

# Package ‘nethet’

April 16, 2024

**Type** Package

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

**Version** 1.34.0

**Date** 2020-09-27

**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, GeneNet, huge, CompQuadForm, ggm, mclust, parallel, GSA, limma, multtest, ICSNP, glmnet, network, ggplot2, grDevices, graphics, stats, utils

**Suggests** knitr, xtable, BiocStyle, testthat

**biocViews** Clustering, GraphAndNetwork

**VignetteBuilder** knitr

**License** GPL-2

**RoxygenNote** 6.1.1

**git\_url** <https://git.bioconductor.org/packages/nethet>

**git\_branch** RELEASE\_3\_18

**git\_last\_commit** e771f90

**git\_last\_commit\_date** 2023-10-24

**Repository** Bioconductor 3.18

**Date/Publication** 2024-04-15

**R topics documented:**

NetHet-package . . . . .	4
agg.pval . . . . .	5
agg.score.iriz.scale . . . . .	5
agg.score.iriz.shift . . . . .	6
aggpval . . . . .	6
aic.glasso . . . . .	7
beta.mat . . . . .	8
beta.mat.diffregr . . . . .	8
bic.glasso . . . . .	9
buildDotPlotDataFrame . . . . .	10
bwprun_mixglasso . . . . .	10
cv.fold . . . . .	12
cv.glasso . . . . .	13
diffnet_multisplit . . . . .	14
diffnet_pval . . . . .	16
diffnet_singlesplit . . . . .	18
diffregr_multisplit . . . . .	20
diffregr_pval . . . . .	22
diffregr_singlesplit . . . . .	23
dot_plot . . . . .	25
error.bars . . . . .	27
est2.my.ev2 . . . . .	27
est2.my.ev2.diffregr . . . . .	28
est2.my.ev3 . . . . .	29
est2.my.ev3.diffregr . . . . .	30
est2.ww.mat.diffregr . . . . .	31
est2.ww.mat2 . . . . .	32
est2.ww.mat2.diffregr . . . . .	32
export_network . . . . .	33
EXPStep.mix . . . . .	34
func.uinit . . . . .	35
generate_2networks . . . . .	36
generate_inv_cov . . . . .	37
getinvcov . . . . .	38
ggmgsa_multisplit . . . . .	38
ggmgsa_singlesplit . . . . .	40
glasso.invcor . . . . .	41
glasso.invcov . . . . .	42
glasso.parcor . . . . .	42
gsea.highdimT2 . . . . .	43
gsea.iriz . . . . .	44
gsea.iriz.scale . . . . .	45
gsea.iriz.shift . . . . .	46
gsea.t2cov . . . . .	46
het_cv_glasso . . . . .	47
hugepath . . . . .	48

inf.mat . . . . .	49
invcov2parcor . . . . .	50
invcov2parcor_array . . . . .	50
lambda.max . . . . .	51
lambdagrid_lin . . . . .	51
lambdagrid_mult . . . . .	52
loglik_mix . . . . .	52
logratio . . . . .	53
logratio.diffregr . . . . .	54
make_grid . . . . .	55
mcov . . . . .	55
mixglasso . . . . .	56
mixglasso_init . . . . .	58
mixglasso_ncomp_fixed . . . . .	60
mle.ggm . . . . .	61
MStepGlasso . . . . .	62
my.ev2.diffregr . . . . .	63
my.p.adjust . . . . .	63
my.ttest . . . . .	64
my.ttest2 . . . . .	64
mytrunc.method . . . . .	65
perm.diffregr_pval . . . . .	65
perm.diffregr_teststat . . . . .	66
plot.diffnet . . . . .	67
plot.diffregr . . . . .	67
plot.gmgmsa . . . . .	68
plot.nethetclustering . . . . .	68
plotCV . . . . .	69
plot_2networks . . . . .	70
print.nethetsummary . . . . .	71
q.matrix.diffregr . . . . .	71
q.matrix.diffregr3 . . . . .	72
q.matrix.diffregr4 . . . . .	73
q.matrix3 . . . . .	73
q.matrix4 . . . . .	74
scatter_plot . . . . .	75
screen_aic.glasso . . . . .	76
screen_bic.glasso . . . . .	77
screen_cv.glasso . . . . .	78
screen_cv1se.lasso . . . . .	79
screen_cvfix.lasso . . . . .	80
screen_cvmin.lasso . . . . .	81
screen_cvsqrt.lasso . . . . .	81
screen_cvtrunc.lasso . . . . .	82
screen_full . . . . .	83
screen_shrink . . . . .	83
shapiro_screen . . . . .	84
sim_mix . . . . .	85

sim_mix_networks . . . . .	86
sparse_conc . . . . .	87
summary.diffnet . . . . .	87
summary.diffregr . . . . .	88
summary.gmgsa . . . . .	88
summary.nethetclustering . . . . .	89
sumoffdiag . . . . .	90
symmkldist . . . . .	90
t2cov.lr . . . . .	91
t2diagcov.lr . . . . .	91
test.sd . . . . .	92
test.t2 . . . . .	92
tr . . . . .	93
twosample_single_regr . . . . .	93
w.kldist . . . . .	94
ww.mat . . . . .	95
ww.mat.diffregr . . . . .	95
ww.mat2 . . . . .	96
ww.mat2.diffregr . . . . .	97
<b>Index</b>	<b>98</b>

---

 NetHet-package

*NetHet-package*


---

## 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

## References

Stadler, N. and Mukherjee, S. (2013). Two-Sample Testing in High-Dimensional Models. Preprint <http://arxiv.org/abs/1210.4584>.

---

agg.pval *P-value aggregation (Meinshausen et al 2009)*

---

**Description**

P-value aggregation

**Usage**

```
agg.pval(gamma, pval)
```

**Arguments**

gamma	see Meinshausen et al 2009
pval	vector of p-values

**Value**

inf-quantile aggregated p-value

**Author(s)**

n.stadler

---

agg.score.iriz.scale *Irizarry aggregate score (scale)*

---

**Description**

Irizarry aggregate score (scale)

**Usage**

```
agg.score.iriz.scale(ttstat, geneset, gene.name)
```

**Arguments**

ttstat	no descr
geneset	no descr
gene.name	no descr

**Value**

no descr

**Author(s)**

n.stadler

agg.score.iriz.shift *Irizarry aggregate score (shift)*

---

**Description**

Irizarry aggregate score (shift)

**Usage**

```
agg.score.iriz.shift(ttstat, geneset, gene.name)
```

**Arguments**

ttstat	no descr
geneset	no descr
gene.name	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

aggpval *Meinshausen p-value aggregation*

---

**Description**

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)
```

---

aic.glasso

*AIC.glasso*

---

**Description**

AIC.glasso

**Usage**

```
aic.glasso(x, lambda, penalize.diagonal = FALSE, plot.it = TRUE,
  use.package = "huge", include.mean = FALSE)
```

**Arguments**

x	no descr
lambda	no descr
penalize.diagonal	no descr
plot.it	no descr
use.package	no descr
include.mean	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

beta.mat	<i>Compute beta-matrix</i>
----------	----------------------------

---

**Description**

Compute beta-matrix

**Usage**

