Package ‘SAGx’

January 15, 2017

Type Package
Title Statistical Analysis of the GeneChip
Version 1.48.0
Author Per Broberg
Maintainer Per Broberg, <pi.broberg@gmail.com>
Depends R (>= 2.5.0), stats, multtest, methods
Suggests KEGG.db, hu6800.db, MASS
Imports Biobase, stats4
Description A package for retrieval, preparation and analysis of data from the Affymetrix GeneChip. In particular the issue of identifying differentially expressed genes is addressed.
License GPL-3
LazyLoad yes
URL http://home.swipnet.se/pibroberg/expression_hemsida1.html
biocViews Microarray, OneChannel, Preprocessing, DataImport,
            DifferentialExpression, Clustering, MultipleComparison,
            GeneExpression, GeneSetEnrichment, Pathways, Regression, KEGG
NeedsCompilation yes

R topics documented:
clin2mim ................................. 2
cluster.q .................................. 3
estimatep0 ................................ 4
fetchSignal ................................ 4
firstpass .................................. 5
fom ....................................... 6
fp.fn ..................................... 7
Fstat ..................................... 8
gap ....................................... 9
GSEA.mean.t .............................. 10
JT.test .................................. 11
list.experiments ......................... 13
list.intersection.p ..................... 13
mat2TeX .................................. 14
Output a script file to WinMIM, linking clinical data and gene expression.

Description

Given a clinical variable, it produces a script file for WinMIM by calculating means and covariances and for the N most highly correlated probes (in absolute value). Here N is an input parameter, but a recommended value 10. WinMIM can find a relevant graphical model for the dependencies between the probes and the clinical variable.

Usage

clin2mim(variable="FEV1.ACTUAL", data=dbs, clindat=clinical, probes=probes, N=10, out="mimscr.txt")

Arguments

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>variable</td>
<td>Clinical variable to be examined</td>
</tr>
<tr>
<td>data</td>
<td>The input data set, with subject id in first column.</td>
</tr>
<tr>
<td>clindat</td>
<td>The input clinical data, with subject id in first column</td>
</tr>
<tr>
<td>probes</td>
<td>The name of the probes in the order of data</td>
</tr>
<tr>
<td>N</td>
<td>The number of highly correlated probes to be studied</td>
</tr>
<tr>
<td>out</td>
<td>The MIM script file</td>
</tr>
</tbody>
</table>

Value

The correlation matrix
Note
David Edwards’ program WinMIM can be found on StatLib (http://lib.stat.cmu.edu/graphmod/). In MIM issue input mimscript.txt and the calculations to find a model will start. When finished go to the Graphics menu and click on Independence Graph. The resulting graph can be exported both to WMF and LaTeX.

Author(s)
Per Broberg

References
Whittaker, Joe (1990) Graphical Models in Multivariate Analysis. Wiley

---

cluster.q

Clustering Goodness measured by Q2

Description
Calculates a goodness of clustering measure based prediction sum squares.

Usage
cluster.q(data,cluster)

Arguments
- data: The data matrix
- cluster: a vector describing the cluster memberships

Value
The clustering mean Q2

Author(s)
Per Broberg

References
estimatep0  

**Estimate proportion unchanged genes**

**Description**

The function uses the vector of p-values to estimate p0.

**Usage**

```r
estimatep0(ps = pp, B = 500, range = seq(0, 0.95, by = 0.05))
```

**Arguments**

- `ps`  
  the vector of p-values, e.g. from firstpass
- `B`  
  the number of Bootstrap samples
- `range`  
  the values considered

**Value**

the value of p0, the proportion unchanged genes

**Author(s)**

Per Broberg

**References**


---

fetchSignal  

**Fetch data from the GATC database**

**Description**

Fetch FILENAME, PROBESET, SIGNAL and ABS\_CALL from the GATC database

**Usage**

```r
fetchSignal(experiment="AZ33 ALI", channel, chip="HG_U95Av2")
```

**Arguments**

- `experiment`  
  The name of the experiment corresponding to an individual chip
- `channel`  
  The channel to the database
- `chip`  
  the chip type

**Value**

dataframe with columns
firstpass

Author(s)

Ported to R by Per Broberg. Original Oracle code by Petter Hallgren, with input from Petra Johansson.

