

Package ‘diggit’

November 21, 2019

Version 1.19.0

Date 2014-08-22

Title Inference of Genetic Variants Driving Cellular Phenotypes

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Depends R (>= 3.0.2), Biobase, methods

Imports ks, viper(>= 1.3.1), parallel

Suggests diggitdata

Description Inference of Genetic Variants Driving Cellular Phenotypes
by the DIGGIT algorithm

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biocViews SystemsBiology, NetworkEnrichment, GeneExpression,
FunctionalPrediction, GeneRegulation

git_url <https://git.bioconductor.org/packages/diggit>

git_branch master

git_last_commit 81ce99a

git_last_commit_date 2019-10-29

Date/Publication 2019-11-20

R topics documented:

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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)
```

Arguments

| | |
|-----------|---|
| dnull | Numerical vector representing the null model |
| symmetric | Logical, whether the distribution should be treated as symmetric around zero and only one tail should be approximated |

Value

function with two parameters, x and alternative

aqtl *Inference of aQTL*

Description

This function infers aQTLs from F-CNVs and VIPER activity

Usage

```
aqtl(x, ...)

## S4 method for signature 'diggit'
aqtl(x, mr = 0.01, mr.adjust = c("none", "fdr",
  "bonferroni"), fcnv = 0.01, fcnv.adjust = c("none", "fdr", "bonferroni"),
  method = c("spearman", "mi", "pearson", "kendall"), mindy = FALSE,
  cores = 1, verbose = TRUE)
```

Arguments

| | |
|-----------|---|
| x | Object of class diggit |
| ... | Additional parameters to pass to the function |
| mr | Either a numerical value between 0 and 1 indicating the p-value threshold for the Master Regulator (MR) selection, or a vector of character strings listing the MRs |
| mr.adjust | Character string indicating the multiple hypothesis test correction for the MRs |
| fcnv | Either a numerical value between 0 and 1 indicating the p-value threshold for the F-CNV, or a vector of character strings listing the F-CNVs |

| | |
|-------------|---|
| fcnv.adjust | Character string indicating the multiple hypothesis test correction for the F-CNVs |
| method | Character string indicating the method for computing the association between F-CNV and regulator activity (aQTL analysis) |
| mindy | Logical, whether only post-translational modulators of each evaluated TF should be considered as putative genetic driver |
| cores | Integer indicating the number of cores to use (1 for Windows-based systems) |
| verbose | Logical, whether progress should be reported |

Value

Updated diggit object with viper and aqtl slots

Examples

```
data(gbm.expression, package="diggitdata")
data(gbm.cnv, package="diggitdata")
data(gbm.aracne, package="diggitdata")
dobj <- diggitClass(expset=gbmExprs, cnv=gbmCNV, regulon=gbmTFregulon)
dobj <- fCNV(dobj)
dobj <- aqtl(dobj, mr=c("CEBPD", "STAT3"), fcnv.adjust="fdr")
dobj
diggitAqtl(dobj)[, 1:4]
```

conditional

Conditional analysis of CNVs

Description

This function performs the conditional analysis of fCNVs

Usage

```
conditional(x, ...)

## S4 method for signature 'diggit'
conditional(x, pheno = "cond", group1, group2 = NULL,
  cnv = 0.2, mr = 0.01, mr.adjust = c("none", "fdr", "bonferroni"),
  modul = 0.01, modul.adjust = c("none", "fdr", "bonferroni"),
  fet.pval = 0.05, cores = 1, verbose = TRUE)
```

Arguments

| | |
|--------|---|
| x | Object of class diggit |
| ... | Additional parameters to pass to the function |
| pheno | Character string indicating the feature for sample groups |
| group1 | Character string indicating the treatment group |
| group2 | Optional character string indicating the reference group |
| cnv | Single number or vector of two numbers indicating the thresholds for CNVs |

| | |
|--------------|--|
| mr | Either vector of character strings indicating the MR genes, or number indicating the corrected p-value threshold for selecting the MRs |
| mr.adjust | Character string indicating the multiple-hypothesis correction to apply to the MR p-values |
| modul | Number indicating the p-value threshold for a modulator to be considered associated with the MR activity |
| modul.adjust | Character string indicating the multiple-hypothesis correction to apply to the aQTL results |
| fet.pval | Number indicating the FET p-value threshold for the association between CNVs and sample groups |
| cores | Integer indicating the number of cores to use (1 for Windows-based systems) |
| verbose | Logical, whether progress should be reported |

Value

Object of class `diggit` with conditional analysis results

Examples

