Package 'CoGAPS'

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Description

CoGAPS implements a Bayesian MCMC matrix factorization algorithm, GAPS, and links it to gene set statistic methods to infer biological process activity. It can be used to perform sparse matrix factorization on any data, and when this data represents biomolecules, to do gene set analysis.

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Author(s)

Maintainer: Elana J. Fertig <ejfertig@jhmi.edu>, Michael F. Ochs <ochsm@tcnj.edu>

References

Fertig EJ, Ding J, Favorov AV, Parmigiani G, Ochs MF. CoGAPS: an R/C++ package to identify patterns and biological process activity in transcriptomic data. Bioinformatics. 2010 Nov 1;26(21):2792-3

binaryA	binaryA creates a binarized heatmap of the A matrix in which the value is 1 if the value in Amean is greater than threshold * Asd and 0 otherwise

calcCoGAPSStat 3

Description

binaryA creates a binarized heatmap of the A matrix in which the value is 1 if the value in Amean is greater than threshold * Asd and 0 otherwise

Usage

```
binaryA(Amean, Asd, threshold = 3)
```

Arguments

Amean the mean estimate for the A matrix
Asd the standard deviations on Amean

threshold the number of standard deviations above zero that an element of Amean must be

to get a value of 1

calcCoGAPSStat CoGAPS gene set statistic

Description

Computes the p-value for the association of underlying patterns from microarray data to activity in gene sets.

Usage

```
calcCoGAPSStat(Amean, Asd, GStoGenes, numPerm=500)
```

Arguments

Amean Sampled mean value of the amplitude matrix A. row.names(Amean) must cor-

respond to the gene names contained in GStoGenes.

Asd Sampled standard deviation of the amplitude matrix A.

GStoGenes List or data frame containing the genes in each gene set. If a list, gene set

names are the list names and corresponding elements are the names of genes contained in each set. If a data frame, gene set names are in the first column and corresponding gene names are listed in rows beneath each gene set name.

numPerm Number of permuations used for the null distribution in the gene set statistic.

(optional; default=500)

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Details

This script links the patterns identified in the columns of P to activity in each of the gene sets specified in GStoGenes using a novel z-score based statistic developed in Ochs et al. (2009). Specifically, the z-score for pattern p and gene set G_i containing G total genes is given by

$$Z_{i,p} = \frac{1}{G} \sum_{ginG_i} A_{gp} / \sigma_{gp}$$

, where g indexes the genes in the set and σ_{gp} is the standard deviation of A_{gp} obtained from MCMC sampling. CoGAPS then uses the specified numPerm random sample tests to compute a consistent p value estimate from that z score.

Value

A list containing:

GSUpreg p-values for upregulation of each gene set in each pattern.

GSDownreg p-values for downregulation of each gene set in each pattern.

GSActEst p-values for activity of each gene set in each pattern.

Author(s)

Elana J. Fertig <ejfertig@jhmi.edu>

References

M.F. Ochs, L. Rink, C. Tarn, S. Mburu, T. Taguchi, B. Eisenberg, and A.K. Godwin. (2009) Detection and treatment-induced changes in signaling pathways in gastrointestinal stromal tumors using transcriptomic data. Cancer Research, 69:9125-9132.

See Also

CoGAPS

COGAPS COGAPS calls the C++ MCMC code through gapsRun and performs

Bayesian matrix factorization returning the two matrices that reconstruct the data matrix and then calls calcCoGAPSStat to estimate gene

set activity with nPerm set to 500

Description

CoGAPS calls the C++ MCMC code through gapsRun and performs Bayesian matrix factorization returning the two matrices that reconstruct the data matrix and then calls calcCoGAPSStat to estimate gene set activity.

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Usage

```
CoGAPS(data, unc, GStoGenes, nFactor = "7", nEquil = 1000, nSample = 1000, nOutR = 1000, output_atomic = "false", simulation_id = "simulation", plot = TRUE, nPerm = 500, alphaA = "0.01", nMaxA = "100000", max_gibbmass_paraA = "100.0", lambdaA_scale_factor = "1.0", alphaP = "0.01", nMaxP = "100000", max_gibbmass_paraP = "100.0", lambdaP_scale_factor = "1.0")
```

Arguments

data data matrix

unc uncertainty matrix (std devs for chi-squared of Log Likelihood)

