

# Package ‘MEAL’

October 16, 2018

**Title** Perform methylation analysis

**Version** 1.10.1

**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 (>= 3.2.0), Biobase, MultiDataSet

**License** Artistic-2.0

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**LazyData** true

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---

analysisRegionResults *Old class to encapsulate results (deprecated in new version)*

---

### Description

Old class to encapsulate results (deprecated in new version)

### Usage

```
analysisRegionResults()
```

### Value

Deprecated

### Examples

```
analysisRegionResults()
```

---

analysisResults	<i>Old class to encapsulate results (deprecated in new version)</i>
-----------------	---

---

**Description**

Old class to encapsulate results (deprecated in new version)

**Usage**

```
analysisResults()
```

**Value**

Deprecated

**Examples**

```
analysisResults()
```

---

calculateRelevantSNPs	<i>Calculate the SNPs correlated to cpgs</i>
-----------------------	--

---

**Description**

This function estimates the correlation between the snps and the cpgs. For each pair cpg-SNP the p-value is returned.

**Usage**

```
calculateRelevantSNPs(set, snps, num_cores = 1)
```

**Arguments**

set	MethylationSet
snps	SnpsSet
num_cores	Numeric with the number of cores to be used.

**Value**

Data.frame with the pvalues for pairs SNPs-cpgs. SNPs are in the rows and cpgs in the columns.

**Examples**

```
## Not run:  
## betamatrix: matrix of beta values  
## phenodf: data.frame with the phenotypes  
## snpsobject: SnpsSet  
set <- prepareMethylationSet(matrix = betamatrix, phenotypes = phenodf)  
relevantSNPs <- calculateRelevantSNPs(set, snpsobject)  
  
## End(Not run)
```

---

computeRDAR2      *Compute signification of RDA test*

---

### Description

Compare R2 obtained in our region of interest with the global R<sup>2</sup> and the R<sup>2</sup> of regions with the same number of probes.

### Usage

```
computeRDAR2(fullMat, varsmode1, covarsmode1 = NULL, featNum, R2,
  num_permutations = 1e+05 - 1)
```

### Arguments

fullMat	Matrix with the whole genome expression or methylation values
varsmode1	Matrix with the model
covarsmode1	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 subtracted 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.
meth_set_name	Character vector with the name of the MultiDataSet's slot containing methylation data.
exprs_set_name	Character vector with the name of the MultiDataSet's slot containing expression data.
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

---

correlationMethSNPs     *Computes the correlation between methylation and SNPs*

---

**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**

```
correlationMethSNPs(multiset, meth_set_name = NULL, snps_set_name = NULL,
  range, variable_names, covariable_names = NULL, snps_cutoff = 0.01,
  verbose = TRUE)
```

**Arguments**

multiset	MultiDataSet containing a methylation and an expression slots.
meth_set_name	Character vector with the name of the MultiDataSet's slot containing methylation data.
snps_set_name	Character vector with the name of the MultiDataSet's slot containing SNPs data.
range	GenomicRanges with the range used in the analysis
variable_names	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.
covariable_names	Character vector with the names of the variables that will be used to adjust the model.
snps_cutoff	Numerical with the threshold to consider a p-value from a SNP-cpg correlation significant.
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**

List with the results:

- 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

---

createRanges	<i>Create GenomicRanges from data.frame</i>
--------------	---

---

**Description**

Create GenomicRanges from data.frame

**Usage**

```
createRanges()
```

**Value**

Deprecated

**Examples**

```
createRanges()
```

---

DARegionAnalysis	<i>Analyse methylation or expression in a specific range</i>
------------------	--

---

**Description**

Analyse methylation or expression in a specific range

**Usage**

```
DARegionAnalysis()
```

**Value**

Deprecated

**Examples**

```
DARegionAnalysis()
```

---

explainedVariance	<i>Calculate R2 for different variables</i>
-------------------	---

---

### Description

Using a data.frame as input, calculates the R2 between a dependent variable and some independent variables. Base adjusting by covariates can also be used.

### Usage

```
explainedVariance(data, num_mainvar = 1, num_covariates = 0,  
  variable_label = NULL)
```

### Arguments

data	Data.frame containing the dependent variable in the first column.
num_mainvar	Numerical with the number of variables that should be grouped. They should be at the beginning.
num_covariates	Numerical with the number of variables that should be considered as covariates. Covariates variables must be at the end.
variable_label	Character with the name of the main variable in the results.

### Details

explainedVariance computes R2 via linear models. The first column is considered to be the dependent variable. Therefore, a lineal model will be constructed for each of the remaining variables. In case that covariates were included, they will be included in all the models and, in addition, a model containing only the covariates will be returned.

Some variables can be grouped in the models to assess their effect together.

### Value

Numeric vector with the R2 explained by each of the variables.

