Package 'MEAL'

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Title Perform methylation analysis

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Description Package to integrate methylation and expression data. It can also perform methylation or expression analysis alone. Several plotting functionalities are included as well as a new region analysis based on redundancy analysis. Effect of SNPs on a region can also be estimated.

Depends R (>= 3.6.0), Biobase, MultiDataSet

License Artistic-2.0

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 ${\tt computeRDAR2}$

Compute signification of RDA test

Description

Compare R2 obtained in our region of interest with the global R^2 and the R^2 of regions with the same number of probes.

```
computeRDAR2(
  fullMat,
  varsmodel,
  covarsmodel = NULL,
  featNum,
  R2,
  num_permutations = 1e+05 - 1
)
```

correlationMethExprs 3

Arguments

fullMat Matrix with the whole genome expression or methylation values

varsmodel Matrix with the model

covarsmodel Matrix with the covariables model

featNum Numeric with the number of features of the RDA model

R2 Numeric with the R2 of the RDA model

num_permutations

Numeric with the number of permutations.

Value

Numeric vector with the probability of finding a region with the same number of probes with a bigger R2 and the global R2.

correlationMethExprs

Computes the correlation between methylation and expression

Description

Estimates the correlation between methylation and expression. When there are known variables that affect methylation and/or expression, their effect can be substracted using a linear model and then the residuals are used.

Usage

```
correlationMethExprs(
  multiset,
  meth_set_name = NULL,
  exprs_set_name = NULL,
  vars_meth = NULL,
  vars_exprs = NULL,
  sel_cpgs,
  flank = 250000,
  betas = TRUE,
  num_cores = 1,
  verbose = TRUE
)
```

Arguments

multiset MultiDataSet containing a methylation and an expression slots.

tion data.

 $\verb|exprs_set_name| Character vector with the name of the \verb|MultiDataSet's slot containing expressions and the model of th$

sion data.

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vars_meth	Character vector with the names of the variables that will be used to obtain the methylation residuals. By default, none is used and residuals are not computed.
vars_exprs	Character vector with the names of the variables that will be used to obtain the expression residuals. By default, none is used and residuals are not computed.
sel_cpgs	Character vector with the name of the CpGs used in the analysis. If empty, all the CpGs of the methylation set will be used.
flank	Numeric with the number of pair bases used to define the cpg-expression probe pairs.
betas	If set is a GenomicRatioSet, should beta values be used? (Default: TRUE)
num_cores	Numeric with the number of cores to be used.
verbose	Logical value. If TRUE, it writes out some messages indicating progress. If FALSE nothing should be printed.

Details

For each cpg, a range is defined by the position of the cpg plus the flank parameter (upstream and downstream). Only those expression probes that are entirely in this range will be selected. For these reason, it is required that the ExpressionSet contains a featureData with the chromosome and the starting and ending positions of the probes.

Value

Data.frame with the results of the linear regression:

- cpg: Name of the cpg
- exprs: Name of the expression probe
- beta: coefficient of the methylation change
- se: standard error of the beta
- P.Value: p-value of the beta coefficient
- adj.P.Val: q-value computed using B&H

exportResults	Exports results data.frames to csv files.	

Description

Exports results to csv files. If more than one variable is present, subfolders with the name of the variable are created. For each variable, four files will be generated: probeResults.csv, dmrCateResults.csv, bumphunterResults.csv and blockFinderResults.csv

filterResults 5

Usage

```
exportResults(
  object,
  dir = "./",
  prefix = NULL,
  fNames = c("chromosome", "start")
)
```

Arguments

object ResultSet

dir Character with the path to export.

prefix Character with a prefix to be added to all file names.

fNames Names of the columns of object fData that will be added to the results data.frame.

Value

Files are saved into the given folder.

Examples

```
if (require(minfiData)){
set <- ratioConvert(mapToGenome(MsetEx[1:10,]))
methyOneVar <- runPipeline(set, variable_names = "sex")
exportResults(methyOneVar)
}</pre>
```

filterResults

Filter the data.frame obtained from probe analysis

Description

Filter the data.frame obtained from probe analysis

Usage

```
filterResults(results, range, position = "position", chr = "chromosome")
```

Arguments

results Data.frame with the results of probe analysis range GenomicRanges with the desired range.

position Character with the name of the column containing the positions chr Character with the name of the column containing the chromosome

Value

Data.frame with the results of the probes of the range

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Get all probes related to a gene

Description

Given a ResultSet and a gene name returns the results of the analysis of all the probes of the gene.

