Package ‘rama’

January 15, 2017

Type Package

Title Robust Analysis of MicroArrays

Version 1.48.0

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Description Robust estimation of cDNA microarray intensities with replicates. The package uses a Bayesian hierarchical model for the robust estimation. Outliers are modeled explicitly using a t-distribution, and the model also addresses classical issues such as design effects, normalization, transformation, and nonconstant variance.

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Depends R(>= 2.5.0)

License GPL (>= 2)

biocViews Microarray, TwoChannel, QualityControl, Preprocessing

NeedsCompilation yes

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arrange.row

Reorder a dataset by increasing row order.

Description

The functions could be used to reorder a dataset to make sure that all the genes are in the same row before fitting any model. The `arrange.row` function is also used by the `weight.plot` function to map all the genes to their position on the slide.

Usage

`arrange.row(data)`

Arguments

- `data` A dataset containing the row indices in the first column and the column indices in the second column. The row indices should all be distinct. All indices should start at zero!

Value

The ordered dataset.

Author(s)

Raphael Gottardo

References

Robust Estimation of cDNA Microarray Intensities with Replicates Raphael Gottardo, Adrian E. Raftery, Ka Yee Yeung, and Roger Bumgarner Department of Statistics, University of Washington, Box 354322, Seattle, WA 98195-4322

See Also

`weight.plot`

Examples

```r
data(hiv)
### Put the indices in the first two columns and
### reorder the first 4 replicates
new.data<-cbind(hiv[,9:10],hiv[,1:4])
ordered.data<-arrange.row(new.data)
```
Estimate the shift used in the log transformation

**Description**

Estimate the shift in the log transformation when fitting the Hierarchical model as in bayes.rob.

**Usage**

```r
est.shift(sample1, sample2, B=1000, min.iter=0, batch=10, mcmc.obj=NULL, dye.swap=FALSE, nb.col1=NULL, all.out=TRUE, verbose=FALSE)
```

**Arguments**

- `sample1`: The matrix of intensity from the sample 1. Each row corresponds to a different gene.
- `sample2`: The matrix of intensity from the sample 2. Each row corresponds to a different gene.
- `B`: The number of iteration used the MCMC algorithm.
- `min.iter`: The length of the burn-in period in the MCMC algorithm. `min.iter` should be less than `B`.
- `batch`: The thinning value to be used in the MCMC. Only every `batch`-th iteration will be stored.
- `mcmc.obj`: An object of type `mcmc.shift`, as returned by `est.shift`. If no `mcmc.obj`, the MCMC is initialized to the least squares estimates.
- `dye.swap`: A logical value indicating if the experiment was a dye swap experiment.
- `nb.col1`: An integer value corresponding to the number of arrays (columns) in the first group of the dye swap experiment. In other words, the number of replicates before the dyes have been swapped.
- `all.out`: A logical value indicating if all the parameters should be outputted. If `all.out` is `FALSE`, only the posterior mean is outputted. This could be used to save memory.
- `verbose`: A logical value indicating if the current MCMC iteration number should be printed out.

**Details**

The estimation is done by fitting the same model (as in `fit.model`) with constant variance, Gaussian errors and a prior for the shift. The main purpose of this function is to estimate the shift in the log transformation. Parameter estimation is carried out using Markov Chain Monte Carlo. The shift is estimated with the posterior mean.

**Value**

An object of type `mcmc.est` containing the sampled values from the posterior distribution.

- `mu`: A vector containing the sampled values from `mu`, the baseline intensity.
- `alpha2`: A vector containing the sampled values from `alpha2`, the sample effect.
- `beta2`: A vector containing the sampled values from `beta2`, the dye effect.
delta22  A vector containing the sampled values from delta_22, the dye*sample interaction.

eta      A matrix, each row contains the sampled values from the corresponding array effect.

gamma1   A matrix, each row contains the sampled values from the corresponding gene effect in sample 1.

gamma2   A matrix, each row contains the sampled values from the corresponding gene effect in sample 1.

lambda.gamma1  A vector containing the sampled values for the precision of the gene effect prior in sample 1.

lambda.gamma2  A vector containing the sampled values for the precision of the gene effect prior in sample 2.

rho       A vector containing the sampled values from between sample correlation coefficient rho

lambda_eps1 A vector containing the sampled values from the gene precision in sample 1.

lambda_eps2 A vector containing the sampled values from the gene precision in sample 2.

shift     A vector containing the sampled values from the shift.