```
beta.mat(ind1, ind2, sig1, sig2, sig)
```

**Arguments**

ind1	no descr
ind2	no descr
sig1	no descr
sig2	no descr
sig	no descr

**Details**

$$\text{beta-matrix} = E[s_{\text{ind1}}(Y; \text{sig1}) s_{\text{ind2}}(Y; \text{sig2})' | \text{sig}]$$
**Value**

no descr

**Author(s)**

n.stadler

---

beta.mat.diffregr	<i>Computation beta matrix</i>
-------------------	--------------------------------

---

**Description**

Computation beta matrix

**Usage**

```
beta.mat.diffregr(ind1, ind2, beta1, beta2, beta, sig1, sig2, sig, Sig)
```



**Arguments**

ind1	no descr
ind2	no descr
beta1	no descr
beta2	no descr
beta	no descr
sig1	no descr
sig2	no descr
sig	no descr
Sig	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

bic.glasso	<i>BIC.glasso</i>
------------	-------------------

---

**Description**

BIC.glasso

**Usage**

```
bic.glasso(x, lambda, penalize.diagonal = FALSE, plot.it = TRUE,  
use.package = "huge", include.mean = FALSE)
```

**Arguments**

x	no descr
lambda	no descr
penalize.diagonal	no descr
plot.it	no descr
use.package	no descr
include.mean	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

 buildDotPlotDataFrame *Build up dataframe for plotting dot plot with ggplot2*


---

**Description**

Internal function

**Usage**

```
buildDotPlotDataFrame(net.clustering, cluster.names, node.names)
```

**Arguments**

```
net.clustering  Clustering
cluster.names   Cluster names
node.names      Node names
```

**Value**

A data frame for plotting the dotPlot with ggplot2 is returned. Column P.Corr contains the partial correlations of each edge as a numeric, column Mean contains the minimum mean expression of the two proteins (e.g. if the edge is e(p1, p2), then the column contains min(mean(p1), mean(p2))), column Edge contains the name of the edge as a character string of the form "p1-p2" and column Type contains the cluster name of the cluster that the edge belongs to as a character string.

---

 bwprun\_mixglasso      *bwprun\_mixglasso*


---

**Description**

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**

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

**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**

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

**Author(s)**

n.stadler

**Examples**

```
##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')
```

---

`cv.fold`*Make folds*

---

**Description**

Make folds

**Usage**`cv.fold(n, folds = 10)`**Arguments**

n	no descr
folds	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

`cv.glasso`*Crossvalidation for GLasso*

---

**Description**

Crossvalidation for GLasso

**Usage**

```
cv.glasso(x, folds = 10, lambda, penalize.diagonal = FALSE,  
plot.it = FALSE, se = TRUE, include.mean = FALSE)
```

**Arguments**

<code>x</code>	no descr
<code>folds</code>	no descr
<code>lambda</code>	lambda-grid (increasing!)
<code>penalize.diagonal</code>	no descr
<code>plot.it</code>	no descr
<code>se</code>	no descr
<code>include.mean</code>	no descr

**Details**

! lambda-grid has to be increasing (see glassopath)

**Value**

no descr

**Author(s)**

n.stadler

---

diffnet\_multisplit      *Differential Network*

---

## Description

Differential Network

## Usage

```
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).
include.mean	Should sample specific means be included in hypothesis? Use include.mean=FALSE (default and recommended) which assumes $\mu_1=\mu_2=0$ and tests the hypothesis $H_0: \Omega_1=\Omega_2$ .
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  $x_1$  and  $x_2$  have mean zero and DiffNet tests the hypothesis  $H_0: \Omega_{11}=\Omega_{22}$ . You might need to center  $x_1$  and  $x_2$ . \* If include.mean=TRUE, then DiffNet tests the hypothesis  $H_0: \mu_1=\mu_2$  &  $\Omega_{11}=\Omega_{22}$  \* However, we recommend to set include.mean=FALSE and to test equality of the means separately. \* You might also want to scale  $x_1$  and  $x_2$ , 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.stadler

## 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
```



**Description**

P-value calculation

**Usage**

```
diffnet_pval(x1, x2, x, sig1, sig2, sig, mu1, mu2, mu, act1, act2, act,  
             compute.evals, include.mean, method.compquadform, acc, epsabs, epsrel,  
             show.warn)
```

**Arguments**

x1	no descr
x2	no descr
x	no descr
sig1	no descr
sig2	no descr
sig	no descr
mu1	no descr
mu2	no descr
mu	no descr
act1	no descr
act2	no descr
act	no descr
compute.evals	no descr
include.mean	no descr
method.compquadform	no descr
acc	no descr
epsabs	no descr
epsrel	no descr
show.warn	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

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.eval = "est2.my.ev3",
  algorithm.mleggm = "glasso_rho0", include.mean = FALSE,
  method.compquadform = "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).
compute.eval	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.
include.mean	Should sample specific means be included in hypothesis? Use include.mean=FALSE (default and recommended) which assumes $\mu_1=\mu_2=0$ and tests the hypothesis $H_0: \Omega_1=\Omega_2$ .
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	Should MLEs be in the output list (default=FALSE)?
...	Additional arguments for screen.meth.

**Details**

Remark:

\* If include.mean=FALSE, then x1 and x2 have mean zero and DiffNet tests the hypothesis  $H_0: \Omega_1 = \Omega_2$ . You might need to center x1 and x2. \* If include.mean=TRUE, then DiffNet tests the hypothesis  $H_0: \mu_1 = \mu_2 \ \& \ \Omega_1 = \Omega_2$  \* 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**

```
##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 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

```

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).
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.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 ( $\mu_1=\mu_2=0$ ). 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.nulldistr	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

```
#####
##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.ivals	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.ivals = "est2.my.ev3.diffregr",
  method.compquadform = "imhof", acc = 1e-04, epsabs = 1e-10,
  epsrel = 1e-10, show.warn = FALSE, n.perm = NULL, ...)
```

**Arguments**

y1	Response vector condition 1.
y2	Response vector condition 2.
x1	Predictor matrix condition 1.
x2	Predictor matrix condition 2.
split1	Samples condition 1 used in screening-step.
split2	Samples condition 2 used in screening-step.
screen.meth	Screening method (default='screen_cvtrunc.lasso').
compute.ivals	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).
...	Other arguments specific to screen.meth.

**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

pval.onesided	"One-sided" p-value.
pval.twosided	"Two-sided" p-value. Ignore all "/*.twosided results.
teststat	2 times Log-likelihood-ratio statistics
weights.null distr	Estimated weights of weighted-sum-of-chi2s.
active	List of active-sets obtained in screening step.
beta	Regression coefficients (MLE) obtained in cleaning-step.

**Author(s)**

n.stadler



**Examples**

```
##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**

```
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))
```

**Arguments**

<code>net.clustering</code>	A network clustering object as returned by <code>het_cv_glasso</code> or <code>mixglasso</code> .
<code>p.corr.thresh</code>	Cutoff for the partial correlations; only edges with absolute partial correlation $>$ <code>p.corr.thresh</code> (in any cluster) will be displayed.
<code>hard.limit</code>	Additional hard limit on the number of edges to display. If <code>p.corr.thresh</code> results in more edges than <code>hard.limit</code> , only <code>hard.limit</code> edges with the highest partial correlation are returned.
<code>display</code>	If TRUE, print the plot to the current output device.
<code>node.names</code>	Names for the nodes in the network.
<code>group.names</code>	Names for the clusters or groups.
<code>dot.size.range</code>	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.corr.thresh=0.5)
```

---

error.bars	<i>Error bars for plotCV</i>
------------	------------------------------

---

**Description**

Error bars for plotCV

**Usage**

