Package ‘orQA’

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Description Assess repeatability, accuracy and cross-platform agreement of titration microarray data based on order restricted inference procedures
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Description

orQA provides methods for quality assessment microarray titration data. These include permutation based trend and shape tests useful for the assessment of accuracy and cross platform consistency as well as methods for the estimation of variance components under order restrictions.

Details

orQA provides methods for quality assessment of microarray titration data. Exploiting the monotonic nature of such measurements accuracy, precision and cross-platform agreement can be derived. For the assessment of accuracy using shape tests see pttest. To evaluate precision using variance component estimates see est.lme. Order restricted inference of monotonic trends for the purpose of cross-platform comparison is provided by e2test. For an example see below.

Author(s)

Florian Klinglmueller
Maintainer: Florian Klinglmueller <float_at_lefant.net>

References

Guo W., Sarkar SK., Peddada SD. (2010) "Controlling False Discoveries in Multidimensional Directional Decisions, with Applications to Gene Expression Data on Ordered Categories" Biometrics

Examples

## Let's assume a titration study with 10 genes 4 titration groups and
## 10 replicates which come from either of 2 biologically different
## samples (i.e. two times 4 technical replicates)

## WARNING: examples are run with a very limited number of permutations

## Titration groups, random factor
g <- rep(1:4,each=8)
r <- rep(rep(1:2,each=4),4)
## No differences (global null)
nulldata <- matrix(rnorm(320),nc=32)
## Differences between titration levels in each gene
alldata <- t(t(nulldata)+g)

## Accuracy are there any significantly non monotonous trends
res <- pttest(nulldata,g,1000,r) # apply shape test
## no significant trends at all
sigdirPttest(res)
## with alternatives
res <- pttest(alldata,g,1000,r) # apply shape test

## some significant trends
sigdirPttest(res)
## type of monotonicity (no significant trend, up, down,
## "anti-monotonous")
table(monotonicity(res))

## Precision - estimate variance components
res <- est.lme(nulldata,g,r)
round(apply(res,2,summary),2)
res <- est.lme(alldata,g,r)
round(apply(res,2,summary),2)

## Trend test and agreement
## some other dataset with some alternatives in both directions
tdir <- sample((1:3)+2,10,rep=TRUE)
alldata2 <- matrix(rnorm(320),nc=32)+ (tdir %*% t(g))
res1 <- e2test(alldata,g,1000,r)
res2 <- e2test(alldata2,g,1000,r)

## trinomial coding for directions (-1 down, 0 non sig., 1 up)
sigdir1 <- sigdirE2test(res1)
sigdir2 <- sigdirE2test(res2)

## contingency table of directional decisions
table(sigdir1,sigdir2)

---

**e2test**

*Perform permutation Barlow’s test on a dataset*
Description

This function computes Barlow’s test for each line of a given matrix. The global null distribution is computed using permutation. FWE control is provided by the maxT procedure.

Usage

e2test(data, g, B, rep = rep(1, length(g)))

Arguments

data a numeric matrix, for the lines of which we want to test the null of no trend across groups
g integer vector with group labels specified as ordered integers ranging from 1 to n where n is the number of ordered categories
B number of permutations or a permutation matrix
rep integer vector with group labels ranging from 1 to m where m is the number of independent samples (e.g. individuals). The ordering is not important.

Details

e2test takes a matrix for each line of which the null hypotheses of no trend across ordered groups is tested using a permutation test based on Barlow’s E2 statistic. By permuting only samples within independent entities of the experimental design, random factors such as technical replicates from the same sample material can be incorporated. Multiple testing control is provided by the maxT procedure.

Value

adj vector with FWE adjusted p.values for each null hypothesis
raw vector with raw p.values
dir vector with the direction of each decision

Author(s)

Florian Klinglmueller <float_at_lefant.net> Part of this function is C code that has been ported by Korbinian Strimmer from R code originally written by Kaspar Rufibach.

References


est.lme

Examples

data <- matrix(rnorm(7200),nc=72)
groups <- rep(1:4,each=18)
ind <- rep(rep(1:3,each=6),4)
out <- e2test(data,groups,B=1000,rep=ind)
sum(out$adj<.05)
data2 <- data+matrix(rep(groups,nrow(data)),nr=nrow(data),byrow=TRUE)
out2 <- e2test(data2,groups,B=1000,rep=ind)
sum(out2$adj<.05)

est.lme

Estimate order restricted variance components for a two way mixed model with interaction.

Description

Estimates variance components of a two way cross classification mixed model with an order restricted fixed effect, a random effect and random interaction term.

Usage

est.lme(y,ia,ib)

Arguments

y a numeric matrix, for the lines of which univariate variance decompositions should be estimated
ia integer vector of length ncol(y) specifying the ordered levels of the order restricted fixed effect as integers between 1 and n where n is the number of levels
ib integer vector or factor specifying the levels of the random term (e.g. individuals)

Details

est.lme estimates the variance components for a two way cross classification mixed model with random interaction. The order restriction on the fixed effect used to improve the estimates by pooling levels of the fixed effect using isotonic regression according to the observed order in the measurements. Estimation is then done using functionality provided by the package <nlme>.