GStoGenes data.frame or list with gene sets

nFactor number of patterns (basis vectors, metagenes)

simulation_id name to attach to atoms files if created
plot logical to determine if plots produced
nPerm number of permutations for gene set test

nEquil number of iterations for burn-in nSample number of iterations for sampling

nOutR how often to print status into R by iterations

output_atomic whether to write atom files (large)
alphaA sparsity parameter for A domain
alphaP sparsity parameter for P domain

max_gibbmass_paraA

limit truncated normal to max size for A

max_gibbmass_paraP

limit truncated normal to max size for P

nMaxA PRESENTLY UNUSED, future = limit number of atoms for A

nMaxP PRESENTLY UNUSED, future = limit number of atoms for P

lambdaA_scale_factor

lambda factor in penalized likelihood for A

lambdaP_scale_factor

lambda factor in penalized likelihood for P

Details

CoGAPS first decomposes the data matrix using GAPS, **D**, into a basis of underlying patterns and then determines the gene set activity in each of these patterns.

The GAPS decomposition is achieved by finding amplitude and pattern matrices (\mathbf{A} and \mathbf{P} , respectively) for which

$$\mathbf{D} = \mathbf{AP} + \Sigma,$$

where Σ is the matrix of uncertainties given by unc. The matrices **A** and **P** are assumed to have the atomic prior described in Sibisi and Skilling (1997) and are found with MCMC sampling.

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Then, the patterns identified in the columns of \mathbf{P} are linked to activity in each of the gene sets specified in GStoGenes using a novel z-score based statistic developed in Ochs et al. (2009). Specifically, the z-score for pattern p and gene set G_i containing \$G\$ total genes is given by

$$Z_{i,p} = \frac{1}{G} \sum_{gin\mathcal{G}_{i}} \frac{\mathbf{A}_{gp}}{Asd_{gp}},$$

where g indexes the genes in the set and Asd_{gp} is the standard deviation of \mathbf{A}_{gp} obtained from MCMC sampling. CoGAPS then uses the specified nPerm random sample tests to compute a consistent p value estimate from that z score. Note that the data from Ochs et al. (2009) are provided with this package in GIST_TS_20084.RData and TFGSList.RData are also provided with this package for further validation.

Value

A list containing:

Amean Sampled mean value of the amplitude matrix **A**.

Asd Sampled standard deviation of the amplitude matrix **A**.

Pmean Sampled mean value of the amplitude matrix \mathbf{P} .

Psd Sampled standard deviation of the amplitude matrix **P**.

Data matrix **D** input to factorization.

Sigma uncertainty matrix (std devs for chi-squared of Log Likelihood)

GSUpreg p-values for upregulation of each gene set in each pattern.

GSDownreg p-values for downregulation of each gene set in each pattern.

GSActEst p-values for activity of each gene set in each pattern.

atomsAEquil Number of atoms in **A** during each iteration of the equilibration phase.

Number of atoms in **A** during each iteration of the sampling phase.

Number of atoms in **P** during each iteration of the equilibration phase.

atomsPSamp Number of atoms in P during each iteration of the sampling phase.

chiSqValues Value of chi^2 at each step during equilibration and sampling.

meanChi2 Value of chi^2 for Amean and Pmean.

See Also

gapsRun,calcCoGAPSStat

Examples

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computeGeneGSProb

CoGAPS gene membership statistic

Description

Computes the p-value for gene set membership using the CoGAPS-based statistics developed in Fertig et al. (2012). This statistic refines set membership for each candidate gene in a set specified in GSGenes by comparing the inferred activity of that gene to the average activity of the set. Specifically, we compute the following summary statistic for each gene g that is a candidate member of gene set g:

$$S_{g,G} = (\sum_p -log(Pr_{G,p})Pw[p](A_{gp}/\sigma_{gp}))/\sum_p -log(Pr_{G,p})Pw[p],$$

where p indexes each of the patterns, $Pr_{G,p}$ is the probability that gene set G is upregulated computed with calcCoGAPSStat, A_{gp} is the mean amplitude matrix from the GAPS matrix factorization, Pw[p] is a prior weighting for each pattern based upon the context to which that pattern relates, and σ_{gp} is the standard deviation of the amplitude matrix. P-values are formulated from a permutation test comparing the value of $S_{g,G}$ for genes in GSGenes relative to the value of $S_{g,G}$ numPerm random gene sets with the same number of targets.

