Package ‘RNAinteractMAPK’

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Type Package

Title Mapping of Signalling Networks through Synthetic Genetic Interaction Analysis by RNAi

Version 1.40.0

Description This package includes all data used in the paper -Mapping of Signalling Networks through Synthetic Genetic Interaction Analysis by RNAi- by Horn, Sandmann, Fischer et al., Nat. Methods, 2011. The package vignette shows the R code to reproduce all figures in the paper.

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LazyLoad yes

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RNAracticMPK-package

Mapping of Signalling Networks through Synthetic Genetic Interaction Analysis by RNAi.

Description

The package contains the data and the source code to reproduce the results and figures from the paper


Details

See vignette("RNAracticMPK") for details.

Package content

See vignette("RNAracticMPK") for more detail on how to obtain the data used for specific figures. In addition this vignette contains the complete analysis and the generation of all figures.

The main screen can be loaded by data("Dmel2PPMAPK", package="RNAracticMPK"). Access to the pairwise interaction data is done via the getData function from the RNAracticMPK-package. See example below.

The following datasets are provided with this package:

Dmel2PPMAPK interaction data of main screen. See example below.
Within this package a number of specialized functions is defined written for the analysis of the MAPK interaction screen and additional experiments shown in the paper. These functions are not intended to be general purpose analysis functions, but should document the steps of analysis of the paper. Therefore, these functions are not exported. A list of functions is given below. A general purpose package for the analysis of genetic interaction screens is the package `RNAinteract`.

The following functions are provided within this package.

Functions used for the classification: `MAPK.predict.classification`, `MAPK.cv.classifier`, `MAPK.getCV`, `MAPK.ternary.plot`, `MAPK.getXY`, `MAPK.plot.classification`.

Functions for the analysis of the interaction surfaces: `MAPK.plot.TPS.single`, `MAPK.plot.TPS.all`, `MAPK.estimate.TPS`, `MAPK.cv.TPS`, `MAPK.screen.as.array`.

A function to write the hit list: `MAPK.report.gene.lists.paper`.

A function to plot a heatmap: `MAPK.plot.heatmap.raster`.

A function to plot smooth scatters: `MAPK.smooth.scatter`.

Author(s)

Bernd Fischer

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References


See Also

`RNAinteractMAPK-package`

Examples

data(Dmel2PPMAPK)
dmel2PPMAPK

# Obtain the pairwise interaction matrix
PI <- getData(Dmel2PPMAPK, type="pi", format="targetMatrix",
             screen="mean", withoutgroups = c("pos", "neg"))
cellTiterGlo

Comparison of interaction experiment with an cellTiterGlo viability assay

Description

For ten gene pairs genetic interactions are measured. The experiment contains 24 different conditions. These are repeated in each row of the three 384 mutli well plates. The data.frame contains the plate annotation as well as the viability readout for the three plates.

Usage

data(cellTiterGlo)

Format

A data frame with 384 observations on the following 6 variables.

Well  a character vector
dsRNA_1 a character vector
dsRNA_2 a character vector
plate1 a numeric vector
plate2 a numeric vector
plate3 a numeric vector

Source

Horn, Sandmann, Fischer, Huber, Boutros, Mapping of Signalling Networks through Synthetic Genetic Interaction Analysis by RNAi, Nature Methods, 2011, Figure S15.

Examples

data(cellTiterGlo)
head(cellTiterGlo)
**Dmel2PPMAPK**

The interaction data of the main screen

**Description**

Dmel2PPMAPK is an object of class `RNAinteract`. It contains the raw data, the computed main effects, pairwise interaction scores, p-values and q-values computed by a t-test. The package vignette contains the complete code and documentation for the statistical analysis.

**Usage**

```r
data(Dmel2PPMAPK)
```

**Format**

An object of class `RNAinteract`.

**Source**


**Examples**

```r
data(Dmel2PPMAPK)
Dmel2PPMAPK

# Obtain the pairwise interaction matrix
PI <- getData(Dmel2PPMAPK, type="pi", format="targetMatrix",
               screen="mean", withoutgroups = c("pos", "neg"))
```

**dsRNAiDilutionSeries**

dsRNA dilution series

**Description**

A dilution series for 6 x 6 gene. For each gene pair all combinations of 8 different concentrations of dsRNA reagent are screened. Three readout channels (nrCells, area, intensity) are available in the data.frame `dsRNAiDilutionSeries`. The plate annotation is given in the data.frame `dsRNAiDilutionSeriesAnno` and precomputed degrees of freedom for thin plate splines are available in the matrix `dsRNAiDilutionSeriesDF`.

**Usage**

```r
data(dsRNAiDilutionSeries)
```
ElpB1phenotype

Ectopic wing vein formation phenotype caused by the EgfrElpB1.