Usage

```
getGeneVals(
  object,
  gene,
  rid = 1,
  genecol = "genes",
  fNames = c("chromosome", "start"),
  ...
)
```

Arguments

object	ResultSet
gene	Character with the name of the gene
rid	Name of the results: "DiffMean" for mean differences, "DiffVar" for variance differences. (Default: DiffMean)
genecol	Character with the column of object fData with the gene information
fNames	Names of the columns of object fData that will be added to the results data.frame.
	Further arguments passed to getProbeResults

Value

data.frame with the results of the analysis of the probes belonging to the gene

Examples

```
## Not run:
if (require(minfiData)){
  set <- ratioConvert(mapToGenome(MsetEx[1:10,]))
methyOneVar <- runPipeline(set, variable_names = "sex")
getGeneVals(methyOneVar, "TSPY4")
}
## End(Not run)</pre>
```

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getProbeResults Obtain probe results from a ResultSet

Description

It computes the statistics from the MArrayLM computed with DiffMeanAnalysis or DiffVarAnalysis. This function allows to specify the contrasts and to get F-statistics for a group of variables.

Usage

```
getProbeResults(
  object,
  rid = "DiffMean",
  coef = 2,
  contrast = NULL,
  fNames = c("chromosome", "start"),
  robust = FALSE,
  ...
)
```

Arguments

object	ResultSet
rid	Name of the results: "DiffMean" for mean differences, "DiffVar" for variance differences. (Default: DiffMean)
coef	Number of the coefficient used to compute the statistics. If a vector is supplied, F-statistics evaluating the global effect of the coefficients are computed. (Default: 2).
contrast	Matrix of contrasts
fNames	Names of the columns of object fData that will be added to the results data.frame.
	Further arguments passed to getAssociation.

Value

data.frame with the probe results.

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getRDAresults

Get a summary of RDA results

Description

Get statistics from RDA result.

Usage

getRDAresults(object)

Arguments

object

ResultSet

Value

Numeric vector with the RDA statistics

MEAL

MEAL (Methylation and Expression AnaLizer): Package for analysing methylation and expression data

Description

MEAL is a package designed to facilitate the analysis methylation and expression data. The package can analyze one dataset and can find correlations between methylation and expression data. MEAL has a vignette that explains the main functionalities of the package.

MEAL-defunct

Defunct functions

Description

These functions are defunct and no longer available.

Details

Defunct functions are: multiCorrMethExprs, DAPipeline, DAProbe, DARegion, RDAset, filterSet, plotBestFeatures, preparePhenotype, createRanges, prepareMethylationSet, calculateRelevantSNPs, correlationMethSNPs, explainedVariance, normalSNP, plotLM

Defunct classes are: analysisRegionResults, analysisResults

plotFeature 9

Description

Plot values of a feature splitted by one or two variables.

Usage

```
plotFeature(set, feat, variables = colnames(pheno)[1], betas = TRUE)
```

Arguments

set ExpressionSet, GenomicRatioSet or SummarizedExperiment.

feat Numeric with the index of the feature or character with its name.

variables Character vector with the names of the variables to be used in the splitting. Two

variables is the maximum allowed.

betas If set is a GenomicRatioSet, should beta values be used? (Default: TRUE)

Value

A plot is generated on the current graphics device.

Examples

```
if (require(minfiData)){
set <- ratioConvert(mapToGenome(MsetEx[1:10,]))
plotFeature(set, 1, variables = "Sample_Group")
}</pre>
```

plotRDA Plot RDA results

Description

Plot RDA results

```
plotRDA(object, pheno = data.frame(), n_feat = 5, main = "RDA plot", alpha = 1)
```

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Arguments

object	ResultSet
pheno	data.frame with the variables used to color the samples.
n_feat	Numeric with the number of cpgs to be highlighted. Default: 5.
main	Character with the plot title.
alpha	Numeric with the alpha level for colour transparance. Default: 1; no transparency.

Value

A plot is generated on the current graphics device.

