Package 'DeMAND'

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Title DeMAND

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Description DEMAND predicts Drug MoA by interrogating a cell context specific regulatory network with a small number (N >= 6) of compound-induced gene expression signatures, to elucidate specific proteins whose interactions in the network is dysregulated by the compound.

Depends R (>= 2.14.0), MASS, methods

License GPL (>= 2)

biocViews SystemsBiology, NetworkEnrichment, GeneExpression, StatisticalMethod, Network

NeedsCompilation no

R topics documented:

bcellAnno *Annotation for the expression data*

Description

Annotation information for the probes of the gene expression matrix

bcellExp *B cell expression data*

Description

subest of a gene expression profiles from DLBCL cells treated by Geldanamycin and by DMSO as control.

bcellNetwork *B cell network*

Description

A subset of a molecular interaction network of Bcell assembled by the ARACNe*Margolin2006* algorithm for protein-DN interactions and Bayesian method*Lefebvre2010* for protein- protein interactions.

caseIndex *Case sample index*

Description

Column indices of the gene expression matrix for the samples treated by Geldanamycin.

controlIndex *Control sample index*

Description

Column indices of the gene expression matrix for the samples treated by DMSO

demand-instance *The DeMAND instance*

Description

This instance stores parameters and results of theDeMAND algorithm

Arguments

exp	A N by M numeric matrix and the rows are N probes and the columns are M samples.
anno	A N by 2 character matrix. The rows are probes but the order should be the same with the *demand* matrix. The first column can be anything (usually probe IDs) but the second column should includes Official Gene Symbol information for each probe.
network	A K by 4 character matrix which contains K interactions. The 1st column and the 2nd column contain pairs of interacted genes. The 3rd and 4th columns indicate whether the interactions are pr otein-protein interaction (ppi) or protein-DNA (pdi) interaction. Column name should be as follows: c("Gene1", "Gene2", "ppi", "pdi")
moa	A data frame contains DeMAND MoA predictions (e.g. Gene, p-value, adjusted p-values)

demandClass *The demand class constructor*

Description

This function generates demand class instances

Usage

```
demandClass(exp, anno, network, moa)
```

Arguments

exp	A N by M numeric matrix and the rows are N probes and the columns are M samples.
anno	A N by 2 character matrix. The rows are probes but the order should be the same with the *demand* matrix. The first column can be anything (usually probe IDs) but the second column should includes Official Gene Symbol information for each probe.

network	A K by 4 character matrix which contains K interactions. The 1st column and the 2nd column contain pairs of interacted genes. The 3rd and 4th columns indicate whether the interactions are protein-protein interaction (ppi) or protein-DNA (pdi) interaction. Column name should be as follows: c("Gene1", "Gene2", "ppi", "pdi")
moa	A data frame contains DeMAND MoA predictions (e.g. Gene, p-value, adjusted p-values)

Value

Instance of class demand

Examples

```
## Load toy example
data(inputExample)
dobj <- demandClass(exp=bcellExp, anno=bcellAnno, network=bcellNetwork)
printDeMAND(dobj)
```

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printDeMAND *Basic methods for class demand*

Description

This document lists a series of basic methods for the class DeMAND

Usage

```
printDeMAND(x)
```

Arguments

x	An instance of class demand which includes: a gene expression data, annotation information, and a molecular interaction network.

Value

printDeMAND returnssummary information about the diggit object

Examples

```
data(inputExample)
dobj <- demandClass(exp=bcellExp, anno=bcellAnno, network=bcellNetwork)
printDeMAND(dobj)
```

runDeMAND *Run DeMAND algorithm*

Description

DeMAND.

This function is based on the realization that drugs affect the protein activity of their targets, but not necessarily their mRNA expression levels. In contrast, the change in protein activity directly affects the mRNA expression levels of downstream genes. Based on this hypothesis, DeMAND identifies drug MoA by comparing gene expression profiles following drug perturbation with control samples, and computing the change in the individual interactions within a pre-determined integrated transcriptional and post-translational regulatory model (interactome).

Usage

```
runDeMAND(dobj, fgIndex, bgIndex)
```

Arguments

dobj	An instance of class demand which includes: a gene expression data, annotation information, and a molecular interaction network.
fgIndex	A numeric vector contains indices of columns which represent case samples (e.g. drug treated). The sample size should be greater than 3.
bgIndex	A numeric vector contains indices of columns which represent control samples (e.g. drug treated). The sample size should be greater than 3.

Details

For each edge in the interactome we determine the two-dimensional probability distribution of the gene expression levels both in the control state, and following drug treatment. Any changes in the probability distribution are estimated using the Kullback-Leibler (KL) divergence, from which we determine the statistical significance of the dysregulation of each edge. In the second step of DeMAND, we interrogate each gene independently to determine whether its interactions are enriched in dysregulated ones, suggesting that it is a candidate mechanism of action.

Value

The moa slot in a DeMAND object will be updated once DeMAND run completes. The prediction is a matrix containing a list of genes, corresponding p-value, and adjusted p-value.

Examples

```
## Load toy example
data(inputExample)
dobj <- demandClass(exp=bcellExp, anno=bcellAnno, network=bcellNetwork, moa=NULL)
dobj <- runDeMAND(dobj, fgIndex=caseIndex, bgIndex=controlIndex)
## results (head)
```

```
printDeMAND(dobj)
## results (all)
print(dobj@moa)
```

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