Package 'fssemR'

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Title Fused Sparse Structural Equation Models to Jointly Infer Gene Regulatory Network

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Description An optimizer of Fused-Sparse Structural Equation Models, which is the state of the art jointly fused sparse maximum likelihood function for structural equation models proposed by Xin Zhou and Xiaodong Cai (2018 <doi:10.1101/466623>).

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Encoding UTF-8

Depends methods

Imports Rcpp, Matrix, stats, igraph, mvtnorm, qtl, stringr, glmnet, MASS, qpdf

Suggests plotly, knitr, rmarkdown, network, ggnetwork

LinkingTo Rcpp, RcppEigen

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NeedsCompilation yes

Repository CRAN

VignetteBuilder knitr

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Contents

`cv.multiFSSEMiPALM` *cv.multiFSSEMiPALM*

Description

cv.multiFSSEMiPALM

Usage

```
cv.multiFSSEMiPALM(
  Xs,
  Ys,
  Bs,
  Fs,
  Sk,
  sigma2,
  nlambda = 20,
  nrho = 20,
  nfold = 5,
  p,
  q,
  wt = TRUE,
  plot = FALSE
)
```

Arguments

Xs	eQTL matrices
Ys	Gene expression matrices
Bs	initialized GRN-matrices
Fs	initialized eQTL effect matrices
Sk	eQTL index of genes
sigma2	initialized noise variance
nlambda	number of hyper-parameter of lasso term in CV
nrho	number of hyper-parameter of fused-lasso term in CV
nfold	CVfold number. Default 5/10
p	number of genes
q	number of eQTLs
wt	use adaptive lasso or not. Default TRUE.
plot	plot contour of cvmean or not. Default FALSE.

Value

list of cross-validation result

cv.multiFSSEMiPALM2 *cv.multiFSSEMiPALM2*

Description

cv.multiFSSEMiPALM2

Usage

```
cv.multiFSSEMiPALM2(
  Xs,
  Ys,
  Bs,
  Fs,
  Sk,
  sigma2,
  nlambda = 20,
  nrho = 20,
  nfold = 5,
  p,
  q,
  wt = TRUE,
  plot = FALSE
)
```

Arguments

Xs	eQTL matrices
Ys	Gene expression matrices
Bs	initialized GRN-matrices
Fs	initialized eQTL effect matrices
Sk	eQTL index of genes
sigma2	initialized noise variance
nlambda	number of hyper-parameter of lasso term in CV
nrho	number of hyper-parameter of fused-lasso term in CV
nfold	CVfold number. Default 5/10
p	number of genes
q	number of eQTLs
wt	use adaptive lasso or not. Default TRUE.
plot	plot contour of cvmean or not. Default FALSE.

Value

list of cross-validation result

cv.multiNFSSEMiPALM2 *cv.multiNFSSEMiPALM2*

Description

cv.multiNFSSEMiPALM2

Usage

```
cv.multiNFSSEMiPALM2(
  Xs,
  Ys,
  Bs,
  Fs,
  Sk,
  sigma2,
  nlambda = 20,
  nrho = 20,
  nfold = 5,
  p,
  q,
  wt = TRUE,
  plot = FALSE
)
```

Arguments

Xs	eQTL matrices
Ys	Gene expression matrices
Bs	initialized GRN-matrices
Fs	initialized eQTL effect matrices
Sk	eQTL index of genes
sigma2	initialized noise variance
nlambda	number of hyper-parameter of lasso term in CV
nrho	number of hyper-parameter of fused-lasso term in CV
nfold	CVfold number. Default 5/10
p	number of genes
q	number of eQTLs
wt	use adaptive lasso or not. Default TRUE.
plot	plot contour of cvmean or not. Default FALSE.

Value

list of cross-validation result for NFSSEM

cv.multiRegression *cv.multiRegression*

Description

cv.multiRegression

Usage

```
cv.multiRegression(Xs, Ys, Sk, ngamma = 20, nfold = 5, n, p, k)
```

Arguments

Xs	eQTL matrices
Ys	Gene expression matrices
Sk	eQTL index of genes
ngamma	number of hyper-parameter in CV
nfold	CVfold number. Default 5/10
n	number of observations
p	number of genes
k	number of eQTLs

Value

gamma_min optimal gamma to minimize cross-validation error

cwiseGradient4FSSEM *cwiseGradient4FSSEM*

Description

function generator function

Usage

```
cwiseGradient4FSSEM(n, c, Y, R, Y2norm, sigma2)
```

Arguments

n	number of observations
c	cofactor vector
Y	Matrix of gene expression
R	Residual matrix
Y2norm	Column of YtY
sigma2	noise variance

Value

function whose argument is column vector bi

FDR *FDR*

Description

False discovery rate for network prediction

Usage

```
FDR(X, B, PREC = 0)
```

Arguments

X	list of predicted network matrices
B	list of true network matrices
PREC	precision threshold for FDR test. Default 0.

