Package 'EBarrays'

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Description EBarrays provides tools for the analysis of replicated/unreplicated microarray data.
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crit.fun

Find posterior probability threshold to control FDR

Description

Find posterior probability threshold to control FDR

Usage

```
crit.fun(x, cc)
```

Arguments

x x is one minus the posterior probabilities of being in a specific DE pattern. If there is only one DE pattern, then x is the posterior probabilities of being EE.

cc cc is FDR to be controlled. For example, to control FDR at 0.05, set cc=0.05.

Value

crit.fun returns a threshold so that if used in identifying genes in a specific DE pattern, FDR can be controlled at cc. Those genes with posterior probability of being in that specific DE pattern greater than this threshold are claimed to be in that specific DE pattern.

Author(s)

Ming Yuan, Ping Wang, Deepayan sarkar, Michael Newton, and Christina Kendziorski

References

Newton, M.A., Noueiry, A., Sarkar, D., and Ahlquist, P. (2004). Detecting differential gene expression with a semiparametric hierarchical mixture model. *Biostatistics* **5**, 155-176.

Examples

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```
gg4.crit <- crit.fun(1-gg4.post.out[,2], 0.05)</pre>
# number of genes in pattern 2, a DE pattern
sum(gg4.post.out[,2] > gg4.crit)
```

EBarrays-internal

Internal EBarrays Functions

Description

Internal EBarrays functions.

Note

These are not to be called by the user (or in some cases are just waiting for proper documentation to be written).

ebarraysFamily-class Class of Families to be used in the EBarrays package

Description

Objects used as family in the emfit function.

The package contains three functions that create such objects for the three most commonly used families, Gamma-Gamma, Lognormal-Normal and Lognormal-Normal with modified variances. Users may create their own families as well.

Usage

```
eb.createFamilyGG()
eb.createFamilyLNN()
eb.createFamilyLNNMV()
```

Details

The emfit function can potentially fit models corresponding to several different Bayesian conjugate families. This is specified as the family argument, which ultimately has to be an object of formal class "ebarraysFamily" with some specific slots that determine the behavior of the 'family'.

For users who are content to use the predefined GG, LNN and LNNMV models, no further details than that given in the documentation for emfit are necessary. If you wish to create your own families, read on.

Value

Objects of class "ebarraysFamily" for the three predefined families Gamma-Gamma, Lognormal-Normal and Lognormal-Normal with modified variances.

Objects from the Class

Objects of class "ebarraysFamily" can be created by calls of the form new("ebarraysFamily", ...). Predefined objects corresponding to the GG, LNN and LNNMV models can be created by eb.createFamilyGG(), eb.createFamilyLNN() and eb.createFamilyLNNMV(). The same effect is achieved by coercing from the strings "GG", "LNN" and "LNNMV" by as("GG", "ebarraysFamily"), as("LNN", "ebarraysFamily") and as("LNNMV", "ebarraysFamily").

Slots

An object of class "ebarraysFamily" extends the class "character" (representing a short hand name for the class) and should have the following slots (for more details see the source code):

description: A not too long character string describing the family

link: function that maps user-visible parameters to the parametrization that would be used in the optimization step (e.g. log(sigma^2) for LNN). This allows the user to think in terms of familiar parametrization that may not necessarily be the best when optimizing w.r.t. those parameters.

invlink: inverse of the link function

- thetaInit: function of a single argument data (matrix containing raw expression values), that calculates and returns as a numeric vector initial estimates of the parameters (in the parametrization used for optimization)
- f0: function taking arguments theta and a list called args. f0 calculates the negative log likelihood at the given parameter value theta (again, in the parametrization used for optimization). This is called from emfit. When called, only genes with positive intensities across all samples are used.
- f0.pp: f0.pp is essentially the same as f0 except the terms common to the numerator and denominator when calculating posterior odds may be removed. It is called from postprob.
- f0.arglist: function that takes arguments data, patterns (of class "ebarraysPatterns") and groupid (for LNNMV family only) and returns a list with two components, common.args and pattern.args. common.args is a list of arguments to f0 that don't change from one pattern to another, whereas pattern.args[[i]][[j]] is a similar list of arguments, but specific to the columns in pattern[[i]][[j]]. Eventually, the two components will be combined for each pattern and used as the args argument to f0.
- logDensity: function of two arguments x (data vector, containing log expressions) and theta (parameters in user-visible parametrization). Returns log marginal density of the natural log of intensity for the corresponding theoretical model. Used in plotMarginal

lower.bound: vector of lower bounds for the argument theta of f0. Used in optim

upper.bound: vector of upper bounds for the argument theta of f0.

Author(s)

Ming Yuan, Ping Wang, Deepayan Sarkar, Michael Newton, and Christina Kendziorski

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References

Newton, M.A., Kendziorski, C.M., Richmond, C.S., Blattner, F.R. (2001). On differential variability of expression ratios: Improving statistical inference about gene expression changes from microarray data. Journal of Computational Biology 8:37-52.

Kendziorski, C.M., Newton, M.A., Lan, H., Gould, M.N. (2003). On parametric empirical Bayes methods for comparing multiple groups using replicated gene expression profiles. Statistics in Medicine 22:3899-3914.

Newton, M.A. and Kendziorski, C.M. Parametric Empirical Bayes Methods for Microarrays in The analysis of gene expression data: methods and software. Eds. G. Parmigiani, E.S. Garrett, R. Irizarry and S.L. Zeger, New York: Springer Verlag, 2003.

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Yuan, M. and Kendziorski, C. (2006). A unified approach for simultaneous gene clustering and differential expression identification. Biometrics 62(4): 1089-1098.

See Also

