Package 'viper'

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`aecdf` *Approximate empirical commulative distribution function*

Description

This function generates an empirical null model that computes a normalized statistics and p-value

Usage

```
aecdf(dnull, symmetric = FALSE, n = 100)
```

Arguments

dnull	Numerical vector representing the null model
symmetric	Logical, whether the distribution should betreated as symmetric around zero and only one tail should be approximated
n	Integer indicating the number of points to evaluate the empirical cummulative probability function

Value

function with two parameters, x and alternative

---

approxk2d *approxk2d*

Description

This function uses a gaussian kernel to estimate the joint density distribution at the specified points

Usage

```
approxk2d(x, gridsize = 128, pos = x)
```

Arguments

x	Matrix of x and y points
gridsize	number or vector indicating the size of the greed where to estimate the density
pos	Matrix of coordinates to evaluate the density

Value

Vector of density estimates

Examples

```
x <- rnorm(500)
y <- x+rnorm(500)
kde2 <- approxk2d(cbind(x, y))
plot(x, y, pch=20, col=hsv(0, kde2/max(kde2), 1))
```

aracne2regulon *Regulon object generation from ARACNe results*

Description

This function generates a regulon object from ARACNe results and the corresponding expression dataset

Usage

```
aracne2regulon(afile, eset, gene = FALSE, format = c("adj", "3col"),
  verbose = TRUE)
```

Arguments

afile	Character string indicating the name of the ARACNe network file
eset	Either a character string indicating the name of the expression-dataset file, a ExpressionSet object or a gene expression matrix with genes (probes) in rows and samples in columns
gene	Logical, whether the probes should be collapsed at the gene level
format	Character string, indicating the format of the aracne file, either adj for adjacency matrixes generated by aracne, or 3col when the interactome is represented by a 3 columns text file, with regulator in the first column, target in the second and mutual information in the third column
verbose	Logical, whether progression messages should be printed in the terminal.

Value

Regulon object

See Also

msviper, viper

Examples

```
data(bcellViper, package="bcellViper")
adjfile <- file.path(find.package("bcellViper"), "aracne", "bcellaracne.adj")
regul <- aracne2regulon(adjfile, dset)
print(regul)
```

aracne2regulon4cnv *Regulon object generation from ARACNe results corrected by cnv*

Description

This function generates a regulon object from ARACNe results and the corresponding expression dataset when correction for CNV have been applied

Usage

```
aracne2regulon4cnv(afile, eset, regeset, gene = FALSE,
  format = c("adj", "3col"), verbose = TRUE)
```

Arguments

afile	Character string indicating the name of the ARACNe network file
eset	Either a character string indicating the name of the expression-dataset file, a ExpressionSet object or a gene expression matrix with genes (probes) in rows and samples in columns, where the expression was corrected by CNV
regeset	Either a character string indicating the name of the expression-dataset file, a ExpressionSet object or a gene expression matrix with genes (probes) in rows and samples in columns
gene	Logical, whether the probes should be collapsed at the gene level
format	Character string, indicating the format of the aracne file, either adj for adjacency matrixes generated by aracne, or 3col when the interactome is represented by a 3 columns text file, with regulator in the first column, target in the second and mutual information in the third column
verbose	Logical, whether progression messages should be printed in the terminal.

Value

Regulon object

See Also

msviper, viper

Examples

```
data(bcellViper, package="bcellViper")
adjfile <- file.path(find.package("bcellViper"), "aracne", "bcellaracne.adj")
regul <- aracne2regulon(adjfile, dset)
print(regul)
```

aREA *analytic Rank-based Enrichment Analysis*

Description

This function performs wREA enrichment analysis on a set of signatues

Usage

```
aREA(eset, regulon, method = c("auto", "matrix", "loop"), minsize = 20,
  cores = 1, wm = NULL, verbose = FALSE)
```

Arguments

eset	Matrix containing a set of signatures, with samples in columns and traits in rows
regulon	Regulon object
method	Character string indicating the implementation, either auto, matrix or loop
minsize	Interger indicating the minimum allowed size for the regulons
cores	Integer indicating the number of cores to use (only 1 in Windows-based systems)
wm	Optional numeric matrix of weights (0; 1) with same dimension as eset
verbose	Logical, whether a progress bar should be shown

Value

List of two elements, enrichment score and normalized enrichment score

as.dist.signatureDistance *Distance matrix from signatureDistance objects*

Description

This function transforms a signatureDistance object into a dist object

Usage

```
## S3 method for class 'signatureDistance'
as.dist(m, diag = FALSE, upper = FALSE)
```

Arguments

m	signatureDistance object
diag	parameter included for compatibility
upper	parameter included for compatibility

Value

Object of class dist

bootstrapmsviper *msviper bootstraps integration*

Description

This function integrates the bootstrap msviper results

Usage

```
bootstrapmsviper(mobj, method = c("mean", "median", "mode"))
```

Arguments

mobj	msviper object
method	Character string indicating the method to use, either mean, median or mode

Value

msviper object

See Also

msviper

Examples

```
data(bcellViper, package="bcellViper")
sig <- bootstrapTtest(dset, "description", c("CB", "CC"), "N")
mra <- msviper(sig, regulon)
plot(mra, cex=.7)
```

bootstrapTtest *Bootstrapped signature by t-test*

Description

This function generates a bootstrapped signature matrix by t-test

Usage

```
bootstrapTtest(x, ...)

## S4 method for signature 'matrix'
bootstrapTtest(x, y, per = 100, seed = 1,
  cores = 1, verbose = TRUE)

## S4 method for signature 'ExpressionSet'
bootstrapTtest(x, pheno, group1, group2,
  per = 100, seed = 1, verbose = TRUE)
```

