Package ‘PROMISE’

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Type Package

Title PRojection Onto the Most Interesting Statistical Evidence

Description A general tool to identify genomic features with a specific biologically interesting pattern of associations with multiple endpoint variables as described in Pounds et. al. (2009) Bioinformatics 25: 2013-2019

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Imports Biobase, GSEABase, stats

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R topics documented:

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**Description**

a tool to identify genomic features with a specific biologically interesting pattern of associations with multiple endpoint variables

**Details**

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The PROMISE (PRojection Onto the Most Interesting Statistical Evidence) is performed by calling function PROMISE. The array data and endpoint data are passed through an ExpressionSet; the gene set definition is passed through a GeneSetCollection, and PROMISE definition is passed through a data frame. promise.genestat and avg.abs.genestat are called internally by PROMISE. Two R routines for calculating association statistics with individual endpoint variable(jung.rstat and spearman.rstat) are provided in this version. Users could provide their own R routines written in a similar fashion.

**Author(s)**

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avg.abs.genestat

Function to Compute Gene Set Statistics

Description

A function to calculate the mean of absolute values of statistics based on a gene set definition

Usage

avg.abs.genestat(gene.res, probes, GS.data)
Arguments

gene.res  
a data frame. Each row gives test statistics for a genomic variable. Each column  
corresponds to an endpoint variable.

probes  
a vector that links the gene.res to GS.data.

GS.data  
a data frame with first column for probe set identifier and second column for  
gene set identifier. Each row assigns a probe set to a gene set. Each probe set  
may be assigned to multiple gene sets or no gene set at all.

Value

Return a matrix of statistics. Each row gives the mean absolute value of test statistics of genes  
belonging to a gene set. The columns are same as in gene.res.

Note

A function internally called by PROMISE.

Author(s)

Stan Pounds <stanley.pounds@stjude.org>; Xueyuan Cao <xueyuan.cao@stjude.org>

References

Goeman JJ and Buhlmann P (2007) Analyzing gene expression data in terms of gene sets: method-  

See Also

PROMISE

Examples

```r
## load sampExprSet sampGeneSet.
data(sampExprSet)
data(sampGeneSet)

## extract expression matrix from sampExprSet
Y <- exprs(sampExprSet)
probes <- rownames(Y)

## convert sampGeneSet to a data frame
GS.data <- NULL
for (i in 1:length(sampGeneSet)){
  tt <- sampGeneSet[[i]][[1]]
  this.name <- unlist(geneIds(tt))
  this.set <- setName(tt)
  GS.data <- rbind.data.frame(GS.data,
    cbind.data.frame(featureID=as.character(this.name),
      setID=rep(as.character(this.set),
      length(this.name))))
```
jung.rstat

}

## Calculate the mean of absolute values of statistics
## This is only a demo, probe expression values are used
## instead of statistics
test <- avg.abs.genestat(Y, probes, GS.data)

---

**jung.rstat**  
*Function to Compute Jung’s Statistics*

**Description**

Compute statistic that measures the correlation of many continuous variables with a censored time-to-event variable.

**Usage**

```r
jung.rstat(x, time.cens, strat = NULL)
```

**Arguments**

- `x`: a data frame with row corresponding to probe set and column corresponding to subjects, the order of columns (subjects) should match the order of rows in `time.cens`.
- `time.cens`: a data frame with number of row equal to number of column in `x`. It contains two columns with first for time and second for censor (1 = event, 0 = censored).
- `strat`: a vector of stratum to calculate stratified r-type association statistics, default = NULL.

**Value**

Returns a vector of Jun’s r-type association statistics.

**Note**

The order of subjects in `x` (column), `time.cens`, and `strat` should all match. The original statistic proposed by Jung, Owzar, and George can be written as a dot-product. The statistic returned by this routine is expressed in the form of a correlation statistic by dividing the dot product by the square root of the lengths of the two vectors in the numerator.

**Author(s)**

Stan Pounds <stanley.pounds@stjude.org>; Xueyuan Cao <xueyuan.cao@stjude.org>

**References**

See Also

PROMISE

Examples

```r
## load sampExprSet.
data(sampExprSet)

## extract expression matrix from sampExprSet
Y <- exprs(sampExprSet)

## extract end point data from sampExprSet
time.cens <- pData(phenoData(sampExprSet))[, 3:4]
strat <- pData(phenoData(sampExprSet))$strat

## compute Jung's r-type association statistics
jungstat <- jung.rstat(Y, time.cens, strat = strat)
```

---

**phPatt**

*Phenotype Pattern Definition Set*

### Description

This hypothetical phenotype pattern definition set *phPatt* has three columns: `stat.coef`, `stat.func`, and `endpt.vars`. It defines an association pattern for three phenotypes.

