Package: LPE (via r-universe)

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Title Methods for analyzing microarray data using Local Pooled Error (LPE) method

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Description This LPE library is used to do significance analysis of microarray data with small number of replicates. It uses resampling based FDR adjustment, and gives less conservative results than traditional 'BH' or 'BY' procedures. Data accepted is raw data in txt format from MAS4, MAS5 or dChip. Data can also be supplied after normalization. LPE library is primarily used for analyzing data between two conditions. To use it for paired data, see LPEP library. For using LPE in multiple conditions, use HEM library.

Imports stats

License LGPL

URL http://www.r-project.org, http://www.healthsystem.virginia.edu/internet/hes/biostat/bioinformatics/, http://sourceforge.net/projects/r-lpe/

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`am.trans` *Transform replicated arrays into (A,M) format*

Description

Transforms expression intensity measurements for replicated arrays of a single experimental condition into (A,M) format: A = (xi+xj)/2, M = (xi-xj) where x1, x2,..., xn are individual chips. This function is used in the estimation of within-bin variances in the LPE function, and not typically by the user.

Usage

```
am.trans(y)
```

Arguments

`y`	y is an ngene by n matrix of expression intensity measurements for replicated arrays under a single experimental condition.

Value

Returns matrix with 2 columns cbind(A.M) and rows comprising all permutations of individual chip columns of the input matrix y. Note that for each pair of chips M is calculated twice, once for xi-xj and once for xj-xi. The resulting matrix thus has twice the number of rows as the input matrix y.

Author(s)

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References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

See Also

lpe

Examples

```
library(LPE)
# Loading the LPE library

# Test data with duplicates
temp1 <- matrix(c(1,20,1.5,23),nrow=2)
am.trans(temp1)
# It gives a matrix of (4*2) as only two permutaions
# are possible for each row with duplicates (X1-X2, and X2-X1)


# Another test data with three replicates
temp2 <- matrix(c(1,20,1.5,23,0.8,19),nrow=2)
am.trans(temp2)
# Now it returns matrix of (12*2) as there are
# 6 possible permutations for each row with triplicates
# (X1-X2, X1-X3, X2-X3, X2-X1, X3-X1 and X3-X2)
```

---

baseOlig.error *Evaluates LPE variance function of M for quantiles of A within and experimental condition and then interpolates it for all genes.*

Description

Calls baseOlig.error.step1 and baseOlig.error.step2 functions in order to calculate the baseline distribution.

Usage

```
baseOlig.error(y, stats=median, q=0.01, min.genes.int=10,div.factor=1)
```

Arguments

y	y is a preprocessed matrix or data frame of expression intensities in which columns are expression intensities for a particular experimental condition and rows are genes.
stats	It determines whether mean or median is to be used for the replicates
q	q is the quantile width; q=0.01 corresponds to 100 quantiles i.e. percentiles. Bins/quantiles have equal number of genes and are split according to the average intensity A.
min.genes.int	Determines the minimum number of genes in a subinterval for selecting the adaptive intervals.
div.factor	Determines the factor by which sigma needs to be divided for selecting adaptive intervals.

Value

Returns object of class baseOlig comprising a data frame with 2 columns: A and var M, and rows for each quantile specified. The A column contains the median values of A for each quantile/bin and the M columns contains the pooled variance of the replicate chips for genes within each quantile/bin.

Author(s)

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References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

See Also

lpe

Examples

```
# Loading the library and the data
library(LPE)
data(Ley)

dim(Ley)
# Gives 12488 by 7
Ley[1:3,]
 # Returns
#       ID          c1   c2   c3    t1    t2    t3
```

```
#   1  AFFX-MurIL2_at 4.06 3.82 4.28 11.47 11.54 11.34
#   2 AFFX-MurIL10_at 4.56 2.79 4.83  4.25  3.72  2.94
#   3  AFFX-MurIL4_at 5.14 4.10 4.59  4.67  4.71  4.67

  Ley[,2:7] <- preprocess(Ley[,2:7],data.type="MAS5")

  subset <- 1:1000
  Ley.subset <- Ley[subset,]

  # Finding the baseline distribution of subset of the data
  # condition one (3 replicates)
  var.1 <- baseOlig.error(Ley.subset[,2:4], q=0.01)
  dim(var.1)
  # Returns a matrix of 1000 by 2 (A,M) format, equal to the nrow(data)
```

`baseOlig.error.step1` *Evaluates LPE variance function of M for quantiles of A within and experimental condition by divinding the A in 100 intervals.*

Description

Genes are placed in bins/quantiles according to their average expression intensity. The function baseOlig.error calculates a pooled variance of M for genes within these bins/quantiles of A for the replicates of the experimental condition contained in y. Here the assumption is that variance of the genes in each interval is similar.