Arguments

x	Matrix containing the test dataset
...	Additional parameters added to keep compatibility
y	Matrix containing the reference dataset
per	Integer indicating the number of permutations
seed	Integer indicating the seed for the permutations, 0 for disable it
cores	Integer indicating the number of cores to use (set to 1 in Windows-based systems)
verbose	Logical whether progress should be reported
pheno	Character string indicating the phenotype data to use
group1	Vector of character strings indicating the category from phenotype pheno to use as test group
group2	Vector of character strings indicating the category from phenotype pheno to use as control group

Value

Matrix of z-scores with genes in rows and permutations in columns

See Also

msviper

Examples

```
data(bcellViper, package="bcellViper")
d1 <- exprs(dset)
sig <- bootstrapTtest(d1[, 1:10], d1[, 11:20], per=100)
dim(sig)
plot(density(sig[1907, ]))
data(bcellViper, package="bcellViper")
sig <- bootstrapTtest(dset, "description", "CB", "N", per=100)
dim(sig)
plot(density(sig[1907, ]))
```

---

bootstrapViper *bootstrapsViper*

Description

This function performs a viper analysis with bootstraps

Usage

```
bootstrapViper(eset, regulon, nes = TRUE, bootstraps = 10,
  eset.filter = FALSE, adaptive.size = TRUE, minsize = 20,
  mvws = 1, cores = 1, verbose = TRUE)
```

Arguments

eset	ExpressionSet object or Numeric matrix containing the expression data, with samples in columns and genes in rows
regulon	Object of class regulon
nes	Logical, whether the enrichment score reported should be normalized
bootstraps	Integer indicating the number of bootstraps iterations to perform. Only the scale method is implemented with bootstraps.
eset.filter	Logical, whether the dataset should be limited only to the genes represented in the interactome
adaptive.size	Logical, whether the weighting scores should be taken into account for computing the regulon size
minsize	Integer indicating the minimum number of targets allowed per regulon
mvws	Number or vector indicating either the exponent score for the metaViper weights, or the inflection point and trend for the sigmoid function describing the weights in metaViper
cores	Integer indicating the number of cores to use (only 1 in Windows-based systems)
verbose	Logical, whether progression messages should be printed in the terminal

Value

A list containing a matrix of inferred activity for each regulator gene in the network across all samples and the corresponding standard deviation computed from the bootstrap iterations.

See Also

viper

Examples

```
data(bcellViper, package="bcellViper")
d1 <- exprs(dset)
res <- viper(d1[, 1:50], regulon, bootstraps=10) # Run only on 50 samples to reduce computation time
dim(d1)
d1[1:5, 1:5]
regulon
dim(res$nes)
res$nes[1:5, 1:5]
res$sd[1:5, 1:5]
```

---

comNames *Combinatorial annotation*

Description

This function convers combinatorial annotations

Usage

```
comNames(x, annot)
```

Arguments

x	Character vector of gene name combinations, where the combinations are separated by –
annot	Vector of gene names with geneID as names attribute

Value

Converted annotations

See Also

msviper

---

distMode *Mode of continuous distributions*

Description

This function computes the mode for continuous distributions

Usage

```
distMode(x, adj = 1)
```

Arguments

x	Numeric data vector
adj	Number indicating the adjustment for the kernel bandwidth

Value

Number

Examples

```
data(bcellViper, package="bcellViper")
d1 <- exprs(dset)
mean(d1[, 1])
median(d1[, 1])
distMode(d1[, 1])
plot(density(d1[, 1]))
abline(v=c(mean(d1[, 1]), median(d1[, 1]), distMode(d1[, 1])), col=c("green", "red", "blue"))
legend("topleft", c("Mean", "Median", "Mode"), col=c("green", "red", "blue"), lwd=4)
```

fcvarna *Variance of columns for arrays with NA values*

Description

This function computes the variance by columns ignoring NA values

Usage

```
fcvarna(x)
```

Arguments

x	Numeric matrix

Value

1-column matrix with the variance by column results

Examples

```
data(bcellViper, package="bcellViper")
tmp <- exprs(dset)[, 1:10]
tmp[round(runif(100, 1, length(tmp)))] <- NA
fcvarna(tmp)
```

filterColMatrix *Filter for columns of a matrix with no loss of col and row names*

Description

This function filters the columns of a matrix returning always a two dimensional matrix

Usage

```
filterColMatrix(x, filter)
```

Arguments

x	Matrix
filter	Logical or numerical index of columns

Value

Matrix

filterCV *Coefficient of variation filter*

Description

This function filter redundant probes based on the highest coefficient of variation

Usage

```
filterCV(expset, ...)

## S4 method for signature 'matrix'
filterCV(expset)

## S4 method for signature 'ExpressionSet'
filterCV(expset)
```

Arguments

expset	Expression set or Matrix containing the gene expression data, with samples in columns and probes in rows. The colnames attribute should contain the sample names and the rownames attribute should contain the unique geneIDs
...	Additional parameters added to keep compatibility