---

flinvB *flinvB*

Description

inversed difference of two B matrices. For adaptive fused lasso penalty

Usage

```
flinvB(Bs)
```

Arguments

Bs	list of network matrices

Value

inversed difference matrices

floneB *floneB*

Description

if you do not want adaptive fused lasso penalty, floneB replace flinvB

Usage

```
floneB(Bs)
```

Arguments

Bs	list of network matrices

Value

matrix whose entries are all 1

---

fssemR *Solving Sparse Structural Equation Model*

Description

An optimizer of Fused-Sparse Structural Equation Models, which is the state of the art jointly fused sparse maximum likelihood function for structural equation models proposed by Xin Zhou and Xiaodong Cai (2018 <doi:10.1101/466623>)

Author(s)

Xin Zhou <<xxz220@miami.edu>>

Examples

```
seed = as.numeric(Sys.time())
N = 100                                          # sample size
Ng = 5                                           # gene number
Nk = 5 * 3                                       # eQTL number
Ns = 1                                           # sparse ratio
sigma2 = 0.01                                    # sigma2
set.seed(seed)
library(fssemR)
data = randomFSSEMdata(n = N, p = Ng, k = Nk, sparse = Ns, df = 0.3, sigma2 = sigma2,
                       u = 5, type = "DG", nhub = 1, dag = TRUE)
gamma = cv.multiRegression(data$Data$X, data$Data$Y, data$Data$Sk, ngamma = 20, nfold = 5,
                           N, Ng, Nk)
fit   = multiRegression(data$Data$X, data$Data$Y, data$Data$Sk, gamma, N, Ng, Nk,
```

```
                      trans = FALSE)
Xs    = data$Data$X
Ys    = data$Data$Y
Sk    = data$Data$Sk

## cross-validation
## cvfitc <- cv.multiFSSEMiPALM(Xs = Xs, Ys = Ys, Bs = fit$Bs, Fs = fit$Fs, Sk = Sk,
##                              sigma2 = fit$sigma2, nlambda = 10, nrho = 10,
##                              nfold = 5, p = Ng, q = Nk, wt = TRUE)

fitm <- opt.multiFSSEMiPALM(Xs = Xs, Ys = Ys, Bs = fit$Bs, Fs = fit$Fs, Sk = Sk,
                            sigma2 = fit$sigma2, nlambda = 10, nrho = 10,
                            p = Ng, q = Nk, wt = TRUE)

fitc0 <- fitm$fit

(TPR(fitc0$Bs[[1]], data$Vars$B[[1]]) + TPR(fitc0$Bs[[2]], data$Vars$B[[2]])) / 2
(FDR(fitc0$Bs[[1]], data$Vars$B[[1]]) + FDR(fitc0$Bs[[2]], data$Vars$B[[2]])) / 2
TPR(fitc0$Bs[[1]] - fitc0$Bs[[2]], data$Vars$B[[1]] - data$Vars$B[[2]])
FDR(fitc0$Bs[[1]] - fitc0$Bs[[2]], data$Vars$B[[1]] - data$Vars$B[[2]])
```

`implFSSEM` *implFSSEM*

Description

implementor function of FSSEM solver

Usage

```
implFSSEM(data = NULL, method = c("CV", "BIC"))
```

Arguments

`data`	Data archive of experiment measurements, includeing eQTL matrices, Gene expression matrices of different conditions, marker of eQTLs and data generation SEM model
`method`	Use cross-validation (CV) or bayesian-information-criterion(BIC)

Value

List of TPR and FDR

`initLambdaiPALM` *initLambdaiPALM*

Description

initLambdaiPALM

Usage

```
initLambdaiPALM(Xs, Ys, Bs, Fs, Sk, sigma2, Wl, Wf, p, k)
```

Arguments

`Xs`	eQTL matrices
`Ys`	Gene expression matrices
`Bs`	initialized GRN-matrices
`Fs`	initialized eQTL effect matrices
`Sk`	eQTL index of genes
`sigma2`	initialized noise variance
`Wl`	weight matrices for adaptive lasso terms
`Wf`	weight matrix for adaptive fused lasso term
`p`	number of genes
`k`	number of eQTL