Author(s)
Raphael Gottardo

References
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See Also
fit.model

Examples

```r
data(hiv)
### Initialize the proposals
mcmc.hiv<-est.shift(hiv[1:10,c(1:4)],hiv[1:10,c(5:8)],B=2000,min.iter=000,batch=1,mcmc.obj=NULL,dye.swap=TRUE,nb.col1=2)
```

Description
Estimate the log transformed intensities of each sample of a replicated microarray experiment. The estimation is done via Hierarchical Bayesian Modeling.

Usage

```r
fit.model(sample1,sample2,B=1000,min.iter=0,batch=10,shift=NULL,mcmc.obj=NULL,dye.swap=FALSE,nb.col1=NULL,all.out=FALSE,ci=0.95,
verbose=FALSE)
```
Arguments

- **sample1**: The matrix of intensity from the sample 1. Each row corresponds to a different gene.
- **sample2**: The matrix of intensity from the sample 2. Each row corresponds to a different gene.
- **B**: The number of iteration used the MCMC algorithm.
- **min.iter**: The length of the burn-in period in the MCMC algorithm. min.iter should be less than B.
- **batch**: The thinning value to be used in the MCMC. Only every batch-th iteration will be stored.
- **mcmc.obj**: An object of type mcmc, as returned by fit.model. mcmc.obj is used to initialized the MCMC. If no mcmc.obj, the MCMC is initialized to the least squares estimates.
- **shift**: The shift to be used in the log transformation. If shift=NULL is specified (default), it is estimated using est.shift.
- **dye.swap**: A logical value indicating if the experiment was a dye swap experiment.
- **nb.col1**: An integer value corresponding to the number of arrays (columns) in the first group of the dye swap experiment. In other words, the number of replicates before the dyes have been swapped.
- **all.out**: A logical value indicating if all the parameters should be outputted. If all.out is FALSE, only the posterior mean is outputted. This could be used to save memory.
- **ci**: A number between 0 and 1 corresponding to the level used when computing log ratio credible intervals. If all.out is FALSE, this option is ignored.
- **verbose**: A logical value indicating if the current MCMC iteration number should be printed out.

Details

The function fits a hierarchical Bayesian model for robust estimation of cDNA microarray intensities. Our model addresses classical issues such as design effects, normalization and transformation. Outliers are modeled explicitly using a t-distribution. Parameter estimation is carried out using Markov Chain Monte Carlo.

Value

An object of type mcmc containing the sampled values from the posterior distribution.

- **mu**: A vector containing the sampled values from mu, the baseline intensity.
- **alpha2**: A vector containing the sampled values from alpha2, the sample effect.
- **beta2**: A vector containing the sampled values from beta2, the dye effect.
- **delta22**: A vector containing the sampled values from delta_22, the dye*sample interaction.
- **eta**: A matrix, each row contains the sampled values from the corresponding array effect.
- **gamma1**: A matrix, each row contains the sampled values from the corresponding gene effect in sample 1.
gamma2

A matrix, each row contains the sampled values from the corresponding gene effect in sample 1.

q.low

A vector containing the lower bounds for the log ratio credible intervals, i.e. the credible intervals for gamma1-gamma2.

q.up

A vector containing the upper bounds for the log ratio credible intervals, i.e. the credible intervals for gamma1-gamma2.

lambda.gamma1

A vector containing the sampled values for the precision of the gene effect prior in sample 1.

lambda.gamma2

A vector containing the sampled values for the precision of the gene effect prior in sample 2.

rho

A vector containing the sampled values from between sample correlation coefficient rho.

lambda_eps1

A matrix, each row contains the sampled values from the corresponding gene precision in sample 1.

lambda_eps2

A matrix, each row contains the sampled values from the corresponding gene precision in sample 2.

a.eps

A vector containing the sampled values for the mean of the prior of the genes precision.

b.eps

A vector containing the sampled values for the variance of the prior of the genes precision.

w

A matrix, each element (i,j) correspond to the posterior mean of the sampled weights of replicate j in gene i. To save memory, we only store the posterior means of the weights.

shift

The value of the shift.

Author(s)

Raphael Gottardo

References

Robust Estimation of cDNA Microarray Intensities with Replicates Raphael Gottardo, Adrian E. Raftery, Ka Yee Yeung, and Roger Bumgarner Department of Statistics, University of Washington, Box 354322, Seattle, WA 98195-4322

See Also

est.shift

Examples

data(hiv)
mcmc.hiv<-fit.model(hiv[1:10,c(1:4)],hiv[1:10,c(5:8)],B=2000,min.iter=000,batch=1,shift=30,mcmc.obj=NULL,dye.swap=TRUE,nb.col1=2)
**hiv**

*Cellular gene expression upon human immunodeficiency virus type 1 infection of CD4+-T-Cell lines*

**Description**

This data set consists of 4 experiments using the same RNA preparation on 4 different slides. The expression levels of ~7000 cellular RNA transcripts were assessed in CD4-T-cell lines at time $t=24$ hour after infection with HIV virus type 1. The first 4 columns correspond to the first treatment state (hiv infected). The second four represent the control state. The experiment is a balanced dye swap experiment. Finally, the last two columns contain the row and column positions of each gene on the array (slide).