Description

Partial suppression of ectopic wing vein formation (in vivo fly phenotype) caused by the EgfrElpB1 in Cka heterozygous mutant backgrounds. The wing vein formation phenotype is classified as strong and not strong. It is tested for three fly mutants.

Usage

data(ElpB1phenotype)
MAPK.cv.classifier

**Format**

A data frame with 3 observations on the following 2 variables.

- `strong` a numeric vector
- `notstrong` a numeric vector

**Source**

Horn, Sandmann, Fischer, Huber, Boutros, Mapping of Signalling Networks through Synthetic Genetic Interaction Analysis by RNAi, Nature Methods, 2011, Figure 5f.

**Examples**

```r
data(ElpB1phenotype)
ElpB1phenotype
```

---

**MAPK.cv.classifier**

A classifier for genetic interaction data.

**Description**

These functions implement a classifier to classify three classes of pathway membership of the RasMAPK and JNK pathway. For each sample and each channel a sparse linear discriminat classifier is trained. The posterior probabilities are averaged over all single classifiers. The classification posterior probabilities of three classes are plotted as a ternary plot (ternary plot adapted from CRAN package vcd).

**Usage**

```r
MAPK.cv.classifier(sgi, traingroups)
MAPK.predict.classification(sgi, traingroups)
MAPK.plot.classification(posterior,
    classes = NULL, classnames = NULL,
    col = "darkgray", y = NULL,
    classcol = NULL,
    main = "predicted classification probabilities",
    pop = TRUE, threshText = 0.3,
    textToLeft = NULL, textToRight = NULL)
```

**Arguments**

- `sgi` An object of class `RNAinteract`
- `traingroups` A list of gene names for the training examples. For each class there should be a vector of gene names.
- `posterior` A matrix of posterior probabilities. Each row represents one gene, each column represents one class.
MAPK.cv.classifier

- **classes**: The three classes to be displayed on the ternary plot.
- **classnames**: The class names to be displayed.
- **col**: The color used for the text labels.
- **y**: A factor representing the class label for each gene in posterior.
- **classcol**: The color used for the three classes.
- **main**: The title of the plot.
- **pop**: If TRUE, all viewports are popped before finishing the function.
- **threshText**: A threshold for the posterior probability of the three classes. Only genes that are assigned with a larger probability to the three classes are shown.
- **textToLeft**: These text labels will be shown on the left hand side.
- **textToRight**: These text labels will be shown on the right hand side.

**Details**

The code for the ternary plot (used by MAPK.plot.classification) is adapted from the function ternaryplot in the CRAN package vcd. Author of the original code is David Meyer (David.Meyer@R-project.org). References: M. Friendly (2000), Visualizing Categorical Data. SAS Institute, Cary, NC. This code is specialized for the publication "Mapping Signalling Networks by RNAi ..." in Nat. Methods. It is highly recommended to use the original code by David Meyer.

**Value**

- **MAPK.cv.classifier** returns a list with the cross validated class assignment probability, as well as the results of the single classifiers.
- **MAPK.predict.classifier** returns the predicted posterior probabilities of new genes as well as the classification results of the single classifier.
- **MAPK.plot.classifier** returns nothing.

**Author(s)**

Bernd Fischer

**References**


**See Also**

RNAinteract, RNAinteractMAPK
**MAPK.estimate.TPS**

---

### Description

Genetic interaction surfaces are estimated from a dilution experiment. Cells are treated with two RNAi’s. The concentration of the RNAi reagent is changed in 8 steps. All 8 x 8 combinations of concentrations are tested for 6 x 6 gene pairs.

### Usage

- `MAPK.screen.as.array(data, Anno)`
- `MAPK.estimate.TPS (A, DF, n.out = 8, channel = 1)`
- `MAPK.cv.TPS (A, range.df = 6:56, channel = 1)`
- `MAPK.plot.TPS.all (TPSmodel, range = c(-6, 6), fill = c("cornflowerblue", "cornflowerblue", "black", "#777700", "yellow"), channel = 1)`
- `MAPK.plot.TPS.single(gene1, gene2, TPSmodel, range = c(-6, 6), fill = c("cornflowerblue", "cornflowerblue", "black", "#777700", "yellow"), channel = 1)`

### Arguments

- **data, Anno**
  - **data**: A data.frame containing the read.out of the dilution screen. Each row is one well. Each column one feature.
  - **Anno**: A data.frame containing the plate configuration. For each row in data there should a row in Anno.
- **A**: An array of dimension concentration x concentration x genes x genes x channel as returned by `MAPK.screen.as.array`.
- **DF**: A 6 x 6 matrix of degrees of freedom for the thin spline plate regression.
- **n.out**: number of points for sampling from the regression function.
- **channel**: The channel used.
- **range.df**: The range of degrees of freedom that is considered for cross validation.
- **range**: The range of pairwise interaction scores that is shown by the colorbar.
- **gene1, gene2**: The genes for which the interaction surface is plotted.
- **TPSmodel**: The TPS model estimated by `MAPK.estimate.TPS`.
- **fill**: The range of colors used for the color code.
Details

