

Package ‘mnem’

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Type Package

Title Mixture Nested Effects Models

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Description Mixture Nested Effects Models (mnem) is an extension of Nested Effects Models and allows for the analysis of single cell perturbation data provided by methods like Perturb-Seq (Dixit et al., 2016) or Crop-Seq (Datlinger et al., 2017). In those experiments each of many cells is perturbed by a knock-down of a specific gene, i.e. several cells are perturbed by a knock-down of gene A, several by a knock-down of gene B, ... and so forth. The observed read-out has to be multi-trait and in the case of the Perturb-/Crop-Seq gene are expression profiles for each cell. mnem uses a mixture model to simultaneously cluster the cell population into k clusters and infer k networks causally linking the perturbed genes for each cluster. The mixture components are inferred via an expectation maximization algorithm.

Depends R (>= 3.6)

License GPL-3

Encoding UTF-8

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app

Processed scRNAseq from pooled CRISPR screens

Description

Example data: mnem results for the Dixit et al., 2016 and Datlinger et al., pooled CRISPR screens. For details see the vignette or function createApp().

Usage

app

References

Datlinger, P., Rendeiro, A., Schmidl, C., Krausgruber, T., Traxler, P., Klughammer, J., Schuster, L. C., Kuchler, A., Alpar, D., and Bock, C. (2017). Pooled crispr screening with single-cell transcriptome readout. *Nature Methods*, 14, 297-301.

Dixit, A., Parnas, O., Li, B., Chen, J., Fulco, C. P., Jerby-Arnon, L., Marjanovic, N. D., Dionne, D., Burks, T., Raychowdhury, R., Adamson, B., Norman, T. M., Lander, E. S., Weissman, J. S., Friedman, N., and Regev, A. (2016). Perturb-seq: Dissecting molecular circuits with scalable single-cell rna profiling of pooled genetic screens. *Cell*, 167(7), 1853-1866.e17.

Examples

data(app)

bootstrap	<i>Bootstrap.</i>
-----------	-------------------

Description

Run bootstrap simulations on the components (phi) of an object of class mnem.

Usage

```
bootstrap(x, size = 1000, p = 1, logtype = 2, complete = FALSE,
  ...)
```

Arguments

x	mnem object
size	size of the bootstrap simulations
p	percentage of samples (e.g. for 100 E-genes p=0.5 means sampling 50)
logtype	logarithm type of the data (e.g. 2 for log2 data or exp(1) for natural)
complete	if TRUE, complete data log likelihood is considered (for very large data sets, e.g. 1000 cells and 1000 E-genes)
...	additional parameters for hte nem function

Value

returns bootstrap support for each edge in each component (phi); list of adjacency matrices

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
data <- (sim$data - 0.5)/0.5
data <- data + rnorm(length(data), 0, 1)
result <- mnem(data, k = 2, starts = 1)
boot <- bootstrap(result, size = 2)
```

clustNEM	<i>Cluster NEM.</i>
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Description

This function clusters the data and performs standard nem on each cluster.

Usage

```
clustNEM(data, k = 2:10, cluster = NULL, starts = 1, logtype = 2,
  nem = TRUE, getprobspars = list(), getaffinitypars = list(), ...)
```

Arguments

data	data of log ratios with cells in columns and features in rows
k	number of clusters to check
cluster	given clustering has to correspond to the columns of data
starts	number of random starts for the kmeans algorithm
logtype	logarithm type of the data
nem	if FALSE only clusters the data
getprobspars	list of parameters for the getProbs function
getaffinitypars	list of parameters for the getAffinity function
...	additional arguments for standard nem function

Value

	family of nems; the first k list entries hold full information of the standard nem search
comp	list of all adjacency matrices phi
mw	vector of mixture weights
probs	fake cell probabilities (see mw: mixture weights)

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
data <- (sim$data - 0.5)/0.5
data <- data + rnorm(length(data), 0, 1)
result <- clustNEM(data, k = 2:3)
```

createApp

Creating app data.