Examples

```
if (require(minfiData)){
  set <- ratioConvert(mapToGenome(MsetEx[1:10,]))
  model <- model.matrix(~set$sex)
  rda <- runRDA(set, model)
  plotRDA(rda, pheno = data.frame(factor(set$sex)))
}</pre>
```

plotRegion

Plot results in a genomic region

Description

Plot the results from the different analyses of a ResultSet in a specific genomic region. It can plot all the results from runPipeline.

```
plotRegion(
    rset,
    range,
    results = names(rset),
    genome = "hg19",
    rset2,
    tPV = 5,
    fNames = c("chromosome", "start", "end"),
    fNames2 = c("chromosome", "start", "end"))
```

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Arguments

rset	ResultSet
range	GenomicRanges with the region coordinates
results	Character with the analyses that will be included in the plot. By default, all analyses available are included.
genome	String with the genome used to retrieve transcripts annotation: hg19, hg38, mm10. (Default: "hg19")
rset2	Additional ResultSet
tPV	Threshold for P-Value
fNames	Names from rset fData
fNames2	Names from rset2 fData

Details

This plot allows to have a quick summary of the methylation or gene expression analyses in a given region. If we use a ResultSet obtained from methylation data, transcripts annotation is obtained from archive. If we use a ResultSet obtained from gene expression data, transcripts annotation is taken from fData.

This plot can be used to plot the results of one dataset (methylation or gene expression) or to represent the association between methylation and gene expression data. If only one dataset is used, the p-values and the coefficients of DiffMean and DiffVar analyses are plotted. If we pass two ResultSets, rset should contain methylation results and a rset2 the gene expression results.

Value

Regional plot

runBlockFinder	$Run\ blockFinder$

Description

Run blockFinder

```
runBlockFinder(
   set,
   model,
   coefficient = 2,
   blockfinder_cutoff = 0.1,
   num_permutations = 0,
   resultSet = FALSE,
   verbose = FALSE,
   ...
)
```

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Arguments

set GenomicRatioSet, eSet derived object or SummarizedExperiment

Model matrix or formula to get model matrix from set.

coefficient Numeric with the column of model matrix used in the analysis. (Default: 2)

blockfinder_cutoff

Numeric with the minimum cutoff to include a probe in a block. (Default: 0.1)

num_permutations

Numeric with the number of permutations run to compute the blocks p-value. (Default: 0)

resultSet Should results be encapsulated in a resultSet? (Default: TRUE)

verbose Logical value. Should the function be verbose? (Default: FALSE)

... Further arguments passed to blockFinder.

Details

This function has been deprecated and will be defunct in the new version.

Value

data.frame or resultSet with the result of blockFinder

See Also

blockFinder

runBumphunter

Run bumphunter

Description

Run bumphunter

```
runBumphunter(
    set,
    model,
    coefficient = 2,
    bumphunter_cutoff = 0.1,
    num_permutations = 0,
    bumps_max = 30000,
    betas = TRUE,
    check_perms = FALSE,
    verbose = FALSE,
    resultSet = FALSE,
    ...
)
```

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Arguments

set GenomicRatioSet, eSet derived object or SummarizedExperiment

model Model matrix or formula to get model matrix from set.

coefficient Numeric with the column of model matrix used in the analysis. (Default: 2)

bumphunter_cutoff

Numeric with the minimum cutoff to include a probe in a block. (Default: 0.1)

num_permutations

Numeric with the number of permutations run to compute the bumps p-value.

(Default: 0)

bumps_max Numeric with the maximum number of bumps used in the permutation. This

parameter only applies when num_permutations is greater than 0. (Default:

30000)

betas If set is a GenomicRatioSet, should beta values be used? (Default: TRUE)

check_perms Logical. Should we check that there are less bumps than bumps_max? This

parameter only applies when num_permutations is greater than 0. (Default:

TRUE)

verbose Logical value. Should the function be verbose? (Default: FALSE)

resultSet Should results be encapsulated in a resultSet? (Default: TRUE)

. . . Further arguments passed to bumphunter.

Details

This function has been deprecated and will be defunct in the new version.

Value

data.frame or resultSet with the result of bumphunter

See Also

bumphunter

runDiffMeanAnalysis Run differen

Run differential mean analysis

Description

Run differential mean analysis using t-moderated statistics. This function relies on lmFit from limma package.

