Package ‘nethet’

March 23, 2017

Type Package

Title A bioconductor package for high-dimensional exploration of biological network heterogeneity

Version 1.6.0

Date 2015-08-18

Author Nicolas Staedler, Frank Dondelinger

Maintainer Nicolas Staedler <staedler.n@gmail.com>,
Frank Dondelinger <fdondelinger.work@gmail.com>

Description Package nethet is an implementation of statistical solid methodology enabling the analysis of network heterogeneity from high-dimensional data. It combines several implementations of recent statistical innovations useful for estimation and comparison of networks in a heterogeneous, high-dimensional setting. In particular, we provide code for formal two-sample testing in Gaussian graphical models (differential network and GGM-GSA; Stadler and Mukherjee, 2013, 2014) and make a novel network-based clustering algorithm available (mixed graphical lasso, Stadler and Mukherjee, 2013).

Imports glasso, mvtnorm, parcor, GeneNet, huge, CompQuadForm, ggm, mclust, parallel, GSA, limma, multtest, ICSNP, glmnet, network, ggplot2

Suggests knitr, xtable, BiocStyle

biocViews Clustering, GraphAndNetwork

VignetteBuilder knitr

License GPL-2

NeedsCompilation yes

R topics documented:

NetHet-package ............................................................... 2
aggpval ................................................................. 3
bwprun_mixglasso ...................................................... 4
diffnet_multisplit ..................................................... 5
diffnet_singlesplit .................................................... 8
diffregr_multisplit ................................................... 10
diffregr_pval ............................................................ 12
diffregr_singlesplit .................................................. 13
Description

A bioconductor package for high-dimensional exploration of biological network heterogeneity

Details

Includes: Network-based clustering (MixGLasso) *Differential network (DiffNet) *Differential regression (DiffRegr) *Gene-set analysis based on graphical models (GGMGSA) *Plotting functions for exploring network heterogeneity
Meinshausen p-value aggregation.

Usage

aggpval(pval, gamma.min = 0.05)

Arguments

pval Vector of p-values.
gamma.min See inf-quantile formula of Meinshausen et al 2009 (default=0.05).

Details

Inf-quantile formula for p-value aggregation presented in Meinshausen et al 2009.

Value

Aggregated p-value.

Author(s)

n.stadler

Examples

pval=runif(50)
aggpval(pval)
Mixglasso with backward pruning

Usage

bwprun_mixglasso(x, n.comp.min = 1, n.comp.max, lambda = sqrt(2 * nrow(x) * log(ncol(x)))/2, pen = "glasso.parcor", selection.crit = "mmdl", term = 10^(-3), min.compsize = 5, init = "kmeans.hc", my.cl = NULL, modelname.hc = "VVV", nstart.kmeans = 1, iter.max.kmeans = 10, reinit.out = FALSE, reinit.in = FALSE, mer = TRUE, del = TRUE, ...)

Arguments

x Input data matrix
n.comp.min Minimum number of components. Take n.comp.min=1!
n.comp.max Maximum number of components
lambda Regularization parameter. Default=sqrt(2*n*log(p))/2
pen Determines form of penalty: glasso.parcor (default), glasso.invcov, glasso.invcor
selection.crit Selection criterion. Default='mmdl'
term Termination criterion of EM algorithm. Default=10^-3
min.compsize Stop EM if any(compsize)<min.compsize; Default=5
init Initialization. Method used for initialization init='cl.init','r.means','random','kmeans','kmeans.hc','hc'. Default='kmeans.hc'
my.cl Initial cluster assignments; need to be provided if init='cl.init' (otherwise this param is ignored). Default=NULL
modelname.hc Model class used in hc. Default="VVV"
nstart.kmeans Number of random starts in kmeans; default=1
iter.max.kmeans Maximal number of iteration in kmeans; default=10
reinit.out Re-initialization if compsize<min.compsize (at the start of algorithm) ?
reinit.in Re-initialization if compsize<min.compsize (at the bwprun-loop level of algorithm) ?
mer Merge closest comps for initialization
del Delete smallest comp for initialization
...
Other arguments. See mixglasso_init

Details

This function runs mixglasso with various number of mixture components: It starts with a too large number of components and iterates towards solutions with smaller number of components by initializing using previous solutions.
**Value**

list consisting of

- **selcrit**: Selcrit for all models with number of components between `n.comp.min` and `n.comp.max`
- **res.init**: Initialization for all components
- **comp.name**: List of names of components. Indicates which states where merged/deleted during backward pruning
- **re.init.in**: Logical vector indicating whether re-initialization was performed or not
- **fit.mixgl.selcrit**: Results for model with optimal number of components. List see `mixglasso_init`

**Author(s)**

n.stadler

**Examples**

```r
##generate data
set.seed(1)
n <- 1000
n.comp <- 3
p <- 10

# Create different mean vectors
Mu <- matrix(0,p,n.comp)

nonzero.mean <- split(sample(1:p),rep(1:n.comp,length=p))
for(k in 1:n.comp){
  Mu[nonzero.mean[[k]],k] <- -2/sqrt(ceiling(p/n.comp))
}
sim <- sim_mix_networks(n, p, n.comp, Mu=Mu)

##run mixglasso

fit <- bwprun_mixglasso(sim$data,n.comp=1,n.comp.max=5,selection.crit='bic')
plot(fit$selcrit,ylab='bic',xlab='Num.Comps',type='b')
```

---

**Description**

Differential Network
diffnet_multisplit

diffnet_multisplit(x1, x2, b.splits = 50, frac.split = 1/2, 
screen.meth = "screen_bic.glasso", include.mean = FALSE, 
gamma.min = 0.05, compute.evals = "est2.my.ev3", 
algorithm.mleggm = "glasso_rho0", method.compquadform = "imhof", 
acc = 1e-04, epsabs = 1e-10, epsrel = 1e-10, show.warn = FALSE, 
save.mle = FALSE, verbose = TRUE, mc.flag = FALSE, mc.set.seed = TRUE, 
mc.preschedule = TRUE, mc.cores = getOption("mc.cores", 2L), ...)

Arguments

x1 Data-matrix sample 1. You might need to center and scale your data-matrix.
x2 Data-matrix sample 1. You might need to center and scale your data-matrix.
b.splits Number of splits (default=50).
frac.split Fraction train-data (screening) / test-data (cleaning) (default=0.5).
screen.meth Screening procedure. Options: 'screen_bic.glasso' (default), 'screen_cv.glasso', 'screen_shrink' (not recommended), 'screen_mb'.
include.mean Should sample specific means be included in hypothesis? Use include.mean=FALSE (default and recommended) which assumes mu1=mu2=0 and tests the hypothesis H0: Omega_1=Omega_2.
gamma.min Tuning parameter in p-value aggregation of Meinshausen et al (2009). (Default=0.05).
compute.evals Method to estimate the weights in the weighted-sum-of-chi2s distribution. The default and (currently) the only available option is the method 'est2.my.ev3'.
algorithm.mleggm Algorithm to compute MLE of GGM. The algorithm 'glasso_rho' is the default and (currently) the only available option.
method.compquadform Method to compute distribution function of weighted-sum-of-chi2s (default='imhof').
acc See ?davies (default 1e-04).
epsabs See ?imhof (default 1e-10).
epsrel See ?imhof (default 1e-10).
show.warn Should warnings be showed (default=FALSE)?
save.mle If TRUE, MLEs (inverse covariance matrices for samples 1 and 2) are saved for all b.splits. The median aggregated inverse covariance matrix is provided in the output as 'medwi'. The default is save.mle=FALSE.
verbose If TRUE, show output progress.
mc.flag If TRUE use parallel execution for each b.splits via function mclapply of package parallel.
mc.set.seed See mclapply. Default=TRUE
mc.preschedule See mclapply. Default=TRUE
mc.cores Number of cores to use in parallel execution. Defaults to mc.cores option if set, or 2 otherwise.
...
Additional arguments for screen.meth.
Details

Remark:
* If include.mean=FALSE, then x1 and x2 have mean zero and DiffNet tests the hypothesis H0: \( \Omega_1 = \Omega_2 \). You might need to center x1 and x2. * If include.mean=TRUE, then DiffNet tests the hypothesis H0: \( \mu_1 = \mu_2 \) & \( \Omega_1 = \Omega_2 \). * However, we recommend to set include.mean=FALSE and to test equality of the means separately. * You might also want to scale x1 and x2, if you are only interested in differences due to (partial) correlations.