Value

sb estimates of the random effect variance component
sg estimates of the interaction term variance component
se estimates of the residual error variance
tss total sum of squares (useful to obtain normalized scales between estimates from different measurements)
Author(s)
Florian Klinglmueller <float@lefant.net>

References

Examples

```r
g <- rep(1:4,each=10)
r <- rep(rep(1:2,each=5),4)

## No differences (global null)
nulldata <- matrix(rnorm(400),nc=40)

## estimation
res <- est.lme(nulldata,g,r)
round(apply(res,2,summary),2)
```

Description

Compute mixed directional FDR controlled test decisions for raw p-values of multidimensional ordered tests

Usage

`guo(p,a)`

Arguments

- `p`: a numeric matrix, of raw p-values from multidimensional ordered tests. Each line corresponds to a group of ordered hypotheses e.g. t-tests between mean measures from consecutive levels of some ordered grouping variable.
- `a`: desired alpha level for the test
misoreg

Details

guo implements the method proposed in Guo et al. (2010) that provides test decisions controlling the mixed directional FDR for multidimensional ordered tests.

Value

A matrix with test decisions TRUE corresponds to significant rejection of the null and FALSE to acceptance of the null.

Author(s)

Florian Klinglmueller <float_at_lefant.net>

References


Guo W., Sarkar SK., Peddada SD. (2010) "Controlling False Discoveries in Multidimensional Directional Decisions, with Applications to Gene Expression Data on Ordered Categories" Biometrics

Examples

data <- matrix(rnorm(7200),nc=72)
groups <- rep(1:4,each=18)
ind <- rep(rep(1:3,each=6),4)
out <- pttest(data,groups,B=1000,rep=ind)
guo(out$unadj,.05)
data2 <- data+matrix(rep(groups,nrow(data)),nr=nrow(data),byrow=TRUE)
out2 <- pttest(data2,groups,B=1000,rep=ind)
guo(out2$unadj,.05)

---

misoreg

Apply isotonic regression to each line of a matrix

Description

This function calculates the isotonic regression (assuming an upward trend) for each line of a given matrix with a given vector of weights. It does so by using the C implementation of the pool adjacent violators algorithm provided in the package <fdrtool>, looping over the lines of the matrix in compiled C++ code. This implementation is approximately 2 orders of magnitude faster than using apply in R.

Usage

misoreg(data, weights)
Arguments

data        a numeric matrix, for the lines of which we want to calculate the isotonic regression
weights     a vector of same length as the columns of data defining the weights

Details

misoreg takes a matrix of values for the lines of which a weighted isotonic regression is to be computed. The weights are assumed to be equal for each line.

Value

result      matrix with lines giving the isotonic regression fit for each line of the input matrix assuming an upward trend
weights     vector with original weights

Author(s)

Florian Klinglmueller <float_at_lefant.net> Part of this function is C code that has been ported by Korbinian Strimmer from R code originally written by Kaspar Rufibach. Many thanks also to Romain Francois and Dirk Eddelbuettel for helping moving the code to the new Rcpp API.

References


Examples

x <- matrix(rnorm(4000),nc=4)
w <- c(3,6,3,6)/18
out <- misoreg(x,w)

monotonicity(o,alpha)

monotonicity

Summarize results from pttest

Description

Translate results from pttest into the four categories: overall upward trend (up), overall downward trend (down), no significant trend (none), significant non-monotonicity (anti).

Usage

monotonicity(o,alpha)
orQA

Arguments
- o: result object from `pttest`
- alpha: desired alpha level for the test

Details
Translate results from `pttest` into the four categories: overall upward trend (up), overall downward trend (down), no significant trend (none), significant non-monotonicity (anti).

Value
A vector of length corresponding to the number of tests coding each result as either "up", "down", "none", or "anti".

Author(s)
Florian Klinglmueller <float_at_lefant.net>

Examples
```r
groups <- rep(1:4, each=18)
ind <- rep(rep(1:3, each=6), 4)
tdir <- sample((1:3)-2, 100, rep=TRUE)
data <- matrix(rnorm(7200), nc=72)+(t(dir% t(groups))
out <- pttest(data, groups, B=1000, rep=ind)
sigdir <- monotonicity(out)
table(sigdir)
```

orQA  

**Order restricted quality assessment of microarray titration data**

Description
orQA provides methods for quality assessment of microarray titration data. These include permutation based trend and shape tests useful for the assessment of accuracy and cross-platform consistency as well as methods for the estimation of variance components under order restrictions.