Value

CV filtered dataset

Examples

```
data(bcellViper, package="bcellViper")
d1 <- exprs(dset)
tmp <- rownames(d1)
tmp[round(runif(10, 1, length(tmp)))] <- tmp[1]
rownames(d1) <- tmp
dim(d1)
d1 <- filterCV(d1)
dim(d1)
```

filterRowMatrix *Filter for rows of a matrix with no loss of col and row names*

Description

This function filters the rows of a matrix returning always a two dimensional matrix

Usage

```
filterRowMatrix(x, filter)
```

Arguments

x	Matrix
filter	Logical or numerical index of rows

Value

Matrix

---

frcv *Coeficient of variations for rows*

Description

This function computes the coefficient of variation (CV) by rows

Usage

```
frcv(x)
```

Arguments

x	Numeric matrix

Value

1-column matrix with the coefficient of variation by row results

Examples

```
data(bcellViper, package="bcellViper")
tmp <- exprs(dset)[1:10, ]
tmp[round(runif(100, 1, length(tmp)))] <- NA
frcv(tmp)
```

---

frvarna *Variance of rows for arrays with NA values*

Description

This function computes the variance by rows ignoring NA values

Usage

```
frvarna(x)
```

Arguments

x	Numeric matrix

Value

1-column matrix with the variance by row results

Examples

```
data(bcellViper, package="bcellViper")
tmp <- exprs(dset)[1:10, ]
tmp[round(runif(100, 1, length(tmp)))] <- NA
frvarna(tmp)
```

`groupPwea3` *Proportionally Weighted Enrichment Analysis for gene-set groups*

Description

This function performs a Proportionally Weighted Enrichment Analysis on groups of gene-sets

Usage

```
groupPwea3(rlist, groups, nullpw = NULL, alternative = c("two.sided",
  "less", "greater"), per = 0, minsize = 5, cores = 1,
  verbose = TRUE)
```

Arguments

`rlist`	Named vector containing the scores to rank the expression profile or matrix where columns contains bootstraped signatures
`groups`	List of gene-sets (regulons), each component is a list of two vectors: *TFmode* containing the TFMoA index (-1; 1) and *likelihood* containing the interaction relative likelihood
`nullpw`	Numerical matrix representing the null model, with genes as rows (geneID as rownames) and permutations as columns
`alternative`	Character string indicating the alternative hypothesis, either two.sided, greater or less
`per`	Integer indicating the number of permutations for the genes in case "nullpw" is ommited
`minsize`	Integer indicating the minimum size for the regulons
`cores`	Integer indicating the number of cores to use (only 1 in Windows-based systems)
`verbose`	Logical, whether progression messages should be printed in the terminal

Value

A list containing four matrices:

es Enrichment score

nes Normalized Enrichment Score

size Regulon size

p.value Enrichment p.value

integrateSignatures *Integrate signatures*

Description

This function integrates signatures represented as columns in the input matrix using self-weighting average

Usage

```
integrateSignatures(signature, score = 1)
```

Arguments

signature	Numeric matrix containing the signatures as z-scores or NES, genes in rows and signatures in columns
score	Number indicating the exponent score for the weight

Value

Vector containing the integrated signatures

Examples

```
data(bcellViper, package="bcellViper")
sig <- bootstrapTtest(dset, "description", "CB", "N", per=100)
isig <- integrateSignatures(sig)
plot(density(sig))
lines(density(isig, adj=1.5), col="red")
```

ledge *Leading-edge analysis*

Description

This function performs a Leading-Edge analysis on an object of class msviper

Usage

```
ledge(mobj)
```

Arguments

mobj	msviper class object

Value

msviper object updated with a ledge slot

See Also

msviper

Examples

```
data(bcellViper, package="bcellViper")
sig <- rowTtest(dset, "description", "CB", "N")$statistic
mra <- msviper(sig, regulon)
mra <- ledge(mra)
summary(mra)
```

---

loadExpset *Loading expression sets*

Description

This function load an expression file into a matrix

Usage

```
loadExpset(filename)
```

Arguments

filename	Character string indicating the name of the expression file

Value

List containing a numeric matrix of expression data with samples in columns and probes in rows; and a vector of gene mapping annotations

---

msviper *msVIPER*

Description

This function performs MAster Regulator INference Analysis

Usage

```
msviper(ges, regulon, nullmodel = NULL, pleiotropy = FALSE,
  minsize = 25, adaptive.size = FALSE, ges.filter = TRUE,
  synergy = 0, level = 10, pleiotropyArgs = list(regulators = 0.05,
  shadow = 0.05, targets = 10, penalty = 20, method = "adaptive"),
  cores = 1, verbose = TRUE)
```

Arguments

ges	Vector containing the gene expression signature to analyze, or matrix with columns containing bootstraped signatures
regulon	Object of class regulon
nullmodel	Matrix of genes by permutations containing the NULL model signatures. A parametric approach equivalent to shuffle genes will be used if nullmodel is ommitted.
pleiotropy	Logical, whether correction for pleiotropic regulation should be performed
minsize	Number indicating the minimum allowed size for the regulons
adaptive.size	Logical, whether the weight (likelihood) should be used for computing the regulon size
ges.filter	Logical, whether the gene expression signature should be limited to the genes represented in the interactome
synergy	Number indicating the synergy computation mode: (0) for no synergy computation; (0-1) for establishing the p-value cutoff for individual TFs to be included in the synergy analysis; (>1) number of top TFs to be included in the synergy analysis
level	Integer, maximum level of combinatorial regulation
pleiotropyArgs	list of 5 numbers for the pleotropy correction indicating: regulators p-value threshold, pleiotropic interaction p-value threshold, minimum number of targets in the overlap between pleiotropic regulators, penalty for the pleiotropic interactions and the pleiotropy analysis method, either absolute or adaptive
cores	Integer indicating the number of cores to use (only 1 in Windows-based systems)
verbose	Logical, whether progression messages should be printed in the terminal