```
emfit, optim, plotMarginal
```

Examples

```
show(eb.createFamilyGG())
show(eb.createFamilyLNN())
show(eb.createFamilyLNNMV())
```

ebplots

Various plotting routines in the EBarrays package

Description

Various plotting routines, used for diagnostic purposes

Usage

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Arguments

data, as a "matrix" or "ExpressionSet"

useRank logical. If TRUE, ranks of means and c.v.-s are used in the scatterplot

f passed on to lowess

fit, x object of class "ebarraysEMfit", typically produced by a call to emfit

model which theoretical model use for Q-Q plot. Partial string matching is allowed

number of bins for checking model assumption.

nb number of data rows included in each bin for checking model assumption

cluster check model assumption for data in that cluster

groupid an integer vector indicating which group each sample belongs to. groupid for

samples not included in the analysis should be 0.

kernel, n, bw, adjust

passed on to density

cond a vector specifying the condition for each replicate

ncolors different number of colors in the plot

xlab, ylab labels for x-axis and y-axis

sep whether or not to draw horizontal lines between clusters transform a function to transform the original data in plotting

plottype a character string specifying the type of the plot. Available options are "cluster"

and "marginal". The default plottype "cluster" employs function 'plotCluster'

whereas the "marginal" plottype uses function 'plotMarginal'.

... extra arguments are passed to the qqmath, histogram and xyplot call used to

produce the final result

Details

checkCCV checks the constant coefficient of variation assumption made in the GG and LNN models. checkModel generates QQ plots for subsets of (log) intensities in a small window. They are used to check the Log-Normal assumption on observation component of the LNN and LNNMV models and the Gamma assumption on observation component of the GG model. checkVarsQQ generates QQ plot for gene specific sample variances. It is used to check the assumption of a scaled inverse chi-square prior on gene specific variances, made in the LNNMV model. checkVarsMar is another diagnostic tool to check this assumption. The density histogram of gene specific sample variances and the density of the scaled inverse chi-square distribution with parameters estimated from data will be plotted. checkMarginal generates predictive marginal distribution from fitted model and compares with estimated marginal (kernel) density of data. Available for the GG and LNN models only. plotCluster generate heatmap for gene expression data with clusters

Value

checkModel, checkVarsQQ and checkVarsMar return an object of class "trellis", using function in the Lattice package. Note that in certain situations, these may need to be explicitly 'print'-ed to have any effect.

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Author(s)

Ming Yuan, Ping Wang, Deepayan Sarkar, Michael Newton, and Christina Kendziorski

References

Newton, M.A., Kendziorski, C.M., Richmond, C.S., Blattner, F.R. (2001). On differential variability of expression ratios: Improving statistical inference about gene expression changes from microarray data. Journal of Computational Biology 8:37-52.

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See Also

```
emfit, lowess
```

emfit

Implements EM algorithm for gene expression mixture model

Description

Implements the EM algorithm for gene expression mixture model

Usage

