Package 'directPA'

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Type Package

Title Direction Pathway Analysis

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Description A package for pathway analysis in experiments with multiple perturbation designs.

License GPL-3

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directPA-package *Direction Pathway Analysis Package*

Description

The directPA-package is designed for analysing pathways in experiments with multiple perturbations. The combination effects of different treatments are tested by rotating polar coordinates in two-dimentional space when the experiment contains two perturbations and corresponding controls, or spherical coordinates in three-dimensional space when the experiment contains three perturbations and corresponding controls.

Details

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Version:	1.0
Date:	2013-10-21
License:	GPL-3

Author(s)

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References

Pengyi Yang, Ellis Patrick, Shi-Xiong Tan, Daniel J. Fazakerley, James Burchfield, Christopher Gribben, Matthew J. Prior, David E. James, Yee Hwa Yang, Direction pathway analysis of large-scale proteomics data reveals novel features of the insulin action pathway, submitted.

directPA *Direction Pathway Analysis*

Description

The main function of direction pathway analysis package.

Usage

```
directPA(Tc, direction, pathway.list, minSize = 5, gene.method = "OSP",
path.method = "Stouffer", visualize = FALSE)
```

Arguments

Tc	The matrix of test statistics where rows correspond to proteins/genes and columns correspond to perturbations compared to controls.
direction	The direction to be tested. For two-dimensional rotation (experiments with two perturbations), directions are specified as degree. For three-dimensional rotation (experiments with three perturbations), directions are specified as contrast. See examples below for more details.
pathway.list	A pathway database in list format. See example below for details.
minSize	The minimum size of the pathway to be included in the report.
gene.method	A p-value integration method for protein/gene level combination. That is integrating information for each protein/gene accross all perturbations (i.e. for each row of matrix Tc, integrating accross the columns). Available methods are Stouffer, OSP, Fisher, and maxP. Default method is OSP.
path.method	A p-value integration method for pathway level combination. That is integrating information of protein/gene included in a pathway, given a pathway database. Available methods are Stouffer, OSP, Fisher, and maxP. Default method is Stouffer.
visualize	A boolean value indicating whether to visualize the protein/gene level integration statistics in a scatter plot.

Value

Return a matrix of test statistics for all given pathway that passed the minimum size cutoff on a specified test direction.

Author(s)

Pengyi Yang & Ellis Patrick

References

Pengyi Yang, Ellis Patrick, Shi-Xiong Tan, Daniel J. Fazakerley, James Burchfield, Christopher Gribben, Matthew J. Prior, David E. James, Yee Hwa Yang, Direction pathway analysis of large-scale proteomics data reveals novel features of the insulin action pathway, submitted.

Examples

```
# Load the example dataset.
data(PM)

# Load the reactome pathway.
data(reactome)

# Display reactome pathways. Could be replaced by any other pathway databases.
reactome.list

# Combine test statistics of each perturbation vs control into a matrix of test statistics.
```

```
Tc = cbind(Ins,Wmn,MK)

## Direction pathway analysis in two-dimensional space. Implemented as rotating by degree.
# (1) Testing combined effect of Ins and Wmn vs controls on original direction.
gst1 <- directPA(Tc[,c(1,2)], direction=0, pathway.list=reactome.list)
# Display the top 20 pathways ranked by integrated p-value.
gst1[order(unlist(gst1[,1])),][1:20,]

# (2) Testing combined effect of Ins and MK vs controls on the pi/2 direction.
gst2 <- directPA(Tc[,c(1,3)], direction=pi/2, pathway.list=reactome.list)
gst2[order(unlist(gst2[,1])),][1:20,]

## Direction pathway analysis in three-dimensional space. Implemnted as rotating by contrast.
# (1) Testing combined effect of all 3 perturbations vs controls on the original direction.
gst3 <- directPA(Tc, direction=c(1,1,1), pathway.list=reactome.list)
gst3[order(unlist(gst3[,1])),][1:20,]

# (2) Testing combined effect of all 3 perturbations vs controls on direction c(1,-1, 0).
# This rotates Ins by 0 degree, Wmn by 90 degree, and MK by 45 degree
gst4 <- directPA(Tc, direction=c(1,-1,0), pathway.list=reactome.list)
gst4[order(unlist(gst4[,1])),][1:20,]

# (3) Testing combined effect of all 3 perturbations vs controls on direction c(1,-1, 1).
# This rotates Ins by 0 degree, Wmn by 90 degree, and MK by 0 degree
gst5 <- directPA(Tc, direction=c(1,-1,1), pathway.list=reactome.list)
gst5[order(unlist(gst5[,1])),][1:20,]
```

`geneStats` *Gene Level Statistics*

Description

Calculating protein/gene level statistics accross multiple perturbations.

Usage

```
geneStats(T, method = "OSP")
```

Arguments

`T`	A matrix of test statistics (normally after rotation), where rows correspond to proteins/genes and columns correspond to perturbations.
`method`	The p-value integration method for combining accross multiple perturbations. Available methods are Stouffer, OSP, Fisher, and maxP. The default method is OSP.

Value

Return the integration p-value for a protein/gene.