Examples

```r
# Not run:
# Do not run example 1. Fetch Probeset, Signal, ABS_CALL and CHIP for one sample.
library(RODBC)
(channel<-odbcConnect("DSN",uid="USERID",pwd="PASSWORD"))
ali.data <-fetchSignal(experiment="AZ33 ALI", channel, chip="hg_u95a")
colnames(ali.data)
# [1] "FILENAME" "PROBESET" "SIGNAL" "ABS_CALL" "CHIP"

# Do not run example 2
(t1 <- paste("select q1.name as name from experiment q1, physical_chip q2, chip_design q3")
  t2 <- paste("where q1.physical_chip_id=q2.id and q3.id=q2.design_id and ")
  t3 <- paste("upper(q1.name) like ' 
Ids <- sqlQuery(channel,paste(t1,t2,t3) )
# fetch Signal from GATC corresponding to the U95A chip for all samples in experiment. #
  tmp <- apply(Ids,1,toupper)
probes <- data.frame(fetchSignal(experiment=tmp[1],channel, chip="hg_u95a"),"PROBESET")
test <- matrix(nrow=nrow(as.data.frame(probes)),ncol=nrow(Ids))
for(i in 1:nrow(as.data.frame(tmp))){
  test[,i] <- fetchSignal(experiment=tmp[i],channel, chip="hg_u95a"),"SIGNAL"]
  }
codes <- data.frame(apply(Ids,1,code<-function(x) substr(x,1,5)))
colnames(test) <- as.character(t(codes))
test <- test[,order(colnames(test))]
# End(Not run)
```

Description

Does a first-pass analysis for a comparative experiment. This includes the calculation of means and confidence intervals for the groups, and finally a Kruskal-Wallis p-value for the null hypothesis of no difference.

Usage

```r
firstpass(data = D, probes = probes , g, log = FALSE, present = NULL, labels = NULL, output.data = FALSE)
```

Arguments

- `data` A data frame with one array in each column
- `probes` a vector containing the names of the probes in the same order as rows in D
- `g` A vector with the groups for the arrays, eg. TREATMENT and CONTROL
- `present` A dataframe with the Present calls, 3 = P, 2 = M, 1 = A.
log

if TRUE then data are log transformed through \( t(x) = \log(1+x) \) and geometric means are calculated

labels

a vector of labels given the group means

output.data

if T the raw data are included in the output

Details

A speed-up for Wilcoxon based on Kronecker products was put in place with SAGx v.1.4.5. Ties are currently not taken into account in Wilcoxon.

Value

A dataframe with the columns PROBES, followed by group means and sd’s, lower confidence intervals and then, upper confidence interval (confidence level 95%), and finally the input data. If present names a dataframe holding the present calls the proportion present is calculated. Furthermore, if there are two groups the difference in group means is added.

Examples

```r
## Not run:
# not run
g <- c(rep(1,4),rep(2,4)); labs <- c("Mean Diet","Mean Control"); probes <- paste("Probe",1:1000)
firstpass(data = utmat[,1:2], probes = probes[,1:2], g, log = FALSE, labels = labs)

# Probesets Mean Diet Mean Control LCL.1 LCL.2 UCL.1 UCL.2 pval
#1 Probe 1 -12.344460036497 -11.7495704973055 -12.9047961446666 -12.2832657957485 -11.7840958626327 -11.2158751988625 0.0433081428107922
#2 Probe 2 -7.99773926405627 -8.02799133391929 -8.47704512876227 -8.19487551919835 -7.51843393935028 -7.86110714864023 0.772829992684449
# Difference Subject 1 Subject 2 Subject 3 Subject 4 Subject 5 Subject 6 Subject 7 Subject 8
## End(Not run)
```

Clustering Figure of Merit

Description

Goodness of clustering measure based on prediction error.

Usage

fom(data,cluster)

Arguments

data The data matrix
cluster a vector describing the cluster memberships

Details

The criterion in the Reference is not correct in the article (i.e. does not follow from the premises), but has been corrected here.
Value

The Figure of Merit measure of the current clustering

Author(s)

Per Broberg

References


fp.fn

Calculation of fp and fn based on a vector of p-values

Description

Based on a vector of p-values the proportion false positive (fp) and the proportion false negative are calculated for each entry, assuming that one to be the last to be called significant. The sum of fp and fn is also calculated (errors). Furthermore, an estimate of the proportion unchanged together with the number of the entry with minimum errors.

Usage

fp.fn(ps = pvals, B = 100)

Arguments

ps a vector of p-values
B the number of bootstrap loops done by the function estimatep0 called by fp.fn

Value

A list with components

p0 the estimated proportion unchanged
fp the estimated proportion false positives
fn the estimated proportion false negatives
N the number of the p-value (significance level) that gives minimum fp + fn

Author(s)

Per Broberg
Fstat

Calculation of F statistic by gene given a linear model

Description

Calculates F statistic.