```
error.bars(x, upper, lower, width = 0.02, ...)
```

**Arguments**

x	no descr
upper	no descr
lower	no descr
width	no descr
...	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

est2.my.ev2	<i>Weights of sum-w-chi2</i>
-------------	------------------------------

---

**Description**

Compute weights of sum-w-chi2 (2nd order simplification)

**Usage**

```
est2.my.ev2(sig1, sig2, sig, act1, act2, act, include.mean = FALSE)
```

**Arguments**

sig1	no descr
sig2	no descr
sig	no descr
act1	no descr
act2	no descr
act	no descr
include.mean	no descr

**Details**

\*expansion of  $W$  in two directions ("dimf>dimg direction" & "dimf>dimg direction") \*simplified computation of weights is obtained by assuming  $H_0$  and that  $X_u \sim X_v$  holds

**Value**

no descr

**Author(s)**

n.stadler

---

est2.my.ev2.diffregr    *Compute weights of sum-w-chi2 (2nd order simplification)*

---

**Description**

\*expansion of  $W$  in two directions ("dimf>dimg direction" & "dimf>dimg direction") \*simplified computation of weights is obtained by assuming  $H_0$  and that  $X_u \sim X_v$  holds

**Usage**

est2.my.ev2.diffregr(y1, y2, x1, x2, beta1, beta2, beta, act1, act2, act)

**Arguments**

y1	no descr
y2	no descr
x1	no descr
x2	no descr
beta1	no descr
beta2	no descr
beta	no descr
act1	no descr
act2	no descr
act	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

`est2.my.ev3`*Compute weights of sum-of-weighted-chi2s*

---

**Description**

Compute weights of sum-of-weighted-chi2s

**Usage**

```
est2.my.ev3(sig1, sig2, sig, act1, act2, act, include.mean = FALSE)
```

**Arguments**

<code>sig1</code>	MLE (covariance matrix) sample 1
<code>sig2</code>	MLE (covariance matrix) sample 2
<code>sig</code>	Pooled MLE (covariance matrix)
<code>act1</code>	Active-set sample 1
<code>act2</code>	Active-set sample 2
<code>act</code>	Pooled active-set
<code>include.mean</code>	Should the mean be included in the likelihood?

**Details**

\*'2nd order simplification': 1) Factor out  $(1-v_i)^{(d1+d2)}$  "expansion in  $\dim f > \dim g$  direction (old terminology)" 2) Factor out  $(1-\mu)^{d0}$  \*simplified computation of weights is obtained without further invoking H0, or assuming  $X_u \sim X_v$

**Value**

Eigenvalues of M, respectively the weights.

**Author(s)**

n.stadler

---

est2.my.ev3.diffregr *Compute weights of sum-of-weighted-chi2s*

---

### Description

Compute weights of sum-of-weighted-chi2s

### Usage

```
est2.my.ev3.diffregr(y1, y2, x1, x2, beta1, beta2, beta, act1, act2, act)
```

### Arguments

y1	Response vector sample 1.
y2	Response vector sample 2.
x1	Predictor matrix sample 1.
x2	Predictor matrix sample 2.
beta1	MLE (regression coefficients) sample 1.
beta2	MLE (regression coefficients) sample 2.
beta	Pooled MLE (regression coefficients).
act1	Active-set sample 1
act2	Active-set sample 2
act	Pooled active-set

### Details

\*'2nd order simplification': 1) Factor out  $(1-v_i)^{(d1+d2)}$  "expansion in  $\dim f > \dim g$  direction (old terminology)" 2) Factor out  $(1-\mu)^{d0}$  \*simplified computation of weights is obtained without further invoking H0, or assuming  $X_u \sim X_v$

### Value

Eigenvalues of M, respectively the weights.

### Author(s)

n.stadler

---

est2.ww.mat.diffregr *Estimate weights*

---

**Description**

Estimate weights

**Usage**

```
est2.ww.mat.diffregr(y1, y2, x1, x2, beta1, beta2, beta, act1, act2, act)
```

**Arguments**

y1	no descr
y2	no descr
x1	no descr
x2	no descr
beta1	no descr
beta2	no descr
beta	no descr
act1	no descr
act2	no descr
act	no descr

**Details**

estimate W-matrix (using plug-in estimates of Beta-matrix); calculate eigenvalues(W-matrix)

**Value**

no descr

**Author(s)**

n.stadler

---

 est2.ww.mat2

*Weights of sum-w-chi2*


---

**Description**

Compute weights of sum-w-chi2 (1st order simplification)

**Usage**

```
est2.ww.mat2(sig1, sig2, sig, act1, act2, act, include.mean = FALSE)
```

**Arguments**

sig1	no descr
sig2	no descr
sig	no descr
act1	no descr
act2	no descr
act	no descr
include.mean	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

 est2.ww.mat2.diffregr *Estimate weights*


---

**Description**

Estimate weights

**Usage**

```
est2.ww.mat2.diffregr(y1, y2, x1, x2, beta1, beta2, beta, act1, act2, act)
```



**Arguments**

y1	no descr
y2	no descr
x1	no descr
x2	no descr
beta1	no descr
beta2	no descr
beta	no descr
act1	no descr
act2	no descr
act	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

export_network	<i>Export networks as a CSV table.</i>
----------------	--

---

**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.

**Usage**

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

**Arguments**

net.clustering	A network clustering object as returned by <a href="#">screen_cv.glasso</a> or <a href="#">mixglasso</a> .
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.corr.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, Mu=Mu)
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',
  p.corr.thresh=0.25, quote=FALSE)

## End(Not run)
```

---

EXPStep.mix

*Performs EStep*

---

**Description**

Performs EStep

**Usage**

```
EXPStep.mix(logphi, mix.prob)
```

**Arguments**

logphi	no descr
mix.prob	no descr

**Value**

list consisting of

u	responsibilities
LL	loglikelihood

**Author(s)**

n.stadler

---

func.uinit

*Initialization of MixGLasso*

---

**Description**

Initialization of responsibilities

**Usage**

```
func.uinit(x, n.comp, init = "kmeans", my.cl = NULL,
  nstart.kmeans = 1, iter.max.kmeans = 10, modelName.hc = "EII")
```

**Arguments**

x	Observed data
n.comp	Number of mixture components
init	Method used for initialization init='cl.init','r.means','random','kmeans','kmeans.hc','hc'
my.cl	Initial cluster assignments; need to be provided if init='cl.init' (otherwise this param is ignored)
nstart.kmeans	Number of random starts in kmeans; default=1
iter.max.kmeans	Maximal number of iteration in kmeans; default=10
modelName.hc	Model class used in hc; default='EII'

**Value**

a list consisting of

u responsibilities

**Author(s)**

n.stadler

---

generate\_2networks      *Generate sparse invcov with overlap*

---

**Description**

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 uncommon 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

## Specifiy 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      *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  $(1-\text{sparsity}) \cdot p(p-1)$  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)
```

---

getinvcov	<i>Generate an inverse covariance matrix with a given sparsity and dimensionality</i>
-----------	---

---

### Description

Generate an inverse covariance matrix with a given sparsity and dimensionality

### Usage