Usage

```
baseOlig.error.step1(y, stats=median, q=0.01, df=10)
```

Arguments

`y`	y is a preprocessed matrix or data frame of expression intensities in which columns are expression intensities for a particular experimental condition and rows are genes.
`stats`	It determines whether mean or median is to be used for the replicates
`q`	q is the quantile width; q=0.01 corresponds to 100 quantiles i.e. percentiles. Bins/quantiles have equal number of genes and are split according to the average intensity A.
`df`	df stands for degrees of freedom. It is used in smooth.spline function to interpolate the variances of all genes. Default value is 10.

Value

Returns object of class baseOlig, comprising a data frame with 2 columns: A and var M. The A column contains the median values of each gene and the M columns contains the corresponding variance. Number of rows of the data-frame is same as that of the number of genes.

Author(s)

Nitin Jain<nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

See Also

lpe

Examples

```
# Loading the library and the data
library(LPE)
data(Ley)

dim(Ley)
# Gives 12488 by 7
Ley[1:3,]
 # Returns
#       ID           c1   c2   c3    t1    t2    t3
#   1  AFFX-MurIL2_at 4.06 3.82 4.28 11.47 11.54 11.34
#   2 AFFX-MurIL10_at 4.56 2.79 4.83  4.25  3.72  2.94
#   3  AFFX-MurIL4_at 5.14 4.10 4.59  4.67  4.71  4.67

Ley[1:1000,2:7] <- preprocess(Ley[1:1000,2:7],data.type="MAS5")
# Finding the baseline distribution of subset of the data
# condition one (3 replicates)
var.1 <- baseOlig.error.step1(Ley[1:1000,2:4], q=0.01)
dim(var.1)
# Returns a matrix of 1000 by 2 (A,M) format
```

---

baseOlig.error.step2 *Evaluates LPE variance function of M for quantiles of A within and experimental condition. It is based on the adaptive number of intervals.*

Description

Similar to baseOlig.error.step1 function, except that now the number of bins are chosen adaptively instead of fixed 100.

Usage

```
baseOlig.error.step2(y,baseOlig.error.step1.res, df=10, stats=median, min.genes.int=10, div.factor=
```

Arguments

y	y is a preprocessed matrix or data frame of expression intensities in which columns are expression intensities for a particular experimental condition and rows are genes.
baseOlig.error.step1.res	It is the result obtained from baseOlig.error.step1 function, in which number of bins are fixed=100
df	df stands for degrees of freedom. It is used in smooth.spline function to interpolate the variances of all genes. Default value is 10.
stats	It determines whether mean or median is to be used for the replicates
min.genes.int	Determines the minimum number of genes in a subinterval for selecting the adaptive intervals.
div.factor	Determines the factor by which sigma needs to be divided for selecting adaptive intervals.

Value

Returns object of class baseOlig comprising a data frame with 2 columns: A and var M, and rows for each quantile specified. The A column contains the median values of A for each quantile/bin and the M columns contains the pooled variance of the replicate chips for genes within each quantile/bin.