### Usage

```r
data(phPatt)
```

---

**PROMISE**

*PRojection onto the Most Interesting Statistical Evidence*

### Description

Perform permutation-based test to identify genes with expression levels having a specific biologically interesting pattern of associations with multiple endpoint variables.

### Usage

```r
PROMISE(exprSet, geneSet=NULL, promise.pattern, strat.var=NULL, proj0=FALSE, seed=13, nbperm=FALSE, max.ntail=100, nperms=10000)
```
Arguments

exprSet an ExpressionSet class contains minimum of exprs (expression matrix) and phenoData (AnnotatedDataFrame of end point data). Please refer to Biobase for details on how to create such an ExpressionSet.

geneSet a GeneSetCollection class with minimum of setName and geneIDs for each GeneSet. Please refer to GSEABase for how to create such a GeneSetCollection class. The default is NULL which will perform no gene set enrichment analysis.

promise.pattern a data frame defining the association pattern of interest. The column names must be stat.coef, stat.func, and endpt.vars. The stat.coef column gives the coefficients for combining the statistics of association of genomic variables with individual endpoint variable into the ultimate PROMISE statistic. If proj0=TRUE, the stat.coef is ignored. The stat.func column gives the name of the R routine that computes the test statistic of association of the endpoint variables. Two R routines (jung.rstat and spearman.rstat) are provided. Users can provide their own routine accordingly. The endpt.vars column gives the name(s) of variable(s) in the endpoint data file needed to compute each term of the PROMISE statistic. A common without a space should be used to separate multiple variables that correspond to the same term in the association pattern definition.

strat.var the name or numeric value of stratum variable in exprSet for stratified analysis. The default is NULL which performs an unstratified analysis.

proj0 indicator of whether projection to 0 is performed. It takes two valid values: TRUE or FALSE. If proj0=TRUE, PROMISE statistics is the sum of squares of individual endpoint statistic and the stat.coeff in promise.pattern is ignored. The default is FALSE.

seed initial seed of random number generator. The default is 13.

nbperm indicator of fast permutation using negative binomial strategy, taking two valid values: FALSE or TRUE. The default is FALSE.

max.ntail number of success if nbperm = T. Further permutation will not be performed for gene(s) or gene set(s) which max.ntail permuted statistics are greater or equal to the observed statistics. The default is 100

nperms number of permutations. The default is 10,000.

Value

$generes individual genes’ test statistics and p-values for each individual endpoint and PROMISE analysis. If nbperm=T, the last column contains number of permutations for each gene.

$setres gene set’s test statistics and p-values for each individual endpoint and PROMISE analysis. If nbperm=T, the last column contains number of permutations for gene set. If geneSet is NULL, the value of this component is also NULL.

Author(s)

Stan Pounds <stanley.pounds@stjude.org>; Xueyuan Cao <xueyuan.cao@stjude.org>
References


See Also

jung.rstat avg.abs.genestat promise.genestat spearman.rstat promise.pattern

Examples

```r
## load sampExprSet, sampGeneSet, phPatt.
data(sampExprSet)
data(sampGeneSet)
data(phPatt)

## Perform PROMISE procedure without GSEA
test1 <- PROMISE(exprSet=sampExprSet,
     geneSet=NULL,
     promise.pattern=phPatt,
     strat.var=NULL,
     proj0=FALSE,
     nbperm=FALSE,
     max.ntail=10,
     seed=13,
     nperms=100)

## Perform PROMISE procedure with GSEA and using fast permutation
test2 <- PROMISE(exprSet=sampExprSet,
     geneSet=sampGeneSet,
     promise.pattern=phPatt,
     strat.var=NULL,
     proj0=TRUE,
     nbperm=TRUE,
     max.ntail=10,
     seed=13,
     nperms=100)
```

promise.genestat  
Function to Calculate PROMISE Statistics

Description

a function to calculate individual gene and PROMISE statistics for a defined pattern of association

Usage

```r
promise.genestat(Y, ph.data, ph.pattern, strat = NULL, proj0=FALSE)
```
Arguments

Y
a data frame with row corresponding to probe set and column corresponding to subjects, the order of column should match order of row in ph.data.

ph.data
a data frame with rows corresponding to subjects and columns corresponding to endpoint variables.