Details
orQA provides methods for quality assessment of microarray titration data. Exploiting the monotonic nature of such measurements accuracy, precision and cross-platform agreement can be derived. For the assessment of accuracy using shape tests see `pttest`. To evaluate precision using variance component estimates see `est.lme`. Order restricted inference of monotonic trends for the purpose of cross-platform comparison is provided by `e2test`. For an example see below.
Author(s)
Florian Klinglmueller
Maintainer: Florian Klinglmueller <float_at_lefant.net>

References
Guo W., Sarkar SK., Peddada SD. (2010) "Controlling False Discoveries in Multidimensional Directional Decisions, with Applications to Gene Expression Data on Ordered Categories" Biometrics

Examples

```r
## Let's assume a titration study with 10 genes 4 titration groups and
## 10 replicates which come from either of 2 biologically different
## samples (i.e. two times 4 technical replicates)

## WARNING: examples are run with a very limited number of permutations

## Titration groups, random factor
g <- rep(1:4,each=8)
r <- rep(rep(1:2,each=4),4)

## No differences (global null)
nulldata <- matrix(rnorm(320),nc=32)
## Differences between titration levels in each gene
altdata <- t(t(nulldata)+g)

## Accuracy are there any significantly non monotonous trends
res <- pttest(nulldata,g,1000,r) # apply shape test

## no significant trends at all
sigdirPtttest(res)

## with alternatives
res <- pttest(altdata,g,1000,r) # apply shape test

## some significant trends
sigdirPtttest(res)

## type of monotonicity (no significant trend, up, down,
pttest

Perform permutation t-tests between consecutive levels of ordered groups

Description
This function computes permutation t-tests for differences in each line of a matrix between consecutive levels of an ordered grouping variable.

Usage
pttest(data,g,B,rep=rep(1,length(g)))

Arguments
data a numeric matrix, for the lines of which we want to test the null of no trend across groups
g integer vector with group labels for the ordered categories coded as integers between 1 and n, where n is the number of ordered categories
B number of permutations or a list of permutation matrices
rep integer vector with group labels ranging from 1 to m where m is the number of independent samples (e.g. individuals). The ordering is not important.
Details

pttest takes a matrix and for each line computes a permutation t-test between consecutive levels of an ordered grouping variable. Random factors e.g. technical replicates can be specified and will be accounted for by permuting samples only within independent units of this factor. A matrix with raw permutation p-values as well as a matrix with the directional decisions are returned. See guo and sigdirPttest for a way to get test decisions with control over the mixed directional false discovery rate.

Value

- **raw**: matrix with raw p.values
- **dir**: matrix with the direction of each decision

Author(s)

Florian Klinglmueller <float_at_lefant.net>

References


Guo W., Sarkar SK., Peddada SD. (2010) "Controlling False Discoveries in Multidimensional Directional Decisions, with Applications to Gene Expression Data on Ordered Categories" Biometrics

Examples

```r
data <- matrix(rnorm(7200),nc=72)
groups <- rep(1:4,each=18)
ind <- rep(rep(1:3,each=6),4)
out <- pttest(data,groups,B=1000,rep=ind)
guo(out$unadj,.05)
data2 <- data+matrix(rep(groups,nrow(data)),nr=nrow(data),byrow=TRUE)
out2 <- pttest(data2,groups,B=1000,rep=ind)
guo(out2$unadj,.05)
```

---

**sigdirE2test**

*Summarize results from e2test*

Description

Translate results from e2test into trinomial coding where 1 signifies an upward trend, 0 a none significant result, and -1 a downward trend.

Usage

```r
sigdirE2test(o, alpha)
```
Arguments

- result object from `e2test`
- alpha  desired alpha level for the test

Details

Translate results from `e2test` into trinomial coding where 1 signifies an upward trend, 0 a none significant result, and -1 a downward trend.

Value

- a vector of length corresponding to the number of tests coding each result as either 1, 0, or -1.

Author(s)

Florian Klinglmueller <float_at_lefant.net>

Examples

groups <- rep(1:4, each=18)
ind <- rep(rep(1:3, each=6), 4)
tdir <- sample((1:3)-2,100,rep=TRUE)
data <- matrix(rnorm(7200), nc=72)*(t(dir %+% t(groups))
out <- e2test(data, groups, B=1000, rep=ind)
sigdir <- sigdirE2test(out)
table(sigdir)

sigdirPtest  Summarize results from `pttest`

Description

Translate results from `pttest` into trinomial coding where 1 signifies an upward trend, 0 a none significant result, and -1 a downward trend.

Usage

`sigdirPtest(o, alpha)`

Arguments

- result object from `pttest`
- alpha  desired alpha level for the test

Details

Translate results from `e2test` into trinomial coding where 1 signifies an upward trend, 0 a none significant result, and -1 a downward trend.
Value

A matrix with rows corresponding to the number of tests and columns corresponding to the number of treatment groups coding each result as either 1, 0, or -1.

Author(s)

Florian Klinglmueller <float_at_lefant.net>

Examples

groups <- rep(1:4, each=18)
ind <- rep(rep(1:3, each=6),4)
tdir <- sample((1:3)-2,1000, rep=TRUE)
data <- matrix(rnorm(7200), nc=72) + (t(dir %*% t(groups))
out <- pttest(data, groups, B=1000, rep=ind)
sigdir <- sigdirPttest(out)
head(sigdir)
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