Author(s)

Pengyi Yang & Ellis Patrick

Examples

```
# Load the example data.
data(PM)


## (1) For three perturbatins vesus controls, use three dimentional rotation.
Tc <- cbind(Ins, Wmn, MK)

# Rotate the test statistics matrix to the direction of interest.
Tc.rotated <- rotate3Sphere(Tc, direction=c(1,-1,0))

# Integrate protein/gene statistics accross perturmations.
gene.pvalues <- apply(Tc.rotated, 1, geneStats)

# Visualize the rotation statistics.
library(rgl)
HC <- rainbow(length(gene.pvalues)*1.2)
plot3d(Tc, col=HC[rank(gene.pvalues)], size=5)
abclines3d(x=0, y=0, z=0, a=diag(3), col="black", lwd=3)
abclines3d(x=0, a=c(1,-1,0), col="pink", lwd=5)


## (2) For two perturbations vesus controls, use two dimentional rotation.
Tc <- cbind(Ins, Wmn)
Tc.rotated <- rotate2Sphere(Tc, degree=pi/4)
gene.pvalues <- apply(Tc.rotated, 1, geneStats)

# Visualize the rotation statistics.
HC = rainbow(length(gene.pvalues)*1.2)
plot(Tc, col=HC[rank(gene.pvalues)], pch=16)
abline(v = 0,h = 0, lty=2, col="gold")
```

Ins *Insulin perturbation vesus control*

Description

The data object contains all quantified proteins with insulin perturbation vesus control in 3T3L1 cell lines.

MK *MK perturbation vesus control*

Description

The data object contains all quantified proteins with MK perturbation vesus control in 3T3L1 cell lines.

pathwayStats *Pathway Level Statistics*

Description

Calculating pathway level statistics by combining protein/gene belong to this pathway.

Usage

```
pathwayStats(PGs, T, minSize, method = "Stouffer")
```

Arguments

PGs	An array of names indicating proteins/genes belong to a given pathway.
T	An array of test statistics of all proteins/genes. This should be the zsore transformed output of geneStats.
minSize	The minimum size of a pathway to be reported.
method	A p-value integration method for combining proteins/genes in a given pathway.

Value

pvalue	Integrated pvalue of the given pathway
size	size of the given pathway

Author(s)

Pengyi Yang & Ellis Patrick

Examples

```
# Load the example data.
data(PM)
Tc = cbind(Ins, Wmn, MK)

# Load reactome pathway.
data(reactome)

# Rotate the test statistics matrix to the direction of interest.
Tc.rotated <- rotate3Sphere(Tc, direction=c(1, -1, 0))

# Integrate protein/gene statistics accross perturmations.
gene.pvalues <- apply(Tc.rotated, 1, geneStats)

# Transform the pvlaue computed from geneStats to zsocres.
gene.zscores <- qnorm(gene.pvalues, lower.tail = FALSE)

# Compute statistics for all reactome pathway
gst <- t(sapply(reactome.list, pathwayStats, gene.zscores, minSize=5))
```

---

reactome.list *Reactome Database*

Description

Reactome database in list format. Each list element contains an array of gene names corresponding to the genes contains in a pathway. The name of the list element is the pathway name.

References

Joshi-Tope, G., et al. Reactome: a knowledgebase of biological pathways. Nucleic Acids Research 33.suppl 1 (2005): D428-D432.

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rotate2Sphere *Polar Coordinates Rotation*

Description

Rotate to the direction of interest in polar coordinates by degree (i.e pi/4).

Usage

```
rotate2Sphere(T, degree = 0)
```

Arguments

T	A matrix of test statistics. The rows correspond to protein/genes and the columns correspond to perturbations. The number of colmuns should be 2.
degree	The degree to be rotated.

Value

A transformed matrix with respect to the direction of interest.

Author(s)

Pengyi Yang & Ellis Patrick

Examples

```
# Load the example dataset.
data(PM)

# Combine two perturbations into a single matrix.
# The matrix contains test statistics of each protein w.r.t each perturbation.
Tc <- cbind(Ins, Wmn)

# Rotate the matrix by pi/2 in polar coordinates.
Tc.rotated <- rotate2Sphere(Tc, degree = pi/2)
```

---

rotate3Sphere *Spherical Coordinates Rotation*

Description

Rotate to the direction of interest in spherical coordinates by contrast (i.e 1, -1, -1).

Usage

```
rotate3Sphere(T, direction = c(1, 1, 1))
```

Arguments

T	A matrix of test statistics. The rows correspond to protein/genes and the columns correspond to perturbations. The number of columns should be 3.
direction	The angle to be rotated in contrast format (see example below).

Value

A transformed matrix with respect to the direction of interest.

Author(s)

Pengyi Yang & Ellis Patrick

Examples

```
# Load the example data.
data(PM)

# Combine three perturbations into a single matrix.
# The matrix contains test statistics of each protein w.r.t each perturbations.
Tc <- cbind(Ins, Wmn, MK)

# Rotate the matrix by contrast 1, -1, -1 in spherical coordinates.
Tc.rotated <- rotate3Sphere(Tc, direction = c(1, -1, -1))
```

Wmn *Wortmannin perturbation vesus control*

Description

The data object contains all quantified proteins with Wortmannin perturbation vesus control in 3T3L1 cell lines.

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