```
getinvcov(p, s, a.diff = 5, b.diff = 5, magn.diag = 0, emin = 0.1)
```

### Arguments

p	Dimensionality
s	Sparsity
a.diff	binomial parameter
b.diff	binomial parameter
magn.diag	Magnitude
emin	e min

### Value

Inverse covariance matrix Internal function

---

ggmgsa_multisplit	<i>Multi-split GGMGSA (parallelized computation)</i>
-------------------	--

---

### 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).
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, $\text{dim}(pval)=(\text{number of gene-sets})\times(\text{number of splits})$
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, $\text{dim}(\text{teststat})=(\text{number of gene-sets})\times(\text{number of splits})$
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
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
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
# fit.dn <- diffnet_multisplit(x1,x2,b.splits=2,verbose=FALSE)
# fit.dn$medagg.pval

## Identify hubs with 'gene-sets'
gene.names <- paste('G',1:p,sep='')
gsets <- split(gene.names,rep(1:3,each=3))

## Run GGM-GSA
fit.gmggsa <- gmggsa_multisplit(x1,x2,b.splits=2,gsets,gene.names,verbose=FALSE)
summary(fit.gmggsa)
fit.gmggsa$medagg.pval#median aggregated p-values
p.adjust(apply(fit.gmggsa$pval,1,median),method='fdr')#or: first median aggregation,
#second fdr-correction
```

---

ggmgsa\_singlesplit      *Single-split GGMGSA*


---

**Description**

Single-split GGMGSA



**Usage**

```
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

---

glasso.invcor

*Graphical Lasso based on inverse covariance penalty*

---

**Description**

Graphical Lasso based on inverse covariance penalty

**Usage**

```
glasso.invcor(s, rho, penalize.diagonal, term = 10^{ -3 })
```

**Arguments**

s	no descr
rho	no descr
penalize.diagonal	no descr
term	no descr

**Value**

w; wi; iter

**Author(s)**

n.stadler

---

`glasso.invcov`*Graphical Lasso based on inverse correlation penalty*

---

**Description**

Graphical Lasso based on inverse correlation penalty

**Usage**`glasso.invcov(s, rho, penalize.diagonal, term = 10^{ -3 })`**Arguments**

<code>s</code>	no descr
<code>rho</code>	no descr
<code>penalize.diagonal</code>	no descr
<code>term</code>	no descr

**Value**

w; wi; iter

**Author(s)**

n.stadler

---

`glasso.parcor`*Graphical Lasso based on partial correlation penalty*

---

**Description**

Graphical Lasso based on partial correlation penalty

**Usage**`glasso.parcor(s, rho, penalize.diagonal, maxiter = 1000, term = 10^{ -3 }, verbose = FALSE)`

**Arguments**

s	no descr
rho	no descr
penalize.diagonal	no descr
maxiter	no descr
term	no descr
verbose	set to TRUE to print out progress.

**Value**

w; wi; iter

**Author(s)**

n.stadler

---

gsea.highdimT2	<i>GSA based on HighdimT2</i>
----------------	-------------------------------

---

**Description**

GSA based on HighdimT2

**Usage**

```
gsea.highdimT2(x1, x2, gene.sets, gene.names, gs.names = NULL,
  method = "test.sd", method.p.adjust = "fdr")
```

**Arguments**

x1	no descr
x2	no descr
gene.sets	no descr
gene.names	no descr
gs.names	no descr
method	no descr
method.p.adjust	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

`gsea.iriz`*Irizarry approach for gene-set testing*

---

**Description**

Irizarry approach for gene-set testing

**Usage**

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

**Arguments**

<code>x1</code>	Expression matrix (condition 1)
<code>x2</code>	Expression matrix (condition 2)
<code>gene.sets</code>	List of gene-sets
<code>gene.names</code>	Gene names
<code>gs.names</code>	Gene-set names
<code>method.p.adjust</code>	Method for p-value adjustment (default='fdr')
<code>alternative</code>	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

<code>pval.shift</code>	p-values measuring shift
<code>pval.scale</code>	p-values measuring scale
<code>pval.combined</code>	combined p-values (minimum of <code>pval.shift</code> and <code>pval.scale</code> )

**Author(s)**

n.stadler

**Examples**

```

n <- 100
p <- 20
x1 <- matrix(rnorm(n*p),n,p)
x2 <- matrix(rnorm(n*p),n,p)
gene.names <- paste('G',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

```

---

gsea.iriz.scale	<i>Irizarry approach (scale only)</i>
-----------------	---------------------------------------

---

**Description**

Irizarry approach (scale only)

**Usage**

```

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

```

**Arguments**

x1	no descr
x2	no descr
gene.sets	no descr
gene.names	no descr
gs.names	no descr
method.p.adjust	
	no descr
alternative	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

gsea.iriz.shift	<i>Irizarry approach (shift only)</i>
-----------------	---------------------------------------

---

**Description**

Irizarry approach (shift only)

**Usage**

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

**Arguments**

x1	no descr
x2	no descr
gene.sets	no descr
gene.names	no descr
gs.names	no descr
method.p.adjust	
	no descr
alternative	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

gsea.t2cov	<i>GSA using T2cov-test</i>
------------	-----------------------------

---

**Description**

GSA using T2cov-test

**Usage**

```
gsea.t2cov(x1, x2, gene.sets, gene.names, gs.names = NULL,
           method = "t2cov.lr", method.p.adjust = "fdr")
```

**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	method for testing equality of covariance matrices
method.p.adjust	method for p-value adjustment (default: 'fdr')

**Value**

list of results

**Author(s)**

n.stadler

---

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.glasso.

**Details**

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.

**Value**

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).

**Examples**

```
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)
```

---

hugepath

*Graphical Lasso path with huge package*


---

**Description**

Graphical Lasso path with huge package

**Usage**

```
hugepath(s, rholist, penalize.diagonal = NULL, trace = NULL)
```

**Arguments**

s	no descr
rholist	no descr
penalize.diagonal	no descr
trace	no descr



**Value**

no descr

**Author(s)**

n.stadler

---

inf.mat

*Information Matrix of Gaussian Graphical Model*

---

**Description**

Compute Information Matrix of Gaussian Graphical Model

**Usage**

```
inf.mat(Sig, include.mean = FALSE)
```

**Arguments**

Sig                    Sig=solve(SigInv) true covariance matrix under H0

include.mean        no descr

**Details**

computes  $E_0[s(Y;\Omega)s(Y;\Omega)']$  where  $s(Y;\Omega)=(d/d\Omega) \text{LogLik}$

**Value**

no descr

**Author(s)**

n.stadler

---

invcov2parcor	<i>Convert inverse covariance to partial correlation</i>
---------------	--

---

**Description**

Convert inverse covariance to partial correlation

**Usage**

```
invcov2parcor(invcov)
```

**Arguments**

invcov	Inverse covariance matrix
--------	---------------------------

**Value**

The partial correlation matrix.

**Examples**

```
inv.cov = generate_inv_cov(p=25)
p.corr = invcov2parcor(inv.cov)
```

---

invcov2parcor_array	<i>Convert inverse covariance to partial correlation for several inverse covariance matrices collected in an array.</i>
---------------------	---

---

**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)
```

---

lambda.max

*Lambdamax*


---

**Description**

Lambdamax

**Usage**

```
lambda.max(x)
```

**Arguments**

x                   no descr

**Value**

no descr

**Author(s)**

n.stadler

---

lambdagrid\_lin

*Lambda-grid*


---

**Description**

Lambda-grid (linear scale)