Description

This function is for the reproduction of the application results in the vignette and publication. See the publication Pirkl & Beerenwinkel (2018) on how to download the data files: GSE92872_CROP-seq_Jurkat_TCR.digital_expression.csv k562_both_filt.txt GSM2396861_k562_ccycle_cbc_gbc_dict.csv GSM2396858_k562_tfs_7_cbc_gbc_dict.csv

Usage

```
createApp(sets = seq_len(3), m = NULL, n = NULL, o = NULL,
  maxk = 5, parallel = NULL, path = "", dataonly = FALSE,
  allcrop = FALSE, multi = FALSE, ...)
```

Arguments

sets	numeric vector with the data sets: 1 (CROPseq), 2, 3 (both PERTURBseq); default is all three
m	number of Sgenes (for testing)
n	number of most variable E-genes (for testing)
o	number of samples per S-gene (for testing)
maxk	maximum number of component in mnem inference (default: 5)
parallel	number of threads for parallelisation
path	path to the data files path/file.csv
dataonly	if TRUE, only fetches and normalizes the data and computes the log odds
allcrop	if TRUE, does not restrict and uses the full CROPseq dataset
multi	if TRUE, includes cells with more than one perturbed gene
...	additional parameters for the mixture nem function

Value

app data object

Author(s)

Martin Pirkl

Examples

```
## recreate the app data object (takes very long, i.e. days)
## Not run:
createApp()

## End(Not run)
data(app)
```

fitacc	<i>Simulation accuracy.</i>
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Description

Computes the accuracy of the fit between simulated and inferred mixture.

Usage

```
fitacc(x, y, strict = FALSE, unique = TRUE, type = "ham")
```

Arguments

x	mnem object
y	simulation object or another mnem object
strict	if TRUE, accounts for over/underfitting, i.e. the number of components
unique	if TRUE, phis of x and y are made unique each (FALSE if strict is TRUE)
type	type of accuracy. "ham" for hamming, "sens" for sensitivity and "spec" for Specificity

Value

plot of EM convergence

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
data <- (sim$data - 0.5)/0.5
data <- data + rnorm(length(data), 0, 1)
result <- mnem(data, k = 2, starts = 1)
fitacc(result, sim)
fitacc(result, sim, type = "sens")
fitacc(result, sim, type = "spec")
fitacc(result, sim, strict = TRUE, type = "sens")
fitacc(result, sim, strict = TRUE, type = "spec")
```

fuzzyindex

Calculate fuzzy ground truth.

Description

Calculates responsibilities and mixture weights based on the ground truth and noisy data.

Usage

```
fuzzyindex(x, data, logtype = 2, complete = FALSE, ...)
```

Arguments

x	mnemsim object
data	noisy data matrix
logtype	logarithm type of the data
complete	if TRUE, complete data log likelihood is considered (for very large data sets, e.g. 1000 cells and 1000 E-genes)
...	additional parameters for the function getAffinity

Value

list with cell log odds mixture weights and log likelihood

Author(s)

Martin Pirkl

Examples

```

sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
data <- sim$data
data[which(sim$data == 1)] <- rnorm(sum(sim$data == 1), 1, 1)
data[which(sim$data == 0)] <- rnorm(sum(sim$data == 0), -1, 1)
fuzzy <- fuzzyindex(sim, data)

```

getAffinity

Calculate responsibilities.

Description

This function calculates the responsibilities of each component for all cells from the expected log distribution of the hidden data.

Usage