```
data(gbm.expression, package="diggitdata")
data(gbm.cnv, package="diggitdata")
data(gbm.aracne, package="diggitdata")
dobj <- diggitClass(expset=gbmExprs, cnv=gbmCNV, regulon=gbmTFregulon)
dobj <- fCNV(dobj)
dobj <- aqtl(dobj, mr=c("CEBPD", "STAT3"), fcnv.adjust="fdr", verbose=FALSE)
dobj <- conditional(dobj, pheno="subtype", group1="MES", group2="PN", mr="STAT3", verbose=FALSE)
dobj
```

| | |
|-------------|-------------------------|
| correlation | <i>Correlation test</i> |
|-------------|-------------------------|

Description

This function computes the correlation between x and y given both are numeric vectors, between the columns of x if it is a numeric matrix, or between the columns of x and y if both are numeric matrixes

Usage

```
correlation(x, y = NULL, method = c("pearson", "spearman", "kendall"),
  pairwise = FALSE)
```

Arguments

| | |
|----------|---|
| x | Numeric vector or matrix |
| y | Optional numeric vector or matrix |
| method | Character string indicating the correlation method |
| pairwise | Logical, whether columns of x and y should be compared in a pairwise manner. x and y must have the same number of columns |

Details

This function computes correlation and associated p-values

Value

Numeric value, vector or matrix of results

Examples

```
x <- seq(0, 10, length=50)
y <- x+rnorm(length(x), sd=2)
correlation(x, y)
```

| | |
|---------------|--------------------------|
| diggitt-class | <i>The diggitt class</i> |
|---------------|--------------------------|

Description

This class stores parameters and results of the diggitt algorithm

This function generates diggitt class objects

Usage

```
diggittClass(expset = NULL, cnv = NULL, regulon = NULL, mindy = NULL,
             fcnv = NULL, mr = NULL, viper = NULL, aqtl = NULL,
             conditional = NULL)
```

Arguments

| | |
|-------------|---|
| expset | ExpressionSet object or numeric matrix of expression data, with features in rows and samples in columns |
| cnv | Numeric matrix of CNV data |
| regulon | Regulon class object containing the transcriptional interactome |
| mindy | Regulon class object containing the post-translational interactome |
| fcnv | Vector of F-CNV p-values |
| mr | Vector of master regulator Z-score (NES) |
| viper | Numeric matrix of VIPER results |
| aqtl | Numeric matrix of aQTL p-values |
| conditional | List containing the conditional analysis results |

Details

see [diggitt-methods](#) for related methods

Value

Object of class diggitt

Slots

expset: ExpressionSet object containing the gene expression data
cnv: Matrix containing the CNV data
regulon: Regulon object containing the transcriptional interactome
mindy: Regulon object containing the post-translational interactome
fcnv: Numeric vector containing the p-values for functional CNVs
mr: Numeric vector of normalized enrichment scores for the MARINa analysis
viper: Numeric matrix of normalized enrichment scores for the VIPER analysis
aqtl: Numeric matrix of association p-values for the aQTL analysis
conditional: List containing the conditional analysis results

Examples

```

data(gbm.expression, package="diggitdata")
data(gbm.aracne, package="diggitdata")
dobj <- diggitClass(expset=gbmExprs, regulon=gbmTFregulon)
print(dobj)

```

fCNV

*Inference of functional CNVs***Description**

This function infers functional CNVs by computing their association with gene expression

Usage

```

fCNV(x, ...)

## S4 method for signature 'diggit'
fCNV(x, expset = NULL, cnv = NULL,
     method = c("spearman", "mi", "pearson", "kendall"), cores = 1,
     verbose = TRUE)

## S4 method for signature 'ExpressionSet'
fCNV(x, cnv, method = c("spearman", "mi", "pearson",
                       "kendall"), cores = 1, verbose = TRUE)

## S4 method for signature 'matrix'
fCNV(x, cnv, method = c("spearman", "mi", "pearson",
                       "kendall"), cores = 1, verbose = TRUE)

## S4 method for signature 'data.frame'
fCNV(x, cnv, method = c("spearman", "mi", "pearson",
                       "kendall"), cores = 1, verbose = TRUE)

```

Arguments

| | |
|---------|--|
| x | Object of class <code>diggit</code> , <code>expressionSet</code> object or numeric matrix of expression data, with features in rows and samples in columns |
| ... | Additional arguments |
| expset | Optional numeric matrix of expression data |
| cnv | Optional numeric matrix of CNVs |
| method | Character string indicating the method for computing the association between CNVs and expression |
| cores | Integer indicating the number of cores to use (1 for Windows-based systems) |
| verbose | Logical, whether to report analysis progress |

Value

Objet of class `diggit` with updated `fCNV` slot

Examples

