

Package ‘discordant’

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Title The Discordant Method: A Novel Approach for Differential Correlation

Depends R (>= 4.1.0)

Description Discordant is an R package that identifies pairs of features that correlate differently between phenotypic groups, with application to -omics data sets. Discordant uses a mixture model that “bins” molecular feature pairs based on their type of coexpression or coabundance. Algorithm is explained further in ‘‘Differential Correlation for Sequencing Data’’ (Siska et al. 2016).

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Suggests BiocStyle, knitr, testthat (>= 3.0.0)

Imports Rcpp, Biobase, stats, biwt, gtools, MASS, tools, dplyr, methods, utils

License GPL-3

URL <https://github.com/siskac/discordant>

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Contents

createVectors	2
discordant	3
discordantRun	4
fishersTrans	6
splitMADOutlier	7
TCGA_Breast_miRNASeq	8
TCGA_Breast_miRNASeq_voom	9
TCGA_Breast_RNASeq	9
TCGA_Breast_RNASeq_voom	10
TCGA_GBM_miRNA_microarray	11
TCGA_GBM_transcript_microarray	11

Index

13

createVectors

Create correlation coefficient vectors based on bivariate data

Description

Calculates correlation coefficients based on two groups of -omics bivariate data. Currently, only two groups of samples can be specified. Used to make input for discordantRun().

Usage

```
createVectors(
  x,
  y = NULL,
  groups,
  cor.method = c("spearman", "pearson", "bwmc", "sparcc")
)
```

Arguments

x	ExpressionSet of -omics data
y	Optional second ExpressionSet of -omics data, induces dual -omics analysis
groups	n-length vector of 1s and 2s matching samples belonging to groups 1 and 2
cor.method	Correlation method to measure association. Options are "spearman", "pearson", "bwmc" and "sparcc"

Details

Creates vectors of correlation coefficients based on feature pairs within x or between x and y. The names of the vectors are the feature pairs taken from x and y.

Value

List of two named numeric vectors. Vectors give the correlation coefficients for groups 1 and 2 respectively, and vector names give the each feature for the respective feature pair separated by an underscore.

Author(s)

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References

Siska C, Bowler R and Kechris K. The Discordant Method: A Novel Approach for Differential Correlation. (2015) Bioinformatics. 32(5): 690-696.

Friedman J and Alm EJ. Inferring Correlation Networks from Genomic Survey Data. (2012) PLoS Computational Biology. 8:9, e1002687.

Examples

```
## load data
data("TCGA_GBM_miRNA_microarray")
data("TCGA_GBM_transcript_microarray")
print(colnames(TCGA_GBM_transcript_microarray)) # look at groups
groups <- c(rep(1,10), rep(2,20))
# transcript-transcript pairs
vectors <- createVectors(TCGA_GBM_transcript_microarray,
                           groups = groups, cor.method = c("pearson"))
# miRNA-transcript pairs
vectors <- createVectors(TCGA_GBM_transcript_microarray,
                           TCGA_GBM_miRNA_microarray, groups = groups)
```

Description

Discordant is a method to determine differential correlation of molecular feature pairs from -omics data using mixture models. Algorithm is explained further in Siska et al.

Author(s)

Charlotte Siska
 Max McGrath
 Katerina Kechris

discordantRun	<i>Run Discordant Algorithm</i>
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Description

Runs discordant algorithm on two vectors of correlation coefficients.

Usage

```
discordantRun(
  v1,
  v2,
  x,
  y = NULL,
  transform = TRUE,
  subsampling = FALSE,
  subSize = NULL,
  iter = 100,
  components = 3
)
```

Arguments

v1	Vector of correlation coefficients in group 1
v2	Vector of correlation coefficients in group 2
x	ExpressionSet of -omics data
y	ExpressionSet of -omics data, induces dual -omics analysis
transform	If TRUE v1 and v2 will be Fisher transformed
subsampling	If TRUE subsampling will be run
subSize	Indicates how many feature pairs to be used for subsampling. Default is the feature size in x
iter	Number of iterations for subsampling. Default is 100
components	Number of components in mixture model.

Details

The discordant algorithm is based on a Gaussian mixture model. If there are three components, correlation coefficients are clustered into negative correlations (-), positive correlations (+) and no correlation (0). If there are five components, then there are two more classes for very negative correlation (-) and very positive correlations (++) . All possible combinations for these components are made into classes. If there are three components, there are 9 classes. If there are five components, there are 25 classes.

The posterior probabilities for each class are generated and outputted into the value probMatrix. The value probMatrix is a matrix where each column is a class and each row is a feature pair. The values discordPPVector and discordPPMatrix are the summed differential correlation posterior probability for each feature pair. The values classVector and classMatrix are the class with the highest posterior probability for each feature pair.