```

getAffinity(x, affinity = 0, norm = TRUE, logtype = 2, mw = NULL,
            data = matrix(0, 2, ncol(x)), complete = FALSE)

```

Arguments

x	log odds for l cells and k components as a kxl matrix
affinity	0 for standard soft clustering, 1 for hard clustering during inference (not recommended)
norm	if TRUE normalises to probabilities (recommended)
logtype	logarithm type of the data (e.g. 2 for log2 data or exp(1) for natural)
mw	mixture weights of the components
data	data in log odds
complete	if TRUE, complete data log likelihood is considered (for very large data sets, e.g. 1000 cells and 1000 E-genes)

Value

responsibilities as a kxl matrix (k components, l cells)

Author(s)

Martin Pirkl

Examples

```

sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
data <- (sim$data - 0.5)/0.5
data <- data + rnorm(length(data), 0, 1)
result <- mnem(data, k = 2, starts = 1)
resp <- getAffinity(result$probs, mw = result$mw, data = data)

```

getIC

Calculate negative penalized log likelihood.

Description

This function calculates a negative penalized log likelihood given a object of class `mnem`. This penalized likelihood is based on the normal likelihood and penalizes complexity of the mixture components (i.e. the networks).

Usage

```
getIC(x, man = FALSE, degree = 4, logtype = 2, pen = 2,
      useF = FALSE, Fnorm = FALSE)
```

Arguments

<code>x</code>	<code>mnem</code> object
<code>man</code>	logical. manual data penalty, e.g. <code>man=TRUE</code> and <code>pen=2</code> for an approximation of the Akaike Information Criterion
<code>degree</code>	different degree of penalty for complexity: positive entries of transitively reduced phis or ϕ^r (<code>degree=0</code>), ϕ^r and mixture components minus one <code>k-1</code> (1), ϕ^r , <code>k-1</code> and positive entries of thetas (2), positive entries of transitively closed phis or ϕ^t , <code>k-1</code> (3), ϕ^t , theta, <code>k-1</code> (4, default), all entries of phis, thetas and <code>k-1</code> (5)
<code>logtype</code>	logarithm type of the data (e.g. 2 for log2 data or <code>exp(1)</code> for natural)
<code>pen</code>	penalty weight for the data (e.g. <code>pen=2</code> for approximate Akaike Information Criterion)
<code>useF</code>	use F (see publication) as complexity instead of phi and theta
<code>Fnorm</code>	normalize complexity of F, i.e. if two components have the same entry in F, it is only counted once

Value

penalized log likelihood

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
data <- (sim$data - 0.5)/0.5
data <- data + rnorm(length(data), 0, 1)
pen <- numeric(3)
result <- list()
for (k in seq_len(2)) {
  result[[k]] <- mnem(data, k = k, starts = 1)
  pen[k] <- getIC(result[[k]])
}
print(pen)
```

hamSim	<i>Accuracy for two phis.</i>
--------	-------------------------------

Description

This function uses the hamming distance to calculate an accuracy for two networks (phi).

Usage

```
hamSim(a, b, diag = 1, symmetric = TRUE)
```

Arguments

a	adjacency matrix (phi)
b	adjacency matrix (phi)
diag	if 1 includes diagonal in distance, if 0 not
symmetric	comparing a to b is asymmetrical, if TRUE includes comparison b to a

Value

normalized hamming accuracy for a and b

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
similarity <- hamSim(sim$Nem[[1]], sim$Nem[[2]])
```

mnem	<i>Mixture NEMs - main function.</i>
------	--------------------------------------

Description

This function simultaneously learns a mixture of causal networks and clusters of a cell population from single cell perturbation data (e.g. log odds of fold change) with a multi-trait readout. E.g. Pooled CRISPR scRNA-Seq data (Perturb-Seq. Dixit et al., 2016, Crop-Seq. Datlinger et al., 2017).

Usage