Usage

Fstat(indata = M, formula1 = as.factor(g), formula0 = "mean", design1 = NULL, design0 = NULL, B = NULL)

Arguments

indata The data matrix
formula1 a formula describing the alternative linear model
data0 a formula describing the null model. Use linear models syntax, except for one-way ANOVA ("mean")
design1 the alternative design matrix. If not NULL it overrides the formula argument
design0 the null design matrix. If not NULL it overrides the formula argument
B the number of bootstrap replicates

Value

A list with the components

Fstat the value of the F statistic
fnum the numerator degrees of freedom
fdenom the denominator degrees of freedom
design1 the alternative design matrix
design0 the null design matrix
SS1 the sum of squares in the denominator of the F-statistic
SS0 the sum of squares in the numerator of the F-statistic
pvalue the p-value for testing the alternative vs the null model

Author(s)

Per Broberg

Examples

## Annette Dobson (1990) "An Introduction to Generalized Linear Models".  
# Page 9: Plant Weight Data.
ctl <- c(4.17,5.58,5.18,6.11,4.50,4.61,5.17,4.53,5.33,5.14)
trt <- c(4.81,4.17,4.41,3.59,5.87,3.83,6.03,4.89,4.32,4.69)
group <- gl(2,10,20, labels=c("Ctl","Trt"))
weight <- c(ctl, trt)
anova(lm.D9 <- lm(weight ~ group))
# Analysis of Variance Table
# Response: weight
# Df Sum Sq Mean Sq F value Pr(>F)
#group 1 0.6882 0.6882 1.4191 0.249
#Residuals 18 8.7292 0.4850

Fstat(indata = rbind(weight,weight),formula1=~group) # Fstat will need at least two genes to work with#
#$Fstat
# weight weight
#1.419101 1.419101

#$fnum
#[1] 18

#$fdenom
#[1] 1

#$design1
# (Intercept) groupTrt
#1 1 0
#2 1 0
#3 1 0
#4 1 0
#5 1 0
#6 1 0
#7 1 0
#8 1 0
#9 1 0
#10 1 0
#11 1 1
#12 1 1
#13 1 1
#14 1 1
#15 1 1
#16 1 1
#17 1 1
#18 1 1
#19 1 1
#20 1 1
#attr("assign")
#[1] 0 1

#$design0
# NULL

#$SS1
# weight weight
#8.72925 8.72925

#$SS0
# weight weight
#0.688205 0.688205

---

gap GAP statistic clustering figure of merit
GSEA.mean.t

**Description**

Calculates a goodness of clustering measure based on the average dispersion compared to a reference distribution.

**Usage**

```
gap(data = swiss, class = g, B = 500, cluster.func = myclus)
```

**Arguments**

- `data`: The data matrix, with samples (observations) in rows and genes (variables) in columns.
- `class`: A vector describing the cluster memberships of the rows of data.
- `B`: The number of bootstrap samples.
- `cluster.func`: A function taking the arguments `data` and `k` (number of clusters) and outputs cluster assignments as list elements `cluster` (accessed by `object$cluster`).

**Value**

The GAP statistic and the standard deviation.

**Author(s)**

Per Broberg

**References**


**Examples**

```
library("MASS")
data(swiss)
cl <- myclus(data = swiss, k = 3)
gap(swiss, cl$cluster)
```

---

**GSEA.mean.t**

*Gene Set Enrichment Analysis using output from samroc*

**Description**

Based on a list of gene sets, e.g. pathways, in terms of Affymtrix identifiers, these sets are ranked with respect to regulation as measured by an effect in a linear model using the SAM statistic. Typical applications include two-group comparisons or simple linear regression to clinical variable or gene expression of a given gene.

**Usage**

```
GSEA.mean.t(samroc = samroc.res, probeset = probeset, pway = kegg, type = c("original", "absolute", "maxmean"), two.side = FALSE, cutoff = c(10,Inf), rest...)```
Arguments

- **samroc**: an object of class `samroc.result`
- **probeset**: the Affymetrix identifiers
- **pway**: a list of pathways or gene sets
- **type**: if "absolute" value of the absolute value of the `samroc` test statistic is used. If "original" no transformation. "maxmean" not available.
- **two.side**: if TRUE a two-sided test is performed. Currently only two-sided test when type = "original" and else one-sided
- **cutoff**: Gene sets with the number of members not falling within the interval given by `cutoff` are excluded
- **restand**: if TRUE a 'restandardization' following Efron and Tibshirani (2006) is performed

Details

Restandardization based on Efron and Tibshirani (2006) introduced. For normal approximation of the gene set statistic both the mean of the statistic, or the variance (and likewise for the Wilcoxon statistic), are obtained from the permutation distribution included in the `samroc.result` object. Note that this will account for the dependency between genes.

Value

A matrix with columns normal approximation p-values, mean statistic, median statistic, and if type = "original", also Wilcoxon signed ranks statistic based p-value.

Author(s)

Per Broberg

References


---

**JT.test**  
*Jonckheere-Terpstra trend test*

Description

The test is testing for a monotone trend in terms of the class parameter. The number of times that an individual of a higher class has a higher gene expression forms a basis for the inference.

Usage

