns. If data is an ExpressionSet object, `cl` can also be a character string naming the column of `pData(data)` that contains the class labels of the samples.
- In the one-class case, `cl` should be a vector of 1's.
- In the two class unpaired case, `cl` should be a vector containing 0's (specifying the samples of, e.g., the control group) and 1's (specifying, e.g., the case group).
- In the two class paired case, `cl` can be either a numeric vector or a numeric matrix. If it is a vector, then `cl` has to consist of the integers between -1 and $-n/2$ (e.g., before treatment group) and between 1 and $n/2$ (e.g., after treatment group), where n is the length of `cl` and k is paired with $-k$, $k = 1, \dots, n/2$. If `cl` is a matrix, one column should contain -1's and 1's specifying, e.g., the before and the after treatment samples, respectively, and the other column should contain integer between 1 and $n/2$ specifying the $n/2$ pairs of observations.
- In the multiclass case and if `method = cat.stat`, `cl` should be a vector containing integers between 1 and g , where g is the number of groups.
- For examples of how `cl` can be specified, see the manual of **siggenes**
- method** a character string or a name specifying the method/function that should be used in the computation of the expression scores d . If `method = d.stat`, a modified t-statistic or F-statistic, respectively, will be computed as proposed by Tusher et al. (2001). If `method = wilc.stat`, a Wilcoxon rank sum statistic or Wilcoxon signed rank statistic will be used as expression score. For an analysis of categorical data such as SNP data, `method` can be set to `cat.stat`. In this case Pearson's Chi-squared statistic is computed for each row. It is also possible to use an user-written function to compute the expression scores. For details, see **Details**
- delta** a numeric vector specifying a set of values for the threshold Δ that should be used. If `NULL`, `n.delta` Δ values will be computed automatically

<code>n.delta</code>	a numeric value specifying the number of Δ values that will be computed over the range of all possible values for Δ if <code>delta</code> is not specified
<code>p0</code>	a numeric value specifying the prior probability π_0 that a gene is not differentially expressed. If NA, <code>p0</code> will be computed by the function <code>pi0.est</code>
<code>lambda</code>	a numeric vector or value specifying the λ values used in the estimation of the prior probability. For details, see <code>?pi0.est</code>
<code>ncs.value</code>	a character string. Only used if <code>lambda</code> is a vector. Either "max" or "paper". For details, see <code>?pi0.est</code>
<code>ncs.weights</code>	a numerical vector of the same length as <code>lambda</code> containing the weights used in the estimation of π_0 . By default no weights are used. For details, see <code>?pi0.est</code>
<code>gene.names</code>	a character vector of length <code>nrow(data)</code> containing the names of the genes. By default the row names of <code>data</code> are used
<code>q.version</code>	a numeric value indicating which version of the q-value should be computed. If <code>q.version=2</code> , the original version of the q-value, i.e. $\min\{\text{pFDR}\}$, will be computed. If <code>q.version=1</code> , $\min\{\text{FDR}\}$ will be used in the calculation of the q-value. Otherwise, the q-value is not computed. For details, see <code>?qvalue.cal</code>
<code>...</code>	further arguments of the specific SAM methods. If <code>method = d.stat</code> , see the help of <code>d.stat</code> . If <code>method = wilc.stat</code> , see the help of <code>wilc.stat</code> . If <code>method = cat.stat</code> , see the help of <code>cat.stat</code>

Details

`sam` provides SAM procedures for several types of analysis (one and two class analyses with either a modified t-statistic or a Wilcoxon rank statistic, a multiclass analysis with a modified F statistic, and an analysis of categorical data). It is, however, also possible to write your own function for another type of analysis. The required arguments of this function must be `data` and `cl`. This function can also have other arguments. The output of this function must be a list containing

- d:** a numeric vector consisting of the expression scores of the genes
- d.bar:** a numeric vector of the same length as `na.exclude(d)` specifying the expected expression scores under the null hypothesis
- p.value:** a numeric vector of the same length as `d` containing the raw, unadjusted p-values of the genes
- vec.false:** a numeric vector of the same length as `d` consisting of the one-sided numbers of falsely called genes, i.e. if $d > 0$ the numbers of genes expected to be larger than d under the null hypothesis, and if $d < 0$, the number of genes expected to be smaller than d under the null hypothesis
- s:** a numeric vector of the same length as `d` containing the standard deviations of the genes. If no standard deviation can be calculated, set `s=numeric(0)`
- s0:** a numeric value specifying the fudge factor. If no fudge factor is calculated, set `s0=numeric(0)`
- mat.samp:** a matrix with `B` rows and `ncol(data)` columns, where `B` is the number of permutations, containing the permutations used in the computation of the permuted d-values. If such a matrix is not computed, set `mat.samp=matrix(numeric(0))`
- msg:** a character string or vector containing information about, e.g., which type of analysis has been performed. `msg` is printed when the function `print` or `summary`, respectively, is called. If no such message should be printed, set `msg=""`
- fold:** a numeric vector of the same length as `d` consisting of the fold changes of the genes. If no fold change has been computed, set `fold=numeric(0)`

If this function is, e.g., called `foo`, it can be used by setting `method = foo` in `sam`. More detailed information and an example will be contained in the `siggenes` manual.