Author(s)

Nitin Jain<nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

See Also

lpe

Examples

```
  # Loading the library and the data
  library(LPE)
  data(Ley)

  dim(Ley)
  # Gives 12488 by 7
  Ley[1:3,]
   # Returns
  #       ID           c1   c2   c3    t1    t2    t3
#   1  AFFX-MurIL2_at 4.06 3.82 4.28 11.47 11.54 11.34
#   2 AFFX-MurIL10_at 4.56 2.79 4.83  4.25  3.72  2.94
#   3  AFFX-MurIL4_at 5.14 4.10 4.59  4.67  4.71  4.67

  Ley[1:1000,2:7] <- preprocess(Ley[1:1000,2:7],data.type="MAS5")
  # Finding the baseline distribution of subset of the data
  # condition one (3 replicates)
  var.1 <- baseOlig.error.step1(Ley[1:1000,2:4], q=0.01, df=10)
  dim(var.1)
  var.11 <- baseOlig.error.step2(Ley[1:1000,2:4], var.1, df=10)
  # Returns a matrix of 1000 by 2 (A,M) format
```

`fdr.adjust` *FDR adjustment procedures*

Description

Based on the type of adjustment, eg: resampling, BH, BY, etc, calls appropriate functions for fdr adjustment

Usage

```
fdr.adjust(lpe.result,adjp="resamp",target.fdr=c(10^-3 ,seq(0.01,0.10,0.01), 0.15, 0.20, 0.50),itera
```

Arguments

`lpe.result`	Data frame obtained from calling lpe function
`adjp`	Type of adjustment procedure. Can be "resamp", "BH", "BY", "Bonferroni" or "mix.all"
`target.fdr`	Desired FDR level (used only for resampling based adjustment)
`iterations`	Number of iterations for stable z-critical.
`ALL`	If TRUE, the FDR corresponding to all the z-statistics, i.e. for every gene intensity is given.

Details

Returns the output similar to lpe function, including adjusted FDR. BH and BY give Benjamini-Hochberg and Benjamini-Yekutieli adjusted FDRs (adopted from multtest procedure), Bonferroni adjusted p-values and "mix.all" gives SAM-like FDR adjustment. For further details on the comparisons of each of these methods, please see the reference paper (Rank-invariant resampling...) mentioned below. Users are encouraged to use FDR instead of Bonferrni adjsusted p-value as initial cutoffs while selecting the significant genes. Bonferroni adjusted p-values are provided under Bonferroni method here just for the sake of completion for the users who want it.

Author(s)

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References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

Examples

```
# Loading the library and the data
library(LPE)
data(Ley)

dim(Ley)
# Gives 12488*7
# First column is ID.

Ley[,2:7] <- preprocess(Ley[,2:7],data.type="MAS5")

# Subsetting the data
subset.Ley <- Ley[1:1000,]


# Finding the baseline distribution of condition 1 and 2.
var.1 <- baseOlig.error(subset.Ley[,2:4], q=0.01)
var.2 <- baseOlig.error(subset.Ley[,5:7], q=0.01)

# Applying LPE
lpe.result <- lpe(subset.Ley[,2:4],subset.Ley[,5:7], var.1, var.2,
               probe.set.name=subset.Ley[,1])


final.result <- fdr.adjust(lpe.result, adjp="resamp", target.fdr=c(0.01,0.05), iterations=1)
final.result
```

`fixbounds.predict.smooth.spline` *Makes the predicted variance non negative*

Description

Makes the predicted variance non negative

Usage

```
fixbounds.predict.smooth.spline(object,x, deriv=0)
```

Arguments

`object`	variance from baseOlig.error function
`x`	vector for which variance needs to be predicted
`deriv`	derivative of the vector required, default =0

Value

Returns the predicted variance for the given vector based on the baseline error distribution. Maximum and minimum predicted values for the vector are same as those of baseline error distribution

Author(s)

Nitin Jain<nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

Examples

```
# Loading the library and the data
 library(LPE)
 data(Ley)

 dim(Ley)
 # Gives 12488*7
 # First column is ID.


 # Subsetting the data
 subset.Ley <- Ley[1:1000,]

  subset.Ley[,2:7] <- preprocess(subset.Ley[,2:7],data.type="MAS5")
  # preprocess the data

 # Finding the baseline distribution of condition 1 and 2.
 var.1 <- baseOlig.error(subset.Ley[,2:4], q=0.01)
  median.x <- apply(subset.Ley[,2:4], 1, median)

 sf.x <- smooth.spline(var.1[, 1], var.1[, 2], df = 10)

 var.test <- fixbounds.predict.smooth.spline(sf.x, median.x)$y
```

`iqr` *Inter-quartile range*

Description

Finds inter-quartile range of the data = {75th percentile - 25th percentile}.