Value

list consisting of

- **ms.pval**: p-values for all b.splits
- **ss.pval**: single-split p-value
- **medagg.pval**: median aggregated p-value
- **meinshagg.pval**: meinshausen aggregated p-value (meinshausen et al 2009)
- **teststat**: test statistics for b.splits
- **weights.nulldistr**: estimated weights
- **active.last**: active-sets obtained in last screening-step
- **medwi**: median of inverse covariance matrices over b.splits
- **sig.last**: constrained mle (covariance matrix) obtained in last cleaning-step
- **wi.last**: constrained mle (inverse covariance matrix) obtained in last cleaning-step

Author(s)

n.statler

Examples

############################################################
##This example illustrates the use of Differential Network##
############################################################

##set seed
set.seed(1)

##sample size and number of nodes
n <- 40
p <- 10

##specifiy sparse inverse covariance matrices
gen.net <- generate_2networks(p,graph='random',n.nz=rep(p,2),
   n.nz.common=ceiling(p*0.8))
invcov1 <- gen.net[[1]]
invcov2 <- gen.net[[2]]
plot_2networks(invcov1,invcov2,label.pos=0,label.cex=0.7)

##get corresponding correlation matrices
cor1 <- cov2cor(solve(invcov1))
cor2 <- cov2cor(solve(invcov2))

## generate data under null hypothesis (both datasets have the same underlying network)
library('mvtnorm')
x1 <- rmvnorm(n,mean = rep(0,p), sigma = cor1)
x2 <- rmvnorm(n,mean = rep(0,p), sigma = cor1)

## run diffnet (under null hypothesis)
dn.null <- diffnet_multisplit(x1,x2,b.splits=1,verbose=FALSE)
dn.null$ss.pval# single-split p-value

## generate data under alternative hypothesis (datasets have different networks)
x1 <- rmvnorm(n,mean = rep(0,p), sigma = cor1)
x2 <- rmvnorm(n,mean = rep(0,p), sigma = cor2)

## run diffnet (under alternative hypothesis)
dn.altn <- diffnet_multisplit(x1,x2,b.splits=1,verbose=FALSE)
dn.altn$ss.pval# single-split p-value
dn.altn$medagg.pval# median aggregated p-value

## typically we would choose a larger number of splits
# dn.altn <- diffnet_multisplit(x1,x2,b.splits=10,verbose=FALSE)
# dn.altn$ms.pval# multi-split p-values
# dn.altn$medagg.pval# median aggregated p-value
# plot(dn.altn)# histogram of single-split p-values

diffnet_singlesplit

Differential Network for user specified data splits

Description
Differential Network for user specified data splits

Usage
diffnet_singlesplit(x1, x2, split1, split2, screen.meth = "screen_bic.glasso", compute.evals = "est2.my.ev3", algorithm.mleggm = "glasso_rho0", include.mean = FALSE, method.comquadform = "imhof", acc = 1e-04, epsabs = 1e-10, epsrel = 1e-10, show.warn = FALSE, save.mle = FALSE, ...)

Arguments

x1 Data-matrix sample 1. You might need to center and scale your data-matrix.
x2 Data-matrix sample 2. You might need to center and scale your data-matrix.
split1 Samples (condition 1) used in screening step.
split2 Samples (condition 2) used in screening step.
screen.meth Screening procedure. Options: 'screen_bic.glasso' (default), 'screen_cv.glasso', 'screen_shrink' (not recommended), 'screen_mb'.
compute.evals Method to estimate the weights in the weighted-sum-of-chi2s distribution. The default and (currently) the only available option is the method 'est2.my.ev3'.
Algorithm to compute MLE of GGM. The algorithm ‘glasso_rho’ is the default and (currently) the only available option.

Should sample specific means be included in hypothesis? Use include.mean=FALSE (default and recommended) which assumes mu1=mu2=0 and tests the hypothesis H0: Omega_1=Omega_2.

Method to compute distribution function of weighted-sum-of-chi2s (default=‘imhof’).

See ?davies (default 1e-04).

See ?imhof (default 1e-10).

See ?imhof (default 1e-10).

Should warnings be showed (default=FALSE)?

Should MLEs be in the output list (default=FALSE)?

Additional arguments for screen.meth.

Remark:

* If include.mean=FALSE, then x1 and x2 have mean zero and DiffNet tests the hypothesis H0: Omega_1=Omega_2. You might need to center x1 and x2. * If include.mean=TRUE, then DiffNet tests the hypothesis H0: mu_1=mu_2 & Omega_1=Omega_2 * However, we recommend to set include.mean=FALSE and to test equality of the means separately. * You might also want to scale x1 and x2, if you are only interested in differences due to (partial) correlations.

Value

list consisting of

pval.onesided p-value

pval.twosided ignore this output

teststat log-likelihood-ratio test statistic

weights.nulldistr estimated weights

active active-sets obtained in screening-step

sig constrained mle (covariance) obtained in cleaning-step

wi constrained mle (inverse covariance) obtained in cleaning-step

mu mle (mean) obtained in cleaning-step

Author(s)

n.stadler

Examples

```r
##set seed
set.seed(1)

##sample size and number of nodes
n <- 40
```
p <- 10

## specify sparse inverse covariance matrices
gen.net <- generate_2networks(p, graph='random', n.nz=rep(p,2), n.nz.common=ceiling(p*0.8))

invcov1 <- gen.net[[1]]
invcov2 <- gen.net[[2]]

plot_2networks(invcov1, invcov2, label.pos=0, label.cex=0.7)

## get corresponding correlation matrices
cor1 <- cov2cor(solve(invcov1))
cor2 <- cov2cor(solve(invcov2))

## generate data under alternative hypothesis
library('mvtnorm')
x1 <- rmvnorm(n, mean = rep(0,p), sigma = cor1)
x2 <- rmvnorm(n, mean = rep(0,p), sigma = cor2)

## run diffnet
split1 <- sample(1:n,20)#samples for screening (condition 1)
split2 <- sample(1:n,20)#samples for screening (condition 2)
dn <- diffnet_singlesplit(x1, x2, split1, split2)
dn$pval.onesided#p-value

---

diffregr_multisplit  
**Differential Regression (multi-split version).**

### Description

Differential Regression (multi-split version).

### Usage

```r
diffregr_multisplit(y1, y2, x1, x2, b.splits = 50, frac.split = 1/2,
  screen.meth = "screen_cvtrunc.lasso", gamma.min = 0.05,
  compute.evals = "est2.my.ev3.diffregr", method.compquadform = "imhof",
  acc = 1e-04, epsabs = 1e-10, epsrel = 1e-10, show.warn = FALSE,
  n.perm = NULL, mc.flag = FALSE, mc.set.seed = TRUE,
  mc.preschedule = TRUE, mc.cores = getOption("mc.cores", 2L), ...)
```

### Arguments

- **y1**: Response vector condition 1.
- **y2**: Response vector condition 2.
- **x1**: Predictor matrix condition 1.
- **x2**: Predictor matrix condition 2.
- **b.splits**: Number of splits (default=50).
- **frac.split**: Fraction train-data (screening) / test-data (cleaning) (default=0.5).
- **screen.meth**: Screening method (default="screen_cvtrunc.lasso").
- **gamma.min**: Tuning parameter in p-value aggregation of Meinshausen et al (2009) (default=0.05).
diffregr_multisplit

calculate.evals  Method to estimate the weights in the weighted-sum-of-chi2s distribution. The default and (currently) the only available option is the method 'est2.my.ev3.diffregr'.

method.compquadform  Algorithm for computing distribution function of weighted-sum-of-chi2 (default='imhof').

acc  See ?davies (default=1e-4).

epsabs  See ?imhof (default=1e-10).

epsrel  See ?imhof (default=1e-10).

show.warn  Show warnings (default=FALSE)?

n.perm  Number of permutation for "split-perm" p-value. Default=NULL, which means that the asymptotic approximation is used.

mc.flag  If TRUE use parallel execution for each b.splits via function mclapply of package parallel.

mc.set.seed  See mclapply. Default=TRUE

mc.preschedule  See mclapply. Default=TRUE

mc.cores  Number of cores to use in parallel execution. Defaults to mc.cores option if set, or 2 otherwise.