Value

A msviper object containing the following components:

signature The gene expression signature

regulon The final regulon object used

es Enrichment analysis results including regulon size, normalized enrichment score and p-value

param msviper parameters, including `minsize`, `adaptive.size`

See Also

`viper`

Examples

```
data(bcellViper, package="bcellViper")
sig <- rowTtest(dset, "description", c("CB", "CC"), "N")$statistic
dnull <- ttestNull(dset, "description", c("CB", "CC"), "N", per=100) # Only 100 permutations to reduce computat
mra <- msviper(sig, regulon, dnull)
plot(mra, cex=.7)
```

msviper-class *The msviper class*

Description

This class contains the results generated by the msviper function

Slots

`signature`: Matrix containing the gene expression signature

`regulon`: Object of class `regulon`

`es`: List containing 6 objects:

`es$es`: Named vector of class `numeric` containing the enrichment scores

`es$nes`: Named vector of class `numeric` containing the normalized enrichment scores

`es$nes.se`: Named vector of class `numeric` containing the standard error for the normalized enrichment score

`es$size`: Named vector of class `numeric` containing the size -number of target genes- for each regulator

`es$p.value`: Named vector of class `numeric` containing the enrichment p-values

`es$nes.bt`: Matrix containing the normalized enrichment score if the msviper test is performed with bootstraps

`param`: List containing 3 elements:

`param$minsize`: Integer indicating the minimum allowed size for the regulons

`param$adaptive.size`: Logical indicating whether the weight (likelihood) should be used for computing the regulon size

`param$iterative`: Logical indicating whether a two step analysis with adaptive redundancy estimation should be performed

`nullmodel`: Matrix of genes by permutations containing the NULL model signatures

`ledge`: List containing the leading edge genes for each regulator. This slot is added by the `ledge` function

`shadow`: Two columns matrix containing the gene names for the shadow pairs. The first column contain the most probble regulator and the second column the one that was identified because a shadow effect

msviperAnnot *msVIPER annotation change*

Description

This function changes the annotation of genes in msviper objects

Usage

```
msviperAnnot(mobj, annot, complete = TRUE)
```

Arguments

mobj	msviper object generated by msviper function
annot	Vector os character strings containing the gene names and gene identifiers as vector names attribute
complete	Logical, whether the signature and target names should be also transformed

Value

msviper object with updated annotations

See Also

msviper

Examples

```
data(bcellViper, package="bcellViper")
sig <- rowTtest(dset, "description", "CB", "N")$statistic
mra <- msviper(sig, regulon)
tmp <- unique(c(names(mra$regulon), rownames(mra$signature)))
annot <- 1:length(tmp)
names(annot) <- tmp
plot(mra, cex=.7)
mra <- msviperAnnot(mra, annot)
plot(mra, cex=.7)
```

---

msviperClass *msVIPER class*

Description

This function generates an instance of the msviper class from a signature, NES signature and regulon object

Usage

```
msviperClass(nes, signature, regulon, nullmodel = NULL)
```

Arguments

nes	Numeric vector of NES values
signature	Numeric vector of gene expression signature
regulon	Instance of class regulon
nullmodel	Optional matrix containing the signatures for the null model

Value

msviper class object

Examples

```
data(bcellViper, package="bcellViper")
sig <- rowTtest(dset, "description", c("CB", "CC"), "N")$statistic
mra <- msviper(sig, regulon)
mra1 <- msviperClass(mra$es$nes, sig, regulon)
summary(mra1)
plot(mra1)
```

`msviperCombinatorial` *msviper combinatorial analysis*

Description

This function performs combinatorial analysis for msviper objects

Usage

```
msviperCombinatorial(mobj, regulators = 100, nullmodel = NULL,
  minsize = NULL, adaptive.size = NULL, level = 10, cores = 1,
  processAll = FALSE, verbose = TRUE)
```

Arguments

`mobj`	msviper object generated by `msviper` function
`regulators`	Either a number between 0 and 1 indicating the p-value cutoff for individual TFs to be included in the combinations analysis; (>1) indicating the number of top TFs to be included in the combinations analysis; or a vector of character strings indicating the TF IDs to be included in the analysis
`nullmodel`	Matrix of genes by permutations containing the NULL model signatures. Taken from `mobj` by default
`minsize`	Number indicating the minimum allowed size for the regulons, taken from `mobj` by default
`adaptive.size`	Logical, whether the weight (likelihood) should be used for computing the size, taken from `mobj` by default
`level`	Integer, maximum level of combinatorial regulation
`cores`	Integer indicating the number of cores to use (only 1 in Windows-based systems)
`processAll`	Logical, whether all pairs, even if not significant, should be processed for synergy
`verbose`	Logical, whether progression messages should be printed in the terminal