Usage

```
iqr(x)
```

Arguments

`x`	x is a vector for which IQR has to be found.

Value

Returns a numeric value representing the difference of 75th percentile and 25th percentile of the vector. It is used for normalization across the chips - basic assumption is that net differential expression of the middle half of the genes in microarray experiment is zero, which is conservative assumption as typically only 5-10 differential expression.

Author(s)

Nitin Jain<nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

See Also

lpe

Examples

```
library(LPE)
# Loading the LPE library

iqr(1:5)
```

Ley *Gene Expression Data from Mouse Immune response study, (2002)*

Description

Affymetrix GeneChip (12488 genes and 3 different conditions, each with 3 replicates) experiment was conducted by Dr. Ley (2002) to understand mouse immune response study. For demonstration purposes, we show data from 2 conditions, i.e. 6 chips, only.

Usage

```
data(Ley)
```

Format

Matrix of 12488 genes by 7 columns. First column is the GeneID, next three columns are replicates in condition one, and last three columns are replicates in condition 2.

For details, contact. Dr. Klaus Ley, <kfl3f@virginia.edu>, http://hsc.virginia.edu/medicine/basic-sci/biomed/ley/

Author(s)

Nitin Jain <nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*. (To appear in Bioinformatics) See http://hesweb1.med.virginia.edu/bioinformatics/research/expression/index.html.

`lowess.normalize` *lowess normalization of the data (based on M vs A graph)*

Description

All the chips are normalized w.r.t. 1st chip

Usage

```
lowess.normalize(x,y)
```

Arguments

x	x is the chip data w.r.t. which other chips would be normalized
y	y is the chip data which would be normalized

Value

Returns the lowess normalized chip intensity.

Author(s)

Nitin Jain<nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

See Also

lpe

Examples

```
library(LPE)
# Loading the LPE library

data(Ley)
# Loading the data set
dim(Ley) #gives 12488 * 7
Ley[1:3,]

Ley[1:1000,2:7] <- preprocess(Ley[1:1000,2:7],data.type="MAS5")
Ley[1:3,]
```

---

lpe *Evaluates local pooled error significance test*

Description

The local pooled error test attempts to reduce dependence on the within-gene estimates in tests for differential expression, by pooling error estimates within regions of similar intensity. Note that with the large number of genes there will be genes with low within-gene error estimates by chance, so that some signal-to-noise ratios will be large regardless of mean expression intensities and fold-change. The local pooled error attempts to avert this by combining within-gene error estimates with those of genes with similar expression intensity.

Usage

```
lpe(x, y, basevar.x,basevar.y, df=10, array.type="olig",
    probe.set.name=NULL, trim.percent=5)
```

Arguments

x	Replicated data from first experimental condition (as matrix or data-frame)
.	
y	Replicated data from second experimental condition (as matrix or data-frame)
.	
basevar.x	Baseline distribution of first condition obtained from function baseOlig.error
basevar.y	Baseline distribution of second condition obtained from function baseOlig.error
df	Degrees of freedom used in fitting smooth.spline to estimates of var.M for bins in A
array.type	Currently supports oligo arrays
probe.set.name	Gene IDs. By default if they are not provided then 1,2,3,... is assigned as GeneID
trim.percent	Percent of (A, var.M) estimates to trim from low end of A

Details

The LPE test statistic numerator is the difference in medians between the two experimental conditions. The test statistic denominator is the combined pooled standard error for the two experimental conditions obtained by looking up the var.M from each baseOlig.error variance function. The conversion to p-values is based on the Gaussian distribution for difference if order statistics (medians). The user may select both the smoother degrees of freedom (smaller is smoother) and the trim percent to obtain a variance function to suit particular issues i.e. variability of genes with low expression intensity.

Value

Data frame including x, median of x, y, median of y, median difference of (x,y), pooled standard deviation of difference, LPE p-value, outlier flag, probability of an outlier within x or y.