Usage

computeGeneGSProb(Amean, Asd, GStoGenes, Pw=rep(1,ncol(Amean)),numPerm=500,PwNull=F)

Arguments

Amean	Sampled mean value of the amplitude matrix ${\bf A}$. row.names(Amean) must correspond to the gene names contained in GStoGenes.
Asd	Sampled standard deviation of the amplitude matrix A .
GStoGenes	Vector containing the prior estimate of members of the gene set of interest.
Pw	Vector containing the weight to assign each pattern in the gene statistic assumed to be computed from the association of the pattern with samples in a given context (optional: default=1 giving all patterns equal weight).
numPerm	Number of permuations used for the null distribution in the gene set statistic. (optional; default=500)
PwNull	Logical value. If TRUE, use pattern weighting in Pw when computing the null distribution for the statistic. If FALSE, do not use the pattern weighting so that the null is context independent. (optional; default=F)

Value

A vector of length GStoGenes containing the p-values of set membership for each gene containined in the set specified in GStoGenes.

Author(s)

```
Elana J. Fertig <ejfertig@jhmi.edu>
```

References

E.J. Fertig, A.V. Favorov, and M.F. Ochs (2013) Identifying context-specific transcription factor targets from prior knowledge and gene expression data. 2012 IEEE Nanobiosciences.

See Also

```
calcCoGAPSStat
```

Examples

```
## Not run:
# Results for GIST data in Fertig et al. (2012) #
# load the data
data(GIST_TS_20084)
data(TFGSList)
# define transcription factors of interest based on Ochs et al. (2009)
TFs <- c("c.Jun", NF.kappaB, Smad4, "STAT3", "Elk.1", "c.Myc", "E2F.1",
        "AP.1", "CREB", "FOXO", "p53", "Sp1")
# run the GAPS matrix factorization
nIter <- 10000
results <- CoGAPS(GIST.D, GIST.S, tf2ugFC,
                nFactor=5,
                nEquil=nIter, nSample=nIter,
                plot=FALSE)
# set membership statistics
permTFStats <- list()</pre>
for (tf in TFs) {
    genes <- levels(tf2ugFC[,tf])</pre>
    genes <- genes[2:length(genes)]</pre>
    permTFStats[[tf]] <- computeGeneTFProb(Amean = GISTResults$Amean,</pre>
                                        Asd = GistResults$Asd, genes)
}
## End(Not run)
```

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gapsMapRun	gapsMapRun calls the C++ MCMC code and performs Bayesian matrix factorization returning the two matrices that reconstruct the data
	matrix; as opposed to gapsRun, this method takes an additional input specifying set patterns in the P matrix

Description

gapsMapRun calls the C++ MCMC code and performs Bayesian matrix factorization returning the two matrices that reconstruct the data matrix; as opposed to gapsRun, this method takes an additional input specifying set patterns in the P matrix

Usage

```
gapsMapRun(D, S, FP, nFactor = "7", simulation_id = "simulation",
    nEquil = "1000", nSample = "1000", nOutR = 1000,
    output_atomic = "FALSE", alphaA = "0.01", nMaxA = "100000",
    max_gibbmass_paraA = "100.0", lambdaA_scale_factor = "1.0",
    alphaP = "0.01", nMaxP = "100000", max_gibbmass_paraP = "100.0",
    lambdaP_scale_factor = "1.0")
```

Arguments

٤	guineiros	
	D	data matrix
	S	uncertainty matrix (std devs for chi-squared of Log Likelihood)
	FP	matrix with rows giving fixed patterns for P
	nFactor	number of patterns (basis vectors, metagenes), which must be greater than or equal to the number of rows of FP
	simulation_id	name to attach to atoms files if created
	nEquil	number of iterations for burn-in
	nSample	number of iterations for sampling
	nOutR	how often to print status into R by iterations
	output_atomic	whether to write atom files (large)
	alphaA	sparsity parameter for A domain
	alphaP	sparsity parameter for P domain
	max_gibbmass_pa	nraA
	•1.1	limit truncated normal to max size in A
	max_gibbmass_pa	
		limit truncated normal to max size in P
	nMaxA	PRESENTLY UNUSED, future = limit number of atoms in A
	nMaxP	PRESENTLY UNUSED, future = limit number of atoms in P
	lambdaA_scale_f	Cactor
		lambda factor in penalized likelihood in A
	lambdaP_scale_f	Cactor

lambda factor in penalized likelihood in P

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Details

The decomposition in GAPS is achieved by finding amplitude and pattern matrices (A and P, respectively) for which

$$\mathbf{D} = \mathbf{AP} + \Sigma$$

, where Σ is the matrix of uncertainties given by S. The matrices $\bf A$ and $\bf P$ are assumed to have the atomic prior described in Sibisi and Skilling (1997) and are found with MCMC sampling. However, some rows of $\bf P$ are fixed to be the values specified in the input argument FP after rescaling to have norm 1.