The screen readout can be reshaped as an array with dimensions concentration x concentration x genes x genes x channel by the function MAPK.screen.as.array. Then the function MAPK.estimate.TPS fits a regression in the 8 x 8 pairwise dilution series. The degrees of freedom for the regression can be estimated automatically by cross validation with the function MAPK.cv.TPS. Finally one can plot the interaction surface for a single gene or an overview of interaction surfaces for all genes with the functions MAPK.plot.TPS.single or MAPK.plot.TPS.all.

Value

- MAPK.screen.as.array returns an array of dimensions concentration x concentration x genes x genes x channel with the screen data.
- MAPK.estimate.TPS returns a regression model estimated by thin plate splines for each pair of genes and subsampled matrices.
- MAPK.cv.TPS.all returns
  - DF a matrix with degrees of freedom.
  - CVerror The prediction error estimated by cross validation.
  - CVerrorSD The standard deviation of the prediction error estimated by cross validation.
- MAPK.plot.TPS.single, MAPK.plot.TPS.all: An object of class "trellis". See levelplot for details.

Author(s)

Bernd Fischer

See Also

RNAinteract-package, RNAinteractMAPK-package

MAPK.plot.heatmap.raster

Plots a heatmap using grid.raster

Description

This functions provides a grid plot that displays the raster image of a heatmap without any axis or label. This function is adapted from the function grid.sgiHeatmap from the package RNAinteract-package. It is highly recommended to use the original function grid.sgiHeatmap.

Usage

MAPK.plot.heatmap.raster(X, subset = NULL,
                        hc.row = NULL, hc.col = NULL,
                        pi.max = NULL)
Arguments

- **X**: A matrix of pairwise interaction scores.
- **subset**: A subset of genes that are displayed in the rows.
- **hc.row**: A hclust object.
- **hc.col**: A hclust object.
- **pi.max**: The maximum interaction score of the colorbar. All interaction scores larger than this value will be displayed in the same color.

Value

Nothing is returned.

Author(s)

Bernd Fischer

See Also

RNAinteract-package, RNAinteractMAPK-package

Description

Reports the hitlist of genetic interactions, with p-values from a t-test with pooled variance estimate, from limma, and from Hotelling T^2 test.

Usage

MAPK.report.gene.lists.paper(sgi, sgilimma, sgi3T2, screen = "mean")

Arguments

- **sgi**: An object of class RNAinteract containing p-values from a t-test with pooled variance estimate.
- **sgilimma**: An object of class RNAinteract containing p-values from limma.
- **sgi3T2**: An object of class RNAinteract containing p-values from a Hotelling T^2 test.
- **screen**: The screen name for which the report should be written.

Details

Writes tab-separated lists for each single test as well as a joint table with all three tests.
Value
Nothing is returned.

Author(s)
Bernd Fischer

See Also
RNAinteract-package, RNAinteractMAPK-package

MAPK.smooth.scatter smooth scatter using grid raster

Description
This function is a reimplementation of smoothScatter. For nicer graphics output the background image is written by grid.raster. It is recommended to use the smoothScatter function from the graphics package.

Usage
MAPK.smooth.scatter(x, y, n = 75,
                   nrpoints = 100, col = "blue",
                   pch = 20, size = unit(0.3, "char"), cex = 1.2,
                   colramp = colorRampPalette(c("white", "blue", "green", "yellow", "red"))(256),
                   xlab = "", ylab = "", respect = FALSE)

Arguments
\begin{itemize}
  \item \textbf{x} x-values.
  \item \textbf{y} y-values. Has to be the same length as x.
  \item \textbf{n} nr of bins used for the kernel density estimation.
  \item \textbf{nrpoints} nrpoints points in the lowest density region will be plotted. This allows the identification of outliers.
  \item \textbf{col} color of points.
  \item \textbf{pch} symbol to plot points.
  \item \textbf{size} The size of the points.
  \item \textbf{cex} The size of the label text.
  \item \textbf{colramp} color ramp for the density plot.
  \item \textbf{xlab,ylab} axis labels.
  \item \textbf{respect} A logical value indicating if the height and width of the axis scales should respect each other.
\end{itemize}
mRNAdoubleKDeficiency

Details

Plots a density plot with grid graphics.