Value

A msviper object

See Also

`msviper`

Examples

```
data(bcellViper, package="bcellViper")
sig <- rowTtest(dset, "description", c("CB", "CC"), "N")$statistic
dnull <- ttestNull(dset, "description", c("CB", "CC"), "N", per=100) # Only 100 permutations to reduce computat
mra <- msviper(sig, regulon, dnull)
mra <- msviperCombinatorial(mra, 20)
plot(mra, cex=.7)
```

`msviperSynergy` *msviper synergy analysis*

Description

This function performs a synergy analysis for combinatorial regulation

Usage

```
msviperSynergy(mobj, per = 1000, seed = 1, cores = 1,
  verbose = TRUE)
```

Arguments

`mobj`	msviper object containing combinatorial regulation results generated by `msviperCombinatorial`
`per`	Integer indicating the number of permutations
`seed`	Integer indicating the seed for the permutations, 0 for disable it
`cores`	Integer indicating the number of cores to use (only 1 in Windows-based systems)
`verbose`	Logical, whether progression messages should be printed in the terminal

Value

Updated msviper object containing the sygergy p-value

See Also

`msviper`

Examples

```
data(bcellViper, package="bcellViper")
sig <- rowTtest(dset, "description", c("CB", "CC"), "N")$statistic
dnull <- ttestNull(dset, "description", c("CB", "CC"), "N", per=100) # Only 100 permutations to reduce computat
mra <- msviper(sig, regulon, dnull)
mra <- msviperCombinatorial(mra, 20)
mra <- msviperSynergy(mra)
summary(mra)
```

plot.msviper *Plot msviper results*

Description

This function generate a plot for msviper results showing the enrichment of the target genes for each significant master regulator on the gene expression signature

Usage

```
## S3 method for class 'msviper'
plot(x, mrs = 10, color = c("cornflowerblue",
  "salmon"), pval = NULL, bins = 500, cex = 0, density = 0,
  smooth = 0, sep = 0.2, hybrid = TRUE, include = c("expression",
  "activity"), gama = 2, ...)
```

Arguments

x	msviper object produced by msviper function
mrs	Either an integer indicating the number of master regulators to include in the plot, or a character vector containing the names of the master regulators to include in the plot
color	Vector of two components indicating the colors for the negative and positive parts of the regulon
pval	Optional matrix of p-values to include in the plot
bins	Number of bins to split the vector of scores in order to compute the density color of the bars
cex	Number indicating the text size scaling, 0 indicates automatic scaling
density	Integrer indicating the number of steps for the kernel density. Zero for not plotting it
smooth	Number indicating the proportion of point for smoothing the density distribution. Zero for not using the smoother
sep	Number indicating the separation from figure and text
hybrid	Logical, whether the 3-tail approach used for computingthe enrichment should be reflected in the plot
include	Vector indicating the information to include as heatmap to the right of the msviper plot: expression and activity
gama	Positive number indicating the exponential transformation for the activity and expression color scale
...	Given for compatibility to the plot generic function

Value

Nothing, a plot is generated in the default output device

See Also

msviper

Examples

```
data(bcellViper, package="bcellViper")
sig <- rowTtest(dset, "description", c("CB", "CC"), "N")$statistic
dnull <- ttestNull(dset, "description", c("CB", "CC"), "N", per=100) # Only 100 permutations to reduce computat
mra <- msviper(sig, regulon, dnull)
plot(mra, cex=.7)
```

---

pruneRegulon *Prune Regulons*

Description

This function limits the maximum size of the regulons

Usage

```
pruneRegulon(regulon, cutoff = 50, adaptive = TRUE,
  eliminate = FALSE, wm = NULL)
```

Arguments

regulon	Object of class regulon
cutoff	Number indicating the maximum size for the regulons (maximum number of target genes)
adaptive	Logical, whether adaptive size should be used (i.e. sum(likelihood^2))
eliminate	Logical whether regulons smalles than cutoff should be eliminated
wm	Optional numeric vector of weights (0; 1) for the genes

Value

Prunned regulon

See Also

viper, msviper

Examples

```
data(bcellViper, package="bcellViper")
hist(sapply(regulon, function(x) sum(x$likelihood)/max(x$likelihood)), nclass=20)
preg <- pruneRegulon(regulon, 400)
hist(sapply(preg, function(x) sum(x$likelihood)/max(x$likelihood)), nclass=20)
```

pwea3NULLf *Null model function*

Description

This function generates the NULL model function, which computes the normalized enrichment score and associated p-value

Usage

```
pwea3NULLf(pwnull, cores = 1, verbose = TRUE)
```

Arguments

pwnull	Object generated by pwea3NULLgroups function
cores	Integer indicating the number of cores to use (only 1 in Windows-based systems)
verbose	Logical, whether progression messages should be printed in the terminal

Value

List of function to compute NES and p-value

pwea3NULLgroups *Regulon-specific NULL model*

Description

This function generates the regulon-specific NULL models

Usage

```
pwea3NULLgroups(pwnull, groups, cores = 1, verbose = TRUE)
```

Arguments

pwnull	Numerical matrix representing the null model, with genes as rows (geneID as rownames) and permutations as columns
groups	List containing the regulons
cores	Integer indicating the number of cores to use (only 1 in Windows-based systems)
verbose	Logical, whether progression messages should be printed in the terminal