Value

lambda_max

`initLambdaiPALM2` *initLambdaiPALM2*

Description

initLambdaiPALM2

Usage

```
initLambdaiPALM2(Xs, Ys, Bs, Fs, Sk, sigma2, Wl, Wf, p, k)
```

Arguments

Xs	eQTL matrices
Ys	Gene expression matrices
Bs	initialized GRN-matrices
Fs	initialized eQTL effect matrices
Sk	eQTL index of genes
sigma2	initialized noise variance
Wl	weight matrices for adaptive lasso terms
Wf	weight matrix for adaptive fused lasso term
p	number of genes
k	number of eQTL

Value

lambda_max

---

initLambdaiPALM3 *initLambdaiPALM3*

Description

initLambdaiPALM3

Usage

```
initLambdaiPALM3(Xs, Ys, Bs, Fs, Sk, sigma2, Wl, Wf, p, k)
```

Arguments

Xs	eQTL matrices
Ys	Gene expression matrices
Bs	initialized GRN-matrices
Fs	initialized eQTL effect matrices
Sk	eQTL index of genes
sigma2	initialized noise variance
Wl	weight matrices for adaptive lasso terms
Wf	weight matrix for adaptive fused lasso term
p	number of genes
k	number of eQTL

Value

lambda_max

`initRhoiPALM` *initRhoiPALM*

Description

initRhoiPALM

Usage

```
initRhoiPALM(Xs, Ys, Bs, Fs, Sk, sigma2, Wl, Wf, lambda, n, p)
```

Arguments

`Xs`	eQTL matrices
`Ys`	Gene expression matrices
`Bs`	initialized GRN-matrices
`Fs`	initialized eQTL effect matrices
`Sk`	eQTL index of genes
`sigma2`	initialized noise variance
`Wl`	weight matrices for adaptive lasso terms
`Wf`	weight matrix for adaptive fused lasso term
`lambda`	lambda w.r.t. rho_max
`n`	number of observations
`p`	number of genes

Value

rho_max

`initRhoiPALM2` *initRhoiPALM2*

Description

initRhoiPALM2

Usage

```
initRhoiPALM2(Xs, Ys, Bs, Fs, Sk, sigma2, Wl, Wf, lambda, n, p)
```

Arguments

Xs	eQTL matrices
Ys	Gene expression matrices
Bs	initialized GRN-matrices
Fs	initialized eQTL effect matrices
Sk	eQTL index of genes
sigma2	initialized noise variance
Wl	weight matrices for adaptive lasso terms
Wf	weight matrix for adaptive fused lasso term
lambda	lambda w.r.t. rho_max
n	number of observations
p	number of genes

Value

rho_max

`initRhoiPALM3` *initRhoiPALM3*

Description

initRhoiPALM3

Usage

```
initRhoiPALM3(Xs, Ys, Bs, Fs, Sk, sigma2, Wl, Wf, lambda, n, p)
```

Arguments

Xs	eQTL matrices
Ys	Gene expression matrices
Bs	initialized GRN-matrices
Fs	initialized eQTL effect matrices
Sk	eQTL index of genes
sigma2	initialized noise variance
Wl	weight matrices for adaptive lasso terms
Wf	weight matrix for adaptive perturbation group lasso term
lambda	lambda w.r.t. rho_max
n	number of observations
p	number of genes

Value

rho_max

`inverseB` *inverseB*

Description

inverse matrices of B network for adaptive FSSEM

Usage

```
inverseB(Bs)
```

Arguments

`Bs`	list of network matrices

Value

list of inversed B matrices

`invoneB` *invoneB*

Description

if you do not want to get inversed B matrces, invoneB gives you a matrix with constant 1 instead in FSSEM

Usage

```
invoneB(Bs)
```

Arguments

`Bs`	list of network matrices

Value

list of invone B matrices

logLikFSSEM *logLikFSSEM*

Description

logLikFSSEM

Usage

```
logLikFSSEM(Bs, Wl, Wf, lambda, rho, sigma2, Dets, n, p)
```

Arguments

Bs	Network matrices
Wl	Weights for lasso term
Wf	Weights for fused term
lambda	Hyperparameter of lasso term
rho	Hyperparameter of fused lasso term
sigma2	noise variance
Dets	determinants of I-B matrices
n	number of observations
p	number of genes

Value

objective value of FSSEM with specified hyper-paramters

logLikNFSSEM *logLikNFSSEM*

Description

logLikNFSSEM

Usage

```
logLikNFSSEM(Bs, Wl, Wf, lambda, rho, sigma2, Dets, n, p)
```

Arguments

Bs	Network matrices
Wl	Weights for lasso term
Wf	Weights for group perturb lasso term
lambda	Hyperparameter of lasso term
rho	Hyperparameter of group fused lasso term
sigma2	noise variance
Dets	determinants of I-B matrices
n	number of observations
p	number of genes