...  Other arguments specific to screen.meth.

Details

Intercepts in regression models are assumed to be zero (mu1=mu2=0). You might need to center the input data prior to running Differential Regression.

Value

List consisting of

ms.pval  p-values for all b.splits

ss.pval  single-split p-value

medagg.pval  median aggregated p-value

meinshagg.pval  meinshausen aggregated p-value (meinshausen et al 2009)

teststat  test statistics for b.splits

weights.nulldist  estimated weights

active.last  active-sets obtained in last screening-step

beta.last  constrained mle (regression coefficients) obtained in last cleaning-step

Author(s)

n.stadler
Examples

```r
# This example illustrates the use of Differential Regression

## set seed
set.seed(1)

## Number of predictors and sample size
p <- 100
n <- 80

## Predictor matrices
x1 <- matrix(rnorm(n*p),n,p)
x2 <- matrix(rnorm(n*p),n,p)

## Active-sets and regression coefficients
act1 <- sample(1:p,5)
act2 <- c(act1[1:3],sample(setdiff(1:p,act1),2))
beta1 <- beta2 <- rep(0,p)
beta1[act1] <- 0.5
beta2[act2] <- 0.5

## Response vectors under null-hypothesis
y1 <- x1%*%as.matrix(beta1)+rnorm(n,sd=1)
y2 <- x2%*%as.matrix(beta1)+rnorm(n,sd=1)

## Diffregr (asymptotic p-values)
fit.null <- diffregr_multisplit(y1,y2,x1,x2,b.splits=5)
fit.null$ms.pval # multi-split p-values
fit.null$medagg.pval # median aggregated p-values

## Response vectors under alternative-hypothesis
y1 <- x1%*%as.matrix(beta1)+rnorm(n,sd=1)
y2 <- x2%*%as.matrix(beta2)+rnorm(n,sd=1)

## Diffregr (asymptotic p-values)
fit.alt <- diffregr_multisplit(y1,y2,x1,x2,b.splits=5)
fit.alt$ms.pval
fit.alt$medagg.pval

## Diffregr (permutation-based p-values; 100 permutations)
fit.alt.perm <- diffregr_multisplit(y1,y2,x1,x2,b.splits=5,n.perm=100)
fit.alt.perm$ms.pval
fit.alt.perm$medagg.pval
```

diffregr_pval

Computation "split-asym" p-values.

Description

Computation "split-asym"/"split-perm" p-values.
Usage

diffregr_pval(y1, y2, x1, x2, beta1, beta2, beta, act1, act2, act,
compute.evals, method.compquadform, acc, epsabs, epsrel, show.warn, n.perm)

Arguments

y1 Response vector condition 1.
y2 Response vector condition 2.
x1 Predictor matrix condition 1.
x2 Predictor matrix condition 2.
beta1 Regression coefficients condition 1.
beta2 Regression coefficients condition 2.
beta Pooled regression coefficients.
act1 Active-set condition 1.
act2 Active-set condition 2.
act Pooled active-set.
compute.evals Method for computation of weights.
method.compquadform Method to compute distribution function of w-sum-of-chi2.
acc See ?davies.
epsabs See ?imhof.
epsrel See ?imhof.
show.warn Show warnings?
n.perm Number of permutations.

Value

P-value, test statistic, estimated weights.

Author(s)

n.stadler

diffregr_singlesplit Differential Regression (single-split version).

Description

Differential Regression (single-split version).

Usage

diffregr_singlesplit(y1, y2, x1, x2, split1, split2,
screen.meth = "screen_cvtrunc.lasso",
compute.evals = "est2.my.ev3.diffregr", method.compquadform = "imhof",
acc = 1e-04, epsabs = 1e-10, epsrel = 1e-10, show.warn = FALSE,
n.perm = NULL, ...)


Arguments

\begin{itemize}
  \item \texttt{y1} \quad \text{Response vector condition 1.}
  \item \texttt{y2} \quad \text{Response vector condition 2.}
  \item \texttt{x1} \quad \text{Predictor matrix condition 1.}
  \item \texttt{x2} \quad \text{Predictor matrix condition 2.}
  \item \texttt{split1} \quad \text{Samples condition 1 used in screening-step.}
  \item \texttt{split2} \quad \text{Samples condition 2 used in screening-step.}
  \item \texttt{screen.meth} \quad \text{Screening method (default='screen_cvtrunc.lasso').}
  \item \texttt{compute.evals} \quad \text{Method to estimate the weights in the weighted-sum-of-chi2s distribution. The default and (currently) the only available option is the method 'est2.my.ev3.diffregr'.}
  \item \texttt{method.compquadform} \quad \text{Algorithm for computing distribution function of weighted-sum-of-chi2 (default='imhof').}
  \item \texttt{acc} \quad \text{See ?davies (default=1e-4).}
  \item \texttt{epsabs} \quad \text{See ?imhof (default=1e-10).}
  \item \texttt{epsrel} \quad \text{See ?imhof (default=1e-10).}
  \item \texttt{show.warn} \quad \text{Show warnings (default=FALSE)?}
  \item \texttt{n.perm} \quad \text{Number of permutation for "split-perm" p-value (default=NULL).}
  \item \texttt{...} \quad \text{Other arguments specific to screen.meth.}
\end{itemize}

Details

Intercepts in regression models are assumed to be zero (\(\mu_1=\mu_2=0\)). You might need to center the input data prior to running Differential Regression.

Value

List consisting of

\begin{itemize}
  \item \texttt{pval.onesided} \quad "One-sided" p-value.
  \item \texttt{pval.twosided} \quad "Two-sided" p-value. Ignore all "*.twosided results.
  \item \texttt{teststat} \quad 2 times Log-likelihood-ratio statistics
  \item \texttt{weights.nulldistr} \quad Estimated weights of weighted-sum-of-chi2s.
  \item \texttt{active} \quad List of active-sets obtained in screening step.
  \item \texttt{beta} \quad Regression coefficients (MLE) obtained in cleaning-step.
\end{itemize}

Author(s)

n.stadler
Examples

```r
## set seed
set.seed(1)

## number of predictors / sample size
p <- 100
n <- 80

## predictor matrices
x1 <- matrix(rnorm(n*p), n, p)
x2 <- matrix(rnorm(n*p), n, p)

## active-sets and regression coefficients
act1 <- sample(1:p, 5)
act2 <- c(act1[1:3], sample(setdiff(1:p, act1), 2))
beta1 <- beta2 <- rep(0, p)
beta1[act1] <- 0.5
beta2[act2] <- 0.5

## response vectors
y1 <- x1 %*% as.matrix(beta1) + rnorm(n, sd = 1)
y2 <- x2 %*% as.matrix(beta2) + rnorm(n, sd = 1)

## run diffregr
split1 <- sample(1:n, 50) # samples for screening (condition 1)
split2 <- sample(1:n, 50) # samples for screening (condition 2)
fit <- diffregr_singlesplit(y1, y2, x1, x2, split1, split2)
fit$pval.onesided # p-value
```

### dot_plot

Create a plot showing the edges with the highest partial correlation in any cluster.

#### Description

This function takes the output of `het_cv_glasso` or `mixglasso` and creates a plot of the highest scoring edges along the y axis, where, the edge in each cluster is represented by a circle whose area is proportional to the smallest mean of the two nodes that make up the edge, and the position along the y axis shows the partial correlation of the edge.

#### Usage

```r
dot_plot(net.clustering, p.corr.thresh = 0.25, hard.limit = 50, display = TRUE, node.names = rownames(net.clustering$Mu), group.names = sort(unique(net.clustering$comp)), dot.size.range = c(3, 12))
```
export_network

Export networks as a CSV table.

Description

This function takes the output of het_cv_glasso or mixglasso and exports it as a text table in CSV format, where each entry in the table records an edge in one group and its partial correlation.

Arguments

net.clustering  A network clustering object as returned by het_cv_glasso or mixglasso.
p.corrs.thresh  Cutoff for the partial correlations; only edges with absolute partial correlation > p.corrs.thresh (in any cluster) will be displayed.
hard.limit     Additional hard limit on the number of edges to display. If p.corrs.thresh results in more edges than hard.limit, only hard.limit edges with the highest partial correlation are returned.
display        If TRUE, print the plot to the current output device.
node.names     Names for the nodes in the network.
group.names    Names for the clusters or groups.
dot.size.range Graphical parameter for scaling the size of the circles (dots) representing an edge in each cluster.