```r
JT.test(data, class, labs = NULL, alternative = c("two-sided", "decreasing", "increasing"), ties =
```
Arguments

data A matrix with genes in rows and subjects in columns
class the column labels, if not an ordered factor it will be redefined to be one.
labs the labels of the categories coded by class
alternative two-sided, decreasing or increasing
ties Adjustment for ties

Details

Assumes that groups are given in increasing order, if the class variable is not an ordered factor, it will be redefined to be one. The p-value is calculated through a normal approximation.

The implementation owes to suggestions posted to R list.

The definition of predictive strength appears in Flandre and O’Quigley.

Value

an object of class JT-test, which extends the class htest, and includes the following slots

statistic the observed JT statistic
parameter the null hypothesis parameter, if other value than 0.
p.value the p-value for the two-sided test of no trend.
method Jonckheere-Terpstra
alternative The relations between the levels: decreasing, increasing or two-sided
data.name the name of the input data
median1 ... median n the medians for the n groups
trend the rank correlation with category
S1 Predictive strength

Author(s)

Per Broberg, acknowledging input from Christopher Andrews at SUNY Buffalo

References

Flandre, Philippe and O’Quigley, John, Predictive strength of Jonckheere’s test for trend: an application to genotypic scores in HIV infection, Statistics in Medicine, 2007, 26, 24, 4441-4454

Examples

# Enter the data as a vector
A <- as.matrix(c(99,114,116,127,146,111, 125,143,148,157,133,139, 149, 160, 184))
# create the class labels
g <- c(rep(1,5),rep(2,5),rep(3,5))
# The groups have the medians
tapply(A, g, median)
# JT.test indicates that this trend is significant at the 5% level
JT.test(data = A, class = g, labs = c("GRP 1", "GRP 2", "GRP 3"), alternative = "two-sided")
list.experiments

Display all experiment names and id's

Description
Display all experiment names and id's in the GATC database

Usage
list.experiments(channel, chip = "HG_U95Av2")

Arguments
channel the ODBC channel set up through RODBC
chip the chip type

Details
The GATC database has caused some problems by switching between upper and lower case in an erratic manner. To solve this all names are changed to upper case in the identification of experiments. Thus the function will not distinguish between the experiments 'A' and 'a', but with any sensible naming strategy, the restriction is without consequence

Value
dataframe with column EXPERIMENT

Examples
# Not run
## Not run: library(Rodbc)
channel <- odbcConnect(DBN, USRID, PWD)
ut <- list.experiments(channel, chip = "hu6800")
colnames(ut)
# [1] "EXPERIMENT"
## End(Not run)

list.intersection.p

p-value for intersection of two gene lists.

Description
Calculates a p-value for observing a number of probe sets common to two lists drawn from the same chip.

Usage
list.intersection.p(N = 14000, N1 = 100, N2 = 200, common = 30)
Arguments

N The selectable number of probe sets
N1 the number of probe sets on the first list.
N2 the number of probe sets on the second list
common the number of probe sets in common to the two lists.

Value

the p-value giving the probability of observing by chance at least as many in common as was actually observed.

Author(s)

Per Broberg

---

mat2TeX  
Output matrix to LaTeX

Description

The function outputs a matrix to a LaTeX table

Usage

mat2TeX(mat, digits = 4, rowNameTitle = "", file = "", roundNum = NULL, rowNameAlign = "l", matAlign = "r", prtHead = TRUE, prtEnd = TRUE, extraTitle = NULL, rowNameCols = 1, append = FALSE)

Arguments

mat a matrix
digits number of digits
rowNameTitle title above row names
file output file
roundNum integer indicating the precision
rowNameAlign alignment of row names, default is "l"
matAlign alignment of columns, default is "r"
prtHead if TRUE the begin{tabular} line is produced
prtEnd if TRUE the end{tabular} line is produced
extraTitle extra title
rowNameCols the row name column, default is 1
append if TRUE the output is appended to file, deafult is FALSE

Author(s)

Juerg Kindermann; code found on R list
**myclus**  
*A clustering function*

**Description**  
Uses a hierarchical clustering to initiate a kmeans clustering.

**Usage**  
```r  
myclus(data = swiss, k = 3)  
```

**Arguments**  
- `data` The data matrix  
- `k` the number of clusters

**Value**  
a list from function `kmeans`

**Author(s)**  
From Ripley and Venables

**References**  

**Examples**  
```r  
library(MASS)  
data(swiss)  
cl <- myclus(data = swiss, k = 3)  
gap(swiss, cl$cluster)  
```

---

**normalise**  
*Normalise arrays*

**Description**  
Normalises arrays against a calculated average array, and calibrated linearly in a cube-root scatter plot.

**Usage**  
```r  
normalise(x, linear=TRUE)  
```

**Arguments**  
- `x` The data matrix  
- `linear` if linear=TRUE then the matrix elements are raised to the power of 3.
one.probeset.per.gene

Value

normalised version of indata

Author(s)

Per Broberg

References


Description

This function takes a vector of probeset identifiers, a vector of gene identifiers and a vector of present rates, and outputs the probeset id per gene that corresponds to the highest present rate.

Usage

one.probeset.per.gene(probeset = probeset, present = present, symbol = symbol)

Arguments

- **probeset**: a vector of probeset id’s
- **present**: a vector of present rates
- **symbol**: a vector of gene symbols

Details

It is assumed that missing gene symbol is coded as "". Note also that other measurements than present rate may be useful as selection criterion, such some variation measure. The function only assumes that high values are desirable.

Value

A vector of probeset id’s.

Note

Experimental function. Feedback appreciated.

Author(s)

Per Broberg
**outlier**

*Identify outliers in the multivariate distribution*

**Description**

A PCA model is fitted to data and two statistics as measures of extremity are calculated. These are the Hotelling t-square and DMODX, the first is a measure of how far away from the centre of the projection subspace the projection of the observation is. The second one measures how remote from the projection the actual observation is. SVD is done directly on the data matrix. The number of significant dimensions is defined as the number of eigenvalues greater than 1. Typically arrays are in different columns.

**Usage**