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Usage

```
runDiffMeanAnalysis(
    set,
    model,
    weights = NULL,
    method = "ls",
    max_iterations = 100,
    betas = TRUE,
    resultSet = TRUE,
    warnings = TRUE
)
```

Arguments

set Matrix, GenomicRatioSet, SummarizedExperiment or ExpressionSet.

model Model matrix or formula to get model matrix from set.

weights weights used in the lmFit model.

method String indicating the method used in the regression: "ls" or "robust". (Default:

"ls")

max_iterations Numeric indicating the maximum number of iterations done in the robust method.

betas If set is a GenomicRatioSet, should beta values be used? (Default: TRUE)

resultSet Should results be encapsulated in a resultSet? (Default: TRUE)

warnings Should warnings be displayed? (Default:TRUE)

Value

MArrayLM or resultSet with the result of the differential mean analysis.

Examples

```
if (require(minfiData)){
  mvalues <- getM(MsetEx)[1:100, ]
  model <- model.matrix(~ Sample_Group, data = pData(MsetEx))
  res <- runDiffMeanAnalysis(mvalues, model, method = "ls")
  res
}</pre>
```

runDiffVarAnalysis

Run differential variance analysis

Description

Run differential variance analysis. This analysis can only be run with categorical variables. This function relies on varFit from missMethyl package.

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Usage

```
runDiffVarAnalysis(
   set,
   model,
   coefficient = NULL,
   resultSet = TRUE,
   betas = TRUE,
   warnings = TRUE,
   ...
)
```

Arguments

Matrix, GenomicRatioSet, SummarizedExperiment or ExpressionSet.

Model matrix or formula to get model matrix from set.

Numeric with the coefficients used to make the groups. If NULL, all possible groups will be computed.

Should results be encapsulated in a resultSet? (Default: TRUE)

betas If set is a GenomicRatioSet, should beta values be used? (Default: TRUE)

warnings Should warnings be displayed? (Default:TRUE)

Further arguments passed to varFit.

Value

MArrayLM or resultSet with the result of the differential variance analysis.

Examples

```
if (require(minfiData)){
  mvalues <- getM(MsetEx)[1:100, ]
  model <- model.matrix(~ Sample_Group, data = pData(MsetEx))
  res <- runDiffVarAnalysis(mvalues, model)
  res
}</pre>
```

runDMRcate Run DMRcate

Description

Run DMRcate

```
runDMRcate(set, model, coefficient = 2, resultSet = FALSE, ...)
```

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Arguments

set	GenomicRatioSet, eSet derived object or SummarizedExperiment
model	Model matrix or formula to get model matrix from set.
coefficient	Numeric with the column of model matrix used in the analysis. (Default: 2)
resultSet	Should results be encapsulated in a resultSet? (Default: TRUE)
	Further arguments passed to cpg. annotate or dmrcate.

Details

This function has been deprecated and will be defunct in the new version.

Value

data.frame or resultSet with the result of bumphunter

See Also

```
dmrcate, cpg.annotate
```

runPipeline

Perform differential methylation analysis

Description

Wrapper for analysing differential methylation and expression at region and probe level.

```
runPipeline(
  set,
 variable_names,
 covariable_names = NULL,
 model = NULL,
 weights = NULL,
 num_vars,
 sva = FALSE,
 betas = TRUE,
  range,
 analyses = c("DiffMean"),
 verbose = FALSE,
 warnings = TRUE,
 DiffMean_params = NULL,
 DiffVar_params = list(coefficient = 1:2),
  rda_params = NULL,
 method = "ls",
 big = FALSE
)
```

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Arguments

set GenomicRatioSet, eSet derived object or SummarizedExperiment

variable_names Character vector with the names of the variables that will be returned as result. covariable_names

Character vector with the names of the variables that will be used to adjust the

model.

model Model matrix or formula to get model matrix from set.

weights weights used in the lmFit model (default NULL)

num_vars Numeric with the number of variables in the matrix for which the analysis will

be performed. Compulsory if equation is not null.

sva Logical. Should Surrogate Variable Analysis be applied? (Default: FALSE)
betas If set is a GenomicRatioSet, should beta values be used? (Default: TRUE)

range GenomicRanges with the region used for RDA

analyses Vector with the names of the analysis to be run (DiffMean and/or DiffVar).

verbose Logical value. If TRUE, it writes out some messages indicating progress. If

FALSE nothing should be printed.

warnings Should warnings be displayed? (Default:TRUE)

DiffMean_params

List with other parameter passed to runBumphunter function.