Value

Returns a ggplot2 object. If display=TRUE, additionally displays the plot.

Examples

n = 500
p = 10
s = 0.9
n.comp = 3

# Create different mean vectors
Mu = matrix(0,p,n.comp)

# Define non-zero means in each group (non-overlapping)
nonzero.mean = split(sample(1:p),rep(1:n.comp,length=p))

# Set non-zero means to fixed value
for(k in 1:n.comp){
  Mu[nonzero.mean[[k]],k] = -2/sqrt(ceiling(p/n.comp))
}

# Generate data
sim.result = sim_mix_networks(n, p, n.comp, s, Mu=Mu)
mixglasso.result = mixglasso(sim.result$data, n.comp=3)
mixglasso.clustering = mixglasso.result$models[[mixglasso.result$bic.opt]]

dot_plot(mixglasso.clustering, p.corrs.thresh=0.5)
Usage

```
export_network(net.clustering, file = "network_table.csv",
               node.names = rownames(net.clustering$Mu),
               group.names = sort(unique(net.clustering$comp)), p.corrs.thresh = 0.2,
               ...)```

Arguments

- `net.clustering`: A network clustering object as returned by `screen_cv.glasso` or `mixglasso`.
- `file`: Filename to save the network table under.
- `node.names`: Names for the nodes in the network. If NULL, names from `net.clustering` will be used.
- `group.names`: Names for the clusters or groups. If NULL, names from `net.clustering` will be used (by default these are integers 1:numClusters).
- `p.corrs.thresh`: Threshold applied to the absolute partial correlations. Edges that are below the threshold in all of the groups are not exported. Using a negative value will export all possible edges (including those with zero partial correlation).
- `...`: Further parameters passed to `write.csv`.

Value

Function does not return anything.

Author(s)

Frank Dondelinger

Examples

```
n = 500
p = 10
s = 0.9
n.comp = 3

# Create different mean vectors
Mu = matrix(0, p, n.comp)

# Define non-zero means in each group (non-overlapping)
nonzero.mean = split(sample(1:p), rep(1:n.comp, length=p))

# Set non-zero means to fixed value
for(k in 1:n.comp){
  Mu[nonzero.mean[[k]],k] = -2/sqrt(ceiling(p/n.comp))
}

# Generate data
sim.result = sim_mix_networks(n, p, n.comp, s)
mixglasso.result = mixglasso(sim.result$data, n.comp=3)
mixglasso.clustering = mixglasso.result$models[[mixglasso.result$bic.opt]]

## Not run:
# Save network in CSV format suitable for Cytoscape import
export_network(mixglasso.clustering, file='nethet_network.csv',
```
generate_2networks

Generate two sparse inverse covariance matrices with overlap

Usage

generate_2networks(p, graph = "random", n.nz = rep(p, 2), n.nz.common = p, n.hub = 2, n.hub.diff = 1, magn.nz.diff = 0.8, magn.nz.common = 0.9, magn.diag = 0, emin = 0.1, verbose = FALSE)

Arguments

p
number of nodes

graph
'random' or 'hub'

n.nz
number of edges per graph (only for graph='random')

n.nz.common
number of edges in common between graphs (only for graph='random')

n.hub
number of hubs (only for graph='hub')

n.hub.diff
number of different hubs

magn.nz.diff
default=0.9

magn.nz.common
default=0.9

magn.diag
default=0

emin
default=0.1 (see ?huge.generator)

verbose
If verbose=FALSE then tracing output is disabled.

Value

Two sparse inverse covariance matrices with overlap

Examples

n <- 70
p <- 30

## Specify sparse inverse covariance matrices,
## with number of edges in common equal to ~ 0.8*p
gen.net <- generate_2networks(p,graph="random",n.nz=rep(p,2),
   n.nz.common=ceiling(p*0.8))

invcov1 <- gen.net[[1]]
invcov2 <- gen.net[[2]]

plot_2networks(invcov1,invcov2,label.pos=0,label.cex=0.7)
generate_inv_cov

Description
Generate an inverse covariance matrix with a given sparsity and dimensionality

Usage
generate_inv_cov(p = 162, sparsity = 0.7)

Arguments
- p: Dimensionality of the matrix.
- sparsity: Determined the proportion of non-zero off-diagonal entries.

Details
This function generates an inverse covariance matrix, with at most \((1 - \text{sparsity}) \times p(p-1)\) non-zero off-diagonal entries, where the non-zero entries are sampled from a beta distribution.

Value
A p by p positive definite inverse covariance matrix.

Examples
generate_inv_cov(p=162)

ggmgsa_multisplit
Multi-split GGMGSA (parallelized computation)

Description
Multi-split GGMGSA (parallelized computation)

Usage
ggmgsa_multisplit(x1, x2, b.splits = 50, gene.sets, gene.names, gs.names = NULL, method.p.adjust = "fdr", order.adj.agg = "agg-adj", mc.flag = FALSE, mc.set.seed = TRUE, mc.preschedule = TRUE, mc.cores = getOption("mc.cores", 2L), verbose = TRUE, ...)
Arguments

x1  Expression matrix for condition 1 (mean zero is required).
x2  Expression matrix for condition 2 (mean zero is required).
b.splits  Number of random data splits (default=50).
gene.sets  List of gene-sets.
gene.names  Gene names. Each column in x1 (and x2) corresponds to a gene.
gs.names  Gene-set names (default=NULL).
genes  Gene-set names (default=NULL).
method.p.adjust  Method for p-value adjustment (default='fdr')..
order.adj.agg  Order of aggregation and adjustment of p-values. Options: ‘agg-adj’ (default), ‘adj-agg’.
mc.flag  If TRUE use parallel execution for each b.splits via function mclapply of package parallel.
mc.set.seed  See mclapply. Default=TRUE
mc.preschedule  See mclapply. Default=TRUE
mc.cores  Number of cores to use in parallel execution. Defaults to mc.cores option if set, or 2 otherwise.
verbose  If TRUE, show output progress.
...
Other arguments (see diffnet_singlesplit).

Details

Computation can be parallelized over many data splits.

Value

List consisting of

medagg.pval  Median aggregated p-values
meinshagg.pval  Meinshausen aggregated p-values
pval  matrix of p-values before correction and adjustment, dim(pval)=(number of gene-sets)x(number of splits)
teststatmed  median aggregated test-statistic
teststatmed.bic  median aggregated bic-corrected test-statistic
teststatmed.aic  median aggregated aic-corrected test-statistic
teststat  matrix of test-statistics, dim(teststat)=(number of gene-sets)x(number of splits)
rel.edgeinter  normalized intersection of edges in condition 1 and 2
df1  degrees of freedom of GGM obtained from condition 1
df2  degrees of freedom of GGM obtained from condition 2
df12  degrees of freedom of GGM obtained from pooled data (condition 1 and 2)

Author(s)
n.stadler
Examples

### This example illustrates the use of GGMGSA

#### Generate networks

```r
set.seed(1)
p <- 9#network with p nodes
n <- 40
hub.net <- generate_2networks(p, graph='hub', n.hub=3, n.hub.diff=1)#generate hub networks
invcov1 <- hub.net[[1]]
invcov2 <- hub.net[[2]]
plot_2networks(invcov1, invcov2, label.pos=0, label.cex=0.7)
```

#### Generate data

```r
library('mvtnorm')
x1 <- rmvnorm(n, mean = rep(0, p), sigma = cov2cor(solve(invcov1)))
x2 <- rmvnorm(n, mean = rep(0, p), sigma = cov2cor(solve(invcov2)))
```

#### Run DiffNet

```r
# fit.dn <- diffnet_multisplit(x1, x2, b.splits=2, verbose=FALSE)
# fit.dn$medagg.pval
```

#### Identify hubs with 'gene-sets'

```r
gene.names <- paste('G', 1:p, sep='')
gsets <- split(gene.names, rep(1:3, each=3))
```

#### Run GGM-GSA

```r
fit.ggmgsa <- ggmgsa_multisplit(x1, x2, b.splits=2, gsets, gene.names, verbose=FALSE)
summary(fit.ggmgsa)
```

```r
p.adjust(apply(fit.ggmgsa$pval, 1, median), method='fdr')#or: first median aggregation,
#second fdr-correction
```

---

**ggmgsa_singlesplit**  
*Single-split GGMGSA*

**Description**

Single-split GGMGSA

**Usage**