Value

an object of class SAM

Note

SAM was developed by Tusher et al. (2001).

!!! There is a patent pending for the SAM technology at Stanford University. !!!

Author(s)

Holger Schwender, <holger.schw@gmx.de>

References

Schwender, H., Krause, A. and Ickstadt, K. (2003). Comparison of the Empirical Bayes and the Significance Analysis of Microarrays. *Technical Report, SFB 475*, University of Dortmund, Germany.

Schwender, H. (2004). Modifying Microarray Analysis Methods for Categorical Data – SAM and PAM for SNPs. To appear in: *Proceedings of the the 28th Annual Conference of the GfKI*.

Tusher, V.G., Tibshirani, R., and Chu, G. (2001). Significance analysis of microarrays applied to the ionizing radiation response. *PNAS*, 98, 5116-5121.

See Also

[SAM-class.d.stat,wilc.stat,cac.stat](#)

Examples

```
## Not run:
# Load the package multtest and the data of Golub et al. (1999)
# contained in multtest.
library(multtest)
data(golub)

# golub.cl contains the class labels.
golub.cl

# Perform a SAM analysis for the two class unpaired case assuming
# unequal variances.
sam.out<-sam(golub,golub.cl,B=100,rand=123)
sam.out

# Obtain the Delta plots for the default set of Deltas
plot(sam.out)

# Generate the Delta plots for Delta = 0.2, 0.4, 0.6, ..., 2
plot(sam.out,seq(0.2,0.4,2))

# Obtain the SAM plot for Delta = 2
plot(sam.out,2)

# Get information about the genes called significant using
# Delta = 3 (since neither the gene names nor the chip type
# has been specified ll is set to FALSE to avoid a warning)
```

```

sam.sum3<-summary(sam.out,3,ll=FALSE)

# Obtain the rows of golub containing the genes called
# differentially expressed
sam.sum3@row.sig.genes

# and their names
golub.gnames[sam.sum3@row.sig.genes,3]

# The matrix containing the d-values, q-values etc. of the
# differentially expressed genes can be obtained by
sam.sum3@mat.sig

# Perform a SAM analysis using Wilcoxon rank sums
sam(golub,golub.cl,method="wilc.stat",rand=123)

# Now consider only the first ten columns of the Golub et al. (1999)
# data set. For now, let's assume the first five columns were
# before treatment measurements and the next five columns were
# after treatment measurements, where column 1 and 6, column 2
# and 7, ..., build a pair. In this case, the class labels
# would be
new.cl<-c(-(1:5),1:5)
new.cl

# and the corresponding SAM analysis for the two-class paired
# case would be
sam(golub[,1:10],new.cl,B=100,rand=123)

# Another way of specifying the class labels for the above paired
# analysis is
mat.cl<-matrix(c(rep(c(-1,1),e=5),rep(1:5,2)),10)
mat.cl

# and the above SAM analysis can also be done by
sam(golub[,1:10],mat.cl,B=100,rand=123)
## End(Not run)

```

sam.plot2

SAM Plot

Description

Generates a SAM plot for a specified value of Delta.

Usage

```

sam.plot2(object, delta, pos.stats = NULL, sig.col = 3, xlim = NULL,
          ylim = NULL, main = NULL, xlab = NULL, ylab = NULL, pty = "s",
          lab = c(10, 10, 7), pch = NULL, sig.cex = 1, ...)

```

Arguments

<code>object</code>	an object of class SAM
<code>delta</code>	a numeric value specifying the value of Δ for which the SAM plot should be generated
<code>pos.stats</code>	an integer between 0 and 2. If <code>pos.stats = 1</code> , general information as the number of significant genes and the estimated FDR for the specified value of <code>delta</code> will be plotted in the upper left corner of the plot. If <code>pos.stats = 2</code> , these information will be plotted in the lower right corner. If <code>pos.stats = 0</code> , no information will be plotted. By default, <code>pos.stats=1</code> if the expression score d can be both positive and negative, and <code>pos.stats = 2</code> if d can only take positive values
<code>sig.col</code>	a specification of the color of the significant genes. If <code>sig.col</code> has length 1, all the points corresponding to significant genes are marked in the color specified by <code>sig.col</code> . If <code>length(sig.col) == 2</code> , the down-regulated genes, i.e. the genes with negative expression score d , are marked in the color specified by <code>sig.col[1]</code> , and the up-regulated genes, i.e. the genes with positive d , are marked in the color specified by <code>sig.col[2]</code> . For a description of how colors are specified, see par
<code>xlim</code>	a numeric vector of length 2 specifying the x limits (minimum and maximum) of the plot
<code>ylim</code>	a numeric vector of length 2 specifying the y limits of the plot
<code>main</code>	a character string naming the main title of the plot
<code>xlab</code>	a character string naming the label of the x axis
<code>ylab</code>	a character string naming the label of the y axis
<code>pty</code>	a character specifying the type of plot region to be used. "s" (default) generates a square plotting region, and "m" the maximal plotting region
<code>lab</code>	a numeric vector of length 3 specifying the approximate number of tickmarks on the x axis and on the y axis and the label size
<code>pch</code>	either an integer specifying a symbol or a single character to be used as the default in plotting points. For a description of how <code>pch</code> can be specified, see par
<code>sig.cex</code>	a numerical value giving the amount by which the symbols of the significant genes should be scaled relative to the default
<code>...</code>	further graphical parameters. See plot.default and par