```

data(gbm.expression, package="diggitdata")
data(gbm.cnv, package="diggitdata")
genes <- intersect(rownames(gbmExprs), rownames(gbmCNV))[1:100]
gbmCNV <- gbmCNV[match(genes, rownames(gbmCNV)), ]
dgo <- diggitClass(expset=gbmExprs, cnv=gbmCNV)

dgo <- fCNV(dgo)
dgo
diggitFcv(dgo)[1:5]
dgo <- fCNV(gbmExprs, gbmCNV)
print(dgo)
diggitFcv(dgo)[1:5]
dgo <- fCNV(exprs(gbmExprs), gbmCNV)
dgo
diggitFcv(dgo)[1:5]
dgo <- fCNV(as.data.frame(exprs(gbmExprs)), gbmCNV)
dgo
diggitFcv(dgo)[1:5]

```

Description

This function infers the master regulators for the transition between two phenotypes

Usage

```
marina(x, ...)
```

```

## S4 method for signature 'matrix'
marina(x, y = NULL, mu = 0, regulon, per = 1000,
       cores = 1, verbose = TRUE)

```

```
## S4 method for signature 'ExpressionSet'
marina(x, pheno = "cond", group1, group2 = NULL,
       mu = 0, regulon, per = 1000, cores = 1, verbose = TRUE)

## S4 method for signature 'diggit'
marina(x, pheno, group1, group2 = NULL, mu = 0,
       regulon = NULL, per = 1000, cores = 1, verbose = TRUE)
```

Arguments

| | |
|---------|--|
| x | Object of class diggit, expressionSet object or numerical matrix containing the test samples |
| ... | Additional arguments |
| y | Numerical matrix containing the control samples |
| mu | Number indicating the control mean when y is omitted |
| regulon | Transcriptional interactome |
| per | Integer indicating the number of permutations to compute the marina null model |
| cores | Integer indicating the number of cores to use (1 for 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

Updated diggit object with Master Regulator results

Examples

```
cores <- 3*(Sys.info()[1] != "Windows")+1
data(gbm.expression, package="diggitdata")
data(gbm.aracne, package="diggitdata")

eset <- exprs(gbmExprs)
samples <- pData(gbmExprs)[["subtype"]]
x <- eset[, samples=="MES"]
y <- eset[, samples=="PN"]
dgo <- marina(x, y, regulon=gbmTFregulon, per=100, cores=cores)
dgo
diggitMR(dgo)[1:5]
dgo <- marina(gbmExprs, pheno="subtype", group1="MES", group2="PN", regulon=gbmTFregulon, per=100, cores=cores)
dgo
diggitMR(dgo)[1:5]
x <- diggitClass(expset=gbmExprs, regulon=gbmTFregulon)
dgo <- marina(x, pheno="subtype", group1="MES", group2="PN", per=100, cores=cores)
dgo
diggitMR(dgo)[1:5]
```

| | |
|------------|---------------------------|
| mutualInfo | <i>Mutual information</i> |
|------------|---------------------------|

Description

This function estimates the mutual information between x and y given both are numeric vectors, between the columns of x if it is a numeric matrix, or between the columns of x and y if both are numeric matrixes

Usage

```
mutualInfo(x, y = NULL, per = 0, pairwise = FALSE, bw = 100,  
           cores = 1, verbose = TRUE)
```

Arguments

| | |
|-----------------------|---|
| <code>x</code> | Numeric vector or matrix |
| <code>y</code> | Optional numeric vector or matrix |
| <code>per</code> | Integer indicating the number of permutations to compute p-values |
| <code>pairwise</code> | Logical, wether columns of x and y should be compared in a pairwise maner. x and y must have the same number of columns |
| <code>bw</code> | Integer indicating the grid size for integrating the joint probability density |
| <code>cores</code> | Integer indicating the number of cores to use (1 for Windows-based systems) |
| <code>verbose</code> | Logical, whether progression bars should be shown |

Details

This function estimates the mutual information between continuous variables using a fix bandwidth implementation

Value

Numeric value, vector or matrix of results

Examples

```
x <- seq(0, pi, length=100)  
y <- 5*sin(x)+rnorm(100)  
cor.test(x, y)  
mutualInfo(x, y, per=100)
```

plot,diggit-method *Diggit plot*

Description

This function generate plots for the diggit conditional analysis

Usage