```r
ggmgsa_singlesplit(x1, x2, gene.sets, gene.names, method.p.adjust = "fdr", 
verbose = TRUE, ...)
```
Arguments

- **x1**: centered (scaled) data for condition 1
- **x2**: centered (scaled) data for condition 2
- **gene.sets**: List of gene-sets.
- **gene.names**: Gene names. Each column in x1 (and x2) corresponds to a gene.
- **method.p.adjust**: Method for p-value adjustment (default='fdr').
- **verbose**: If TRUE, show output progress.
- **...**: Other arguments (see `diffnet_singlesplit`).

Value

List of results.

Author(s)

n.stadler

---

**gsea.iriz**

*Irizarry approach for gene-set testing*

Description

Irizarry approach for gene-set testing

Usage

```r
gsea.iriz(x1, x2, gene.sets, gene.names, gs.names = NULL, 
method.p.adjust = "fdr", alternative = "two-sided")
```

Arguments

- **x1**: Expression matrix (condition 1)
- **x2**: Expression matrix (condition 2)
- **gene.sets**: List of gene-sets
- **gene.names**: Gene names
- **gs.names**: Gene-set names
- **method.p.adjust**: Method for p-value adjustment (default='fdr')
- **alternative**: Default='two-sided' (uses two-sided p-values).

Details

Implements the approach described in "Gene set enrichment analysis made simple" by Irizarry et al (2011). It tests for shift and/or change in scale of the distribution.
Value

List consisting of

- pval.shift: p-values measuring shift
- pval.scale: p-values measuring scale
- pval.combined: combined p-values (minimum of pval.shift and pval.scale)

Author(s)

n.stadler

Examples

```r
n <- 100
p <- 20
x1 <- matrix(rnorm(n*p),n,p)
x2 <- matrix(rnorm(n*p),n,p)
gene.names <- paste("'Var\'G'\'Var",1:p,sep="'")
gsets <- split(gene.names,rep(1:4,each=5))
fit <- gsea.iriz(x1,x2,gsets,gene.names)
fit$pvals.combined

x2[,1:3] <- x2[,1:3]+0.5#variables 1-3 of first gene-set are upregulated
fit <- gsea.iriz(x1,x2,gsets,gene.names)
fit$pvals.combined
```

het_cv_glasso

Cross-validated glasso on heterogeneous dataset with grouping

Description

Run glasso on a heterogeneous dataset to obtain networks (inverse covariance matrices) of the variables in the dataset for each pre-specified group of samples.

Usage

`het_cv_glasso(data, grouping = rep(1, dim(data)[1]), mc.flag = FALSE, 
use.package = "huge", normalise = FALSE, verbose = FALSE, ...)`

Arguments

data: The heterogenous network data. Needs to be a num.samples by dim.samples matrix or dataframe.
grouping: The grouping of samples; a vector of length num.samples, with num.groups unique elements.
mc.flag: Whether to use parallel processing via package mclapply to distribute the glasso estimation over different groups.
use.package: 'glasso' for glasso package, or 'huge' for huge package (default)
normalise: If TRUE, normalise the columns of the data matrix before running glasso.
verbose: If TRUE, output progress.
...: Further parameters to be passed to screen_cv.lasso.
This function runs the graphical lasso with cross-validation to determine the best parameter lambda for each group of samples. Note that this function defaults to using package huge (rather than package glasso) unless otherwise specified, as it tends to be more numerically stable.

Returns a list with named elements ‘Sig’, ‘SigInv’, ‘Mu’, ‘Sigma.diag’, ‘group.names’ and ‘var.names. The variables Sig and SigInv are arrays of size dim.samples by dim.samples by num.groups, where the first two dimensions contain the (inverse) covariance matrix for the network obtained by running glasso on group k. Variables Mu and Sigma.diag contain the mean and variance of the input data, and group.names and var.names contains the names for the groups and variables in the data (if specified as colnames of the input data matrix).

n = 100
p = 25

# Generate networks with random means and covariances.
sim.result = sim_mix_networks(n, p, n.comp=3)
test.data = sim.result$data
test.labels = sim.result$comp

# Reconstruct networks for each component
networks = het_cv_glasso(data=test.data, grouping=test.labels)

invcov2parcor

Convert inverse covariance to partial correlation

invcov2parcor

Inverse covariance matrix

The partial correlation matrix.

inv.cov = generate_inv_cov(p=25)
p.corr = invcov2parcor(inv.cov)
invcov2parcor_array  Convert inverse covariance to partial correlation for several inverse covariance matrices collected in an array.

Description
Convert inverse covariance to partial correlation for several inverse covariance matrices collected in an array.

Usage
invcov2parcor_array(invcov.array)

Arguments
invcov.array  Array of inverse covariance matrices, of dimension numNodes by numNodes by numComps.

Value
Array of partial correlation matrices of dimension numNodes by numNodes by numComps

Examples
invcov.array = sapply(1:5, function(x) generate_inv_cov(p=25), simplify='array')
p.corr = invcov2parcor_array(invcov.array)

logratio  Log-likelihood-ratio statistics used in DiffNet

Description
Log-likelihood-ratio statistics used in Differential Network

Usage
logratio(x1, x2, x, sig1, sig2, sig, mu1, mu2, mu)

Arguments
x1  data-matrix sample 1
x2  data-matrix sample 2
x  pooled data-matrix
sig1  covariance sample 1
sig2  covariance sample 2
sig  pooled covariance
mu1  mean sample 1
mu2  mean sample 2
mu  pooled mean
Value

Returns a list with named elements 'twiceLR', 'sig1', 'sig2', 'sig'. 'twiceLR' is twice the log-likelihood-ratio statistic.

Author(s)

n.stadler

Examples

```r
x1 = matrix(rnorm(100), 50, 2)
x2 = matrix(rnorm(100), 50, 2)
logratio(x1, x2, rbind(x1, x2), diag(1, 2), diag(1, 2), diag(1, 2), c(0, 0), c(0, 0), c(0, 0))$twiceLR
```

Description

mixglasso

Usage

```r
mixglasso(x, n.comp, lambda = sqrt(2 * nrow(x) * log(ncol(x))))/2,
pen = "glasso.parcor", init = "kmeans hc", my.cl = NULL,
modelname.hc = "VVV", nstart.kmeans = 1, iter.max.kmeans = 10,
term = 10^{-3}, min.compsize = 5, save.allfits = FALSE,
filename = "mixglasso_fit.rda", mc.flag = FALSE, mc.set.seed = FALSE,
mc.preschedule = FALSE, mc.cores = getOption("mc.cores", 2L), ...)
```

Arguments

- **x**: Input data matrix
- **n.comp**: Number of mixture components. If n.comp is a vector, mixglasso will estimate a model for each number of mixture components, and return a list of models, as well as their BIC and MMDL scores and the index of the best model according to each score.
- **lambda**: Regularization parameter. Default=sqrt(2*n*log(p))/2
- **pen**: Determines form of penalty: glasso.parcor (default) to penalise the partial correlation matrix, glasso.inv cov to penalise the inverse covariance matrix (this corresponds to classical graphical lasso), glasso.inv cor to penalise the inverse correlation matrix.
- **init**: Initialization. Method used for initialization init='cl.init','r.means','random','kmeans','kmeans.hc','hc'. Default='kmeans'
- **my.cl**: Initial cluster assignments; need to be provided if init='cl.init' (otherwise this param is ignored). Default=NULL
- **modelname.hc**: Model class used in hc. Default="VVV"
- **nstart.kmeans**: Number of random starts in kmeans; default=1
Detailed information about the parameters of the `mixglasso` function:

- **iter.max.kmeans**: Maximal number of iteration in kmeans; default=10
- **term**: Termination criterion of EM algorithm. Default=10^-3
- **min.compsize**: Stop EM if any(compsize)<min.compsize; Default=5
- **save.allfits**: If TRUE, save output of mixglasso for all k's.
- **filename**: If save.allfits is TRUE, output of mixglasso will be saved as `paste(filename, _fit.mixgl_k.rda, sep=')`.
- **mc.flag**: If TRUE use parallel execution for each n.comp via function `mclapply` of package parallel.
- **mc.set.seed**: See mclapply. Default=FALSE
- **mc.preschedule**: See mclapply. Default=FALSE
- **mc.cores**: Number of cores to use in parallel execution. Defaults to mc.cores option if set, or 2 otherwise.
- **...**: Other arguments. See mixglasso_init

Details

Runs mixture of graphical lasso network clustering with one or several numbers of mixture components.

Value

A list with elements:

- **models**: List with each element i containing an S3 object of class 'nethetclustering' that contains the result of fitting the mixture graphical lasso model with n.comps[i] components. See the documentation of mixglasso_ncomp_fixed for the description of this object.
- **bic**: BIC for all fits.
- **mmdl**: Minimum description length score for all fits.
- **comp**: Component assignments for all fits.
- **bix.opt**: Index of model with optimal BIC score.
- **mmdl.opt**: Index of model with optimal MMDL score.

Author(s)

n.stadler

Examples