Value

a SAM plot

Author(s)

Holger Schwender, (holger.schw@gmx.de)

References

Tusher, V.G., Tibshirani, R., and Chu, G. (2001). Significance analysis of microarrays applied to the ionizing radiation response. *PNAS*, 98, 5116-5121.

See Also[SAM-class,sam](#)**Examples**

```
## Not run:
# Load the package multtest and the data of Golub et al. (1999)
# contained in multtest.
library(multtest)
data(golub)

# Perform a SAM analysis for the two class unpaired case assuming
# unequal variances.
sam.out<-sam(golub,golub.cl,B=100,rand=123)

# Generate a SAM plot for Delta = 2
sam.plot2(sam.out,2)

# Alternatively way of generating the same SAM plot
plot(sam.out,2)

## End(Not run)
```

```
shortenGeneDescription
      Shorten the Gene Description
```

Description

Shorten the entries of the column of a data frame containing the genes associated with the SNPs for which the data frame comprises annotations. Typically used in combination with, i.e. either within or after an application of, [buildSNPannotation](#)

Usage

```
shortenGeneDescription(dat, colname = "Gene", max.length = 2,
  sep = "///", add.ldots = TRUE)
```

Arguments

dat	a data frame. Typically, the output of buildSNPannotation
colname	character string comprising the name of the column of dat containing the gene description
max.length	integer specifying the maximum number of genes associated with the respective SNP that should be stored in the data frame. By default, the first two genes are retained. Shortened entries are marked by . . . at the end of the entries, when add.ldots = TRUE
sep	character string specifying the separation symbol between the different genes
add.ldots	should . . . be added at the entries which are shortened?

Value

the same data frame as `dat` with shortened entries in the column of `dat` named `colname`

Author(s)

Holger Schwender, (holger.schw@gmx.de)

See Also

[buildSNPannotation](#), [link.genes](#), [link.siggenes](#), [sam2html](#)

siggenes2excel

CSV file of a SAM or an EBAM object

Description

Generates a csv file for either a SAM or an EBAM object for the use in Excel. This csv file can contain general information as the number of differentially expressed genes and the estimated FDR, and gene-specific information on the differentially expressed genes.

Usage

```
sam2excel(object, delta, file, excel.version=1, n.digits = 3, what = "both",
          chip = "", quote = FALSE)
```

```
ebam2excel(object, delta, file, excel.version=1, n.digits = 4, what = "both",
           chip = "", quote = FALSE)
```

Arguments

<code>object</code>	either a SAM or an EBAM object
<code>delta</code>	a numerical value specifying the Delta value
<code>file</code>	character string naming the file in which the output should be stored. Must have the suffix ".csv"
<code>excel.version</code>	either 1 or 2. If <code>excel.version=1</code> (default) a csv file for the use in an Excel version with American standard settings (<code>sep=","</code> and <code>dec="."</code>) will be generated. If <code>excel.version=2</code> a csv file for the European standard setting (<code>sep=";"</code> and <code>dec=","</code>) will be generated
<code>n.digits</code>	integer specifying the number of decimal places used in the output
<code>what</code>	either "both", "stats" or "genes". If "stats" general information will be shown. If "genes" gene-specific information will be given. If "both" both general and gene-specific information will be shown
<code>entrez</code>	logical indicating if both the Entrez links and the symbols of the genes will be added to the output
<code>chip</code>	character string naming the chip type used in this analysis. Must be specified as in the meta-data section of Bioconductor (e.g., "hgu133a" for the Affymetrix HG-U133A chip). Only needed if <code>ll=TRUE</code> . If the argument <code>data</code> in <code>sam(data, cl, ...)</code> has been specified by an <code>ExpressionSet</code> object <code>chip</code> need not to be specified

quote logical indicating if character strings and factors should be surrounded by double quotes. For details see [write.table](#)

Author(s)

Holger Schwender, <holger.schw@gmx.de>

See Also

[sam](#), [sam2html](#), [ebam](#), [ebam2html](#)

siggenes2html *HTML page for a SAM or an EBAM object*

Description

Generates a html page for a SAM or an EBAM object. This html page can contain general information as the number of differentially expressed genes and the estimated FDR, the SAM or EBAM plot, and gene-specific information on the differentially expressed genes.