Value

A list containing two elements:

groups Regulon-specific NULL model containing the enrichment scores

ss Direction of the regulon-specific NULL model

regulon-class *The regulon class*

Description

This class contains interactome data

Slots

List of regulators with the following slots:

tfmode: Named vector of class numeric containing the regulator mode of action scores, with target genes as name attribute

likelihood: Vector of class numeric containing the relative likelihood for each target gene

rowTtest *Student's t-test for rows*

Description

This function performs a Student's t-test on each row of a matrix

Usage

```
rowTtest(x, ...)

## S4 method for signature 'matrix'
rowTtest(x, y = NULL, mu = 0,
  alternative = "two.sided")

## S4 method for signature 'ExpressionSet'
rowTtest(x, pheno, group1, group2 = NULL,
  mu = 0, alternative = "two.sided")
```

Arguments

x	ExpressionSet object or Numerical matrix containing the test samples
...	Additional parameters added to keep compatibility
y	Optional numerical matrix containing the reference samples. If ommited x will be tested against mean = mu
mu	Number indicating the alternative hypothesis when y is ommited
alternative	Character string indicating the tail for the test, either two.sided, greater or lower
pheno	Character string indicating the phenotype data to use
group1	Vector of character strings indicating the category from phenotype pheno to use as test group
group2	Vector of character strings indicating the category from phenotype pheno to use as control group

Value

List of Student-t-statistic (`statistic`) and p-values (`p.value`)

Examples

```
data(bcellViper, package="bcellViper")
d1 <- exprs(dset)
res <- rowTtest(d1[, 1:10], d1[, 11:20])
res$statistic[1:5, ]
res$p.value[1:5, ]
data(bcellViper, package="bcellViper")
res <- rowTtest(dset, "description", "CB", "N")
res$statistic[1:5, ]
res$p.value[1:5, ]
```

---

scale.signatureDistance *Scaling of signatureDistance objects*

Description

This function scales the signatureDistance so its range is (-1, 1)

Usage

```
## S3 method for class 'signatureDistance'
scale(x, center = TRUE, scale = TRUE)
```

Arguments

`x`	signatureDistance object
`center`	Not used, given for compatibility with the generic funtion scale
`scale`	Not used, given for compatibility with the generic function scale

Value

Scaled signatureDistance object

---

scaleGroups *Signatures with grouping variable*

Description

`scaleGroups` compares each group vs. the remaining groups using a Student's t-test

Usage

```
scaleGroups(x, groups)
```

Arguments

x	Numerical matrix with genes in rows and samples in columns
groups	Vector of same length as columns has the dset containing the labels for grouping the samples

Details

This function compute signatures using groups information

Value

Numeric matrix of signatures (z-scores) with genes in rows and groups in columns

Examples

```
data(bcellViper, package="bcellViper")
res <- scaleGroups(exprs(dset)[, 1:20], rep(1:4, rep(5, 4)))
res[1:5, ]
```

---

shadow *Shadow analysis for msviper objects*

Description

This function performs shadow analysis on msviper objects

Usage

```
shadow(mobj, regulators = 0.01, targets = 10, shadow = 0.01,
  per = 1000, nullmodel = NULL, minsize = NULL,
  adaptive.size = NULL, iterative = NULL, seed = 1, cores = 1,
  verbose = TRUE)
```

Arguments

mobj	msviper object generated by msviper
regulators	This parameter represent different ways to select a subset of regulators for performing the shadow analysis, it can be either a p-value cutoff, the total number of regulons to be used for computing the shadow effect, or a vector of regulator ids to be considered
targets	Integer indicating the minimum number of common targets to compute shadow analysis
shadow	Number indicating the p-value threshold for the shadow effect
per	Integer indicating the number of permutations
nullmodel	Null model in marix format
minsize	Integer indicating the minimum size allowed for the regulons
adaptive.size	Logical, whether the target weight should be considered when computing the regulon size

iterative	Logical, whether a two step analysis with adaptive redundancy estimation should be performed
seed	Integer indicating the seed for the permutations, 0 for disable it
cores	Integer indicating the number of cores to use (only 1 in Windows-based systems)
verbose	Logical, whether progression messages should be printed in the terminal

Value

An updated msviper object with an additional slot (shadow) containing the shadow pairs

See Also

msviper

Examples

```
data(bcellViper, package="bcellViper")
sig <- rowTtest(dset, "description", c("CB", "CC"), "N")$statistic
dnull <- ttestNull(dset, "description", c("CB", "CC"), "N", per=100) # Only 100 permutations to reduce computat
mra <- msviper(sig, regulon, dnull)
mra <- shadow(mra, regulators=10)
summary(mra)
```

---

shadowRegulon *Correction for pleiotropy*

Description

This function penalyze the regulatory interactions based on pleiotropy analysis

Usage

```
shadowRegulon(ss, nes, regul, regulators = 0.05, shadow = 0.05,
  targets = 10, penalty = 2, method = c("absolute", "adaptive"))
```

Arguments

ss	Named vector containing the gene expression signature
nes	Named vector containing the normalized enrichment scores
regul	Regulon object
regulators	Number indicating the number of top regulators to consider for the analysis or the p-value threshold for considering significant regulators
shadow	Number indicating the p-value threshold for considering a significant shadow effect
targets	Integer indicating the minimal number of overlaping targets to consider a pair of regulators for pleiotropy analysis
penalty	Number higher than 1 indicating the penalty for the pleiotropic interactions. 1 = no penalty
method	Character string indicating the method to use for computing the pleiotropy, either absolute or adaptive