```
## S4 method for signature 'diggit'  
plot(x, mr = NULL, cluster = NULL, sub = NULL, ...)
```

Arguments

| | |
|---------|--|
| x | Diggit class object |
| mr | Optional vector of character strings indicating the MR names |
| cluster | Optional vector of cluster names |
| sub | Optional sub-title for the plot |
| ... | Additional parameters to pass to the plot function |

Value

Nothing, plots are generated in the default output device

Examples

```
data(gbm.expression, package="diggitdata")  
data(gbm.cnv, package="diggitdata")  
data(gbm.aracne, package="diggitdata")  
dobj <- diggitClass(expset=gbmExprs, cnv=gbmCNV, regulon=gbmTFregulon)  
dobj <- fCNV(dobj)  
dobj <- aqtl(dobj, mr=c("CEBPD", "STAT3"), fcnv.adjust="fdr", verbose=FALSE)  
dobj <- conditional(dobj, pheno="subtype", group1="MES", group2="PN", mr="STAT3", verbose=FALSE)  
plot(dobj, cluster="3")
```

print,diggit-method *Basic methods for class diggit*

Description

This document lists a series of basic methods for the class diggit

Usage

```
## S4 method for signature 'diggit'  
print(x, pval = 0.05)  
  
## S4 method for signature 'diggit'  
show(object)  
  
## S4 method for signature 'diggit'  
exprs(object)  
  
## S4 method for signature 'diggit'  
diggitCNV(x)  
  
## S4 method for signature 'diggit'  
diggitRegulon(x)  
  
## S4 method for signature 'diggit'  
diggitMindy(x)  
  
## S4 method for signature 'diggit'  
diggitFcnv(x)  
  
## S4 method for signature 'diggit'  
diggitMR(x)  
  
## S4 method for signature 'diggit'  
diggitViper(x)  
  
## S4 method for signature 'diggit'  
diggitAqtl(x)  
  
## S4 method for signature 'diggit'  
diggitConditional(x)  
  
## S4 method for signature 'diggit'  
summary(object)  
  
## S4 method for signature 'diggit'  
head(x, rows = 4, cols = 4)  
  
## S4 method for signature 'diggit'  
mindyFiltering(x, mr = 0.01, mr.adjust = c("none", "fdr",  
      "bonferroni"))
```

Arguments

| | |
|--------|--|
| x | Object of class diggit |
| pval | P-value threshold for the conditional analysis |
| object | Object of class diggit |
| rows | Integer indicating the maximum number of rows to show |
| cols | Integer indicating the maximum number of columns to show |

| | |
|------------------------|---|
| <code>mr</code> | Either a numerical value between 0 and 1 indicating the p-value threshold for the Master Regulator (MR) selection, or a vector of character strings listing the MRs |
| <code>mr.adjust</code> | Character string indicating the multiple hypothesis test correction for the MRs |

Value

`print` returns summary information about the diggit object

`show` returns summary information about the object of class diggit

`exprs` returns the ExpressionSet object containing the expression profile data

`diggitCNV` returns a matrix containing the CNV data

`diggitRegulon` returns a regulon object containing the transcriptional interactome

`diggitMindy` returns a regulon object containing the post-translational interactome

`diggitFcv` returns a vector of p-values for the F-CNVs

`diggitMR` returns a vector of master regulators NES

`diggitViper` returns a matrix of VIPER results

`diggitAqtl` returns a matrix of aQTLs (p-value)

`diggitConditional` returns a list containing the conditional analysis results

`summary` returns the integrated results from the conditional analysis

`head` returns a list containing a reduced view for an object of class diggit

`mindyFiltering` returns a diggit class object with CNV and aQTL slots filtered to contain only MINDY post-translational modulators of the MRs

Examples

```
data(gbm.expression, package="diggitdata")
data(gbm.cnv, package="diggitdata")
data(gbm.aracne, package="diggitdata")
dobj <- diggitClass(expset=gbmExprs, cnv=gbmCNV, regulon=gbmTFregulon)
print(dobj)
show(dobj)
exprs(dobj)
diggitCNV(dobj)[1:3, 1:3]
diggitRegulon(dobj)
diggitMindy(dobj)
diggitFcv(dobj)
diggitMR(dobj)
diggitViper(dobj)
diggitAqtl(dobj)
diggitConditional(dobj)
head(dobj)
data(gbm.expression, package="diggitdata")
data(gbm.cnv, package="diggitdata")
data(gbm.mindy, package="diggitdata")
dobj <- diggitClass(expset=gbmExprs, cnv=gbmCNV, mindy=gbmMindy)
dobj <- fCNV(dobj)
dobj
dobj <- mindyFiltering(dobj, mr=c("STAT3", "CEBPD"))
dobj
```

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