```
outlier(M)
```

**Arguments**

- `M` matrix

**Value**

Dataframe with columns Hotelling and DMODX

**Author(s)**

Per Broberg

**References**


**Examples**

```r
## Not run:
# not run
ut<-outlier(M)
# [1] "The number of significant dimensions is 19"
colnames(ut)
# [1] "Hotelling" "DMODX"

## End(Not run)
```
p0.mom

Estimate proportion unchanged genes

Description
The function uses the vector of p-values to estimate p0.

Usage
p0.mom(ps = pvalues)

Arguments
ps
the vector of p-values, e.g. from firstpass

Value
the value of p0, the proportion unchanged genes as a list with components

mgf
estimate from the mgf method
PRE
estimate from the PRE method
experimental1
experimental2

Author(s)
Per Broberg

References
Broberg, P. A new estimate of the proportion unchanged genes, 2005, Genome Biology 5:p10
Broberg, P. A comparative review of estimates of the proportion unchanged genes and the false

pava

Pooling of Adjacent Violators

Description
The PAVA algorithm

Usage
pava(x, wt = rep(1, length(x)))

Arguments
x
A numeric sequence
wt
observation weights; 1 by default.
**Details**

The algorithm will turn a non-increasing into a non-decreasing one. `pava` is an internal function used to force monotonicity, e.g. of `p1` in function `Zfreq`.

**Value**

A non-decreasing sequence

**Author(s)**

R.F. Raubertas, code from S list

**Examples**

```r
pava(c(1,2,4,3,5))
# [1] 1.0 2.0 3.5 3.5 5.0
```

---

**Description**

Estimates tail area and local false discovery rate using isotonic regression

**Usage**

```r
pava.fdr(ps = pvalues, p0 = NULL)
```

**Arguments**

- `ps` the vector of p-values, e.g. from firstpass
- `p0` an estimate of the proportion unchanged genes

**Details**

If `p0 = NULL` the PRE estimate of `p0` is calculated.

**Value**

a list with components

- `pava.fdr` estimate of the FDR
- `p0` estimate of `p0`
- `pava.local.fdr` estimate of the local FDR

**Author(s)**

Per Broberg
References


---

**R2BASE**

*Produces a BASE file*

**Description**

The function produces a BASE file for import to Gene Data Viewer.

**Usage**