```r
###########################################
##This an example of how to use MixGLasso##
###########################################
##generate data
set.seed(1)
n <- 1000
n.comp <- 3
p <- 10
```
# Create different mean vectors
Mu <- matrix(0,p,n.comp)

nonzero.mean <- split(sample(1:p),rep(1:n.comp,length=p))
for(k in 1:n.comp){
  Mu[nonzero.mean[[k]],k] <- -2/sqrt(ceiling(p/n.comp))
}

sim <- sim_mix_networks(n, p, n.comp, Mu=Mu)

##run mixglasso
set.seed(1)
fit1 <- mixglasso(sim$data,n.comp=1:6)
fit1$bic
set.seed(1)
fit2 <- mixglasso(sim$data,n.comp=6)
fit2$bic
set.seed(1)
fit3 <- mixglasso(sim$data,n.comp=1:6,lambda=0)
set.seed(1)
fit4 <- mixglasso(sim$data,n.comp=1:6,lambda=Inf)
set.seed(1)
fit5 <- bwprun_mixglasso(sim$data,n.comp=1,n.comp.max=5,selection.crit='bic')
plot(fit5$selcrit,ylab='bic',xlab='Num.Comps',type='b')

##compare bic
library('ggplot2')
plotting.frame <- data.frame(BIC= c(fit1$bic, fit3$bic, fit4$bic),
  Num.Comps=rep(1:6, 3), Lambda=rep(
    c('Default',
    'Lambda = 0',
    'Lambda = Inf'),
    each=6))

p <- ggplot(plotting.frame) +
  geom_line(aes(x=Num.Comps, y=BIC, colour=Lambda))

print(p)

### Description

mixglasso_init (initialization and lambda set by user)

### Usage

```r
mixglasso_init(x, n.comp, lambda, u.init, mix.prob.init, gamma = 0.5,
  pen = "glasso.parcor", penalize.diagonal = FALSE, term = 10^-3,
  miniter = 5, maxiter = 1000, min.compsize = 5, show.trace = FALSE)
```
mixglasso_init

Arguments

x       Input data matrix
n.comp   Number of mixture components
lambda   Regularization parameter
u.init   Initial responsibilities
mix.prob.init Initial component probabilities
gamma   Determines form of penalty
pen      Determines form of penalty: glasso.parcor (default), glasso.invcov, glasso.invcor
penalize.diagonal Should the diagonal of the inverse covariance matrix be penalized? Default=FALSE (recommended)
term    Termination criterion of EM algorithm. Default=10^-3
miniter Minimal number of EM iteration before ‘stop EM if any(compsize)<min.compsize’ applies. Default=5
maxiter Maximal number of EM iteration. Default=1000
min.compsize Stop EM if any(compsize)<min.compsize; Default=5
show.trace Should information during execution be printed? Default=FALSE

details

This function runs mixglasso; requires initialization (u.init,mix.prob.init)

Value

list consisting of
mix.prob Component probabilities
Mu       Component specific mean vectors
Sig      Component specific covariance matrices
SigInv   Component specific inverse covariance matrices
iter     Number of EM iterations
loglik   Log-likelihood
bic      -loglik+log(n)*DF/2
mmdl     -loglik+penmmdl/2
u        Component responsibilities
comp     Component assignments
compsize Size of components
pi.comps Component probabilities
warn     Warnings during EM algorithm

Author(s)
n.stadler
Description
Plotting function for object of class 'diffnet'

Usage
## S3 method for class 'diffnet'
plot(x, ...)

Arguments
x
...  object of class 'diffnet'
   Further arguments.

Value
Histogram over multi-split p-values.

Author(s)
nicolas

Description
Plotting function for object of class 'diffregr'

Usage
## S3 method for class 'diffregr'
plot(x, ...)

Arguments
x
...  object of class 'diffregr'
   Further arguments.

Value
Histogram over multi-split p-values.

Author(s)
nicolas
plot.ggmgsa

Plotting function for object of class 'ggmgmsa'

Description
Plotting function for object of class 'ggmgmsa'

Usage
## S3 method for class 'ggmgmsa'
plot(x, ...)

Arguments
x          object of class 'ggmgmsa'
...        Further arguments.

Value
Boxplot of single-split p-values.

Author(s)
nicolas

plot.nethetclustering

Plot networks

Description
This function takes the output of screen_cv.glasso or mixglasso and creates a network plot using the network library.

Usage
## S3 method for class 'nethetclustering'
plot(x, node.names = rownames(net.clustering$Mu),
     group.names = sort(unique(net.clustering$comp)), p.corrs.thresh = 0.2,
     print.pdf = FALSE, pdf.filename = "networks", ...)

Arguments
x                  A network clustering object as returned by screen_cv.glasso or mixglasso.
node.names         Names for the nodes in the network. If NULL, names from net.clustering will be used.
group.names        Names for the clusters or groups. If NULL, names from net.clustering will be used (by default these are integers 1:numClusters).
p.corrs.thresh     Threshold applied to the absolute partial correlations. Edges that are below the threshold in all of the groups are not displayed.
print.pdf  If TRUE, save the output as a PDF file.
df.filename  If print.pdf is TRUE, specifies the file name of the output PDF file.

Value
Returns NULL and prints out the networks (or saves them to pdf if print.pdf is TRUE. The networks are displayed as a series of nComps+1 plots, where in the first plot edge widths are shown according to the maximum partial correlation of the edge over all groups. The following plots show the edges for each group. Positive partial correlation edges are shown in black, negative ones in blue. If an edge is below the threshold on the absolute partial correlation, it is displayed in gray or light blue respectively.

---

**plot_2networks**

*Plot two networks (GGMs)*

**Description**
Plot two networks (GGMs)

**Usage**

```r
plot_2networks(invcov1, invcov2, node.label = paste("X", 1:nrow(invcov1), sep = ""), main = c("", ""), ...)```

**Arguments**

- `invcov1`: Inverse covariance matrix of GGM1.
- `invcov2`: Inverse covariance matrix of GGM2.
- `node.label`: Names of nodes.
- `main`: Vector (two elements) with network names.
- `...`: Other arguments (see plot.network).

**Value**
Figure with two panels (for each network).

**Author(s)**
nicolas

**Examples**

```r
n <- 70
p <- 30

## Specify sparse inverse covariance matrices,
## with number of edges in common equal to ~ 0.8*p
gen.net <- generate_2networks(p, graph=’random’, n.nz=rep(p, 2), n.nz.common=ceiling(p*0.8))
```
```r
invcov1 <- gen.net[[1]]
invcov2 <- gen.net[[2]]
plot_2networks(invcov1, invcov2, label.pos=0, label.cex=0.7)
```

---

### print.nethetsummary

**Print function for object of class 'nethetsummary'**

**Description**

Print function for object of class 'nethetsummary'

**Usage**

```r
## S3 method for class 'nethetsummary'
print(x, ...)
```

**Arguments**

- `x` object of class 'nethetsummary'
- `...` Other arguments

**Value**

Function does not return anything.

**Author(s)**

frankd

---

### scatter_plot

Create a scatterplot showing correlation between specific nodes in the network for each pre-specified group.

**Description**

This function takes the output of `het_cv_glasso` or `mixglasso` and creates a plot showing the correlation between specified node pairs in the network for all groups. The subplots for each node pair are arranged in a numPairs by numGroups grid. Partial correlations associated with each node pair are also displayed.