Value

discordPPVector Vector of differentially correlated posterior probabilities.

discordPPMatrix Matrix of differentially correlated posterior probabilities where rows and columns reflect features

classVector Vector of classes that have the highest posterior probability

classMatrix Matrix of classes that have the highest posterior probability where rows and columns reflect features

probMatrix Matrix of posterior probabilities where rows are each molecular feature pair and columns are nine different classes

loglik Final log likelihood

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References

Siska C, Bowler R and Kechris K. The Discordant Method: A Novel Approach for Differential Correlation (2015), Bioinformatics. 32 (5): 690-696.

Lai Y, Zhang F, Nayak TK, Modarres R, Lee NH and McCaffrey TA. Concordant integrative gene set enrichment analysis of multiple large-scale two-sample expression data sets. (2014) BMC Genomics 15, S6.

Lai Y, Adam B-l, Podolsky R, She J-X. A mixture model approach to the tests of concordance and discordance between two large-scale experiments with two sample groups. (2007) Bioinformatics 23, 1243-1250.

Examples

```
# Load Data
data(TCGA_GBM_miRNA_microarray)
data(TCGA_GBM_transcript_microarray)
```

```

print(colnames(TCGA_GBM_transcript_microarray)) # look at groups
groups <- c(rep(1,10), rep(2,20))

## DC analysis on only transcripts pairs

vectors <- createVectors(TCGA_GBM_transcript_microarray,
                           groups = groups)
result <- discordantRun(vectors$v1, vectors$v2,
                           TCGA_GBM_transcript_microarray)

## DC analysis on miRNA-transcript pairs

vectors <- createVectors(TCGA_GBM_transcript_microarray,
                           TCGA_GBM_miRNA_microarray, groups = groups,
                           cor.method = c("pearson"))
result <- discordantRun(vectors$v1, vectors$v2,
                           TCGA_GBM_transcript_microarray,
                           TCGA_GBM_miRNA_microarray)

```

fishersTrans*Fisher Transformation of Pearson Correlation Coefficients to Z Scores***Description**

Transforms Pearson's correlation coefficients into z scores using Fisher's method.

Usage

```
fishersTrans(rho)
```

Arguments

<code>rho</code>	Integer or numeric vector of Pearson's correlation coefficients
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Details

Fisher's transformation is when correlation coefficients are transformed into a z score. These z scores have an approximately normal distribution.

Value

Returns Fisher-transformed correlation coefficients

References

Fisher, R.A. (1915). "Frequency distribution of the values of the correlation coefficient in samples of an indefinitely large population". *Biometrika* (Biometrika Trust) 10 (4).

Examples

```
## Create integer or list of Pearson's correlation coefficients.

library(MASS)
rhoV <- as.vector(cor(t(mvrnorm(10,rep(3,100),diag(100)))))

## Determine Fisher-Transformed z scores of rho
zV <- fishersTrans(rhoV)
```

splitMADOutlier	<i>Outliers using left and right MAD</i>
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Description

Identify features with outliers using left and right median absolute deviation (MAD).

Usage

```
splitMADOutlier(mat, filter0 = TRUE, threshold = 2)
```

Arguments

mat	m by n matrix of -omics data, where rows are features and columns samples.
filter0	Option to filter out features if they have at least one 0 value. Default is TRUE.
threshold	Threshold of how many MADs outside the left or right median is used to determine features with outliers.

Details

The purpose of this function is to determine outliers in non-symmetric distributions. The distribution is split by the median. Outliers are identified by being however many median absolute deviations (MAD) from either split distribution.

Value

mat.filtered Input matrix where features with outliers filtered out.

index Index of features that have no outliers.

References

Leys C, Klein O, Bernard P and Licata L. "Detecting Outliers: Do Not Use Standard Deviation Around the Mean, Use Absolute Deviation Around the Median." *Journal of Experimental Social Psychology*, 2013. 49(4), 764-766.

Magwene, PM, Willis JH, Kelly JK and Siepel A. "The Statistics of Bulk Segregant Analysis Using Next Generation Sequencing." *PLoS Computational Biology*, 2011. 7(11), e1002255.

Examples

```
## Simulate matrix of continuous -omics data.
data(TCGA_Breast_miRNASeq)

## Filter matrix based on outliers.
mat.filtered <- splitMADOutlier(TCGA_Breast_miRNASeq)$mat.filtered
```

TCGA_Breast_miRNASeq *Example breast miRNA-Seq count dataset.*

Description

This dataset contains TMM normalized voom-transformed miRNA count values from miRNASeq that was taken from the Cancer Genome Atlas, or TCGA. The dataset has 100 miRNA and 57 samples. The original dataset has 212 miRNA and 57 samples.