**Usage**

```
lambdagrid_lin(lambda.min, lambda.max, nr.gridpoints)
```

**Arguments**

lambda.min       no descr  
lambda.max       no descr  
nr.gridpoints    no descr

**Value**

no descr

**Author(s)**

n.stadler

---

lambdagrid_mult	<i>Lambda-grid</i>
-----------------	--------------------

---

**Description**

Lambda-grid (log scale)

**Usage**

```
lambdagrid_mult(lambda.min, lambda.max, nr.gridpoints)
```

**Arguments**

lambda.min	no descr
lambda.max	no descr
nr.gridpoints	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

loglik_mix	<i>Log-likelihood for mixture model</i>
------------	---

---

**Description**

Log-likelihood for mixture model

**Usage**

```
loglik_mix(x, mix.prob, Mu, Sig)
```

**Arguments**

x	no descr
mix.prob	no descr
Mu	no descr
Sig	no descr

**Value**

log-likelihood

**Author(s)**

n.stadler

---

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**

```
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
```

---

logratio.diffregr      *Log-likelihood ratio statistics for Differential Regression.*

---

**Description**

Log-likelihood ratio statistics for Differential Regression.

**Usage**

```
logratio.diffregr(y1, y2, y, xx1, xx2, xx, beta1, beta2, beta)
```

**Arguments**

y1	Response vector condition 1.
y2	Response vector condition 2.
y	Pooled response vector.
xx1	Predictor matrix condition 1.
xx2	Predictor matrix condition 2.
xx	Pooled predictor matrix
beta1	Regression coefficients condition 1.
beta2	Regression coefficients condition 2.
beta	Pooled regression coefficients.

**Value**

2 times log-likelihood ratio statistics.

**Author(s)**

n.stadler

---

make_grid	<i>Make grid</i>
-----------	------------------

---

**Description**

Make grid

**Usage**

```
make_grid(lambda.min, lambda.max, nr.gridpoints,  
          method = "lambdagrid_mult")
```

**Arguments**

lambda.min	no descr
lambda.max	no descr
nr.gridpoints	no descr
method	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

mcov	<i>Compute covariance matrix</i>
------	----------------------------------

---

**Description**

Compute covariance matrix

**Usage**

```
mcov(x, include.mean, covMethod = "ML")
```

**Arguments**

x	no descr
include.mean	no descr
covMethod	no descr

**Value**

no descr

**Author(s)**

n.stadler

mixglasso

*mixglasso***Description**

mixglasso

**Usage**

```

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.invcov to penalise the inverse covariance matrix (this corresponds to classical graphical lasso), glasso.invcor 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
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

```
#####
##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)

```

---

mixglasso\_init

*mixglasso\_init*


---

### Description

`mixglasso_init` (initialization and lambda set by user)

**Usage**

```

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)

```

**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.invcov
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

---

 mixglasso\_ncomp\_fixed *mixglasso\_ncomp\_fixed*


---

**Description**

mixglasso\_ncomp\_fixed

**Usage**

```

mixglasso_ncomp_fixed(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, ...)

```

**Arguments**

x	Input data matrix
n.comp	Number of mixture components
lambda	Regularization parameter. Default=sqrt(2*n*log(p))/2
pen	Determines form of penalty: glasso.parcor (default), glasso.invcov, glasso.invcor
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
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
...	Other arguments. See mixglasso_init

**Details**

This function runs mixglasso

**Value**

see return mixglasso\_init. list consisting of

mix.prob	
Mu	
Sig	
SigInv	
iter	
loglik	
bic	-loglik+log(n)*DF/2
mmdl	-loglik+penmmdl/2
u	responsibilities
comp	component assignments
compsize	size of components
pi.comps	
warn	warnings during optimization

**Author(s)**

n.stadler

---

mle.ggm

*MLE in GGM*

---

**Description**

MLE in GGM

**Usage**

```
mle.ggm(x, wi, algorithm = "glasso_rho0", rho = NULL, include.mean)
```

**Arguments**

x	no descr
wi	no descr
algorithm	no descr
rho	no descr
include.mean	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

MStepGlasso
*MStep of MixGLasso***Description**

MStep of MixGLasso

**Usage**

```
MStepGlasso(x, chromosome = NULL, u, v = NULL, lambda, gamma, pen,
  penalize.diagonal, equal.prob.trans = NULL, term, model = "hmm")
```

**Arguments**

x	no descr
chromosome	no descr
u	no descr
v	no descr
lambda	no descr
gamma	no descr
pen	no descr
penalize.diagonal	no descr
equal.prob.trans	no descr
term	no descr
model	no descr

**Value**

list consisting of mix.prob, Mu, Sig, SigInv

**Author(s)**

n.stadler

---

my.ev2.diffregr      *Computation eigenvalues*

---

**Description**

Computation eigenvalues

**Usage**

```
my.ev2.diffregr(Sig, act, act1, act2)
```

**Arguments**

Sig	no descr
act	no descr
act1	no descr
act2	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

my.p.adjust      *P-value adjustment*

---

**Description**

P-value adjustment

**Usage**

```
my.p.adjust(p, method = "fdr")
```

**Arguments**

p	Vector of p-values.
method	Method for p-value adjustment (default='fdr').

**Value**

Vector of adjusted p-values.

**Author(s)**

n.stadler

---

`my.ttest`*T-test*

---

**Description**

T-test (equal variances)

**Usage**`my.ttest(x1, x2)`**Arguments**

x1            no descr

x2            no descr

**Value**

no descr

**Author(s)**

n.stadler

---

`my.ttest2`*T-test*

---

**Description**

T-test (unequal variances)

**Usage**`my.ttest2(x1, x2)`**Arguments**

x1            no descr

x2            no descr

**Value**

no descr



**Author(s)**

n.stadler

---

mytrunc.method      *Additional thresholding*

---

**Description**

Additional thresholding

**Usage**

```
mytrunc.method(n, wi, method = "linear.growth", trunc.k = 5)
```

**Arguments**

n	no descr
wi	no descr
method	no descr
trunc.k	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

perm.diffregr\_pval      *Computation "split-perm" p-value.*

---

**Description**

Computation "split-perm" p-value.

**Usage**

```
perm.diffregr_pval(y1, y2, x1, x2, act1, act2, act, n.perm)
```

**Arguments**

y1	Response vector condition 1.
y2	Response vector condition 2.
x1	Predictor matrix condition 1.
x2	Predictor matrix condition 2.
act1	Active-set condition 1.
act2	Active-set condition 2.
act	Pooled active-set.
n.perm	Number of permutations.

**Value**

Permutation based p-value.

**Author(s)**

n.stadler

---

perm.diffregr\_teststat

*Auxiliary function for computation of "split-perm" p-value.*

---

**Description**

Auxiliary function for computation of "split-perm" p-value.

**Usage**