```
emfit(data,
     family,
     hypotheses,
     ...)
```

Arguments

data

a matrix

family

an object of class "ebarraysFamily" or a character string which can be coerced to one. Currently, only the characters "GG" and "LNN", and "LNNMV" are valid. For LNNMV, a groupid is required. See below. Other families can be

supplied by constructing them explicitly.

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hypotheses

an object of class "ebarraysPatterns" representing the hypotheses of interest. Such patterns can be generated by the function ebPatterns

. . .

other arguments. These include:

cluster if type=1, cluster is a vector specifying the fixed cluster membership for each gene; if type=2, cluster specifies the number of clusters to be fitted

type if type=1, the cluster membership is fixed as input cluster; if type=2, fit the data with a fixed number of clusters

criterion only used when type=2 and cluster contains more than one integers. All numbers of clusters provided in cluster will be fitted and the one that minimizes criterion will be returned. Possible values now are "BIC", "AIC" and "HQ"

cluster.init only used when type=2. Specify the initial clustering membership. **num.iter** number of EM iterations

verbose logical or numeric (0,1,2) indicating desired level of information printed for the user

optim.control list passed unchanged to optim for finer control

groupid an integer vector indicating which group each sample belongs to, required in the "LNNMV" model. It does not depend on "hypotheses".

Details

There are many optional arguments. So a call might look more like this:

emfit(data, family, hypotheses, cluster, type=2, criterion="BIC", cluster.init = NULL, num.iter = 20, verbose = getOption("verbose"), optim.control = list(), ...)

Value

an object of class "ebarraysEMfit", that can be summarized by show() and used to generate posterior probabilities using postprob

Author(s)

Ming Yuan, Ping Wang, Deepayan Sarkar, Michael Newton, and Christina Kendziorski

References

Newton, M.A., Kendziorski, C.M., Richmond, C.S., Blattner, F.R. (2001). On differential variability of expression ratios: Improving statistical inference about gene expression changes from microarray data. Journal of Computational Biology 8:37-52.

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Newton, M.A., Noueiry, A., Sarkar, D., and Ahlquist, P. (2004). Detecting differential gene expression with a semiparametric hierarchical mixture model. Biostatistics 5: 155-176.

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See Also

```
ebPatterns, ebarraysFamily-class
```

Examples

gould

A dataset of class matrix

Description

This dataset is part of a dataset from a study of gene expression patterns of mammary epithelial cells in a rat model of breast cancer, consisting of 5000 genes in 4 biological conditions; 10 arrays total.

Usage

```
data(gould)
```

Format

The data are originally from Affymetrix chips, subsequently processed by dChip and then exported to R for analysis.

Source

Dr. M.N. Gould's laboratory in UW-Madison

Examples

```
data(gould)
```

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postprob

Calculates posterior probabilities for expression patterns

Description

Takes the output from emfit and calculates the posterior probability of each of the hypotheses, for each gene.

Usage

```
postprob(fit, data, ...)
```

Arguments

fit output from emfit

data a numeric matrix or an object of class "ExpressionSet" containing the data, typ-

ically the same one used in the emfit fit supplied below.

... other arguments, ignored

Value

An object of class "ebarraysPostProb". Slot joint is an three dimensional array of probabilities. Each element gives the posterior probability that a gene belongs to certain cluster and have certain pattern. cluster is a matrix of probabilities with number of rows given by the number of genes in data and as many columns as the number of clusters for the fit. pattern is a matrix of probabilities with number of rows given by the number of genes in data and as many columns as the number of patterns for the fit. It additionally contains a slot 'hypotheses' containing these hypotheses.

Author(s)

Ming Yuan, Ping Wang, Deepayan Sarkar, Michael Newton, and Christina Kendziorski

References

Newton, M.A., Kendziorski, C.M., Richmond, C.S., Blattner, F.R. (2001). On differential variability of expression ratios: Improving statistical inference about gene expression changes from microarray data. Journal of Computational Biology 8:37-52.

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See Also

emfit

Examples

utilities

Utility functions for the EBarrays package

Description

Utility functions for the EBarrays package

Usage

```
ebPatterns(x, ordered=FALSE)
```

Arguments

Х

x can be a character vector (of length > 2) (see example), or an arbitrary connection which should provide patterns, one line for each pattern. If x is a character vector of length 1, it is assumed to be the name of a file (since there's no point in a patterns object with only one pattern) which is then opened and treated as a

connection.

ordered

logical variable specifying whether the pattern is ordered or not

Details

ebPatterns creates objects that represent a collection of hypotheses to be used by emfit.

Value

ebPatterns creates an Object of class "ebarraysPatterns", to be used in other functions such as emfit. This is nothing more than a list (and can be treated as such as far as indexing goes) and is used only for method dispatch.

Author(s)

Ming Yuan, Ping Wang, Deepayan Sarkar, Michael Newton, and Christina Kendziorski

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References

Newton, M.A., Kendziorski, C.M., Richmond, C.S., Blattner, F.R. (2001). On differential variability of expression ratios: Improving statistical inference about gene expression changes from microarray data. Journal of Computational Biology 8:37-52.

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Yuan, M. and Kendziorski, C. (2006). A unified approach for simultaneous gene clustering and differential expression identification. Biometrics 62(4): 1089-1098.

See Also

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