```
mnem(D, inference = "em", search = "greedy", phi = NULL,
     theta = NULL, mw = NULL, method = "llr", parallel = NULL,
     reduce = FALSE, runs = 1, starts = 3, type = "random",
     complete = FALSE, p = NULL, k = NULL, kmax = 10,
     verbose = FALSE, max_iter = 100, parallel2 = NULL,
     converged = -Inf, redSpace = NULL, affinity = 0,
     evolution = FALSE, lambda = 1, subtopoX = NULL, ratio = TRUE,
     logtype = 2, domean = TRUE, modulesize = 5, compress = FALSE,
     increase = TRUE, fpdfn = c(0.1, 0.1), multi = FALSE,
     ksel = c("kmeans", "silhouette", "cor"))
```

Arguments

D	data with cells indexing the columns and features (E-genes) indexing the rows
inference	inference method "em" for expectation maximization
search	search method for single network inference "greedy", "exhaustive" or "modules" (also possible: "small", which is greedy with only one edge change per M-step to make for a smooth convergence)
phi	a list of n lists of k networks for n starts of the EM and k components
theta	a list of n lists of k attachment vector for the E-genes for n starts of the EM and k components
mw	mixture weights; if NULL estimated or uniform
method	"llr" for log ratios or foldchanges as input (see ratio)
parallel	number of threads for parallelization of the number of em runs
reduce	logical - reduce search space for exhaustive search to unique networks
runs	number of runs for greedy search
starts	number of starts for the em
type	initialize with responsibilities either by "random", "cluster" (each S-gene is clustered and the different S-gene clustered differently combined for several starts), "cluster2" (clustNEM is used to infer reasonable phis, which are then used as a start for one EM run), "cluster3" (global clustering as a start), or "networks" (initialize with random phis)
complete	if TRUE, optimizes the expected complete log likelihood of the model, otherwise the log likelihood of the observed data
p	initial probabilities as a k (components) times l (cells) matrix
k	number of components
kmax	maximum number of components when k=NULL is inferred
verbose	verbose output
max_iter	maximum iteration, if likelihood does not converge
parallel2	if parallel=NULL, number of threads for single component optimization
converged	absolute distance for convergence between new and old log likelihood; if set to -Inf, the EM stops if neither the phis nor thetas were changed in the most recent iteration
redSpace	space for "exhaustive" search
affinity	0 is default for soft clustering, 1 is for hard clustering

evolution	logical. If TRUE components are penalized for being different from each other.
lambda	smoothness value for the prior put on the components, if evolution set to TRUE
subtopoX	hard prior on theta as a vector with entry i equal to j, if E-gene i is attached to S-gene j
ratio	logical, if true data is log ratios, if false foldchanges
logtype	logarithm type of the data (e.g. 2 for log2 data or exp(1) for natural)
domean	average the data, when calculating a single NEM (speed improvement)
modulesize	max number of S-genes per module in module search
compress	compress networks after search (warning: penalized likelihood not interpretable)
increase	if set to FALSE, the algorithm will not stop if the likelihood decreases
fprfn	numeric vector of length two with false positive and false negative rates for discrete data
multi	set to TRUE if the data contains multiple perturbation per sample; make sure the samples are reasonably named, e.g. "IRF1_CTNNB1"
kse1	character vector of methods for the inference of k; can combine "hc" (hierarchical clustering) or "kmeans" with "silhouette", "BIC" or "AIC"; can also include "cor" for correlation distance (preferred) instead of euclidean

Value

object of class mnem	
comp	list of the component with each component being a list of the causal network phi and the E-gene attachment theta
data	input data matrix
limits	list of results for all independent searches
ll	log likelihood of the best model
lls	log likelihood ascent of the best model search
mw	vector with mixture weights
probs	kx1 matrix containing the cell log likelihoods of the model

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
data <- (sim$data - 0.5)/0.5
data <- data + rnorm(length(data), 0, 1)
result <- mnem(data, k = 2, starts = 1)
```

mnemh	<i>Hierarchical mixture.</i>
-------	------------------------------

Description

This function does a hierarchical mixture. That means it uses the approximate BIC to check, if there are more than one component. It recursively splits the data if there is evidence for $k > 1$ components.