Author(s)

Nitin Jain<nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

Examples

```
 # Loading the library and the data
 library(LPE)
 data(Ley)

 dim(Ley)
 # Gives 12488*7
 # First column is ID.



 # Subsetting the data
 subset.Ley <- Ley[1:1000,]

  subset.Ley[,2:7] <- preprocess(subset.Ley[,2:7],data.type="MAS5")

 # Finding the baseline distribution of condition 1 and 2.
var.11 <- baseOlig.error.step1(subset.Ley[,2:4])
 var.1 <- baseOlig.error(subset.Ley[,2:4], q=0.01)
 var.2 <- baseOlig.error(subset.Ley[,5:7], q=0.01)
```

```
# Applying LPE
lpe.result <- lpe(subset.Ley[,2:4],subset.Ley[,5:7], var.1, var.2,
 probe.set.name=subset.Ley[,1])
```

`mt.rawp2adjp.LPE` *Adjusted p-values for simple multiple testing procedures*

Description

This function computes adjusted p-values for simple multiple testing procedures from a vector of raw (unadjusted) p-values. The procedures include the Bonferroni, Holm (1979), Hochberg (1988), and Sidak procedures for strong control of the family-wise Type I error rate (FWER), and the Benjamini & Hochberg (1995) and Benjamini & Yekutieli (2001) procedures for (strong) control of the false discovery rate (FDR).

Usage

```
mt.rawp2adjp.LPE(rawp, proc=c("Bonferroni", "Holm", "Hochberg", "SidakSS", "SidakSD", "BH", "BY"))
```

Arguments

`rawp`	A vector of raw (unadjusted) p-values for each hypothesis under consideration. These could be nominal p-values, for example, from t-tables, or permutation p-values as given in `mt.maxT` and `mt.minP`. If the `mt.maxT` or `mt.minP` functions are used, raw p-values should be given in the original data order, `rawp[order(index)]`.
`proc`	A vector of character strings containing the names of the multiple testing procedures for which adjusted p-values are to be computed. This vector should include any of the following: `"Bonferroni"`, `"Holm"`, `"Hochberg"`, `"SidakSS"`, `"SidakSD"`, `"BH"`, `"BY"`.

Details

Adjusted p-values are computed for simple FWER and FDR controlling procedures based on a vector of raw (unadjusted) p-values.

Bonferroni Bonferroni single-step adjusted p-values for strong control of the FWER.

Holm Holm (1979) step-down adjusted p-values for strong control of the FWER.

Hochberg Hochberg (1988) step-up adjusted p-values for strong control of the FWER (for raw (unadjusted) p-values satisfying the Simes inequality).

SidakSS Sidak single-step adjusted p-values for strong control of the FWER (for positive orthant dependent test statistics).

SidakSD Sidak step-down adjusted p-values for strong control of the FWER (for positive orthant dependent test statistics).

BH adjusted p-values for the Benjamini & Hochberg (1995) step-up FDR controlling procedure (independent and positive regression dependent test statistics).

BY adjusted p-values for the Benjamini & Yekutieli (2001) step-up FDR controlling procedure (general dependency structures).

Value

A list with components

`adjp` A matrix of adjusted p-values, with rows corresponding to hypotheses and columns to multiple testing procedures. Hypotheses are sorted in increasing order of their raw (unadjusted) p-values.

`index` A vector of row indices, between 1 and `length(rawp)`, where rows are sorted according to their raw (unadjusted) p-values. To obtain the adjusted p-values in the original data order, use `adjp[order(index),]`.

Author(s)

Sandrine Dudoit, http://www.stat.berkeley.edu/~sandrine,
Yongchao Ge, <gyc@stat.berkeley.edu>.

References

Y. Benjamini and Y. Hochberg (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J. R. Statist. Soc. B*. Vol. 57: 289-300.

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S. Dudoit, J. P. Shaffer, and J. C. Boldrick (Submitted). Multiple hypothesis testing in microarray experiments.