Value

A list containing:

Amean Sampled mean value of the amplitude matrix A.

Asd Sampled standard deviation of the amplitude matrix A.

Pmean Sampled mean value of the amplitude matrix \mathbf{P} .

Psd Sampled standard deviation of the amplitude matrix **P**.

atomsAEquil Number of atoms in $\bf A$ during each iteration of the equilibration phase. Number of atoms in $\bf A$ during each iteration of the sampling phase. Number of atoms in $\bf P$ during each iteration of the equilibration phase. Number of atoms in $\bf P$ during each iteration of the sampling phase. Value of chi^2 at each step during equilibration and sampling.

meanChi2 Value of chi^2 for Amean and Pmean.

See Also

CoGAPS,gapsRun

Examples

gapsRun 11

gapsRun gapsRun calls the C++ MCMC code and performs Bayesian matrix factorization returning the two matrices that reconstruct the data matrix		
	gapsRun	factorization returning the two matrices that reconstruct the data ma-

Description

gapsRun calls the C++ MCMC code and performs Bayesian matrix factorization returning the two matrices (A and P) whose product reconstruct the data matrix (D).

Usage

```
gapsRun(D, S, nFactor = "7", simulation_id = "simulation",
    nEquil = "1000", nSample = "1000", nOutR = 1000,
    output_atomic = "FALSE", alphaA = "0.01", nMaxA = "100000",
    max_gibbmass_paraA = "100.0", lambdaA_scale_factor = "1.0",
    alphaP = "0.01", nMaxP = "100000", max_gibbmass_paraP = "100.0",
    lambdaP_scale_factor = "1.0")
```

Arguments

D	data matrix
S	uncertainty matrix (std devs for chi-squared of Log Likelihood)
nFactor	number of patterns (basis vectors, metagenes)
simulation_id	name to attach to atoms files if created
nEquil	number of iterations for burn-in
nSample	number of iterations for sampling
nOutR	how often to print status into R by iterations
output_atomic	whether to write atom files (large)
alphaA	sparsity parameter for A domain
alphaP	sparsity parameter for P domain
max_gibbmass_pa	araA
	limit truncated normal to max size in A
max_gibbmass_pa	araP
	limit truncated normal to max size in P
nMaxA	PRESENTLY UNUSED, future = limit number of atoms in A
nMaxP	PRESENTLY UNUSED, future = limit number of atoms in P
lambdaA_scale_	factor
	lambda factor in penalized likelihood in A
lambdaP_scale_	factor

lambda factor in penalized likelihood in P

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Details

The decomposition in GAPS is achieved by finding amplitude and pattern matrices (\mathbf{A} and \mathbf{P} , respectively) for which

$$\mathbf{D} = \mathbf{AP} + \Sigma$$

, where Σ is the matrix of uncertainties given by S. The matrices **A** and **P** are assumed to have the atomic prior described in Sibisi and Skilling (1997) and are found with MCMC sampling.

Value

A list containing:

Amean Sampled mean value of the amplitude matrix A.

Asd Sampled standard deviation of the amplitude matrix **A**.

Pmean Sampled mean value of the amplitude matrix **P**.

Psd Sampled standard deviation of the amplitude matrix **P**.

atomsAEquil Number of atoms in A during each iteration of the equilibration phase.

atomsASamp Number of atoms in **A** during each iteration of the sampling phase.

atomsPEquil Number of atoms in P during each iteration of the equilibration phase.

atomsPSamp Number of atoms in P during each iteration of the sampling phase.

chiSqValues Value of chi^2 at each step during equilibration and sampling.

meanChi2 Value of chi^2 for Amean and Pmean.

See Also

CoGAPS

Examples

GIST.D

GIST.D

Sample GIST gene expression data from Ochs et al. (2009).