Usage

```
ebam2html(object, delta, filename, addStats = TRUE, addPlot = TRUE,
  addGenes = TRUE, findA0 = NULL, varName = NULL, entrez = TRUE,
  refseq = TRUE, symbol = TRUE, omim = FALSE, ug = FALSE,
  fullname = FALSE, chipname = "", cdfname = NULL,
  which.refseq = "NM", refsnp = NULL, max.associated = 2,
  n.digits = 3, bg.col = "white", text.col = "black", link.col = "blue",
  plotArgs = plotArguments(), plotFindArgs = plotFindArguments(),
  bg.plot.adjust = FALSE, plotname = NULL, plotborder = 0,
  tableborder = 1, new.window = TRUE, load = TRUE, ...)
```

```
sam2html(object, delta, filename, addStats = TRUE, addPlot = TRUE,
  addGenes = TRUE, varName = NULL, entrez = TRUE, refseq = TRUE,
  symbol = TRUE, omim = FALSE, ug = FALSE, fullname = FALSE,
  bonf = FALSE, chipname = "", cdfname = NULL, which.refseq = "NM",
  refsnp = NULL, max.associated = 2, n.digits = 3, bg.col = "white",
  text.col = "black", link.col = "blue", plotArgs = plotArguments(),
  bg.plot.adjust = FALSE, plotname = NULL, plotborder = 0,
  tableborder = 1, new.window = TRUE, load = TRUE, ...)
```

Arguments

object	a SAM or an EBAM object
delta	a numerical value specifying the Delta value
filename	character string naming the file in which the output should be stored. Must have the suffix ".html"
addStats	logical indicating if general information as the number of differentially expressed genes and the estimated FDR should be added to the html page
addPlot	logical indicating if the SAM/EBAM plot should be added to the html page

<code>addGenes</code>	logical indicating if gene-specific information on the differentially expressed genes should be added to the html page
<code>findA0</code>	an object of class <code>FindA0</code> . If specified, the numbers of differentially expressed genes and the estimated FDRs for the different possible values of the fudge factor and the corresponding plot of the logit-transformed posterior probabilities are included in the html file
<code>varName</code>	character string indicating how the variables should be named. If <code>NULL</code> , the variables will be referred to as SNPs in the output if <code>method = cat.stat</code> , and as Genes otherwise
<code>entrez</code>	logical indicating if Entrez links should be added to the output. Ignored if <code>addGenes = FALSE</code>
<code>refseq</code>	logical indicating if RefSeq links should be added to the output. Ignored if <code>addGenes = FALSE</code>
<code>symbol</code>	logical indicating if the gene symbols should be added to the output. Ignored if <code>addGenes = FALSE</code>
<code>omim</code>	logical indicating if OMIM links should be added to the output. Ignored if <code>addGenes = FALSE</code>
<code>ug</code>	logical indicating if UniGene links should be added to the output. Ignored if <code>addGenes = FALSE</code>
<code>fullname</code>	logical indicating whether the full gene names should be added to the output. Ignored if <code>addGenes = FALSE</code>
<code>bonf</code>	logical indicating whether Bonferroni adjusted p-values should be added to the output. Ignored if <code>addGenes = FALSE</code>
<code>chipname</code>	character string specifying the chip type used in the analysis. Must be specified as in the meta-data section of Bioconductor (e.g., "hgu133a" for the Affymetrix HG-U133A chip). Needs not to be specified if <code>cdfname</code> is specified. For Affymetrix SNP chips (starting with the 500k array set), <code>chipname</code> can be specified by the metadata package name, i.e. either by "pd.genomewidesnp.5", by "pd.genomewidesnp.6", by "pd.mapping250k.nsp", or by "pd.mapping250k.st" to add links to the Affymetrix webpage of the SNPs to the html output. Ignored if <code>addGenes = FALSE</code>
<code>cdfname</code>	character string specifying the cdf name of the used chip. Must exactly follow the nomenclatur of the Affymetrix chips (e.g., "HG-U133A" for the Affymetrix HG-U133A chip). If specified, links to the Affymetrix webpage for the interesting genes will be added to the output. If SNP chips are considered, <code>chipname</code> instead of <code>cdfname</code> must be specified for obtaining these links. Ignored if <code>addGenes = FALSE</code>
<code>which.refseq</code>	character string or vector naming the first two letters of the RefSeq links that should be displayed in the html file
<code>refsnp</code>	either a character vector or a data frame. If the former, <code>refsnp</code> contains the RefSNP IDs of the SNPs used in the SAM/EBAM analysis, where <code>names(refsnp)</code> specifies the names of these SNPs, i.e. their probe set IDs. If a data frame, then one column of <code>refsnp</code> must contain the RefSNP IDs of the SNPs, and the name of this column must be <code>RefSNP</code> . The other columns can contain additional annotations such as the chromosome or the physical position of each SNPs. The row names of <code>refsnp</code> must specify the SNPs, i.e. must be the probe set IDs of the SNPs. See buildSNPannotation for an automatical way to construct such a data frame given the corresponding metadata package