### Examples

```
data(mtcars)  
R2 <- explainedVariance(mtcars)  
R2
```



---

exportResults	<i>Exports results data.frames to csv files.</i>
---------------	--

---

### 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

### Usage

```
exportResults(object, dir = "./", prefix = NULL, fName = 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)
}
```

---

filterResults	<i>Filter the data.frame obtained from probe analysis</i>
---------------	---

---

### 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

---

getGeneVals	<i>Get all probes related to a gene</i>
-------------	---

---

**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",
            fName = c("chromosome", "start"), ...)
```

**Arguments**

object	<code>ResultSet</code>
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 <code>fData</code> with the gene information
fNames	Names of the columns of object <code>fData</code> that will be added to the results <code>data.frame</code> .
...	Further arguments passed to <code>getProbeResults</code>

**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)
```

---

getProbeResults	<i>Obtain probe results from a ResultSet</i>
-----------------	--

---

**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"), ...)
```

**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.

---

getRDAResults	<i>Get a summary of RDA results</i>
---------------	-------------------------------------

---

**Description**

Get statistics from RDA result.

**Usage**

```
getRDAResults(object)
```

**Arguments**

object	ResultSet
--------	-----------

**Value**

Numeric vector with the RDA statistics

---

MEAL	<i>MEAL (Methylation and Expression AnaLizer): Package for analysing methylation and expression data</i>
------	--

---

### 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	<i>Defunct functions</i>
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---

### Description

These functions are defunct and no longer available.

### Details

Defunct functions are: multiCorrMethExprs, DAPipeline, DAProbe, DARegion, RDAsset, filterSet, plotBestFeatures, preparePhenotype

---

normalSNP	<i>Normalize SNPs values</i>
-----------	------------------------------

---

### Description

SNPs values, introduced as numerical, are normalized to be used in lineal models.

### Usage

```
normalSNP(snps)
```

### Arguments

snps	Numerical vector or matrix representing the SNPs in the form: 0 homozygote recessive, 1 heterozygote, 2 homozygote dominant.
------	--

### Value

Numerical vector or matrix with the snps normalized.

### Examples

```
snps <- c(1, 0, 0, 1, 0, 0, 2, 1, 2)
normSNPs <- normalSNP(snps)
normSNPs
```

---

plotFeature	<i>Plot values of a feature</i>
-------------	---------------------------------

---

**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")
}
```

---

plotLM	<i>Plot a vector of R2</i>
--------	----------------------------

---

**Description**

Plot a vector of R2 where the first value is the main variable and the last one, if named *covariates* is treated as covariates.

**Usage**

```
plotLM(Rsquares, title = paste("Variance Explained in", feat_name),
  feat_name = NULL, variable_name = names(Rsquares)[1], max_columns = 6)
```

**Arguments**

Rsquares	Numerical vector of R2
title	Character with the plot title
feat_name	Name of the feature used in default title.
variable_name	Character for the first column name
max_columns	Numerical with the maximum number of columns to be plotted.

**Value**

A plot in the graphical device

**Examples**

```
data(mtcars)
R2 <- explainedVariance(mtcars, variable_label = "cyl") ## variable equals to cyl column
plotLM(R2)
```

---

plotRDA

*Plot RDA results*

---

**Description**

Plot RDA results

**Usage**

```
plotRDA(object, pheno, n_feat = 5, main = "RDA plot")
```

**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.
main	Character with the plot title.

**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)))
}
```

---

plotRegion	<i>Plot results in a genomic region</i>
------------	---

---

### Description

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

### Usage

```
plotRegion(rset, range, results = names(rset), genome = "hg19", rset2,
           tPV = 5, fName1 = c("chromosome", "start", "end"),
           fName2 = c("chromosome", "start", "end"))
```

### Arguments

rset	<code>ResultSet</code>
range	<code>GenomicRanges</code> 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 <code>ResultSet</code>
tPV	Threshold for P-Value
fName1	Names from rset fData
fName2	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 `ResultSet`s, rset should contain methylation results and a rset2 the gene expression results.

### Value

Regional plot

---

```
prepareMethylationSet Generating a MethylationSet
```

---

**Description**

Generating a MethylationSet

**Usage**

```
prepareMethylationSet()
```

**Value**

Deprecated

**Examples**

```
prepareMethylationSet()
```

---

```
runBlockFinder Run blockFinder
```

---

**Description**

Run blockFinder to a methylation dataset. This function contains all steps of blockFinder analysis, from model.matrix creation to running the analysis.

**Usage**

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

**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)
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**

runBlockFinder is a wrapper for minfi blockFinder. This function runs all the steps required prior running blockFinder from the methylation set and the formula of the model. This implementation allows running blockFinder to other objects than GenomicRatioSet. The result can be encapsulated in a ResultSet to take advantage of its plotting capabilities.

**Value**

data.frame or resultSet with the result of blockFinder

**See Also**

[blockFinder](#)

---

runBumphunter	<i>Run bumphunter</i>
---------------	-----------------------

---

**Description**

Run bumphunter to a methylation dataset. This function contains all steps of bumphunter analysis, from model.matrix creation to running the analysis.

**Usage**

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

**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**

runBumphunter is a wrapper for minfi bumphunter. This function runs all the steps required prior running bumphunter from the methylation set and the formula of the model. This implementation allows running bumphunter to other objects than GenomicRatioSet. The result can be encapsulated in a ResultSet to take advantage of its plotting capabilities.

If the user wants to run permutations to calculate p-values, this implementation can filter the bumps to avoid doing a very high number of permutations and to reduce computation time. To do so, we can set the maximum number of bumps that we want to permute with the bumps\_max parameter. runBumphunter increases bumphunter\_cutoff value until the number of bumps is lower than bumps\_max.

**Value**

data.frame or resultSet with the result of bumphunter

**See Also**

[bumphunter](#)

---

runDiffMeanAnalysis    *Run differential mean analysis*

---

**Description**

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

**Usage**