Description

Gene expression data from gastrointestinal stromal tumor cell lines treated with Gleevec.

Usage

GIST_TS_20084

Format

Matrix with 1363 genes by 9 samples of mean gene expression data.

References

Ochs, M., Rink, L., Tarn, C., Mburu, S., Taguchi, T., Eisenberg, B., and Godwin, A. (2009). Detection of treatment-induced changes in signaling pathways in gastrointestinal stromal tumors using transcriptomic data. Cancer Res, 69(23), 9125-9132.

GIST.S

Sample GIST gene expression data from Ochs et al. (2009).

Description

Standard deviation of gene expression data from gastrointestinal stromal tumor cell lines treated with Gleevec.

Usage

GIST_TS_20084

Format

Matrix with 1363 genes by 9 samples containing standard deviation (GIST.S) of the gene expression data.

References

Ochs, M., Rink, L., Tarn, C., Mburu, S., Taguchi, T., Eisenberg, B., and Godwin, A. (2009). Detection of treatment-induced changes in signaling pathways in gastrointestinal stromal tumors using transcriptomic data. Cancer Res, 69(23), 9125-9132.

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GSets

Simulated dataset to quantify gene set membership.

Description

Simulated gene sets used to generate amplitude matrix in SimpSim. A and corresponding data SimpSim. D.

Usage

GSets

Format

A list containing names of genes in two simulated gene sets used to generate the data in SimpSim.D.

plotAtoms

plotAtoms a simple plot of the number of atoms from one of the vectors returned with atom numbers

Description

plotAtoms a simple plot of the number of atoms during the sampling period or equilibration periodfrom one of either A or P as specified in type.

Usage

```
plotAtoms(gapsRes, type = "sampA")
```

Arguments

gapsRes the list resulting from applying GAPS

 $type \hspace{1cm} the \ atoms \ to \ plot, \ values \ are \ samp A, \ samp P \ , \ equil A, \ or \ equil P \ to \ plot \ sampling$

or equilibration teop atome numbers

plotDiag 15

plotDiag

plotDiag plots a series of diagnostic plots

Description

plotDiag plots a series of diagnostic plots

Usage

```
plotDiag(gapsRes)
```

Arguments

gapsRes

list returned by gapsRun, gapsMapRun, or CoGAPS

plotGAPS

Plotter for GAPS decomposition results

Description

Plots the A and P matrices obtained from the GAPS matrix decomposition.

Usage

```
plotGAPS(A, P, outputPDF="")
```

Arguments

A The amplitude matrix **A** obtained from GAPS.

P The pattern matrix **P** obtained from GAPS.

outputPDF Name of an pdf file to which the results will be output. (Optional; default=""

will output plots to screen).

Note

If the plot option is true in CoGAPS, this function will be called automatically to plot results to the screen.

Author(s)

```
Elana J. Fertig <efertig@jhmi.edu>
```

See Also

CoGAPS

16 plotSmoothPatterns

plotP

plotP plots the P matrix in a line plot with error bars

Description

plotP plots the P matrix in a line plot with error bars

Usage

```
plotP(PMean_Mat, P_SD)
```

Arguments

PMean_Mat matrix of mean values of P

P_SD matrix of standard deviation values of P

plotSmoothPatterns

Plot loess smoothed CoGAPS patterns

Description

Plots the sampled mean value of the pattern matrix \mathbf{P} obtained from the CoGAPS matrix factorization vs. a specificed X value for each sample in the columns of \mathbf{P} . Lines plot loess normalized values of \mathbf{P} vs specified X variables.

Usage

plotSmoothPatterns(P, x=NULL, breakS=NULL, breakStyle=T, orderP=!all(is.null(x)), plotPTS=F, pointCo

Arguments

Χ

P	A [p, M] pattern matrix (P.mean) obtained from the CoGAPS matrix factoriza-
	tion.

A [M, 1] matrix of values for the X axis for each of the corresponding M

columns of P. (Optional: Default: x=1:M)

breaks A vector of X values at which breaks in plotting should occur. Loess lines fit to

data will start and stop at breaks. (Optional: Default: no breaks). May also be specified as an integer to determine the number of equal groups into which to

divide the data.

breakStyle A logical vector. If TRUE, the corresponding break will start a new plot on the

row for each pattern. If FALSE, a vertical line will demarcate the break point. (Optional: Defaults to all hard breaks). Note, if one logical value is used, that

value will determine the break type at each break point.