<code>max.associated</code>	integer specifying the maximum number of genes associated with the respective SNP displayed in the html output. If all entries should be shown, set <code>max.associated = 0</code> . This however might result in a very large html output. For details, see shortenGeneDescription
<code>n.digits</code>	integer specifying the number of decimal places used in the output
<code>bg.col</code>	specification of the background color of the html page. See par for how colors can be specified
<code>text.col</code>	specification of the color of the text used in the html page. See par for how colors can be specified
<code>link.col</code>	specification of the color of the links used in the html file. See par for how colors can be specified
<code>plotArgs</code>	further arguments for generating the SAM/EBAM plot. These are the arguments used by the SAM/EBAM specific <code>plot</code> method. See the help of plotArguments for these arguments. Ignored if <code>addPlot = FALSE</code>
<code>plotFindArgs</code>	further arguments for generating the (logit-transformed) posterior probabilities for the different values of the fudge factor. Ignored if <code>findA0 = NULL</code> . See the help of plotFindArguments for these arguments
<code>bg.plot.adjust</code>	logical indicating if the background color of the SAM plot should be the same as the background color of the html page. If <code>FALSE</code> (default) the background of the plot is white. Ignored if <code>addPlot = FALSE</code>
<code>plotname</code>	character string naming the file in which the SAM/EBAM plot is stored. This file is needed when the SAM/EBAM plot should be added to the html page. If not specified the SAM/EBAM plot will be stored as png file in the same folder as the html page. Ignored if <code>addPlot = FALSE</code>
<code>plotborder</code>	integer specifying the thickness of the border around the plot. By default, <code>plotborder = 0</code> , i.e. no border is drawn around the plot. Ignored if <code>addPlot = FALSE</code>
<code>tableborder</code>	integer specifying the thickness of the border of the table. Ignored if <code>addGenes = FALSE</code>
<code>new.window</code>	logical indicating if the links should be opened in a new window
<code>load</code>	logical value indicating whether to attempt to load the required annotation data package if it is not already loaded. For details, see the man page of <code>lookUp</code> in the package annotate
<code>...</code>	further graphical arguments for the SAM/EBAM plot. See plot.default and par . Ignored if <code>addPlot = FALSE</code>

Author(s)

Holger Schwender, <holger.schw@gmx.de>

See Also

[SAM-class](#), [sam](#), [EBAM-class](#), [ebam](#), [link.genes](#), [link.siggenes](#), [plotArguments](#), [plotFindArguments](#)

`sumSAM-class`*Classes sumSAM and sumEBAM*

Description

These classes are just used for a nicer output of the summary of an object of class SAM or EBAM, respectively.

Objects from the Class

Objects can be created by calls of the form `new("sumSAM", ...)`, or by using the function `summary(object)` when `object` is a SAM-class object.

Objects can be created by calls of the form `new("sumEBAM", ...)`, or by using the function `summary(object)` when `object` is an EBAM-class object.

Slots

row.sig.genes: Object of class "numeric" consisting of the row numbers of the significant genes in the data matrix

mat.fdr: Object of class "matrix" containing general information as the number of differentially expressed genes and the estimated FDR for either one or several values of Delta.

mat.sig: Object of class "data.frame" containing gene-specific statistics as the d-values (or z-values) and the q-values or (the local FDR) of the differentially expressed genes.

list.args: Object of class "list" consisting of some of the specified arguments of `summary` needed for internal use.

Methods

print `signature(x = "sumSAM")`: Prints the output of the SAM-specific method summary.

show `signature(object = "sumSAM")`: Shows the output of the summary of a SAM analysis.

print `signature(x = "sumEBAM")`: Prints the output of the EBAM-specific method summary.

show `signature(object = "sumEBAM")`: Shows the output of the summary of a EBAM analysis.

Author(s)

Holger Schwender, <holger.schw@gmx.de>

See Also

[SAM-class](#), [EBAM-class](#)

 wilc.ebam

EBAM Analysis Using Wilcoxon Rank Statistics

Description

Generates the required statistics for an Empirical Bayes Analysis of Microarrays analysis using standardized Wilcoxon rank statistics.

Should not be called directly, but via `ebam(..., method = wilc.ebam)`.

Usage

```
wilc.ebam(data, cl, approx50 = TRUE, ties.method = c("min", "random",
  "max"), use.offset = TRUE, df.glm = 5, use.row = FALSE, rand = NA)
```

Arguments

<code>data</code>	a matrix or a data frame. Each row of <code>data</code> must correspond to a variable, and each column to a sample
<code>cl</code>	a numeric vector of length <code>ncol(data)</code> containing the class labels of the samples. In the two class paired case, <code>cl</code> can also be a matrix with <code>ncol(data)</code> rows and 2 columns. For details on how <code>cl</code> should be specified, see ebam
<code>approx50</code>	if <code>TRUE</code> , the null distribution will be approximated by the standard normal distribution. Otherwise, the exact null distribution is computed. This argument will automatically be set to <code>FALSE</code> if there are less than 50 samples in each of the groups
<code>ties.method</code>	either "min" (default), "random", or "max". If "random", the ranks of ties are randomly assigned. If "min" or "max", the ranks of ties are set to the minimum or maximum rank, respectively. For details, see the help of rank . If <code>use.row = TRUE</code> , then <code>ties.method = "max"</code> is used. For the handling of Zeros, see Details
<code>use.offset</code>	should an offset be used in the Poisson regression employed to estimate the density of the observed Wilcoxon rank sums? If <code>TRUE</code> , the log-transformed values of the null density is used as offset
<code>df.glm</code>	integer specifying the degrees of freedom of the natural cubic spline employed in the Poisson regression
<code>use.row</code>	if <code>TRUE</code> , rowWilcoxon is used to compute the Wilcoxon rank statistics
<code>rand</code>	numeric value. If specified, i.e. not <code>NA</code> , the random number generator will be set into a reproducible state