```r
R2BASE(context.data = clingen, sample.ids = AZID, expression.data = dats, annotation = annots, out = "u:/temp/temp.base")
```

**Arguments**

- `context.data`: e.g. a clinical database
- `sample.ids`: Sample Ids, that names the columns of the expression data.
- `expression.data`: a matrix with the gene expression data, samples correspond to columns and probesets to rows. It is assumed that probeset identifiers are found in the first column.
- `annotation`: annotations of the probesets, i.e. the rows in the expression.data. It is assumed that probeset identifiers are found in the first column.
- `out`: the output file including path

**Value**

The file produced complies with an old BASE format. However, none of these formats are documented, as far as I know. So, essentially this function defines a data format that can be read by e.g. Gene Data Viewer.

**Author(s)**

Per Broberg
Description

Given a candidate probe, it produces a script file for WinMIM by calculating means and covariances and for the N most highly correlated probes (in absolute value). Here N is an input parameter, but a recommended value 10. WinMIM can find a relevant graphical model for the dependencies between the probes.

Usage

R2mim(probe="12345_at", N=10, data=inm, out="u:/study/copd/mimscr.txt")

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>probe</td>
<td>The name of the candidate probe</td>
</tr>
<tr>
<td>N</td>
<td>The number of highly correlated probes to be studied</td>
</tr>
<tr>
<td>data</td>
<td>The input data set</td>
</tr>
<tr>
<td>out</td>
<td>The MIM script file</td>
</tr>
</tbody>
</table>

Value

The correlation matrix

Note

David Edwards’ program WinMIM can be found on StatLib (http://lib.stat.cmu.edu/graphmod/). In MIM issue input mimscr.txt and the calculations to find a model will start. When finished go to the Graphics menu and click on Independence Graph. The resulting graph can be exported both to WMF and LaTeX.

Author(s)

Per Broberg

References

Whittaker, Joe (1990) *Graphical Models in Multivariate Analysis*. Wiley
**rank.genes**

*Rank genes with respect to multiple criteria*

**Description**

It is assumed that genes come in rows and the criteria in columns. Furthermore, high values should be good. After ranking the genes with respect to each criterion, the function does a PCA on the ranks, uses the first PC to obtain the final ranks. In principle it could happen that genes are ranked in the opposite direction to the one intended, but that should be evident from a quick glance at the results.

**Usage**

```r
data = indats
```

**Arguments**

- `data`: A matrix with the criteria in columns.

**Value**

The total ranks of the genes.

**Author(s)**

Per Broberg

---

**rank.trend**

*Trend analysis based on ranks*

**Description**

Ranks are used to score genes with respect to degree of agreement to a given trend or pattern, Lehmann (1974) p.294.

**Usage**