Value

Corrected regulon object

`signatureDistance` *Signature Distance*

Description

This function computes the similarity between columns of a data matrix

Usage

```
signatureDistance(dset1, dset2 = NULL, nn = NULL, groups = NULL,
  scale. = TRUE, two.tails = TRUE, ws = 2)
```

Arguments

`dset1`	Dataset of any type in matrix format, with features in rows and samples in columns
`dset2`	Optional Dataset. If provided, distance between columns of dset and dset2 are computed and reported as rows and columns, respectively; if not, distance between all possible pairs of columns from dset are computed
`nn`	Optional size for the signature, default is either the full signature or 10 percent of it, depending or whether `ws=0` or not
`groups`	Optional vector indicating the group ID of the samples
`scale.`	Logical, whether the data should be scaled
`two.tails`	Logical, whether a two tails, instead of 1 tail test should be performed
`ws`	Number indicating the exponent for the weighting the signatures, the default of 0 is uniform weighting, 1 is weighting by SD

Value

Object of class `signatureDistance` as a matrix of normalized enrichment scores

Examples

```
data(bcellViper, package="bcellViper")
dd <- signatureDistance(exprs(dset))
dd[1:5, 1:5]
scale(dd)[1:5, 1:5]
as.matrix(as.dist(dd))[1:5, 1:5]
```

signatureDistance-class *signatureDistance*

Description

This class contains the results generated by `signatureDistance` function.

Slots

Matrix of class `numeric` containing the similarity scores

sigT *Sigmoid transformation*

Description

This function transforms a numeric vector using a sigmoid function

Usage

```
sigT(x, slope = 20, inflection = 0.5)
```

Arguments

`x`	Numeric vector
`slope`	Number indicating the slope at the inflection point
`inflection`	Number indicating the inflection point

Value

Numeric vector

summary.msviper *List msviper results*

Description

This function generates a table of msviper results

Usage

```
## S3 method for class 'msviper'
summary(object, mrs = 10, ...)
```

Arguments

object	msviper object
mrs	Either number of top MRs to report or vector containing the genes to display
...	Given for compatibility with the summary generic function

Value

Data.frame with results

---

ttestNull *Null model by sample permutation testing*

Description

This function performs sample permutation and t-test to generate a null model

Usage

```
ttestNull(x, ...)

## S4 method for signature 'matrix'
ttestNull(x, y, per = 1000, repos = TRUE,
  seed = 1, cores = 1, verbose = TRUE)

## S4 method for signature 'ExpressionSet'
ttestNull(x, pheno, group1, group2, per = 1000,
  repos = TRUE, seed = 1, verbose = TRUE)
```

Arguments

x	ExpressionSet object or Matrix containing the test dataset
...	Additional parameters added to keep compatibility
y	Matrix containing the reference dataset
per	Integer indicating the number of permutations
repos	Logical, whether the permutations should be performed with reposition
seed	Integer indicating the seed for the permutations, 0 for disable it
cores	Integer indicating the number of cores to use (set to 1 in windows systems)
verbose	Logical, whether progression messages should be printed in the terminal
pheno	Character string indicating the phenotype data to use
group1	Vector of character strings indicating the category from phenotype pheno to use as test group
group2	Vector of character strings indicating the category from phenotype pheno to use as control group

Value

Matrix of z-scores with genes in rows and permutations in columns

See Also

msviper, viper

Examples

```
data(bcellViper, package="bcellViper")
d1 <- exprs(dset)
dnull <- ttestNull(d1[, 1:10], d1[, 11:20], per=100)
dim(dnull)
plot(density(dnull))
data(bcellViper, package="bcellViper")
dnull <- ttestNull(dset, "description", "CB", "CC", per=100)
dim(dnull)
plot(density(dnull))
```

---

viper *VIPER*

Description

This function performs Virtual Inference of Protein-activity by Enriched Regulon analysis

Usage

```
viper(eset, regulon, dnull = NULL, pleiotropy = FALSE, nes = TRUE,
  method = c("none", "scale", "rank", "mad", "ttest"), bootstraps = 0,
  minsize = 25, adaptive.size = FALSE, eset.filter = TRUE,
  mvws = 1, pleiotropyArgs = list(regulators = 0.05, shadow = 0.05,
  targets = 10, penalty = 20, method = "adaptive"), cores = 1,
  verbose = TRUE)
```

Arguments

eset	ExpressionSet object or Numeric matrix containing the expression data or gene expression signatures, with samples in columns and genes in rows
regulon	Object of class regulon or list of objects of class regulon for metaVIPER analysis
dnull	Numeric matrix for the null model, usually generated by nullTtest
pleiotropy	Logical, whether correction for pleiotropic regulation should be performed
nes	Logical, whether the enrichment score reported should be normalized
method	Character string indicating the method for computing the single samples signature, either scale, rank, mad, ttest or none
bootstraps	Integer indicating the number of bootstraps iterations to perform. Only the scale method is implemented with bootstraps.
minsize	Integer indicating the minimum number of targets allowed per regulon
adaptive.size	Logical, whether the weighting scores should be taken into account for computing the regulon size
eset.filter	Logical, whether the dataset should be limited only to the genes represented in the interactome #' @param mvws Number or vector indicating either the exponent score for the metaViper weights, or the inflection point and trend for the sigmoid function describing the weights in metaViper

pleiotropyArgs	list of 5 numbers for the pleotropy correction indicating: regulators p-value threshold, pleiotropic interaction p-value threshold, minimum number of targets in the overlap between pleiotropic regulators, penalty for the pleiotropic interactions and the method for computing the pleiotropy, either absolute or adaptive
cores	Integer indicating the number of cores to use (only 1 in Windows-based systems)
verbose	Logical, whether progression messages should be printed in the terminal