```
runDiffMeanAnalysis(set, model, 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.
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
}

```

---

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.

**Usage**

```

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

```

**Arguments**

set	Matrix, GenomicRatioSet, SummarizedExperiment or ExpressionSet.
model	Model matrix or formula to get model matrix from set.
coefficient	Numeric with the coefficients used to make the groups. If NULL, all possible groups will be computed.
resultSet	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
}

```

---

runDMRcate	<i>Run DMRcate</i>
------------	--------------------

---

### Description

Run DMRcate to a methylation dataset. This function contains all steps of DMRcate analysis, from model.matrix creation to running the analysis.

### Usage

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

### 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

runDMRcate is a wrapper for dmrcate function. runDMRcate runs all the steps required prior running blockFinder from the methylation set and the formula of the model. This implementation allows running blockFinder to other objects than GenomicRatioSet. The result can be encapsulated in a ResultSet to take advantage of its plotting capabilities.

### Value

data.frame or resultSet with the result of bumhunter

### See Also

[dmrcate](#), [cpg.annotate](#)

---

runPipeline	<i>Perform differential methylation analysis</i>
-------------	--

---

### Description

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

### Usage

```
runPipeline(set, variable_names, covariable_names = NULL, model = NULL,
  num_vars, sva = FALSE, betas = TRUE, range,
  region_methods = c("bumhunter", "blockFinder", "DMRcate"),
  verbose = FALSE, warnings = TRUE, DiffMean_params = NULL,
  DiffVar_params = list(coefficient = 1:2), bumhunter_params = NULL,
  blockFinder_params = NULL, dmr_cate_params = NULL, rda_params = NULL)
```

**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.
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
region_methods	Character vector with the methods used in runRegionAnalysis. If "none", region analysis is not performed.
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.
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.
rda_params	List with other parameter passed to runRDA function.

**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

**Examples**

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

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**

<code>set</code>	MethylationSet, ExpressionSet or matrix
<code>model</code>	Model matrix or formula to get model matrix from set.
<code>num_vars</code>	Numeric with the number of variables in the matrix for which the analysis will be performed. Compulsory if equation is not null.
<code>range</code>	GenomicRanges with the region used for RDA
<code>betas</code>	If set is a GenomicRatioSet, should beta values be used? (Default: TRUE)
<code>resultSet</code>	Should results be encapsulated in a resultSet? (Default: TRUE)
<code>num_permutations</code>	Numeric with the number of permutations run to compute the p-value. (Default: 1e4)

**Value**

Object of class `rda` or `resultSet`

**See Also**

[rda](#)

**Examples**

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

---

runRegionAnalysis      *Run different DMR detection methods*

---

### Description

This function is a wrapper of two known region differentially methylated detection methods: *Bumphunter*, *blockFinder* and *DMRcate*.

### 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)

### Details

runRegionAnalysis performs a methylation region analysis using *bumphunter*, *blockFinder* and *DMRcate*. *Bumphunter* allows the modification of several parameters that should be properly used.

Cutoff will determine the number of bumps that will be detected. The smaller the cutoff, the higher the number of positions above the limits, so there will be more regions and they will be greater. *Bumphunter* can pick a cutoff using the null distribution, i.e. permutating the samples. There is no standard cutoff and it will depend on the features of the experiment. Permutations are used to estimate p-values and, if needed, can be used to pick a cutoff. The advised number of permutation is 1000. The number of permutations will define the maximum number of bumps that will be considered for analysing. The more bumps, the longer permutation time. As before, there is not an accepted limit but *minfi* tutorial recommends not to exceed 30000 bumps. Finally, if supported, it is very advisable to use parallelization to perform the permutations.

Due to *minfi* design, *BlockFinder* can only be run using own *minfi* annotation. This annotation is based on hg19 and Illumina 450k chipset. CpG sites not named like in this annotation package will not be included. As a result, the use of *BlockFinder* is not recommended.

*DMRcate* uses a first step where linear regression is performed in order to estimate coefficients of the variable of interest. This first step is equal to the calculation performed in *DAProbe*, but using in this situation linear regression and not robust linear regression.

**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
}
```

---

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)
}
```



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