Details

Standardized versions of the Wilcoxon rank statistics are computed. This means that $W^* = (W - W_{mean})/W_{sd}$ is used as expression score z , where W is the usual Wilcoxon rank sum statistic or Wilcoxon signed rank statistic, respectively.

In the computation of these statistics, the ranks of ties are by default set to the minimum rank. In the computation of the Wilcoxon signed rank statistic, zeros are randomly set either to a very small positive or negative value.

If there are less than 50 observations in each of the groups, the exact null distribution will be used. If there are more than 50 observations in at least one group, the null distribution will by default be approximated by the standard normal distribution. It is, however, still possible to compute the exact null distribution by setting `approx50` to `FALSE`.

Value

a list of statistics required by `ebam`

Author(s)

Holger Schwender, holger.schw@gmx.de

References

Efron, B., Storey, J.D., Tibshirani, R. (2001). Microarrays, empirical Bayes methods, and the false discovery rate, *Technical Report*, Department of Statistics, Stanford University.

Schwender, H., Krause, A. and Ickstadt, K. (2003). Comparison of the Empirical Bayes and the Significance Analysis of Microarrays. *Technical Report*, SFB 475, University of Dortmund, Germany.

See Also

[ebam](#)

wilc.stat

SAM Analysis Using Wilcoxon Rank Statistics

Description

Generates the required statistics for a Significance Analysis of Microarrays analysis using standardized Wilcoxon rank statistics.

Should not be called directly, but via `sam(..., method = wilc.stat)`.

Usage

```
wilc.stat(data, cl, gene.names = NULL, R.fold = 1, use.dm = FALSE,
          R.unlog = TRUE, na.replace = TRUE, na.method = "mean",
          approx50 = TRUE, ties.method=c("min", "random", "max"),
          use.row = FALSE, rand = NA)
```

Arguments

<code>data</code>	a matrix or a data frame. Each row of <code>data</code> must correspond to a gene, and each column to a sample
<code>cl</code>	a numeric vector of length <code>ncol(data)</code> containing the class labels of the samples. In the two class paired case, <code>cl</code> can also be a matrix with <code>ncol(data)</code> rows and 2 columns. For details on how <code>cl</code> should be specified, see <code>?sam</code>
<code>gene.names</code>	a character vector of length <code>nrow(data)</code> containing the names of the genes

<code>R.fold</code>	a numeric value. If the fold change of a gene is smaller than or equal to <code>R.fold</code> , or larger than or equal to $1/R.fold$, respectively, then this gene will be excluded from the SAM analysis. The expression score d of excluded genes is set to NA. By default, <code>R.fold</code> is set to 1 such that all genes are included in the SAM analysis. Setting <code>R.fold</code> to 0 or a negative value will avoid the computation of the fold change. The fold change is only computed in the two-class unpaired case
<code>use.dm</code>	if TRUE, the fold change is computed by 2 to the power of the difference between the mean log2 intensities of the two groups, i.e. 2 to the power of the numerator of the test statistic. If FALSE, the fold change is determined by computing 2 to the power of <code>data</code> (if <code>R.unlog = TRUE</code>) and then calculating the ratio of the mean intensity in the group coded by 1 to the mean intensity in the group coded by 0. The latter is the default, as this definition of the fold change is used in Tusher et al. (2001)
<code>R.unlog</code>	if TRUE, the anti-log of <code>data</code> will be used in the computation of the fold change. Otherwise, <code>data</code> is used. This transformation should be done if <code>data</code> is log2-transformed. (In a SAM analysis, it is highly recommended to use log2-transformed expression data.) Ignored if <code>use.dm = TRUE</code>
<code>na.replace</code>	if TRUE, missing values will be removed by the genewise/rowwise statistic specified by <code>na.method</code> . If a gene has less than 2 non-missing values, this gene will be excluded from further analysis. If <code>na.replace = FALSE</code> , all genes with one or more missing values will be excluded from further analysis. The expression score d of excluded genes is set to NA
<code>na.method</code>	a character string naming the statistic with which missing values will be replaced if <code>na.replace=TRUE</code> . Must be either "mean" (default) or median
<code>approx50</code>	if TRUE, the null distribution will be approximated by the standard normal distribution. Otherwise, the exact null distribution is computed. This argument will automatically be set to FALSE if there are less than 50 samples in each of the groups
<code>ties.method</code>	either "min" (default), "random", or "max". If "random", the ranks of ties are randomly assigned. If "min" or "max", the ranks of ties are set to the minimum or maximum rank, respectively. For details, see the help of rank . If <code>use.row = TRUE</code> , <code>ties.method = "max"</code> will be used. For the handling of Zeros, see Details
<code>use.row</code>	if TRUE, <code>rowWilcoxon</code> is used to compute the Wilcoxon rank statistics
<code>rand</code>	numeric value. If specified, i.e. not NA, the random number generator will be set into a reproducible state

