

Package ‘DeconRNASeq’

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Type Package

Title Deconvolution of Heterogeneous Tissue Samples for mRNA-Seq data

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Depends R (>= 2.14.0), limSolve, pcaMethods, ggplot2, grid

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Description DeconSeq is an R package for deconvolution of heterogeneous tissues based on mRNA-Seq data. It modeled expression levels from heterogeneous cell populations in mRNA-Seq as the weighted average of expression from different constituting cell types and predicted cell type proportions of single expression profiles.

License GPL-2

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DeconRNASeq-package *package DeconRNASeq contains function "DeconRNASeq", implementing the decomposition of RNA-Seq expression profilings of heterogeneous tissues into cell/tissue type specific expression and cell type concentration based on cell-type-specific reference measurements.*

Description

Main function "DeconRNASeq" implements a nonnegative decomposition by quadratic programming as $\text{datasets} = \text{signature} * A$, where "datasets" are the originally measured data matrix (e.g. genes by samples), "signature" is the signature matrix (genes by cell types) and "A" the cell type concentration matrix (cell types by samples)

Details

Package: DeconRNASeq
 Type: Package
 Version: 1.0
 Date: 2012-05-25
 License: GPL version 2 or later

DeconRNASeq(datasets, signature)

Author(s)

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References

Gong, T., et al. (2011) Optimal Deconvolution of Transcriptional Profiling Data Using Quadratic Programming with Application to Complex Clinical Blood Samples, PLoS One, 6, e27156.

all.datasets	<i>data objects for rat liver_brain samples</i>
--------------	---

Description

A data frame providing the expression profilings of GSE19830 microarray samples.

Usage

```
all.datasets
```

Format

A matrix with expression studies in the GSE19830 microarray samples: the first three columns are corresponding to the liver, while the last three samples are corresponding to the brain.

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

Examples

```
data(rat_liver_brain)
```

array.proportions *proportions for rat liver and brain mixing samples*

Description

array.proportions: a data frame providing the fractions for liver and brain from the microarray GSE 19830 study

Usage

```
array.proportions
```

Format

a matrix whose rows are mixing samples' name and columns are fractions from pure liver and brain tissues

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

Examples

```
data(rat_liver_brain)
```

array.signatures	<i>data objects for rat liver and brain pure samples</i>
------------------	--

Description

array.signatures: a data frame providing the expression values from rat pure liver and brain samples, each has three replicates

Usage

```
array.signatures
```

Format

a data matrix with 30 expressions from rat pure liver and brain tissues

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

Examples

```
data(rat_liver_brain)
```

condplot	<i>Draw the plot of the condition numbers vs. the number of genes in the signature matrix</i>
----------	---

Description

A function is used to draw the plot of the condition number of signature matrices of all sizes, from a handful of genes in one extreme to the whole signature in the other.

Usage

```
condplot(step, cond)
```

Arguments

step	an array with the number of genes used to calculate the condition numbers of signature matrices, default stepwise = 20
cond	an array with the condition numbers of signature matrices

Value

a plot for the condition numbers of signature matrices

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

References

Gong, T., et al. (2011) Optimal Deconvolution of Transcriptional Profiling Data Using Quadratic Programming with Application to Complex Clinical Blood Samples, PLoS One, 6, e27156.

Examples

```
library(DeconRNASeq)
#####
## toy data example:

step <- seq(20,1000, by=20) #every 20 genes
## cell type-specific gene expression matrix:
x.signature <- matrix(rexp(2000),ncol=2)
sig.cond <- sapply(step, function(x) kappa(scale(x.signature[1:x,])))
function (step, cond)
```

datasets

data objects for liver and kidney mixing samples

Description

A data frame providing the RPKM of seven mixing samples.

Usage

```
datasets
```

Format

A data frame with 31979 genes' expression on the 7 mixing samples: reads.1, reads.2, reads.3, reads.4, reads.5, reads.6, reads.7

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

Examples

```
data(liver_kidney)
```

decon.bootstrap	<i>Estimate the confidence interval for the proportions predicted by deconvolution</i>
-----------------	--

Description

A function is used to estimate the the confidence interval for the proportions predicted by deconvolution through bootstrapping.

Usage

```
decon.bootstrap(data.set, possible.signatures, n.sig, n.iter)
```

Arguments

data.set	the data object for mixing samples
possible.signatures	a data frame providing the expression values from pure tissue samples
n.sig	the number of genes/transcripts used for estimation of proportions from our deconvolution
n.iter	the number of bootstraps for our deconvolution

Value

A three dimensional array to store means and 95% confidence interval

Author(s)

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References

Gong, T., et al. (2011) Optimal Deconvolution of Transcriptional Profiling Data Using Quadratic Programming with Application to Complex Clinical Blood Samples, PLoS One, 6, e27156.