Author(s)

Bernd Fischer

See Also

RNAinteractMAPK-package, smoothScatter

---

mRNAdoubleKDeficiency

mRNA levels for double knock downs

Description

qPCR measurements for the mRNA level after a double gene knock down (ratio relative to wild type control). The experiments tests the knock down efficiency in the presence of a second gene knock down.

Usage

data(mRNAdoubleKDeficiency)

Format

A data frame with 320 observations on the following 5 variables.

- template: an ordered factor with levels Fluc < CG10417 < CG13197 < CG9391 < egr < lic < PRL-1 < Rho1 < Tak1
- qPCR.target: a factor with levels CG10417 CG13197 CG9391 egr lic PRL-1 Rho1 Tak1
- passage: a factor with levels passage 4 passage 42
- RNAi: a numeric vector

Source

Horn, Sandmann, Fischer, Huber, Boutros, Mapping of Signalling Networks through Synthetic Genetic Interaction Analysis by RNAi, Nature Methods, 2011, Figure S2.

Examples

data(mRNAdoubleKDeficiency)
head(mRNAdoubleKDeficiency)
mRNAsingleKDefficiency

*mRNA levels for single gene knock downs*

**Description**

qPCR measurements for the mRNA level after a single gene knock down (ratio relative to wild type control). The experiments is done for two independent designs of RNAi reagents.

**Usage**

data(mRNAsingleKDefficiency)

**Format**

A data frame with 89 observations on the following 5 variables.

- **Symbol**: a character vector
- **MeanDesign1**: a numeric vector
- **StderrDesign1**: a numeric vector
- **MeanDesign2**: a numeric vector
- **StderrDesign2**: a numeric vector

**Source**

Horn, Sandmann, Fischer, Huber, Boutros, Mapping of Signalling Networks through Synthetic Genetic Interaction Analysis by RNAi, Nature Methods, 2011, Figure S1.

**Examples**

data(mRNAsingleKDefficiency)
head(mRNAsingleKDefficiency)

---

Networks

*Knock interaction networks*

**Description**

This dataset is a subset of the DroID database. It contains the known (genetic) interactions between the genes regarded in the main screen.

**Usage**

data(Networks)
pathwayMembership

Format
A data frame with 402 observations on the following 5 variables.
gene1 a character vector
gene2 a character vector
correlation a numeric vector
genetic a numeric vector
human a numeric vector

Source
Data as used in Horn, Sandmann, Fischer, Huber, Boutros, Mapping of Signalling Networks through Synthetic Genetic Interaction Analysis by RNAi, Nature Methods, 2011, Figure S12.
The data is a subset from the drosophila interactions database (DroID), http://www.droidb.org, Data version 2010_10 updated 20 October 2010.

Examples
data(Networks)
head(Networks)

pathwayMembership Pathway membership of genes.

Description
The membership of the tested genes in the four pathways JAK/STAT, RasMAPK, JNK, and p38.

Usage
data(pathwayMembership)

Format
The format is: chr "pathwayMembership"

Source
Horn, Sandmann, Fischer, Huber, Boutros, Mapping of Signalling Networks through Synthetic Genetic Interaction Analysis by RNAi, Nature Methods, 2011, Figure S13.

Examples
data(pathwayMembership)
head(pathwayMembership)
**PhysicalInteractions**  
*Known physical interactions*

**Description**

This dataset contains a collection of known physical interactions assembled from the literature. It contains the known pathway structure of the RasMAPK and the JNK pathway.

**Usage**

```r
data(PhysicalInteractions)
```

**Format**

A data frame with 29 observations on the following 2 variables.

- `V1`: a character vector
- `V2`: a character vector

**Source**

Horn, Sandmann, Fischer, Huber, Boutros, Mapping of Signalling Networks through Synthetic Genetic Interaction Analysis by RNAi, Nature Methods, 2011, Figure S13.

**Examples**

```r
data(PhysicalInteractions)
head(PhysicalInteractions)
```

---

**singleKDRphenotype**  
*Single knockdown phenotype*

**Description**

This data.frame `singleKDRphenotype` contains a screen assessing the single knock down phenotypes (nrCells, intensity, and area) of the tested genes. `singleKDRphenotypeAnno` is a data.frame describing the plate annotation.

**Usage**

```r
data(singleKDRphenotype)
```

**Format**

The format is: chr "singleKDRphenotype" chr "singleKDRphenotypeAnno"
**Source**

Horn, Sandmann, Fischer, Huber, Boutros, Mapping of Signalling Networks through Synthetic Genetic Interaction Analysis by RNAi, Nature Methods, 2011, Figure S3.

**Examples**

```r
data(singleKDphenotype)
head(singleKDphenotype)
head(singleKDphenotypeAnno)
```
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* Optionally other standard keywords, one per line, from file

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