```r
data = x, pattern = c(1:nrow(data)), har = FALSE
```

**Arguments**

- `data`: A data frame with one array in each column
- `pattern`: A permutation of the integers 1:nrow(data)
- `har`: logical parameter indicating whether or not a score based on Hardy’s theorem shall be calculated.

**Details**

The rank scores gives a higher weight to a deviation from trend in more distant observations than a deviation between neighbouring observations. The p-values are calculated through a normal approximation.
rsd.test

Value

A list with the components

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>score</td>
<td>the rank score for each gene</td>
</tr>
<tr>
<td>hardy</td>
<td>if har = TRUE the hardy score, NULL otherwise</td>
</tr>
<tr>
<td>pvals</td>
<td>the p-values for the null hypothesis of no trend</td>
</tr>
</tbody>
</table>

Author(s)

Per Broberg

References


Examples

# not run
D <- c(123, 334, 578, 762, 755, 890)
rank.trend(data = t(as.matrix(D)), har = TRUE)
# Trend score Hardy score p-value for no trend
# [1,] 2 90 0.01750284

rsd.test

Compare two groups with respect to their RSD (CV)

Description

A by row comparison of the Relative Standard Deviation (RSD), aka Coefficient of Variation (CV), is done using a bootstrap

Usage

rsd.test(data1 = x, data2 = y, B = NULL)

Arguments

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>data1</td>
<td>A matrix with the samples for group 1 in columns.</td>
</tr>
<tr>
<td>data2</td>
<td>A matrix with the samples for group 2 in columns.</td>
</tr>
<tr>
<td>B</td>
<td>the number of bootstrap iterations. If NULL no bootstrap is performed.</td>
</tr>
</tbody>
</table>

Value

A list with the components

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>cv1</td>
<td>A vector of the RSD’s for sample 1</td>
</tr>
<tr>
<td>cv2</td>
<td>A vector of the RSD’s for sample 2</td>
</tr>
<tr>
<td>t.stat</td>
<td>the test statistic</td>
</tr>
<tr>
<td>p.vals</td>
<td>A vector of p-values for the comparison between cv1 and cv2</td>
</tr>
</tbody>
</table>
Author(s)
Per Broberg

References

Class “samroc.result” for results of the function samrocN

Description
The class samroc.result is the output of a call to samrocN and the input of various other functions.

Slots

- **d**: Object of class "numeric". Observed test statistic.
- **diff**: Object of class "numeric". Estimate of effect, e.g. difference between group means.
- **se**: Object of class "numeric". Standard error of diff.
- **d0**: Object of class "matrix". Permutation test statistics.
- **p0**: Object of class "numeric". The estimated proportion unaffected genes.
- **s0**: Object of class "numeric". The fudge factor.
- **pvalues**: Object of class "numeric". The p-values.
- **N.list**: Object of class "integer". The optimal top list size among the sizes suggested.
- **errors**: Object of class "numeric". The sum of false positives and false negatives given a list that includes the current gene.
- **formula**: Object of class "formula". The linear model formula used.
- **contrast**: Object of class "numeric". The contrast estimated.
- **annotation**: Object of class "character". Annotation or comments regarding the analysis. By default the date.
- **N.sample**: Object of class "integer". The number of samples.
- **B**: Object of class "integer". The number of permutations.
- **call**: Object of class "character". The call to the function.
- **id**: Object of class "character". The probeset ids.
- **error.df**: Object of class "integer". The error degrees of freedom.
- **design**: Object of class "matrix". The design matrix.

Methods

- **show** (samroc.result): Summarizes the test result.
- **plot** (samroc.result): Plots the density of the observed test statistic and that of the corresponding null distribution.
Author(s)

Per Broberg

See Also

samrocN

calculate ROC curve based SAM statistic

Description

Calculation of the regularised t-statistic which minimises the false positive and false negative rates.

Usage

samrocN(data=M, formula=~as.factor(g), contrast=c(0,1), N = c(50, 100, 200, 300), B=100, perc = 0.6, smooth = FALSE, w = 1, measure = "euclid", p0 = NULL, probeset = NULL)

Arguments

data The data matrix, or ExpressionSet
formula a linear model formula
contrast the contrast to be estimated
N the size of top lists under consideration
B the number of bootstrap iterations
perc the largest eligible percentile of SE to be used as fudge factor
smooth if TRUE, the std will be estimated as a smooth function of expression level
w the relative weight of false positives
measure the goodness criterion
p0 the proportion unchanged probesets; if NULL p0 will be estimated
probeset probeset ids; if NULL then "probeset 1", "probeset 2", ... are used.

Details

The test statistic is based on the one in Tusher et al (2001):

\[
d = \frac{\text{diff}}{s_0 + s}
\]

where \( \text{diff} \) is a the estimate of a constraint, \( s_0 \) is the regularizing constant and \( s \) the standard error.

At the heart of the method lies an estimate of the false negative and false positive rates. The test is calibrated so that these are minimised. For calculation of \( p \)-values a bootstrap procedure is invoked. Further details are given in Broberg (2003). Note that the definition of \( p \)-values follows that in Davison and Hinkley (1997), in order to avoid \( p \)-values that equal zero.

The \( p \)-values are calculated through permuting the residuals obtained from the null model, assuming that this corresponds to the full model except for the parameter being tested, corresponding to the contrast coefficient not equal to zero. This means that factors not tested are kept fixed. NB This may be adequate for testing a factor with two levels or a regression coefficient (correlation), but it is not adequate for all linear models.
Value

An object of class samroc.result.

Author(s)

Per Broberg

References


---

**samrocNboot**

*Calculate ROC curve based SAM statistic*

**Description**

A c-code version of samrocN. Calculation of the regularised t-statistic which minimises the false positive and false negative rates.

**Usage**