DeconRNASeq	<i>Function for Deconvolution of Complex Samples from RNA-Seq.</i>
-------------	--

Description

This function predicts proportions of constituting cell types from gene expression data generated from RNA-Seq data. Perform nonnegative quadratic programming to get per-sample based globally optimized solutions for constituting cell types .

Usage

```
DeconRNASeq(datasets, signatures, proportions = NULL, checksig = FALSE, known.prop = FALSE, use.sc
```

Arguments

datasets	measured mixture data matrix, genes (transcripts) e.g. gene counts by samples, . The user can choose the appropriate counts, RPKM, FPKM etc..
signatures	signature matrix from different tissue/cell types, genes (transcripts) by cell types. For gene counts, the user can choose the appropriate counts, RPKM, FPKM etc..
proportions	proportion matrix from different tissue/cell types.
checksig	whether the condition number of signature matrix should be checked, default = FALSE
known.prop	whether the proportions of cell types have been known in advanced for proof of concept, default = FALSE
use.scale	whether the data should be centered or scaled, default = TRUE
fig	whether to generate the scatter plots of the estimated cell fractions vs. the true proportions of cell types, default = TRUE

Details

Data in the originally measured mixture sample matrix: datasets and reference matrix: signatures, need to be non-negative. We recommend to deconvolute without log-scale.

Value

Function DeconRNA-Seq returns a list of results

out.all	estimated cell type fraction matrix for all the mixture samples
out.pca	svd calculated PCA on the mixture samples to estimate the number of pure sources according to the cumulative R2
out.rmse	averaged root mean square error (RMSE)) measuring the differences between fractions predicted by our model and the truth fraction matrix for all the tissue types

Author(s)

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References

Gong, T., et al. (2011) Optimal Deconvolution of Transcriptional Profiling Data Using Quadratic Programming with Application to Complex Clinical Blood Samples, PLoS One, 6, e27156.

Examples

```
## Please refer our demo
##source("DeconRNASeq.R")
### multi_tissue: expression profiles for 10 mixing samples from multiple tissues
#data(multi_tissue.rda)

#datasets <- x.data[,2:11]
#signatures <- x.signature.filtered.optimal[,2:6]
#proportions <- fraction

#DeconRNASeq(datasets, signatures, proportions, checksig=FALSE, known.prop = TRUE, use.scale = TRUE)
#
```

fraction	<i>mixing fractions for multi-tissues mixing samples</i>
----------	--

Description

A data frame providing the fractions from multiple tissues in the mixing samples

Usage

```
fraction
```

Format

A matrix whose rows are mixing samples' name and columns are fractions from pure tissues including brain, muscle, lung, liver and heart

Author(s)

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Examples

```
data(multi_tissue)
```

liver_kidney	<i>data objects for liver and kidney mixing samples</i>
--------------	---

Description

a list containing:

- 1) datasets: a data frame providing the RPKM of seven mixing samples.
- 2) proportions: a data frame providing the fractions for liver and kidney in the mixing samples
- 3) signatures: a data frame providing the expression values from pure liver and kidney samples

Usage

```
liver_kidney
```

Format

A list 1) a data frame with 31979 genes' expression on the 7 mixing samples: reads.1, reads.2, reads.3, reads.4, reads.5, reads.6, reads.7

2) a matrix whose rows are mixing samples' name and columns are fractions from pure liver and kidney tissues

3) a data matrix with 630 expressions from pure liver and kidney tissues

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

Examples

```
data(liver_kidney)
```

multiplot	<i>Draw the plots of proportions of cells determined from deconvolution vs. proportions of the cells actually mixed (when available) with RMSE.</i>
-----------	---

Description

A function is used to draw the multiple plots of proportions of cells determined from deconvolution vs. proportions of the cells actually mixed. Each plot corresponds to one tissue/cell.

Usage

```
multiplot(..., plotlist = NULL, cols)
```

Arguments

...	any number of the plot objects that store the scatter plots for all the cells/tissue types
plotlist	any other plot objects
cols	columns of the plots, default = 1

Value

A pdf file with the plots of proportions of cells determined from deconvolution vs. proportions of the cells actually mixed with RMSE

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

References

Gong, T., et al. (2011) Optimal Deconvolution of Transcriptional Profiling Data Using Quadratic Programming with Application to Complex Clinical Blood Samples, PLoS One, 6, e27156.