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See Also

`lpe`

Examples

```
# Loading the library and the data
 library(LPE)
 data(Ley)

 dim(Ley)
 # Gives 12488*7
 # First column is ID.


 # Subsetting the data
 subset.Ley <- Ley[1:1000,]

 subset.Ley[,2:7] <- preprocess(subset.Ley[,2:7],data.type="MAS5")

 # Finding the baseline distribution of condition 1 and 2.
 var.1 <- baseOlig.error(subset.Ley[,2:4], q=0.01)
 var.2 <- baseOlig.error(subset.Ley[,5:7], q=0.01)

 # Applying LPE
 lpe.result <- lpe(subset.Ley[,2:4],subset.Ley[,5:7], var.1, var.2,
  probe.set.name=subset.Ley[,1])
 fdr.BH <- fdr.adjust(lpe.result, adjp="BH")
```

`n.genes.adaptive.int` *Calcuates the number of genes in various intervals adaptively.*

Description

Instead of dividing the genes equally in 100 intervals, this function divides them adaptively based on three rules: a) min. number of genes (default =10), b) max. number of genes = total/100; c) based on Median + fraction(SD) from the starting gene of each interval

Usage

```
n.genes.adaptive.int(baseOlig.error.step1.res,
  min.genes.int=10, div.factor=1)
```

Arguments

`baseOlig.error.step1.res`	It is the result from baseOlig.error.step1 function.
`min.genes.int`	It is the minimum number of genes in the interval, default=10.
`div.factor`	(1/div.factor) is the fraction of Standard Deviation which we wish to include in each interval to calculate number of genes in each interval

Value

Returns a vector respresenting the number of genes in each interval.

Author(s)

Nitin Jain<nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

See Also

lpe

Examples

```
  # Loading the library and the data
  library(LPE)
  data(Ley)

  dim(Ley)
  # Gives 12488 by 7
  Ley[1:3,]
   # Returns
  #       ID           c1   c2   c3    t1    t2    t3
#   1  AFFX-MurIL2_at 4.06 3.82 4.28 11.47 11.54 11.34
#   2 AFFX-MurIL10_at 4.56 2.79 4.83  4.25  3.72  2.94
#   3  AFFX-MurIL4_at 5.14 4.10 4.59  4.67  4.71  4.67

  Ley[1:1000,2:7] <- preprocess(Ley[1:1000,2:7],data.type="MAS5")
  # Finding the baseline distribution of subset of the data
  # condition one (3 replicates)
  var.1 <- baseOlig.error.step1(Ley[1:1000,2:4], q=0.01)
  dim(var.1)
  # Returns a matrix of 1000 by 2 (A,M) format
  n.genes.subint <- n.genes.adaptive.int(var.1, min.genes.int=10, div.factor=1)
```

---

permute *Calculating all possible permutations of a vector*

Description

Given a vector, all possible combinations of vector are obtained

Usage

```
permute(a)
```

Arguments

a	a is any numeric vector.

Details

Used in am.trans. Does all permutations for columns within an experimental condition so that A and M can be calculated for all permutations of chips within a treatment.

Value

A vector containing the possible combinations.

Author(s)

Nitin Jain<nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

See Also

lpe

Examples

```
# Loading LPE library
library(LPE)

# A test vector
permute(1:3)

# Returns a 2 by 3 matrix
#       [,1] [,2] [,3]
#  [1,]   2    3    1
#  [2,]   3    1    2
```

preprocess *Preprocessing the data (IQR normalization, thresholding, log- transformation, and lowess normalization)*

Description

Finds inter-quartile range of the data = (75th percentile - 25th percentile), thresholds low intensity MAS4, MAS5 and dChip data to 1, then log transforms the data (base 2), and does lowess normalization

Usage

```
preprocess(x, data.type="MAS5",threshold=1,LOWESS=FALSE)
```

Arguments

x	x is the data-set which needs preprocessing.
data.type	Three types of data accepted in the current version : MAS4 (Microarray suite software) , MAS5 and dChip
threshold	threshold is the 'thresholding value' below which all data would be thresholded (default = 1).
LOWESS	LOWESS is a logical variable which determines if lowess normalization needs to be performed.

Value

Returns a data-set of same dimensions as that of the input data. It has IQR normalization for MAS4 and MAS5 data. Low intensities of MAS4, MAS5 and dChip data are thresholded to 1. Then data is transformed to base 2. If LOWESS normalization parameter is set as TRUE, then lowess normalization is performed.