Usage

```
data(TCGA_Breast_miRNASeq)
```

Format

An ExpressionSet with 100 features, 57 samples

Source

<http://cancergenome.nih.gov/>

References

National Institutes of Health. The Cancer Genome Atlas.

Examples

```
data(TCGA_Breast_miRNASeq)
```

TCGA_Breast_miRNASeq_voom

Example breast miRNA-Seq voom-transformed count dataset.

Description

This dataset contains TMM normalized voom-transformed miRNA count values from miRNASeq that was taken from the Cancer Genome Atlas, or TCGA. The dataset has 100 miRNA and 57 samples. The original dataset has 212 miRNA and 57 samples.

Usage

```
data(TCGA_Breast_miRNASeq_voom)
```

Format

An ExpressionSet with 100 features and 57 samples

Source

<http://cancergenome.nih.gov/>

References

Charity W Law, Yunshun Chen, Wei Shi, Gordon K Smyth. voom: precision weights unlock linear model analysis tools for RNA-seq read counts. 2014. *Genome Biology*, 15:R29.

National Institutes of Health. The Cancer Genome Atlas.

Examples

```
data(TCGA_Breast_miRNASeq_voom)
```

TCGA_Breast_RNASeq

TCGA Breast Cancer RNASeq Sample Dataset

Description

This dataset contains TMM normalized RNA count values from RNASeq that was taken from the Cancer Genome Atlas, or TCGA. It has 100 features and 57 samples. The original dataset had 17972 features and 57 samples.

Usage

```
data(TCGA_Breast_RNASeq)
```

Format

An ExpressionSet with 100 features and 57 samples

Source

<http://cancergenome.nih.gov/>

References

Charity W Law, Yunshun Chen, Wei Shi, Gordon K Smyth. voom: precision weights unlock linear model analysis tools for RNA-seq read counts. 2014. *Genome Biology*, 15:R29.

National Institutes of Health. The Cancer Genome Atlas.

Examples

```
data(TCGA_Breast_RNASeq)
```

TCGA_Breast_RNASeq_voom

TCGA Breast Cancer RNASeq Sample Dataset

Description

This dataset contains TMM normalized voom-transformed RNA count values from RNASeq that was taken from the Cancer Genome Atlas, or TCGA.

Usage

```
data(TCGA_Breast_miRNASeq_voom)
```

Format

An ExpressionSet with 100 features and 57 samples

Source

<http://cancergenome.nih.gov/>

References

Charity W Law, Yunshun Chen, Wei Shi, Gordon K Smyth. voom: precision weights unlock linear model analysis tools for RNA-seq read counts. 2014. *Genome Biology*, 15:R29.

National Institutes of Health. The Cancer Genome Atlas.

Examples

```
data(TCGA_Breast_miRNASeq_voom)
```

TCGA_GBM_miRNA_microarray

TCGA Glioblastoma Multiforme miRNA Sample Dataset

Description

This dataset contains miRNA expression values from a microarray that was taken from the Cancer Genome Atlas, or TCGA. It has 10 features and 30 samples. The original dataset had 331 features and 30 samples.

Usage

```
data(TCGA_GBM_miRNA_microarray)
```

Format

An ExpressionSet with 10 features, 30 samples

Source

<http://cancergenome.nih.gov/>

References

National Institutes of Health. The Cancer Genome Atlas.

Examples

```
data(TCGA_GBM_miRNA_microarray)
```

TCGA_GBM_transcript_microarray

TCGA Glioblastoma Multiforme Transcript Sample Dataset

Description

This dataset contains transcript expression values from a microarray that was taken from the Cancer Genome Atlas, or TCGA. It has 10 features and 30 samples. The original dataset had 72656 features and 30 samples.

Usage

```
data(TCGA_GBM_transcript_microarray)
```

Format

An ExpressionSet with 10 features, 30 samples

Source

<http://cancergenome.nih.gov/>

References

National Institutes of Health. The Cancer Genome Atlas.

Examples

```
data(TCGA_GBM_transcript_microarray)
```

Index

* datasets

TCGA_Breast_miRNASeq, 8
TCGA_Breast_miRNASeq_voom, 9
TCGA_Breast_RNASeq, 9
TCGA_Breast_RNASeq_voom, 10
TCGA_GBM_miRNA_microarray, 11
TCGA_GBM_transcript_microarray, 11

createVectors, 2

discordant, 3

discordantRun, 4

fishersTrans, 6

splitMADOutlier, 7

TCGA_Breast_miRNASeq, 8
TCGA_Breast_miRNASeq_voom, 9
TCGA_Breast_RNASeq, 9
TCGA_Breast_RNASeq_voom, 10
TCGA_GBM_miRNA_microarray, 11
TCGA_GBM_transcript_microarray, 11