```
perm.diffregr_teststat(y1, y2, y12, x1, x2, x12)
```

**Arguments**

y1	Response vector condition 1.
y2	Response vector condition 2.
y12	Pooled response vector.
x1	Predictor matrix condition 1.
x2	Predictor matrix condition 2.
x12	Pooled predictor matrix

**Value**

Test statistic (log-likelihood-ratio statistic).

**Author(s)**

n.stadler

---

plot.diffnet	<i>Plotting function for object of class 'diffnet'</i>
--------------	--

---

**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

---

plot.diffregr	<i>Plotting function for object of class 'diffregr'</i>
---------------	---

---

**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.gmgmsa`*Plotting function for object of class 'ggmgmsa'*

---

**Description**

Plotting function for object of class 'ggmgmsa'

**Usage**

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

**Arguments**

<code>x</code>	object of class 'ggmgmsa'
<code>...</code>	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.corr.thresh = 0.2, print.pdf = FALSE, pdf.filename = "networks",  
  ...)
```

**Arguments**

x	A network clustering object as returned by <code>screen_cv.glasso</code> or <code>mixglasso</code> .
node.names	Names for the nodes in the network. If NULL, names from <code>net.clustering</code> will be used.
group.names	Names for the clusters or groups. If NULL, names from <code>net.clustering</code> will be used (by default these are integers 1:numClusters).
p.corr.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.
pdf.filename	If <code>print.pdf</code> is TRUE, specifies the file name of the output PDF file.
...	Further arguments

**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.

---

plotCV	<i>plotCV</i>
--------	---------------

---

**Description**

plotCV

**Usage**

```
plotCV(lambda, cv, cv.error, se = TRUE, type = "b", ...)
```

**Arguments**

lambda	no descr
cv	no descr
cv.error	no descr
se	no descr
type	no descr
...	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

plot\_2networks      *Plot two networks (GGMs)*


---

**Description**

Plot two networks (GGMs)

**Usage**

```
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**

```
n <- 70
p <- 30

## Specifiy 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)
```

---

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

---

**Description**

Print function for object of class 'nethetsummary'

**Usage**

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

**Arguments**

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

**Value**

Function does not return anything.

**Author(s)**

frankd

---

q.matrix.diffregr     *Computation Q matrix*

---

**Description**

Computation Q matrix

**Usage**

```
q.matrix.diffregr(Sig, a, b, s)
```

**Arguments**

Sig	no descr
a	no descr
b	no descr
s	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

`q.matrix.diffregr3`     *Computation Q matrix*

---

**Description**

Computation Q matrix

**Usage**

```
q.matrix.diffregr3(beta.a, beta.b, beta, sig.a, sig.b, sig, Sig, act.a,  
act.b, ss)
```

**Arguments**

beta.a	no descr
beta.b	no descr
beta	no descr
sig.a	no descr
sig.b	no descr
sig	no descr
Sig	no descr
act.a	no descr
act.b	no descr
ss	no descr

**Value**

no descr

**Author(s)**

n.stadler



---

q.matrix.diffregr4      *Computation Q matrix*

---

**Description**

Computation Q matrix

**Usage**

```
q.matrix.diffregr4(b.mat, act.a, act.b, ss)
```

**Arguments**

b.mat	no descr
act.a	no descr
act.b	no descr
ss	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

q.matrix3      *Compute Q-matrix*

---

**Description**

Compute Q-matrix

**Usage**

```
q.matrix3(sig, sig.a, sig.b, act.a, act.b, ss)
```

**Arguments**

sig	no descr
sig.a	no descr
sig.b	no descr
act.a	no descr
act.b	no descr
ss	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

q.matrix4

*q.matrix4*

---

**Description**

q.matrix4

**Usage**

q.matrix4(b.mat, act.a, act.b, ss)

**Arguments**

b.mat           no descr

act.a           no descr

act.b           no descr

ss               no descr

**Value**

no descr

**Author(s)**

n.stadler

---

scatter_plot	<i>Create a scatterplot showing correlation between specific nodes in the network for each pre-specified group.</i>
--------------	---

---

### Description

This function takes the output of `het_cv_lasso` 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

```
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

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

### 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]]

# 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)

```

---

screen\_aic.glasso

*AIC-tuned glasso with additional thresholding*


---

## Description

AIC-tuned glasso with additional thresholding

## Usage

```

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 ( $\text{rho.opt}=2*\text{la.opt}/n$ ). The variables wi and wi.orig are matrices of size  $\text{dim.samples}$  by  $\text{dim.samples}$  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_aic.glasso(x,length.lambda=5)$wi
```

---

screen\_bic.glasso       *BIC-tuned glasso with additional thresholding*

---

**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  $\text{num.samples}$  by  $\text{dim.samples}$  matrix.  
 include.mean       Include mean in likelihood. TRUE / FALSE (default).  
 length.lambda      Length of lambda path to consider (default=20).  
 lambdamin.ratio    Ratio  $\text{lambda.min}/\text{lambda.max}$ .  
 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 ( $\text{rho.opt}=2*\text{la.opt}/n$ ). The variables wi and wi.orig are matrices of size  $\text{dim.samples}$  by  $\text{dim.samples}$  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
```

---

screen\_cv.glasso      *Cross-validated glasso with additional thresholding*

---

**Description**

Cross-validated glasso with additional thresholding

**Usage**

```
screen_cv.glasso(x, include.mean = FALSE, folds = min(10, dim(x)[1]),
  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, 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).
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.
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 ( $\text{rho.opt}=2*\text{la.opt}/n$ ). 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)
wihat=screen_cv.glasso(x,folds=2)$wi
```

---

screen\_cv1se.lasso      *Cross-validated Lasso screening (lambda.lse-rule)*

---

**Description**

Cross-validated Lasso screening (lambda.lse-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	<i>Cross-validated Lasso screening and upper bound on number of predictors.</i>
--------------------	---

---

**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,

**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))
```



---

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\_cvsqrt.lasso      *Cross-validated Lasso screening and sqrt-truncation.*

---

**Description**

Cross-validated Lasso screening and sqrt-truncation.

**Usage**

```
screen_cvsqrt.lasso(x, y)
```

**Arguments**

x	Predictor matrix.
y	Response vector.

**Details**

Computes Lasso coefficients (cross-validation optimal lambda). Truncates smallest coefficients to zero, such that there are no more than  $\sqrt{n}$  non-zero coefficients.

**Value**

Active-set.

**Author(s)**

n.stadler

**Examples**

```
screen_cvsqrt.lasso(matrix(rnorm(5000), 50, 100), rnorm(50))
```

---

screen\_cvtrunc.lasso *Cross-validated Lasso screening and additional truncation.*

---

**Description**

Cross-validated Lasso screening and additional truncation.

**Usage**

```
screen_cvtrunc.lasso(x, y, k.trunc = 5)
```

**Arguments**

x	Predictor matrix.
y	Response vector.
k.trunc	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_full	<i>Screen_full</i>
-------------	--------------------

---

**Description**

Screen\_full

**Usage**

```
screen_full(x, include.mean = NULL, length.lambda = NULL,
            trunc.method = NULL, trunc.k = NULL)
```

**Arguments**

x	no descr
include.mean	no descr
length.lambda	no descr
trunc.method	no descr
trunc.k	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

screen_shrink	<i>Shrinkage approach for estimating Gaussian graphical model</i>
---------------	---

---

**Description**

Shrinkage approach for estimating Gaussian graphical model

**Usage**