Details

Standardized versions of the Wilcoxon rank statistics are computed. This means that $W_* = (W - W_{mean})/W_{sd}$ is used as expression score d , where W is the usual Wilcoxon rank sum statistic or Wilcoxon signed rank statistic, respectively.

In the computation of these statistics, the ranks of ties are by default set to the minimum rank. In the computation of the Wilcoxon signed rank statistic, zeros are randomly set either to a very small positive or negative value.

If there are less than 50 observations in each of the groups, the exact null distribution will be used. If there are more than 50 observations in at least one group, the null distribution will by default be approximated by the standard normal distribution. It is, however, still possible to compute the exact null distribution by setting `approx50` to FALSE.

Value

a list containing statistics required by `sam`

Author(s)

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References

Schwender, H., Krause, A. and Ickstadt, K. (2003). Comparison of the Empirical Bayes and the Significance Analysis of Microarrays. *Technical Report, SFB 475*, University of Dortmund, Germany.

Tusher, V.G., Tibshirani, R., and Chu, G. (2001). Significance analysis of microarrays applied to the ionizing radiation response. *PNAS*, 98, 5116-5121.

See Also

[SAM-class,sam](#)

z.ebam

EBAM analysis Using t- or F-test

Description

Computes the required statistics for an Empirical Bayes Analysis with a modified t- or F-test.

Should not be called directly, but via `ebam(..., method = z.ebam)` or `find.a0(..., method = z.find)`, respectively.

Usage

```
z.ebam(data, cl, a0 = NULL, quan.a0 = NULL, B = 100, var.equal = FALSE,
       B.more = 0.1, B.max = 30000, n.subset = 10, fast = FALSE,
       n.interval = 139, df.ratio = NULL, rand = NA)

z.find(data, cl, B = 100, var.equal = FALSE, B.more = 0.1,
       B.max = 30000)
```

Arguments

<code>data</code>	a matrix, data frame or ExpressionSet object. Each row of <code>x</code> (or <code>exprs(x)</code>) must correspond to a gene, and each column to a sample
<code>cl</code>	a numeric vector of length <code>ncol(x)</code> containing the class labels of the samples. For details on how <code>cl</code> should be specified, see ebam
<code>a0</code>	a numeric value specifying the fudge factor
<code>quan.a0</code>	a numeric value between 0 and 1 specifying the quantile of the standard deviations of the genes that is used as fudge factor
<code>B</code>	an integer indicating how many permutations should be used in the estimation of the null distribution

<code>var.equal</code>	should the ordinary t-statistic assuming equal group variances be computed? If FALSE (default), Welch's t-statistic will be computed
<code>B.more</code>	a numeric value. If the number of all possible permutations is smaller than or equal to $(1+B.more)*B$, full permutation will be done. Otherwise, B permutations are used. This avoids that B permutations will be used – and not all permutations – if the number of all possible permutations is just a little larger than B
<code>B.max</code>	a numeric value. If the number of all possible permutations is smaller than or equal to <code>B.max</code> , B randomly selected permutations will be used in the computation of the null distribution. Otherwise, B random draws of the group labels are used. In the latter way of permuting, it is possible that some of the permutations are used more than once
<code>n.subset</code>	an integer specifying in how many subsets the B permutations should be split when computing the permuted test scores. Note that the meaning of <code>n.subset</code> differs between the SAM and the EBAM functions
<code>fast</code>	if FALSE the exact number of permuted test scores that are more extreme than a particular observed test score is computed for each of the genes. If TRUE, a crude estimate of this number is used
<code>n.interval</code>	the number of intervals used in the logistic regression with repeated observations for estimating the ratio f_0/f
<code>df.ratio</code>	integer specifying the degrees of freedom of the natural cubic spline used in the logistic regression with repeated observations
<code>rand</code>	integer. If specified, i.e. not NA, the random number generator will be set into a reproducible state

Value

a list of object required by `find.a0` or `ebam`, respectively

Author(s)

Holger Schwender, <holger.schw@gmx.de>

References

Efron, B., Tibshirani, R., Storey, J.D. and Tusher, V. (2001). Empirical Bayes Analysis of a Microarray Experiment, *JASA*, 96, 1151-1160.

Schwender, H., Krause, A. and Ickstadt, K. (2003). Comparison of the Empirical Bayes and the Significance Analysis of Microarrays. *Technical Report*, SFB 475, University of Dortmund, Germany.