DiffVar_params List with other parameter passed to runBumphunter function.

rda_params List with other parameter passed to runRDA function.

method String indicating the method used in the regression: "ls" or "robust". (Default:

"ls")

big Logical value indicating whether SmartSVA should be instead of SVA (TRUE

recommended for methylation or when having large number of samples). De-

fault is FALSE.

Details

This function is the main wrapper of the package. First, it simplifies the the set to only contain the common samples between phenotype and features. In addition, it allows to change the class of the variables and to apply genomic models (more information on preparePhenotype). Afterwards, analysis per probe and per region are done merging the results in an AnalysisResults object.

Default linear model will contain a sum of the variables and covariables. If interactions are desired, a costum formula can be specified. In that case, variables and covariables must also be specified in order to assure the proper work of the resulting AnalysisResult. In addition, the number of variables of the model for which the calculation will be done **must** be specified.

Value

ResultSet object

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Examples

```
if (require(minfiData)){
set <- ratioConvert(mapToGenome(MsetEx[1:10,]))
res <- runPipeline(set, variable_names = "Sample_Group")
res
}</pre>
```

runRDA

Calculate RDA for a set

Description

Perform RDA calculation for a AnalysisRegionResults. Feature values will be considered the matrix X and phenotypes the matrix Y. Adjusting for covariates is done using a model matrix passed in covarsmodel.

Usage

```
runRDA(
    set,
    model,
    num_vars = ncol(model),
    range,
    betas = FALSE,
    resultSet = TRUE,
    num_permutations = 10000,
    ...
)
```

Arguments

set MethylationSet, ExpressionSet or matrix

model Model matrix or formula to get model matrix from set.

be performed. Compulsory if equation is not null.

range GenomicRanges with the region used for RDA

betas If set is a GenomicRatioSet, should beta values be used? (Default: TRUE)

resultSet Should results be encapsulated in a resultSet? (Default: TRUE)

num_permutations

Numeric with the number of permutations run to compute the p-value. (Default:

1e4)

... Further arguments passed to rda.

Value

Object of class rda or resultSet

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See Also

rda

Examples

```
if (require(minfiData)){
set <- ratioConvert(mapToGenome(MsetEx[1:10,]))
model <- model.matrix(~set$age)
rda <- runRDA(set, model)
rda
}</pre>
```

runRegionAnalysis

Run different DMR detection methods

Description

Run different DMR detection methods

Usage

```
runRegionAnalysis(
    set,
    model,
    methods = c("blockFinder", "bumphunter", "DMRcate"),
    coefficient = 2,
    bumphunter_params = NULL,
    blockFinder_params = NULL,
    dmrcate_params = NULL,
    verbose = FALSE,
    resultSet = TRUE
)
```

Arguments

set GenomicRatioSet, eSet derived object or SummarizedExperiment

model Model matrix representing a linear model.

methods Character vector with the names of the methods used to estimate the regions.

Valid names are: "blockFinder", "bumphunter" and "DMRcate".

coefficient Numeric with the index of the model matrix used to perform the analysis.

bumphunter_params

List with other parameter passed to runBumphunter function.

blockFinder_params

List with other parameter passed to runBlockFinder function.

dmrcate_params List with other parameter passed to runDMRcate function.

verbose Logical value. Should the function be verbose? (Default: FALSE) resultSet Should results be encapsulated in a resultSet? (Default: TRUE)

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Details

This function has been deprecated and will be defunct in the new version.

Value

List or resultSet with the result of the DMR detection methods.

See Also

```
bumphunter, blockFinder, dmrcate
```

Examples

```
if (require(minfiData)){
set <- ratioConvert(mapToGenome(MsetEx[1:10,]))
model <- model.matrix(~Sample_Group, data = pData(MsetEx))
res <- runRegionAnalysis(set, model)
res
}</pre>
```

topRDAhits

Get the top features associated with the RDA

Description

Get a list of the features significantly associated to the first two RDA components

Usage

```
topRDAhits(object, tPV = 0.05)
```

Arguments

object ResultSet

tPV numeric with the p-value threshold. Only features with a p-values below this

threshold will be shown.

Value

data.frame with the features, the component, the correlation and the p-value

Examples

```
if (require(minfiData) & require(GenomicRanges)){
  set <- ratioConvert(mapToGenome(MsetEx[1:10,]))
  model <- model.matrix(~set$sex)
  rda <- runRDA(set, model)
  topRDAhits(rda)
}</pre>
```

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