Author(s)

Nitin Jain <nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

See Also

lpe

Examples

```
library(LPE)
# Loading the LPE library

data(Ley)
# Loading the data set
dim(Ley) #gives 12488 * 7
Ley[1:3,]

Ley[1:1000,2:7] <- preprocess(Ley[1:1000,2:7],data.type="MAS5",
 threshold=1, LOWESS=TRUE)
Ley[1:3,]
```

---

quan.norm *Finding quartile range*

Description

Finds quartile range of the data (default is IQR = 75th percentile - 25th percentile).

Usage

```
quan.norm(x, percent=50)
```

Arguments

x	x is a vector for which quartile range has to be found.
percent	Percentage for which quartile range is needed

Value

Returns a numeric value representing the difference of 75th percentile and 25th percentile of the vector. It is used for normalization across the chips - basic assumption is that net differential expression of the middle half of the genes in microarray experiment is zero, which is conservative assumption as typically only 5-10 differential expression.

Author(s)

Nitin Jain<nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

See Also

lpe

Examples

```
library(LPE)
# Loading the LPE library

quan.norm(1:5)
```

`quartile.normalize` *Normalization based on quartile range*

Description

Does Normalization based on quartile range

Usage

```
quartile.normalize(x, percent=50)
```

Arguments

`x`	x is a matrix or data.frame on which normalization has to be performed.
`percent`	Percentage for which normalization is needed

Value

Returns the normalized data based on quartile normalization

Author(s)

Nitin Jain<nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

See Also

lpe

Examples

```
library(LPE)
# Loading the LPE library

data(Ley)

dim(Ley)
# Gives 12488*7
# First column is ID.

subset <- 1:1000
Ley[subset,2:7] <- quartile.normalize(Ley[subset,2:7],percent=50)
```

`resamp.adj` *Resampling based fdr adjustment*

Description

Adjusts the fdr based on rank invariant genes

Usage

```
resamp.adj(x,y, q=0.01, iterations=5, min.genes.int=10)
```

Arguments

x	Replicated data from first experimental condition (as matrix or data-frame)
.	
y	Replicated data from second experimental condition (as matrix or data-frame)
.	

q	q is the quantile width; q=0.01 corresponds to 100 quantiles
.	
iterations	Number of iterations to be performed to obtain critical z-statistics
.	
min.genes.int	Determines the minimum number of genes in a subinterval for selecting the adaptive intervals.

Details

Returns the z-statistics for the null distribution, obtained from resampling the rank invariant genes within each quantile. These z-statistic values are compared with z-statiscs from the original data, and fdr is calculated.

Author(s)

Nitin Jain<nitin.jain@pfizer.com>

References

J.K. Lee and M.O.Connell(2003). *An S-Plus library for the analysis of differential expression*. In The Analysis of Gene Expression Data: Methods and Software. Edited by G. Parmigiani, ES Garrett, RA Irizarry ad SL Zegar. Springer, NewYork.

Jain et. al. (2003) *Local pooled error test for identifying differentially expressed genes with a small number of replicated microarrays*, Bioinformatics, 1945-1951.

Jain et. al. (2005) *Rank-invariant resampling based estimation of false discovery rate for analysis of small sample microarray data*, BMC Bioinformatics, Vol 6, 187.

Examples

```
 # Loading the library and the data
library(LPE)
data(Ley)

dim(Ley)
# Gives 12488*7
# First column is ID.

# Subsetting the data
subset.Ley <- Ley[1:1000,]

 subset.Ley[,2:7] <- preprocess(subset.Ley[,2:7],data.type="MAS5")

# Finding the baseline distribution of condition 1 and 2.
var.1 <- baseOlig.error(subset.Ley[,2:4], q=0.01)
var.2 <- baseOlig.error(subset.Ley[,5:7], q=0.01)

# Applying LPE
lpe.result <- lpe(subset.Ley[,2:4],subset.Ley[,5:7], var.1, var.2,
```

```
  probe.set.name=subset.Ley[,1])


z.stats.null <- resamp.adj(subset.Ley[,2:4], subset.Ley[,5:7], q=0.01, iterations=2,min.genes.int=10 )
```

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