Examples

```
## The function is currently defined as
function (... , plotlist = NULL, cols)
{
  pdf("scatterplots.pdf")
  require(grid)
  plots <- c(list(...), plotlist)
  numPlots = length(plots)
  plotCols = cols
  plotRows = ceiling(numPlots/plotCols)
  grid.newpage()
  pushViewport(viewport(layout = grid.layout(plotRows, plotCols)))
```

```

vplayout <- function(x, y) viewport(layout.pos.row = x, layout.pos.col = y)
for (i in 1:numPlots) {
  curRow = ceiling(i/plotCols)
  curCol = (i - 1)%%plotCols + 1
  print(plots[[i]], vp = vplayout(curRow, curCol))
}
dev.off()
}

```

multi_tissue

data objects for multi-tissues mixing samples

Description

a list containing:

- 1) x.data: a data frame providing the RPKM of nine mixing samples.
- 2) x.signatures: a data frame providing the expression values from pure brain, muscle, lung, liver and heart samples.
- 3) x.signatures.filtered: a data frame providing the expression values from pure brain, muscle, lung, liver and heart samples after filtering.
- 4) x.signatures.filtered.optimal: a data frame providing the expression values from pure brain, muscle, lung, liver and heart samples used for the example in DeconRNA-Seq.
- 5) fraction: a data frame providing the fractions from 5 tissues in the mixing samples

Usage

```
multi_tissue
```

Format

A list 1) a matrix with all the genes' expression in the mixing samples: the first two columns are corresponding to the RefSeq accession numbers and gene symbols

- 2) a matrix whose rows are gene symbols and columns are RPKM expressions from pure tissues.
- 3) a matrix whose rows are gene symbols and columns are RPKM expressions from pure tissues: the genes with RPKM less than 200 within any of the five tissues have been filtered.
- 4) a matrix whose rows are gene symbols and columns are RPKM expressions from pure tissues: based on the filtered signature matrix, the optimal number of genes have been selected for the deconvolution according to the condition numbers
- 5) a matrix whose rows are mixing samples' name and columns are fractions from pure tissues including brain, muscle, lung, liver and heart

Author(s)

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Examples

```
data(multi_tissue)
```

proportions	<i>proportions for liver and kidney mixing samples</i>
-------------	--

Description

proportions: a data frame providing the fractions for liver and kidney in the mixing samples

Usage

```
proportions
```

Format

a matrix whose rows are mixing samples' name and columns are fractions from pure liver and kidney tissues

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

Examples

```
data(liver_kidney)
```

rmse	<i>Calculate the differences between proportions predicted by deconvolution and the values actually measured</i>
------	--

Description

A function is used to calculate the root-mean-square error (RMSE) for the accuracy of estimated proportions.

Usage

```
rmse(x, y)
```

Arguments

x	proportions from the actual measurement
y	estimated proportions from our deconvolution

Value

A number for RMSE

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

References

Gong, T., et al. (2011) Optimal Deconvolution of Transcriptional Profiling Data Using Quadratic Programming with Application to Complex Clinical Blood Samples, PLoS One, 6, e27156.

signatures	<i>data objects for liver and kidney pure samples</i>
------------	---

Description

signatures: a data frame providing the expression values from pure liver and kidney samples

Usage

signatures

Format

a data matrix with 630 expressions from pure liver and kidney tissues

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

Examples

data(liver_kidney)

x.data	<i>data objects for multi-tissues mixing samples</i>
--------	--

Description

A data frame providing the RPKM of nine mixing samples.

Usage

x.data

Format

A matrix with all the genes' expression in the mixing samples: the first two columns are corresponding to the RefSeq accession numbers and gene symbols

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

Examples

data(multi_tissue)

x.signature *data objects for multi-tissues pure samples*

Description

A data frame providing the expression values from pure brain, muscle, lung, liver and heart samples.

Usage

```
x.signature
```

Format

A matrix whose rows are gene symbols and columns are RPKM expressions from pure tissues.

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

Examples

```
data(multi_tissue)
```

x.signature.filtered *filtered signatures for multi-tissues pure samples*

Description

A data frame providing the expression values from pure brain, muscle, lung, liver and heart samples after filtering.

Usage

```
x.signature.filtered
```

Format

A matrix whose rows are gene symbols and columns are RPKM expressions from pure tissues: the genes with RPKM less than 200 within any of the five tissues have been filtered.

Author(s)

Ting Gong <tinggong@gmail.com> Joseph D. Szustakowski <joseph.szustakowski@novartis.com>

Examples

```
data(multi_tissue)
```

```
x.signature.filtered.optimal
```

selected signatures from multi-tissues pure samples

Description

A data frame providing the expression values from pure brain, muscle, lung, liver and heart samples used for the example in DeconRNA-Seq.

Usage

```
x.signature.filtered.optimal
```

Format

A matrix whose rows are gene symbols and columns are RPKM expressions from pure tissues: based on the filtered signature matrix, the optimal number of genes have been selected for the deconvolution according to the condition numbers

Author(s)

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Examples

```
data(multi_tissue)
```

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