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orderP	A logical value. If TRUE, vertical ordering of patterns will be determined in order of the value of x at which they peak. If FALSE, vertical ordering will be determined by the rows in the P matrix. (Optional: Default: FALSE)
plotPTS	A logical value. If TRUE, plot will include points for each value of the P matrix in addition to the loess smoothed curve. If FALSE, only the loess smoothed values of P will be plotted. (Optional: Default: FALSE)
pointCol	Color of points of the P matrix plotted when plotPTS=TRUE. (Optional: Default: black)
lineCol	Color of loess smoothed values of the P matrix. (Optional: Default: grey)
add	A logical value. If TRUE, plot will be added to existing graphics device. If FALSE, will create a new graphics device. (Optional: Default: FALSE)
	Additional arguments to plotting functions.

Author(s)

Genevieve Stein-O'Brien <gsteino1@jhmi.edu>

See Also

CoGAPS

Examples

```
## Not run:
# create simulated data
P <- rbind(1:10 + rnorm(10), seq(from=10,to=1) + rnorm(10))

# saved as PDF since figure margins are often too large for the null device with this function
# and the null device may also have trouble with the overlay
pdf(Test.pdf, width=10)
plotSmoothPatterns(P=P, x=rep(seq(from=1,to=10,by=2),each=2), breaks=3, breakStyle=c(F,T,T), plotPTS=T)

# demonstrating the overlay of the plot
plotSmoothPatterns(P=P, x=rep(seq(from=1,to=10,by=2),each=2), breaks=c(0.992,3.660,6.340,9.010), breakStyle=c(dev.off())

## End(Not run)</pre>
```

 ${\it reorder} {\it ByPatternMatch} \quad {\it Match two sets of patterns found with CoGAPS}$

Description

Matches two sets of pattern matrices (of the same size) found with CoGAPS. Matches are identified by finding identifying subsequently decreasing correlations between patterns in the respective matrices.

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Usage

```
reorderByPatternMatch(P, matchTo)
```

Arguments

P Pattern matrix for which rows will be arranged to match the matrix in matchTo matchTo Pattern matrix to which P is matched.

Value

Pattern matrix derived from reordering columns of P

residuals residuals calculate residuals and produce heatmap

Description

residuals calculate residuals and produce heatmap

Usage

```
residuals(AMean_Mat, PMean_Mat, D, S)
```

Arguments

AMean_Mat matrix of mean values for A from GAPS

PMean_Mat matrix of mean values for P from GAPS

D original data matrix run through GAPS

S original standard deviation matrix run through GAPS

SimpSim. A Simulated data

Description

True amplitude matrix generated from gene sets in GSets used to generate simulated data in SimpSim.D.

Usage

SimpSim.A

Format

Matrix with 30 genes by 3 patterns of true amplitude used to generate simulated data.

SimpSim.D

SimpSim.D

Simulated data

Description

Simulated gene expression data from true patterns in SimpSim.P and amplitude in SimpSim.A.

Usage

SimpSim.D

Format

Matrix with 30 genes by 20 samples of simulated gene expression data.

SimpSim.P

Simulated data

Description

True pattern matrix used to generate simulated data in SimpSim. D.

Usage

SimpSim.P

Format

Matrix with 3 patterns by 20 samples of true patterns used to generate simulated data.

SimpSim.S

Simulated data

Description

Standard deviation of simulated gene expression data from true patterns in SimpSim.P and amplitude in SimpSim.A.

Usage

SimpSim.S

Format

Matrix with 30 genes by 20 samples of containing standard deviation of simulated gene expression data.

20 tf2ugFC

tf2ugFC

Gene sets defined by transcription factors defined from TRANSFAC.

Description

List of genes contained in gastrointestinal stromal tumor cell line measurements that are regulated by transcription factors in the TRANSFAC database. Used for the gene set analysis in Ochs et al. (2009).

Usage

TFGSList

Format

Data.frame containing genes (rows) regulated by each transcription factor (columns).

References

Ochs, M., Rink, L., Tarn, C., Mburu, S., Taguchi, T., Eisenberg, B., and Godwin, A. (2009). Detection of treatment-induced changes in signaling pathways in gastrointestinal stromal tumors using transcriptomic data. Cancer Res, 69(23), 9125-9132.

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