```r
samrocNboot(data=M,formula=~as.factor(g), contrast=c(0,1), N = c(50, 100, 200, 300), B=100, perc = 0.6, smooth=FALSE, w = 1, measure = "euclid", probeset = NULL)
```

**Arguments**

- `data` The data matrix
- `formula` a linear model formula
- `contrast` the contrast to be estimated
- `N` the size of top lists under consideration
- `B` the number of bootstrap iterations
- `perc` the largest eligible percentile of SE to be used as fudge factor
- `smooth` if TRUE, the std will be estimated as a smooth function of expression level
- `w` the relative weight of false positives
- `measure` the goodness criterion
- `probeset` probeset ids; if NULL then "probeset 1", "probeset 2", ... are used.
The test statistic is based on the one in Tusher et al (2001):

\[ d = \frac{\text{diff}}{s_0 + s} \]

where \text{diff} is a the estimate of a contrast, \( s_0 \) is the regularizing constant and \( s \) the standard error. At the heart of the method lies an estimate of the false negative and false positive rates. The test is calibrated so that these are minimised. For calculation of \( p \)-values a bootstrap procedure is invoked. Further details are given in Broberg (2003).

The \( p \)-values are calculated through permuting the rows of the design matrix. NB This is not adequate for all linear models.

\text{samrocNboot} uses C-code to speed up the bootstrap loop.

Value
An object of class \text{samroc.result}.

Author(s)
Per Broberg and Freja Vamborg

References


Examples
library(multtest)
# Loading required package: genefilter
# Loading required package: survival
# Loading required package: splines
# Loading required package: reposTools
data(golub)
# This makes the expression data from Golub et al available
# in the matrix golub, and the sample labels in the vector golub.cl
set.seed(849867)
samroc.res <- samrocNboot(data = golub, formula = ~as.factor(golub.cl))
# The proportion of unchanged genes is estimated at
samroc.res@p0
# The fudge factor equals
samroc.res@s0
# A histogram of p-values
hist(samroc.res@pvalues)
# many genes appear changed
union.of.pways

Create the union of two pathway lists

Description

This function takes two lists where each component is a vector of probe sets ids and create a new such list that contains all probe sets and pathways from the two lists.

Usage

union.of.pways(x, y)

Arguments

x the first list
y the second list

Details

The function `merge.list` in package `RCurl` forms a basis for this function which adds the ability to add new probe sets to existing pathways.

Value

A list which is the union of the two input lists.

Note

Experimental function. Feedback appreciated.

Author(s)

Per Broberg

Examples

```r
X = list(a=c(1,2), c=c(1,2)); Y = list(a=c(3,4), d=c(1,2))
union.of.pways(X, Y)
```
**Xprep**

**Fitting of a linear model**

**Description**

The function fits a linear model to a microarray data matrix.

**Usage**

```r
Xprep(indata=M, formula=~as.factor(g), contrast=c(0,1), design=NULL)
```

**Arguments**

- `indata` The data matrix
- `formula` a linear model formula in the `lm` format
- `contrast` a vector defining the contrast of interest
- `design` the design matrix

**Value**

- `Mbar` estimate of the contrast
- `Vest` the error variance
- `k` inverse of the scale factor turning `Vest` into a standard error
- `f` the degrees of freedom of `Vest`
- `design` the design matrix

**Author(s)**

Per Broberg

---

**Xprep.resid**

**Calculation of input of residuals from linear model**

**Description**

The function fits a linear model to a microarray data matrix and calculates the residuals.

**Usage**

```r
Xprep.resid(data=M, formula=~as.factor(g), design=NULL)
```

**Arguments**

- `data` The data matrix
- `formula` a linear model formula in the `lm` format
- `design` the design matrix
Value
A matrix with the residuals

Author(s)
Per Broberg
Index

*Topic **IO**
  mat2TeX, 14
*Topic **database**
  fetchSignal, 4
  list.experiments, 13
*Topic **distribution**
  list.intersection.p, 13
*Topic **htest**
  estimatep0, 4
  fp.fn, 7
  pava.fdr, 19
  samrocN, 25
  samrocNboot, 26
*Topic **methods**
  samroc.result-class, 24
*Topic **models**
  Fstat, 8
  R2BASE, 20
  Xprep, 29
  Xprep.resid, 29
*Topic **multivariate**
  clin2mim, 2
  cluster.q, 3
  fom, 6
  gap, 9
  GSEA.mean.t, 10
  myclus, 15
  normalise, 15
  one.probeset.per.gene, 16
  outlier, 17
  R2mim, 21
  rank.genes, 22
  union.of.pways, 28
*Topic **nonparametric**
  firstpass, 5
  JT.test, 11
  p0.mom, 18
  rsd.test, 23
*Topic **regression**
  pava, 18
*Topic **robust**
  rank.trend, 22

clin2mim, 2

cluster.q, 3
estimatep0, 4
fetchSignal, 4
firstpass, 5
fom, 6
fp.fn, 7
Fstat, 8
gap, 9
GSEA.mean.t, 10
JT.test, 11
list.experiments, 13
list.intersection.p, 13
mat2TeX, 14
myclus, 15
normalise, 15
one.probeset.per.gene, 16
outlier, 17
p0.mom, 18
pava, 18
pava.fdr, 19
plot,samroc.result,ANY-method
(samroc.result-class), 24
plot,samroc.result-method
(samroc.result-class), 24
R2BASE, 20
R2mim, 21
rank.genes, 22
rank.trend, 22
rsd.test, 23

samroc.result-class, 24
samrocN, 24, 25, 25
samrocNboot, 26
show,samroc.result-method
(samroc.result-class), 24
INDEX

union.of.pways, 28
Xprep, 29
Xprep.resid, 29