**Usage**

```r
scatter_plot(net.clustering, data, node.pairs, display = TRUE,
            node.names = rownames(net.clustering$Mu),
            group.names = sort(unique(net.clustering$comp)), cex = 1)
```
Arguments

net.clustering  A network clustering object as returned by `het_cv_glasso` or `mixglasso`.
data  Observed data for the nodes, a numObs by numNodes matrix. Note that nodes need to be in the same ordering as in node.names.
node.pairs  A matrix of size numPairs by 2, where each row contains a pair of nodes to display. If node.names is specified, names in node.pairs must correspond to elements of node.names.
display  If TRUE, print the plot to the current output device.
node.names  Names for the nodes in the network. If NULL, names from net.clustering will be used.
group.names  Names for the clusters or groups. If NULL, names from net.clustering will be used (by default these are integers 1:numClusters).
cex  Scale factor for text and symbols in plot.

Value

Returns a ggplot2 object. If display=TRUE, additionally displays the plot.

Examples

```r
n = 500
p = 10
s = 0.9
n.comp = 3

# Create different mean vectors
Mu = matrix(0,p,n.comp)

# Define non-zero means in each group (non-overlapping)
nonzero.mean = split(sample(1:p),rep(1:n.comp,length=p))

# Set non-zero means to fixed value
for(k in 1:n.comp){
  Mu[nonzero.mean[[k]],k] = -2/sqrt(ceiling(p/n.comp))
}

# Generate data
sim.result = sim_mix_networks(n, p, n.comp, s, Mu=Mu)
mixglasso.result = mixglasso(sim.result$data, n.comp=3)
mixglasso.clustering = mixglasso.result$models[[mixglasso.result$bic.opt]]

# Specify edges
node.pairs = rbind(c(1,3), c(6,9),c(7,8))

# Create scatter plots of specified edges
scatter_plot(mixglasso.clustering, data=sim.result$data,
  node.pairs=node.pairs)
```
**Description**

AIC-tuned glasso with additional thresholding

**Usage**

```r
screen_aic.glasso(x, include.mean = TRUE, length.lambda = 20,
    lambdamin.ratio = ifelse(ncol(x) > nrow(x), 0.01, 0.001),
    penalize.diagonal = FALSE, plot.it = FALSE,
    trunc.method = "linear.growth", trunc.k = 5, use.package = "huge",
    verbose = FALSE)
```

**Arguments**

- **x**: The input data. Needs to be a num.samples by dim.samples matrix.
- **include.mean**: Include mean in likelihood. TRUE / FALSE (default).
- **length.lambda**: Length of lambda path to consider (default=20).
- **lambdamin.ratio**: Ratio lambda.min/lambda.max.
- **penalize.diagonal**: If TRUE apply penalization to diagonal of inverse covariance as well. (default=FALSE)
- **plot.it**: TRUE / FALSE (default)
- **trunc.method**: None / linear.growth (default) / sqrt.growth
- **trunc.k**: truncation constant, number of samples per predictor (default=5)
- **use.package**: ‘glasso’ or ‘huge’ (default).
- **verbose**: If TRUE, output la.min, la.max and la.opt (default=FALSE).

**Value**

Returns a list with named elements ‘rho.opt’, ‘wi’, ‘wi.orig’. Variable rho.opt is the optimal (scaled) penalization parameter (rho.opt=2*la.opt/n). The variables wi and wi.orig are matrices of size dim.samples by dim.samples containing the truncated and untruncated inverse covariance matrix.

**Author(s)**

n.stadler

**Examples**

```r
n=50
p=5
x=matrix(rnorm(n*p),n,p)
wihat=screen_aic.glasso(x,length.lambda=5)$wi
```
Description

BIC-tuned glasso with additional thresholding

Usage

    screen_bic.glasso(x, include.mean = TRUE, length.lambda = 20,
                      lambdamin.ratio = ifelse(ncol(x) > nrow(x), 0.01, 0.001),
                      penalize.diagonal = FALSE, plot.it = FALSE,
                      trunc.method = "linear.growth", trunc.k = 5, use.package = "huge",
                      verbose = FALSE)

Arguments

x              The input data. Needs to be a num.samples by dim.samples matrix.
include.mean   Include mean in likelihood. TRUE / FALSE (default).
length.lambda  Length of lambda path to consider (default=20).
lambdamin.ratio Ratio lambda.min/lambda.max.
penalize.diagonal If TRUE apply penalization to diagonal of inverse covariance as well. (default=FALSE)
plot.it        TRUE / FALSE (default)
trunc.method   None / linear.growth (default) / sqrt.growth
trunc.k        truncation constant, number of samples per predictor (default=5)
use.package    'glasso' or 'huge' (default).
verbose        If TRUE, output la.min, la.max and la.opt (default=FALSE).

Value

Returns a list with named elements 'rho.opt', 'wi', 'wi.orig'. Variable rho.opt is the optimal (scaled) penalization parameter (rho.opt=2*la.opt/n). The variables wi and wi.orig are matrices of size dim.samples by dim.samples containing the truncated and untruncated inverse covariance matrix.

Author(s)

n.stadler

Examples

    n=50
    p=5
    x=matrix(rnorm(n*p),n,p)
    wihat=screen_bic.glasso(x,length.lambda=5)$wi
Description

Cross-validated glasso with additional thresholding

Usage

```r
screen_cv.glasso(x, include.mean = FALSE, folds = 10, length.lambda = 20,
     lambdamini.ratio = ifelse(ncol(x) > nrow(x), 0.01, 0.001),
     penalize.diagonal = FALSE, trunc.method = "linear.growth", trunc.k = 5,
     plot.it = FALSE, se = FALSE, use.package = "huge", verbose = FALSE)
```

Arguments

- **x** The input data. Needs to be a num.samples by dim.samples matrix.
- **include.mean** Include mean in likelihood. TRUE / FALSE (default).
- **folds** Number of folds in the cross-validation (default=10).
- **length.lambda** Length of lambda path to consider (default=20).
- **lambdamini.ratio** Ratio lambda.min/lambda.max.
- **penalize.diagonal** If TRUE apply penalization to diagonal of inverse covariance as well. (default=FALSE)
- **trunc.method** None / linear.growth (default) / sqrt.growth
- **trunc.k** truncation constant, number of samples per predictor (default=5)
- **plot.it** TRUE / FALSE (default)
- **se** default=FALSE.
- **use.package** 'glasso' or 'huge' (default).
- **verbose** If TRUE, output la.min, la.max and la.opt (default=FALSE).

Details

Run glasso on a single dataset, using cross-validation to estimate the penalty parameter lambda. Performs additional thresholding (optionally).

Value

Returns a list with named elements 'rho.opt', 'w', 'wi', 'wi.orig', 'mu'. Variable rho.opt is the optimal (scaled) penalization parameter (rho.opt=2*la.opt/n). Variable w is the estimated covariance matrix. The variables wi and wi.orig are matrices of size dim.samples by dim.samples containing the truncated and untruncated inverse covariance matrix. Variable mu is the mean of the input data.

Author(s)

n.stadler
Examples

n=50
p=5
x=matrix(rnorm(n*p),n,p)
whihat=screen_cv.gllasso(x,folds=2)$wi

screen_cv1se.lasso     Cross-validated Lasso screening (lambda.1se-rule)

Description
Cross-validated Lasso screening (lambda.1se-rule)

Usage

screen_cv1se.lasso(x, y)

Arguments

x Predictor matrix
y Response vector

Value
Active-set

Author(s)
n.stadler

Examples

screen_cv1se.lasso(matrix(rnorm(5000),50,100),rnorm(50))

screen_cvfix.lasso     Cross-validated Lasso screening and upper bound on number of predictors.

Description
Cross-validated Lasso screening and upper bound on number of predictors

Usage

screen_cvfix.lasso(x, y, no.predictors = 10)

Arguments

x Predictor matrix.
y Response vector.
no.predictors Upper bound on number of active predictors,
screen_cvmin.lasso

Details

Computes Lasso coefficients (cross-validation optimal lambda). Truncates smallest coefficients to zero such that there are no more than no.predictors non-zero coefficients.

Value

Active-set.