Usage

```
mnemh(data, k = 2, logtype = 2, getprobspars = list(), ...)
```

Arguments

data	data matrix either binary or log odds
k	number of maximal components for each hierarchy leaf
logtype	log type of the data
getprobspars	list of parameters for the getProbs function
...	additional parameters for the mnem function

Value

object of class mnem

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
data <- (sim$data - 0.5)/0.5
data <- data + rnorm(length(data), 0, 1)
result <- mnemh(data, starts = 1, k = 1)
```

mnemk	<i>Learn the number of components K and optimize the mixture.</i>
-------	---

Description

High level function for learning the number of components k , if unknown.

Usage

```
mnemk(D, ks = seq_len(5), man = FALSE, degree = 4, logtype = 2,
      pen = 2, useF = FALSE, Fnorm = FALSE, ...)
```

Arguments

D	data with cells indexing the columns and features (E-genes) indexing the rows
ks	vector of number of components k to test
man	logical. manual data penalty, e.g. man=TRUE and pen=2 for an approximation of the Akaike Information Criterion
degree	different degree of penalty for complexity: positive entries of transitively reduced phis or ϕ^r (degree=0), ϕ^r and mixture components minus one k-1 (1), ϕ^r , k-1 and positive entries of thetas (2), positive entries of transitively closed phis or ϕ^t , k-1 (3), ϕ^t , theta, k-1 (4, default), all entries of phis, thetas and k-1 (5)
logtype	logarithm type of the data (e.g. 2 for log2 data or exp(1) for natural)
pen	penalty weight for the data (e.g. pen=2 for approximate Akaike Information Criterion)
useF	use F (see publication) as complexity instead of phi and theta
Fnorm	normalize complexity of F, i.e. if two components have the same entry in F, it is only counted once
...	additional parameters for the mnem main function

Value

list containing the result of the best k as an mnem object and the raw and penalized log likelihoods

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
data <- (sim$data - 0.5)/0.5
data <- data + rnorm(length(data), 0, 1)
result <- mnemk(data, ks = seq_len(2), starts = 1)
```

plot.bootmnem

Plot bootstrap mnem result.

Description

Plot bootstrap mnem result.

Usage

```
## S3 method for class 'bootmnem'
plot(x, reduce = TRUE, ...)
```

Arguments

x	bootmnem object
reduce	if TRUE transitively reduces the graphs
...	additional parameters for the plotting function plotDNF

Value

visualization of bootstrap mnem result with Rgraphviz

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
data <- (sim$data - 0.5)/0.5
data <- data + rnorm(length(data), 0, 1)
result <- mnem(data, k = 2, starts = 1)
boot <- bootstrap(result, size = 2)
plot(boot)
```

plot.mnem

Plot mnem result.

Description

Plot mnem result.

Usage

```
## S3 method for class 'mnem'
plot(x, oma = c(3, 1, 1, 3), main = "M&NEM",
     anno = TRUE, cexAnno = 1, scale = NULL, global = TRUE,
     egenes = TRUE, sep = FALSE, tsne = FALSE, affinity = 0,
     logtype = 2, cells = TRUE, pch = ".", legend = FALSE,
     showdata = FALSE, bestCell = TRUE, showprobs = FALSE,
     shownull = TRUE, ratio = TRUE, method = "llr",
     showweights = TRUE, ...)
```

Arguments

x	mnem object
oma	outer margin
main	main text
anno	annotate cells by their perturbed gene
cexAnno	text size of the cell annotations
scale	scale cells to show relative and not absolute distances
global	if TRUE clusters all cells, if FALSE clusters cells within a component
egenes	show egene attachments, i.e. number of E-genes assigned to each S-gene
sep	separate clusters and not put them on top of each other for better visualization
tsne	if TRUE use tsne instead of pca
affinity	use hard clustering if TRUE
logtype	logarithm type of the data (e.g. 2 for log2 data or exp(1) for natural)

cells	show cell attachments, .i.e how many cells are assigned to each S-gene
pch	cell symbol
legend	show legend
showdata	show data if TRUE
bestCell	show probability of best fitting cell for each S-gene
showprobs	if TRUE, shows responsibilities for all cells and components
shownull	if TRUE, shows the null node
ratio	use log ratios (TRUE) or foldchanges (FALSE)
method	"llr" for ratios
showweights	if TRUE, shows mixture weights for all components
...	additional parameters

Value

visualization of mnem result with Rgraphviz

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
data <- (sim$data - 0.5)/0.5
data <- data + rnorm(length(data), 0, 1)
result <- mnem(data, k = 2, starts = 1)
plot(result)
```