ph.pattern
a data frame with column headers: stat.coef, stat.func, endpt.vars. The stat.coef column gives the coefficients for combining the statistics of association of genomic variable with individual endpoint variable into the ultimate PROMISE statistic. If proj0=TRUE, the stat.coef is ignored. The stat.func column gives the name of the R routine that computes the test statistic of association of the end point variables. jung.rstat and spearman.rstat are provided. Users can provide their own routines accordingly. The endpt.vars column gives the name(s) of variable(s) in ph.data needed to compute each term of the PROMISE statistic. A comma without a space should be used to separate multiple variables that correspond to the same term in the association pattern definition.

strat
a vector of stratum to calculate stratified statistics. The default is NULL.

proj0
indicator of whether projection to 0 is performed. It takes two valid values: TRUE or FALSE. If proj0=TRUE, PROMISE statistics is the sum of squares of individual statistics. The default is FALSE.

Value

a matrix of statistics. Each row gives gene's statistics of each individual endpoint and the PROMISE statistics defined in ph.pattern.

Note

a function internally called by PROMISE.

Author(s)

Stan Pounds <stanley.pounds@stjude.org>; Xueyuan Cao <xueyuan.cao@stjude.org>

References


See Also

PROMISE

Examples

## load sampExprSet, phPatt.
data(sampExprSet)
data(phPatt)
Y <- exprs(sampExprSet)
ph.data <- pData(phenoData(sampExprSet))

test <- promise.genestat(Y, ph.data, phPatt, strat=ph.data[, 5])
test2 <- promise.genestat(Y, ph.data, phPatt, strat=ph.data[, 5], proj0=TRUE)

promise.pattern

### Description

PROMISE pattern is a data frame of association pattern definition, consisting of three columns.

### Format

PROMISE pattern: The column names must be `stat.coef`, `stat.func`, and `endpt.vars`.

* `stat.coef` column gives the coefficients for combining the statistics of association of genomic variable with individual endpoint variable into the ultimate PROMISE statistic.

* `stat.func` column gives the name of the R routine that computes the test statistic of association of the endpoint variables. Two R routines (`jung.rstat` and `spearman.rstat`) are provided in current release. Users can provide their own routine accordingly.

* `endpt.vars` column gives the name(s) of variable(s) in the endpoint data frame needed to compute each term of the PROMISE statistic. If more than one variables involve in one term, they should be separated by a `comma` without space.

### Author(s)

Stan Pounds <stanley.pounds@stjude.org>; Xueyuan Cao <xueyuan.cao@stjude.org>

### References


### See Also

PROMISE
**sampExprSet**

*An Example Expression Set*

**Description**

This hypothetical expression set *sampExprSet* belongs to an *ExpressionSet* class. It contains 100 genomic features (probe_1 to probe_100) for 50 subjects (array_1 to array_50) and phenotype data of drugLevel, residualDisease, obsTime, obsCensor and strat. The expression values can be accessed by `exprs(sampExprSet)`. The phenotype data can be accessed by `pData(phenoData(sampExprSet))`.

**Usage**

```r
data(sampExprSet)
```

---

**sampGeneSet**

*An Example Gene Set Collection*

**Description**

This hypothetical gene set *sampGeneSet* belongs to a *GeneSetCollection* class. It contains 10 gene sets (*GeneSet* class).

**Usage**

```r
data(sampGeneSet)
```

---

**spearman.rstat**

*Function to Calculate Spearman Correlation Statistics*

**Description**

A function to calculate Spearman rank correlation of each gene in an array data with a continuous variable.

**Usage**

```r
spearman.rstat(Y, x, strat = NULL)
```

**Arguments**

- `Y` a numeric data frame. Each row gives values of one genomic variable.
- `x` a vector of continuous variable.
- `strat` a vector of stratum to calculate stratified correlation statistics, default = NULL.
Value

Return a vector of Spearman rank correlation statistics.

Author(s)

Stan Pounds <stanley.pounds@stjude.org>; Xueyuan Cao <xueyuan.cao@stjude.org>

References

Spearman C. (1904) The proof and measurement of association between two things. Amer. J. Psychol. 15: 72-101

See Also

PROMISE

Examples

```r
## load sampExprSet.
data(sampExprSet)

## extract expression matrix from sampExprSet
Y <- exprs(sampExprSet)

## extract end point data from sampExprSet
x <- pData(phenoData(sampExprSet))$drugLevel
strat <- pData(phenoData(sampExprSet))$strat

## Calculate Spearman correlation statistics
test <- spearman.rstat(Y, x, strat = strat)
```
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