Author(s)

n.stadler

Examples

screen_cvfix.lasso(matrix(rnorm(5000),50,100),rnorm(50))

desc

screen_cvmin.lasso(matrix(rnorm(5000),50,100),rnorm(50))

screen_cvmin.lasso

Cross-validation lasso screening (lambda.min-rule)

Description

Cross-validated Lasso screening (lambda.min-rule)

Usage

screen_cvmin.lasso(x, y)

Arguments

x  Predictor matrix
y  Response vector

Value

Active-set

Author(s)

n.stadler

Examples

screen_cvmin.lasso(matrix(rnorm(5000),50,100),rnorm(50))
screen_cvtrunc.lasso  \textit{Cross-validated Lasso screening and additional truncation.}

\textbf{Description}

Cross-validated Lasso screening and additional truncation.

\textbf{Usage}

\begin{verbatim}
screen_cvtrunc.lasso(x, y, k.trunc = 5)
\end{verbatim}

\textbf{Arguments}

- \textit{x}  \hspace{1cm} Predictor matrix.
- \textit{y}  \hspace{1cm} Response vector.
- \textit{k.trunc}  \hspace{1cm} Truncation constant="number of samples per predictor" (default=5).
Details

Computes Lasso coefficients (cross-validation optimal lambda). Truncates smallest coefficients to zero, such that there are no more than n/k.trunc non-zero coefficients.

Value

Active-set.

Author(s)

n.stadler

Examples

screen_cvtrunc.lasso(matrix(rnorm(5000),50,100),rnorm(50))

screen_mb

Node-wise Lasso-regressions for GGM estimation

Description

Node-wise Lasso-regressions for GGM estimation

Usage

screen_mb(x, include.mean = NULL, folds = 10, length.lambda = 20, lambdamin.ratio = ifelse(ncol(x) > nrow(x), 0.01, 0.001), penalize.diagonal = FALSE, trunc.method = "linear.growth", trunc.k = 5, plot.it = FALSE, se = FALSE, verbose = FALSE)

Arguments

x The input data. Needs to be a num.samples by dim.samples matrix.
include.mean Include mean in likelihood. TRUE / FALSE (default).
folds Number of folds in the cross-validation (default=10).
length.lambda Length of lambda path to consider (default=20).
lambdamin.ratio Ratio lambda.min/lambda.max.
penalize.diagonal If TRUE apply penalization to diagonal of inverse covariance as well. (default=FALSE)
trunc.method None / linear.growth (default) / sqrt.growth
trunc.k truncation constant, number of samples per predictor (default=5)
plot.it TRUE / FALSE (default)
se default=FALSE.
verbose If TRUE, output la.min, la.max and la.opt (default=FALSE).

Details

(Meinshausen-Buehlmann approach)
Value

Returns a list with named elements 'rho.opt', 'wi'. Variable rho.opt is the optimal (scaled) penalization parameter (rho.opt=2*la.opt/n). The variables wi is a matrix of size dim.samples by dim.samples containing the truncated inverse covariance matrix. Variable Mu mean of the input data.

Author(s)

n.stadler

Examples

n=50
p=5
x=matrix(rnorm(n*p),n,p)
what=screen_mb(x)$wi

Description

Simulate from mixture model with multi-variate Gaussian or t-distributed components.

Usage

sim_mix(n, n.comp, mix.prob, Mu, Sig, dist = "norm", df = 2)

Arguments

n      sample size
n.comp number of mixture components ("comps")
mix.prob mixing probabilities (need to sum to 1)
Mu     matrix of component-specific mean vectors
Sig    array of component-specific covariance matrices
dist   'norm' for Gaussian components, 't' for t-distributed components
df     degrees of freedom of the t-distribution (not used for Gaussian distribution), default=2

Value

a list consisting of:

S  component assignments
X  observed data matrix

Author(s)

n.stadler
**Examples**

```r
comp = 4
p = 5 # dimensionality
Mu = matrix(rep(0, p), p, n.comp)
Sigma = array(diag(p), c(p, p, n.comp))
mix.prob = rep(0.25, n.comp)
sim_mix(100, n.comp, mix.prob, Mu, Sigma)
```

**Description**

Generate inverse covariances, means, mixing probabilities, and simulate data from resulting mixture model.

**Usage**

```r
sim_mix_networks(n, p, n.comp, sparsity = 0.7, mix.prob = rep(1/n.comp, n.comp), Mu = NULL, Sig = NULL, ...)
```

**Arguments**

- `n`: Number of data points to simulate.
- `p`: Dimensionality of the data.
- `n.comp`: Number of components of the mixture model.
- `sparsity`: Determines the proportion of non-zero off-diagonal entries.
- `mix.prob`: Mixture probabilities for the components; defaults to uniform distribution.
- `Mu`: Means for the mixture components, a p by n.comp matrix. If NULL, sampled from a standard Gaussian.
- `Sig`: Covariances for the mixture components, a p by p by n.comp array. If NULL, generated using `generate_inv_cov`.
- `...`: Further arguments passed to `sim_mix`.

**Details**

This function generates `n.comp` mean vectors from a standard Gaussian and `n.comp` covariance matrices, with at most \((1 - \text{sparsity}) \cdot p(p-1)/2\) non-zero off-diagonal entries, where the non-zero entries are sampled from a beta distribution. Then it uses `sim_mix` to simulate from a mixture model with these means and covariance matrices.

Means `Mu` and covariance matrices `Sig` can also be supplied by the user.

**Value**

A list with components: Mu Means of the mixture components. Sig Covariances of the mixture components. data Simulated data, a n by p matrix. S Component assignments, a vector of length n.

**Examples**

```r
# Generate dataset with 100 samples of dimensionality 30, and 4 components
test.data = sim_mix_networks(n=100, p=30, n.comp=4)
```
**summary.diffnet**  
*Summary function for object of class 'diffnet'*

**Description**  
Summary function for object of class 'diffnet'

**Usage**  
```r
## S3 method for class 'diffnet'
summary(object, ...)
```

**Arguments**
- `object`  
  object of class 'diffnet'
- `...`  
  Other arguments.

**Value**  
aggregated p-values

**Author(s)**
nicolas

---

**summary.diffregr**  
*Summary function for object of class 'diffregr'*

**Description**  
Summary function for object of class 'diffregr'

**Usage**  
```r
## S3 method for class 'diffregr'
summary(object, ...)
```

**Arguments**
- `object`  
  object of class 'diffregr'
- `...`  
  Other arguments

**Value**  
aggregated p-values

**Author(s)**
nicolas
### summary.ggmgsa

**Summary function for object of class ‘ggmgsa’**

**Description**

Summary function for object of class ‘ggmgsa’

**Usage**

```r
## S3 method for class 'ggmgsa'
summary(object, ...)
```

**Arguments**

- `object` : object of class ‘ggmgsa’
- `...` : Other arguments

**Value**

aggregated p-values

**Author(s)**

nicolas

---

### summary.nethetclustering

**Summary function for object of class ‘nethetclustering’**

**Description**

Summary function for object of class ‘nethetclustering’

**Usage**

```r
## S3 method for class 'nethetclustering'
summary(object, ...)
```

**Arguments**

- `object` : object of class ‘nethetclustering’
- `...` : Other arguments

**Value**

Network statistics (a ’nethetsummary’ object)

**Author(s)**

frankd
Index

aggpval, 3
bwprun_mixglasso, 4
diffnet_multisplit, 5
diffnet_singlesplit, 8
diffregr_multisplit, 10
diffregr_pval, 12
diffregr_singlesplit, 13
dot_plot, 15
export_network, 16
generate_2networks, 18
generate_inv_cov, 19, 43
ggmsa_multisplit, 19
ggmsa_singlesplit, 21
gsea.iriz, 22
het_cv_glasso, 15, 16, 23, 33, 34
invcov2parcor, 24
invcov2parcor_array, 25
logratio, 25
mixglasso, 15–17, 26, 31, 33, 34
mixglasso_init, 28
NetHet-package, 2
plot.diffnet, 30
plot.diffregr, 30
plot.ggmgsa, 31
plot.nethetclustering, 31
plot_2networks, 32
print.nethetsummary, 33
scatter_plot, 33
screen_aic.glasso, 35
screen_bic.glasso, 36
screen_cv.glasso, 17, 31, 37
screen_cv1se.lasso, 38
screen_cvfix.lasso, 38
screen_cvmmin.lasso, 39
screen_cvsqrt.lasso, 40
screen_cvtrunc.lasso, 40
screen_mb, 41
sim_mix, 42, 43
sim_mix_networks, 43
summary.diffnet, 44
summary.diffregr, 44
summary.ggmgsa, 45
summary.nethetclustering, 45
write.csv, 17