```
screen_shrink(x, include.mean = NULL, trunc.method = "linear.growth",
              trunc.k = 5)
```

**Arguments**

x	The input data. Needs to be a num.samples by dim.samples matrix.
include.mean	Include mean in likelihood. TRUE / FALSE (default).
trunc.method	None / linear.growth (default) / sqrt.growth
trunc.k	truncation constant, number of samples per predictor (default=5)

**Value**

Returns a list with named elements 'rho.opt', 'wi', 'wi.orig'. Variable rho.opt=NULL (no tuning parameter involved). 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

---

shapiro_screen	<i>Filter "non-normal" genes</i>
----------------	----------------------------------

---

**Description**

Filter "non-normal" genes

**Usage**

```
shapiro_screen(x1, x2, sign.level = 0.001)
```

**Arguments**

x1	expression matrix (condition 1)
x2	expression matrix (condition 2)
sign.level	sign.level in Shapiro-Wilk tests (default: sign.level=0.001)

**Details**

Discarding genes which have Shapiro-Wilk p-value (corrected for multiplicity) smaller than sign.level in either of the two conditions. We used sign.level=0.001 in the GGMGSA paper.

**Value**

list consisting of

x1.filt	expression matrix (condition 1) after filtering
x2.filt	expression matrix (condition 2) after filtering

**Author(s)**

n.stadler

---

sim_mix	<i>Simulate from mixture model.</i>
---------	-------------------------------------

---

**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**

```
n.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)
```

---

sim\_mix\_networks      *sim\_mix\_networks*

---

### Description

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

### Usage

```
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 <a href="#">generate_inv_cov</a> .
...	Further arguments passed to <a href="#">sim_mix</a> .

### Details

This function generates n.comp mean vectors from a standard Gaussian and n.comp covariance matrices, with at most  $(1-\text{sparsity}) * p(p-1)/2$  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

```
# Generate dataset with 100 samples of dimensionality 30, and 4 components
test.data = sim_mix_networks(n=100, p=30, n.comp=4)
```

---

sparse_conc	<i>Generates sparse inverse covariance matrices</i>
-------------	---

---

**Description**

Generates sparse inverse covariance matrices

**Usage**

```
sparse_conc(p, K, s, s.common, magn.nz = 0.5, scale.parcor = TRUE)
```

**Arguments**

p	Dimensionality of inverse covariance matrix
K	Number of inverse covariance matrices
s	Number of non-zero entries per inverse covariance matrix
s.common	Number of non-zero entries shared across different inverse covariance matrices
magn.nz	Magnitude of non-zero elements
scale.parcor	Should SigInv be scaled to have diagonal equal one, <code>siginv=parcor</code> ?

**Value**

SigInv: list of inverse covariance matrices

**Author(s)**

n.stadler

---

summary.diffnet	<i>Summary function for object of class 'diffnet'</i>
-----------------	---

---

**Description**

Summary function for object of class 'diffnet'

**Usage**

```
## 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**

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

**Arguments**

object	object of class 'diffregr'
...	Other arguments

**Value**

aggregated p-values

**Author(s)**

nicolas

---

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

---

**Description**

Summary function for object of class 'gmgmsa'

**Usage**

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



**Arguments**

object            object of class 'ggmsa'  
...                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**

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

**Arguments**

object            object of class 'nethetclustering'  
...                Other arguments

**Value**

Network statistics (a 'nethetsummary' object)

**Author(s)**

frankd

---

sumoffdiag	<i>Sum of non-diag elements of a matrix</i>
------------	---

---

**Description**

Sum of non-diag elements of a matrix

**Usage**

sumoffdiag(m)

**Arguments**

m	no descr
---	----------

**Value**

Sum of non-diag elements

**Author(s)**

n.stadler

---

symmkldist	<i>Compute symmetric kull-back leibler distance</i>
------------	---

---

**Description**

Compute symmetric kull-back leibler distance

**Usage**

symmkldist(mu1, mu2, sig1, sig2)

**Arguments**

mu1	no descr
mu2	no descr
sig1	no descr
sig2	no descr

**Value**

symmetric kull-back leibler distance

**Author(s)**

n.stadler

---

t2cov.lr	<i>Classical likelihood-ratio test</i>
----------	--

---

**Description**

Classical likelihood-ratio test (equality of covariance matrices)

**Usage**

```
t2cov.lr(x1, x2, include.mean = FALSE)
```

**Arguments**

x1	no descr
x2	no descr
include.mean	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

t2diagcov.lr	<i>Diagonal-restricted likelihood-ratio test</i>
--------------	--

---

**Description**

Diagonal-restricted likelihood-ratio test

**Usage**

```
t2diagcov.lr(x1, x2, include.mean = FALSE)
```

**Arguments**

x1	no descr
x2	no descr
include.mean	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

test.sd*High-Dim Two-Sample Test (Srivastava, 2006)*

---

**Description**

High-Dim Two-Sample Test (Srivastava, 2006)

**Usage**

test.sd(x1, x2)

**Arguments**

x1           no descr

x2           no descr

**Value**

no descr

**Author(s)**

n.stadler

---

test.t2*HotellingsT2*

---

**Description**

HotellingsT2

**Usage**

test.t2(x1, x2)

**Arguments**

x1           no descr

x2           no descr

**Value**

no descr

**Author(s)**

n.stadler

---

tr                                      *Compute trace of matrix*

---

**Description**

Compute trace of matrix

**Usage**

tr(m)

**Arguments**

m                                      no descr

**Value**

trace of matrix

**Author(s)**

n.stadler

---

twosample\_single\_regr    *old single-split function for diffregr*

---

**Description**

Old single-split function for diffregr

**Usage**

```
twosample_single_regr(y1, y2, x1, x2, n.screen.pop1 = 100,  
  n.screen.pop2 = 100, screen.meth = "screen_cvmin.lasso",  
  compute.evals = "est2.my.ev3.diffregr")
```

**Arguments**

y1	no descr
y2	no descr
x1	no descr
x2	no descr
n.screen.pop1	no descr
n.screen.pop2	no descr
screen.meth	no descr
compute.eval	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

w.kldist

*Distance between comps based on symm. kl-distance*

---

**Description**

Distance between comps based on symm. kl-distance

**Usage**

w.kldist(Mu, Sig)

**Arguments**

Mu	no descr
Sig	no descr

**Value**

list consisting of

- comp.kldist
- min.comp.kldist

**Author(s)**

n.stadler

---

ww.mat                      *Weight-matrix and eigenvalues*

---

**Description**

Calculates weight-matrix and eigenvalues

**Usage**

```
ww.mat(imat, act, act1, act2)
```

**Arguments**

imat	no descr
act	I_uv
act1	I_u
act2	I_v

**Details**

calculation based on true information matrix

**Value**

no descr

**Author(s)**

n.stadler

---

ww.mat.diffregr              *Computation M matrix and eigenvalues*

---

**Description**

Computation M matrix and eigenvalues

**Usage**

```
ww.mat.diffregr(Sig, act, act1, act2)
```

**Arguments**

Sig	no descr
act	no descr
act1	no descr
act2	no descr

**Value**

no descr

**Author(s)**

n.stadler

---

ww.mat2

*Calculates eigenvalues of weight-matrix (using 1st order simplification)*

---

**Description**

Calculates eigenvalues of weight-matrix (using 1st order simplification)

**Usage**