plot.mnemsim

Plot simulated mixture.

Description

Plot simulated mixture.

Usage

```
## S3 method for class 'mnemsim'
plot(x, data = NULL, logtype = 2,
     fuzzypars = list(), ...)
```

Arguments

x	mnemsim object
data	noisy data matrix (optional)
logtype	logarithm type of the data
fuzzypars	list of parameters for the function fuzzyindex
...	additional parameters for the plotting function plotDNF

Value

visualization of simulated mixture with Rgraphviz

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
plot(sim)
```

plotConvergence	<i>Plot convergence of EM</i>
-----------------	-------------------------------

Description

This function plots the convergence of the different EM iterations (four figures, e.g. `par(mfrow=(2,2))`).

Usage

```
plotConvergence(x, col = NULL, type = "b", convergence = 0.1, ...)
```

Arguments

x	mnem object
col	vector of colors for the iterations
type	see <code>?plot.default</code>
convergence	difference of when two log likelihoods are considered equal; see also <code>convergence</code> for the function <code>mnem()</code>
...	additional parameters ofr the plots/lines functions

Value

plot of EM convergence

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
data <- (sim$data - 0.5)/0.5
data <- data + rnorm(length(data), 0, 1)
result <- mnem(data, k = 2, starts = 1)
par(mfrow=c(2,2))
plotConvergence(result)
```


plotDnf

*Plot disjunctive normal form.***Description**

This function visualizes a graph encoded as a disjunctive normal form.

Usage

```
plotDnf(dnf = NULL, freq = NULL, stimuli = c(), signals = c(),
        inhibitors = c(), connected = TRUE, CNOList = NULL, cex = NULL,
        fontsize = NULL, labelsize = NULL, type = 2, lwd = 1,
        edgelwd = 1, legend = 0, x = 0, y = 0, xjust = 0, yjust = 0,
        width = 1, height = 1, layout = "dot", main = "", sub = "",
        cex.main = 1.5, cex.sub = 1, col.sub = "grey", fontcolor = NULL,
        nodestates = NULL, simulate = NULL, edgecol = NULL,
        labels = NULL, labelcol = "blue", nodelabel = NULL,
        nodecol = NULL, bordercol = NULL, nodeshape = NULL,
        verbose = FALSE, edgestyle = NULL, nodeheight = NULL,
        nodewidth = NULL, edgewidth = NULL, lty = NULL, hierarchy = NULL,
        showall = FALSE, edgehead = NULL, edgelabel = NULL,
        edgetail = NULL, bool = TRUE, draw = TRUE, ...)
```

Arguments

dnf	Hyper-graph in disjunctive normal form, e.g. $c("A=B", "A=C+D", "E=!B")$ with the child on the left and the parents on the right of the equation with $"A=C+D"$ for $A = C \text{ AND } D$. Alternatively, dnf can be an adjacency matrix, which is converted on the fly to a disjunctive normal form.
freq	Frequency of hyper-edges which are placed on the edges.
stimuli	Highlights vertices which can be stimulated.
signals	Highlights vertices which regulate E-genes.
inhibitors	Highlights vertices which can be inhibited.
connected	If TRUE, only includes vertices which are connected to other vertices.
CNOList	CNOList object. Optional instead of stimuli, inhibitors or signals. See package CellNOptR.
cex	Global font size.
fontsize	Vertice label size.
labelsize	Edge label size.
type	Different plot types. 2 for Rgraphviz and 1 for graph.
lwd	Line width.
edgelwd	Edgeline width.
legend	0 shows no legend. 1 shows legend as a graph. 2 shows legend in a standard box.
x	x coordinate of box legend.
y	y coordinate of box legend.