Value

A matrix of inferred activity for each regulator gene in the network across all samples

See Also

msviper

Examples

```
data(bcellViper, package="bcellViper")
d1 <- exprs(dset)
res <- viper(d1, regulon)
dim(d1)
d1[1:5, 1:5]
regulon
dim(res)
res[1:5, 1:5]
```

---

viperRPT *viperRPT*

Description

This function computes residual post-translational activity

Usage

```
viperRPT(vipermat, expmat, weights = matrix(1, nrow(vipermat),
  ncol(vipermat), dimnames = list(rownames(vipermat), colnames(vipermat))),
  method = c("spline", "lineal", "rank"), robust = FALSE, cores = 1)
```

Arguments

vipermat	Numeric matrix containing the viper protein activity inferences
expmat	Numeric matrix or expressionSet containing the expression data
weights	List of numeric matrix of sample weights
method	Character string indicating the method to use, either rank, lineal or spline
robust	Logical, whether the contribution of outliers is down-weighted by using a gaussian kernel estimate for the join probability density
cores	Integer indicating the number of cores to use

Value

Matrix of RPT-activity values

See Also

viper

Examples

```
data(bcellViper, package="bcellViper")
vipermat <- viper(dset, regulon)
rpt <- viperRPT(vipermat, dset)
rpt[1:5, 1:5]
```

---

viperSignature *Generic S4 method for signature and sample-permutation null model for VIPER*

Description

This function generates a viperSignature object from a test dataset based on a set of samples to use as reference

Usage

```
viperSignature(eset, ...)

## S4 method for signature 'ExpressionSet'
viperSignature(eset, pheno, refgroup,
  method = c("zscore", "ttest", "mean"), per = 100, bootstrap = TRUE,
  seed = 1, cores = 1, verbose = TRUE)

## S4 method for signature 'matrix'
viperSignature(eset, ref, method = c("zscore",
  "ttest", "mean"), per = 100, bootstrap = TRUE, seed = 1,
  cores = 1, verbose = TRUE)
```

Arguments

eset	ExpressionSet object or numeric matrix containing the test dataset, with genes in rows and samples in columns
...	Additional parameters added to keep compatibility
pheno	Character string indicating the phenotype data to use
refgroup	Vector of character string indicatig the category of pheno to use as reference group
method	Character string indicating how to compute the signature and null model, either ttest, zscore or mean
per	Integer indicating the number of sample permutations
bootstrap	Logical, whether null model should be estimated with bootstrap. In this case, only reference samples are used.

seed	Integer indicating the seed for the random sample generation. The system default is used when set to zero
cores	Integer indicating the number of cores to use (only 1 in Windows-based systems)
verbose	Logical, whether progression messages should be printed in the terminal
ref	Numeric matrix containing the reference samples (columns) and genes in rows

Value

viperSignature S3 object containing the signature and null model

Examples

```
data(bcellViper, package="bcellViper")
ss <- viperSignature(dset, "description", c("N", "CB", "CC"), per=100) # Only 100 permutations to reduce comput
res <- viper(ss, regulon)
dim(exprs(dset))
exprs(dset)[1:5, 1:5]
regulon
dim(res)
exprs(res)[1:5, 1:5]
data(bcellViper, package="bcellViper")
d1 <- exprs(dset)
pos <- pData(dset)[["description"]] %in% c("N", "CB", "CC")
ss <- viperSignature(d1[, !pos], d1[, pos], per=100) # Only 100 permutations to reduce computation time, but it
res <- viper(ss, regulon)
dim(d1)
d1[1:5, 1:5]
regulon
dim(res)
res[1:5, 1:5]
```

---

viperSignature-class *viperSignature*

Description

This class contains the results produced by the `viperSignature` function

Slots

`signature`**:** Matrix of class `numeric` with genes in rows and samples in columns containing the gene expression signatures

`nullmodel`**:** Matrix of class `numeric` with genes in rows and permutations in columns ontaining the sample-permutation based signatures to be used as NULL model

`viperSimilarity` *VIPER similarity*

Description

If ws is a single number, weighting is performed using an exponential function. If ws is a 2 numbers vector, weighting is performed with a symmetric sigmoid function using the first element as inflection point and the second as trend.

Usage

```
viperSimilarity(x, nn = NULL, ws = c(4, 2), method = c("two.sided",
  "greater", "less"))
```

Arguments

`x`	Numeric matrix containing the VIPER results with samples in columns and regulators in rows
`nn`	Optional number of top regulators to consider for computing the similarity
`ws`	Number indicating the weighting exponent for the signature, or vector of 2 numbers indicating the inflection point and the value corresponding to a weighting score of .1 for a sigmoid transformation, only used if `nn` is ommited
`method`	Character string indicating whether the most active (greater), less active (less) or both tails (two.sided) of the signature should be used for computing the similarity

Details

This function computes the similarity between VIPER signatures

Value

signatureDistance object

Examples

```
data(bcellViper, package="bcellViper")
dd <- viperSimilarity(exprs(dset))
dd[1:5, 1:5]
scale(dd)[1:5, 1:5]
as.matrix(as.dist(dd))[1:5, 1:5]
```

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