```
ww.mat2(imat, act, act1, act2)
```

**Arguments**

imat	no descr
act	I_uv
act1	I_u
act2	I_v

**Details**

calculation based on true information matrix

**Value**

no descr

**Author(s)**

n.stadler



---

ww.mat2.diffregr      *Computation M matrix and eigenvalues*

---

**Description**

Computation M matrix and eigenvalues

**Usage**

ww.mat2.diffregr(Sig, act, act1, act2)

**Arguments**

Sig	no descr
act	no descr
act1	no descr
act2	no descr

**Value**

no descr

**Author(s)**

n.stadler

# Index

- \* **Removed**
  - screen\_shrink, 83
- \* **examples**
  - screen\_shrink, 83
- \* **export**
  - screen\_shrink, 83
- \* **fixed.**
  - screen\_shrink, 83
- \* **internal**
  - agg.pval, 5
  - agg.score.iriz.scale, 5
  - agg.score.iriz.shift, 6
  - aic.glasso, 7
  - beta.mat, 8
  - beta.mat.diffregr, 8
  - bic.glasso, 9
  - buildDotPlotDataFrame, 10
  - cv.fold, 12
  - cv.glasso, 13
  - diffnet\_pval, 16
  - error.bars, 27
  - est2.my.ev2, 27
  - est2.my.ev2.diffregr, 28
  - est2.my.ev3, 29
  - est2.my.ev3.diffregr, 30
  - est2.ww.mat.diffregr, 31
  - est2.ww.mat2, 32
  - est2.ww.mat2.diffregr, 32
  - EXPStep.mix, 34
  - func.uinit, 35
  - getinvcov, 38
  - glasso.invcov, 41
  - glasso.invcov, 42
  - glasso.parcov, 42
  - gsea.highdimT2, 43
  - gsea.iriz.scale, 45
  - gsea.iriz.shift, 46
  - gsea.t2cov, 46
  - hugepath, 48
  - inf.mat, 49
  - lambda.max, 51
  - lambdagrid\_lin, 51
  - lambdagrid\_mult, 52
  - loglik\_mix, 52
  - logratio.diffregr, 54
  - make\_grid, 55
  - mcov, 55
  - mixglasso\_ncomp\_fixed, 60
  - mle.ggm, 61
  - MStepGlasso, 62
  - my.ev2.diffregr, 63
  - my.p.adjust, 63
  - my.ttest, 64
  - my.ttest2, 64
  - mytrunc.method, 65
  - perm.diffregr\_pval, 65
  - perm.diffregr\_teststat, 66
  - plotCV, 69
  - q.matrix.diffregr, 71
  - q.matrix.diffregr3, 72
  - q.matrix.diffregr4, 73
  - q.matrix3, 73
  - q.matrix4, 74
  - screen\_full, 83
  - screen\_shrink, 83
  - shapiro\_screen, 84
  - sparse\_conc, 87
  - sumoffdiag, 90
  - symmkldist, 90
  - t2cov.lr, 91
  - t2diagcov.lr, 91
  - test.sd, 92
  - test.t2, 92
  - tr, 93
  - twosample\_single\_regr, 93
  - w.kldist, 94
  - ww.mat, 95
  - ww.mat.diffregr, 95

- ww.mat2, 96
  - ww.mat2.diffregr, 97
  - \* **is**
    - screen\_shrink, 83
  - \* **n=50**
    - screen\_shrink, 83
  - \* **p=5**
    - screen\_shrink, 83
  - \* **package**
    - screen\_shrink, 83
  - \* **parcor**
    - screen\_shrink, 83
  - \* **until**
    - screen\_shrink, 83
  - \* **wihat=screen\_shrink(x)\$wi**
    - screen\_shrink, 83
  - \* **x=matrix(rnorm(n\*p),n,p)**
    - screen\_shrink, 83
- agg.pval, 5
- agg.score.iriz.scale, 5
- agg.score.iriz.shift, 6
- aggpval, 6
- aic.glasso, 7
- beta.mat, 8
- beta.mat.diffregr, 8
- bic.glasso, 9
- buildDotPlotDataFrame, 10
- bwprun\_mixglasso, 10
- cv.fold, 12
- cv.glasso, 13
- diffnet\_multisplit, 14
- diffnet\_pval, 16
- diffnet\_singlesplit, 18
- diffregr\_multisplit, 20
- diffregr\_pval, 22
- diffregr\_singlesplit, 23
- dot\_plot, 25
- error.bars, 27
- est2.my.ev2, 27
- est2.my.ev2.diffregr, 28
- est2.my.ev3, 29
- est2.my.ev3.diffregr, 30
- est2.ww.mat.diffregr, 31
- est2.ww.mat2, 32
- est2.ww.mat2.diffregr, 32
- export\_network, 33
- EXPStep.mix, 34
- func.uinit, 35
- generate\_2networks, 36
- generate\_inv\_cov, 37, 86
- getinvcov, 38
- ggmgsa\_multisplit, 38
- ggmgsa\_singlesplit, 40
- glasso.invcov, 41
- glasso.invcov, 42
- glasso.parcor, 42
- gsea.highdimT2, 43
- gsea.iriz, 44
- gsea.iriz.scale, 45
- gsea.iriz.shift, 46
- gsea.t2cov, 46
- het\_cv\_glasso, 25, 26, 33, 47, 75
- hugepath, 48
- inf.mat, 49
- invcov2parcor, 50
- invcov2parcor\_array, 50
- lambda.max, 51
- lambdagrid\_lin, 51
- lambdagrid\_mult, 52
- loglik\_mix, 52
- logratio, 53
- logratio.diffregr, 54
- make\_grid, 55
- mcov, 55
- mixglasso, 25, 26, 33, 56, 68, 69, 75
- mixglasso\_init, 58
- mixglasso\_ncomp\_fixed, 60
- mle.ggm, 61
- MStepGlasso, 62
- my.ev2.diffregr, 63
- my.p.adjust, 63
- my.ttest, 64
- my.ttest2, 64
- mytrunc.method, 65
- NetHet-package, 4
- perm.diffregr\_pval, 65

perm.diffregr\_teststat, 66  
plot.diffnet, 67  
plot.diffregr, 67  
plot.gmgsa, 68  
plot.nethetclustering, 68  
plot\_2networks, 70  
plotCV, 69  
print.nethetsummary, 71  
  
q.matrix.diffregr, 71  
q.matrix.diffregr3, 72  
q.matrix.diffregr4, 73  
q.matrix3, 73  
q.matrix4, 74  
  
scatter\_plot, 75  
screen\_aic.glasso, 76  
screen\_bic.glasso, 77  
screen\_cv.glasso, 33, 68, 69, 78  
screen\_cv1se.lasso, 79  
screen\_cvfix.lasso, 80  
screen\_cvmin.lasso, 81  
screen\_cvsqrt.lasso, 81  
screen\_cvtrunc.lasso, 82  
screen\_full, 83  
screen\_shrink, 83  
shapiro\_screen, 84  
sim\_mix, 85, 86  
sim\_mix\_networks, 86  
sparse\_conc, 87  
summary.diffnet, 87  
summary.diffregr, 88  
summary.gmgsa, 88  
summary.nethetclustering, 89  
sumoffdiag, 90  
symmklldist, 90  
  
t2cov.lr, 91  
t2diagcov.lr, 91  
test.sd, 92  
test.t2, 92  
tr, 93  
twosample\_single\_regr, 93  
  
w.kldist, 94  
write.csv, 34  
ww.mat, 95  
ww.mat.diffregr, 95  
ww.mat2, 96  
ww.mat2.diffregr, 97