xjust	Justification of legend box left, right or center (-1,1,0).
yjust	Justification of legend box top, bottom or middle (-1,1,0).
width	Vertice width.
height	Vertice height.
layout	Graph layout. See graphvizCapabilities()\$layoutTypes.
main	Main title.
sub	Subtitle.
cex.main	Main title font size.
cex.sub	Subtitle font size.
col.sub	Font color of subtitle.
fontcolor	Global font color.
nodestates	Binary state of each vertice.
simulate	Simulate stimulation and inhibition of a list of vertices. E.g. simulate = list(stimuli = c("A", "B"), inhibitors = c("C", "D")).
edgecol	Vector with colors for every edge of the graph (not hyper-graph). E.g. an AND gate consists of three distinct edges.
labels	Vector with labels for the edges.
labelcol	Vector with label colors for the edges.
nodelabel	List of vertices with labels as input. E.g. labels = list(A="test", B="label for B").
nodecol	List of vertices with colors as input.
bordercol	List of vertices with colors as input.
nodeshape	List of vertices with shapes (diamond, box, square,...).
verbose	Verbose output.
edgestyle	set the edge style like dashed, can be numerical
nodeheight	List of vertices with height as input.
nodewidth	List of vertices with width as input.
edgewidth	Vector with edge widths.
lty	Vector with edge styles (line, dotted,...).
hierarchy	List with the hierarchy of the vertices. E.g. list(top = c("A", "B"), bottom = c("C", "D")).
showall	See "connected" above.
edgehead	Vector with edge heads.
edgelaabel	Vector with edge labels.
edgetail	Vector with edge tails.
bool	If TRUE, only shows normal graph and no AND gates.
draw	Do not plot the graph and only output the graphNEL object.
...	additional arguments

Value

Rgraphviz object

Author(s)

Martin Pirkl

Examples

```
g <- c("!A+B+C=G", "C=G", "!D=G")
plotDnf(g)
```

simData

*Simulate data.***Description**

This function simulates single cell data from a random mixture of networks.

Usage

```
simData(Sgenes = 5, Egenes = 1, Nems = 2, reps = NULL, mw = NULL,
        evolution = FALSE, nCells = 1000, uninform = 0, unitheta = FALSE,
        edgeprob = 0.25, multi = FALSE, subsample = 1, scalefree = FALSE,
        ...)
```

Arguments

Sgenes	number of Sgenes
Egenes	number of Egenes
Nems	number of components
reps	number of replicates, if set (not realistic for cells)
mw	mixture weights (has to be vector of length Nems)
evolution	evolving and not purely random network, if set to TRUE
nCells	number of cells
uninform	number of uninformative Egenes
unitheta	uniform theta, if TRUE
edgeprob	edge probability, value between 0 and 1 for sparse or dense networks
multi	a vector with the percentages of cell with multiple perturbations, e.g. c(0.2,0.1,0) for 20 no quadruple knock-downs
subsample	range to subsample data. 1 means the full simulated data is used
scalefree	if TRUE, graph is scale free
...	additional parameters for the scale free network sampler (see 'nem' package)

Value

simulation object with meta information and data

Nem	list of adjacency matrixes generatign the data
theta	E-gene attachments
data	data matrix
index	index for which Nem generated which cell (data column)
mw	vector of input mixture weights

Author(s)

Martin Pirkl

Examples

```
sim <- simData(Sgenes = 3, Egenes = 2, Nems = 2, mw = c(0.4,0.6))
```

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