See Also

[ebam](#), [find.a0](#)

Index

*Topic **IO**

- link.genes, 28
- link.siggenes, 29
- list.siggenes, 31
- siggenes2excel, 45
- siggenes2html, 46

*Topic **classes**

- EBAM-class, 1
- FindA0class, 3
- SAM-class, 4
- sumSAM-class, 49

*Topic **documentation**

- help.ebam, 25
- help.finda0, 26
- help.sam, 27

*Topic **file**

- link.genes, 28
- link.siggenes, 29
- list.siggenes, 31
- siggenes2excel, 45
- siggenes2html, 46

*Topic **hplot**

- delta.plot, 15
- plotArguments, 34
- plotFindArguments, 35
- sam.plot2, 42

*Topic **htest**

- cat.ebam, 8
- cat.stat, 11
- d.stat, 12
- ebam, 17
- find.a0, 20
- findDelta, 23
- pi0.est, 33
- qvalue.cal, 36
- rowWilcoxon, 38
- sam, 39
- wilc.ebam, 50
- wilc.stat, 51
- z.ebam, 53

*Topic **misc**

- buildSNPannotation, 7

*Topic **optimize**

- fudge2, 24

*Topic **smooth**

- denspr, 16
- pi0.est, 33

*Topic **utilities**

- nclass.wand, 32
- shortenGeneDescription, 44

- args.ebam (*help.ebam*), 25
- args.finda0 (*help.finda0*), 26
- args.sam, 6
- args.sam (*help.sam*), 27

- buildSNPannotation, 7, 28, 30, 44, 45, 47

- cat.ebam, 8, 17–19
- cat.stat, 11, 40, 41

- d.stat, 12, 40, 41
- delta.plot, 6, 15
- denspr, 10, 16, 33

- EBAM (*EBAM-class*), 1
- ebam, 2, 4, 17, 22, 24, 25, 31, 32, 46, 48, 50, 51, 53, 54

- EBAM-class, 4, 19, 25, 48, 49
- EBAM-class, 1
- ebam2excel (*siggenes2excel*), 45
- ebam2html, 31, 35, 36, 46
- ebam2html (*siggenes2html*), 46

- find.a0, 2–4, 18, 19, 20, 26, 54
- FindA0 (*FindA0class*), 3
- FindA0-class, 2, 22, 26
- FindA0-class (*FindA0class*), 3
- FindA0class, 3
- findDelta, 23
- fudge2, 24

- help.ebam, 25
- help.finda0, 26
- help.sam, 27

- identify, SAM-method (*SAM-class*), 4

- link.genes, 8, 28, 31, 45, 48
- link.siggenes, 8, 29, 29, 45, 48
- list.siggenes, 31

- nclass.scott, 16
- nclass.wand, 32

- par, 34–36, 43, 48
- pi0.est, 18, 21, 33, 37
- plot, EBAM-method (*EBAM-class*), 1
- plot, FindA0-method (*FindA0class*), 3
- plot, SAM-method (*SAM-class*), 4
- plot.default, 43, 48
- plotArguments, 34, 48
- plotFindArguments, 35, 48
- print, EBAM-method (*EBAM-class*), 1
- print, FindA0-method (*FindA0class*), 3
- print, SAM-method (*SAM-class*), 4
- print, sumEBAM-method (*sumSAM-class*), 49
- print, sumSAM-method (*sumSAM-class*), 49

- qvalue.cal, 34, 36

- rank, 50, 52
- rowRanksWilc (*rowWilcoxon*), 38
- rowWilcoxon, 38, 50, 52

- SAM (*SAM-class*), 4
- sam, 6, 10, 12, 14, 15, 24, 27, 29, 31, 32, 34, 37, 39, 44, 46, 48, 53
- SAM-class, 10, 12, 14, 15, 24, 27, 29, 34, 37, 41, 44, 48, 49, 53
- SAM-class, 4
- sam.dstat, 6, 24, 27
- sam.dstat (*d.stat*), 12
- sam.plot2, 6, 42
- sam.snp, 6, 27
- sam.snp (*cat.stat*), 11
- sam.wilc, 6, 27
- sam.wilc (*wilc.stat*), 51
- sam2excel (*siggenes2excel*), 45
- sam2html, 8, 29, 31, 35, 45, 46
- sam2html (*siggenes2html*), 46
- shortenGeneDescription, 8, 29, 30, 44, 48
- show, EBAM-method (*EBAM-class*), 1
- show, FindA0-method (*FindA0class*), 3
- show, SAM-method (*SAM-class*), 4

- show, sumEBAM-method (*sumSAM-class*), 49
- show, sumSAM-method (*sumSAM-class*), 49

- siggenes2excel, 45
- siggenes2html, 46
- sumEBAM-class (*sumSAM-class*), 49
- summary, EBAM-method (*EBAM-class*), 1
- summary, SAM-method (*SAM-class*), 4
- sumSAM-class, 49

- wilc.ebam, 18, 19, 38, 50
- wilc.stat, 38, 40, 41, 51
- write.table, 46

- z.ebam, 18, 19, 53
- z.find, 21
- z.find (*z.ebam*), 53