**Usage**

data(hiv)

**Source**


**References**


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**is.row.na**

*Test if a matrix contains missing values*

**Description**

The function returns a vector of logical variables, one for each row of the matrix. The variable is TRUE if the row does not contain any missing values and FALSE otherwise.

**Usage**

is.row.na(data)

**Arguments**

data The data matrix.

**Value**

The vector of logical variable

**Author(s)**

Raphael Gottardo
See Also

is.na

Examples

### Generate a matrix
M<-matrix(rnorm(100),10,10)
M[1,1]<-NA
M[1,2]<- -Inf
M[3,10]<-NA

### Indices of the rows without missing values
ind<-is.row.na(M)

### Submatrix of M with finite values
M.finite<-M[ind,]

ls.effect

Compute the least squares estimates of the all the effects of the general model.

Description

Compute the least squares estimates of the all the effects of the general model.

Usage

ls.effect(sample1,sample2,dye.swap=FALSE,nb.col1=NULL)

Arguments

- **sample1**: The matrix of intensity from the sample 1. Each row corresponds to a different gene.
- **sample2**: The matrix of intensity from the sample 2. Each row corresponds to a different gene.
- **dye.swap**: A logical value indicating if the experiment was a dye swap experiment.
- **nb.col1**: An integer value corresponding to the number of arrays (columns) in the first group of the dye swap experiment. In other words, the number of replicates before the dyes have been swapped.

Value

- **mu**: The baseline intensity
- **alpha2**: The sample effect
- **beta2**: The dye effect
- **delta22**: The dye*sample interaction
- **eta**: The array effects
- **gamma1**: The genes effects in sample 1
### Compute the least squares effects on the log scale
```
data(hiv)
ls.fx<-ls.effect(log2(hiv[,c(1:4)]),log2(hiv[,c(5:8)]),dye.swap=TRUE.nb.col1=2)
```
ratio.plot

See Also
mean, sd

Examples

data(hiv)
sample1<-hiv[,1:4]
ms1<-mat.mean(sample1)

ratio.plot
Plot the estimated log ratios against the overall intensities

Description
Plot the estimated log2(gamma1/gamma2) against log2(gamma1*gamma2)/2.

Usage
ratio.plot(mcmc.obj,col=1,pch=1)

Arguments
mcmc.obj An object of class mcmc as returned by fit.model
col The color to be used for the symbols
pch The type of symbols to be used.

Value
The graph!

Author(s)
Raphael Gottardo

References
Robust Estimation of cDNA Microarray Intensities with Replicates Raphael Gottardo, Adrian E. Raftery, Ka Yee Yeung, and Roger Bumgarner Department of Statistics, University of Washington, Box 354322, Seattle, WA 98195-4322

See Also
fit.model

Examples

data(hiv)
### Initialize the proposals
mcmc.hiv<-fit.model(hiv[1:10,c(1:4)],hiv[1:10,c(5:8)],B=2000,min.iter=000,batch=1,shift=30,mcmc.obj=NULL,dye.swap=TRUE,nb.col1=2)
ratio.plot(mcmc.hiv,col=1,pch=1)
weight.plot

Plot the weights of a given array using the spatial location of the genes on the slide

Description

Plot the weights of a given array using the spatial location of the genes on the slide. This function is a useful diagnostic tool.

Usage

weight.plot(mcmc.obj, coordinate, array = 1)

Arguments

- **mcmc.obj**: An object of class `mcmc` as returned by `fit.model`
- **coordinate**: The coordinate of each gene on the corresponding array. The coordinates should be a two column integer valued matrix containing the row indices (column 1) and the column indices (column 2). The row indices should all be distinct. All indices should start at zero!
- **array**: An integer corresponding to the array number to be plotted.

Value

The image plot of the weights. A small weight (bright color) correspond to an outlier.

Author(s)

Raphael Gottardo

References

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See Also

`arrange.row`

Examples

data(hiv)
### Initialize the proposals
mcmc.hiv <- fit.model(hiv[1:640, c(1:4)], hiv[1:640, c(5:8)], B = 1000, min.iter = 500, batch = 1, shift = 30, mcmc.obj = NULL, dye.swap = TRUE, nb.col1 = 2)
weight.plot(mcmc.hiv, hiv[1:640, 9:10], array = 3)
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