Value

objective value of NFSSEM with specified hyper-paramters

---

multiFSSEMiPALM *multiFSSEMiPALM*

Description

Implementing FSSELM algorithm for network inference. If Xs is identify for different conditions, multiFSSEMiPALM will be use, otherwise, please use `multiFSSEMiPALM2` for general cases

Usage

```
multiFSSEMiPALM(
  Xs,
  Ys,
  Bs,
  Fs,
  Sk,
  sigma2,
  lambda,
  rho,
  Wl,
  Wf,
  p,
  maxit = 100,
  inert = inert_opt("linear"),
  threshold = 1e-06,
  verbose = TRUE,
  sparse = TRUE,
  trans = FALSE,
  B2norm = NULL,
  strict = FALSE
)
```

Arguments

Xs	eQTL matrices
Ys	Gene expression matrices
Bs	initialized GRN-matrices
Fs	initialized eQTL effect matrices
Sk	eQTL index of genes
sigma2	initialized noise variance from ridge regression
lambda	Hyperparameter of lasso term in FSSEM
rho	Hyperparameter of fused-lasso term in FSSEM
Wl	weight matrices for adaptive lasso terms
Wf	weight matrix for adaptive fused lasso term
p	number of genes
maxit	maximum iteration number. Default 100
inert	inertial function for iPALM. Default as k-1/k+2
threshold	convergence threshold. Default 1e-6
verbose	Default TRUE
sparse	Sparse Matrix or not
trans	Fs matrix is transposed to k x p or not. If Fs from ridge regression, trans = TRUE, else, trans = FALSE
B2norm	B2norm matrices generated from ridge regression. Default NULL.
strict	Converge strictly or not. Default False

Value

fit List of FSSEM model

Bs coefficient matrices of gene regulatory networks

Fs coefficient matrices of eQTL-gene effect

mu Bias vector

sigma2 estimate of covariance in SEM

Examples

```
seed = 1234
N = 100                                          # sample size
Ng = 5                                           # gene number
Nk = 5 * 3                                       # eQTL number
Ns = 1                                           # sparse ratio
sigma2 = 0.01                                    # sigma2
set.seed(seed)
library(fssemR)
data = randomFSSEMdata(n = N, p = Ng, k = Nk, sparse = Ns, df = 0.3, sigma2 = sigma2,
                       u = 5, type = "DG", nhub = 1, dag = TRUE)
```

```
## If we assume that different condition has different genetics perturbations (eQTLs)
## gamma = cv.multiRegression(data$Data$X, data$Data$Y, data$Data$Sk, ngamma = 20, nfold = 5,
##                            N, Ng, Nk)
gamma = 0.6784248     ## optimal gamma computed by cv.multiRegression
fit   = multiRegression(data$Data$X, data$Data$Y, data$Data$Sk, gamma, N, Ng, Nk,
                        trans = FALSE)
Xs    = data$Data$X
Ys    = data$Data$Y
Sk    = data$Data$Sk


cvfitc <- cv.multiFSSEMiPALM(Xs = Xs, Ys = Ys, Bs = fit$Bs, Fs = fit$Fs, Sk = Sk,
                             sigma2 = fit$sigma2, nlambda = 5, nrho = 5,
                             nfold = 5, p = Ng, q = Nk, wt = TRUE)

fitc0 <- multiFSSEMiPALM(Xs = Xs, Ys = Ys, Bs = fit$Bs, Fs = fit$Fs, Sk = Sk,
                         sigma2 = fit$sigma2, lambda = cvfitc$lambda, rho = cvfitc$rho,
                         Wl = inverseB(fit$Bs), Wf = flinvB(fit$Bs),
                         p = Ng, maxit = 100, threshold = 1e-5, sparse = TRUE,
                         verbose = TRUE, trans = TRUE, strict = TRUE)


(TPR(fitc0$Bs[[1]], data$Vars$B[[1]]) + TPR(fitc0$Bs[[2]], data$Vars$B[[2]])) / 2
(FDR(fitc0$Bs[[1]], data$Vars$B[[1]]) + FDR(fitc0$Bs[[2]], data$Vars$B[[2]])) / 2
TPR(fitc0$Bs[[1]] - fitc0$Bs[[2]], data$Vars$B[[1]] - data$Vars$B[[2]])
FDR(fitc0$Bs[[1]] - fitc0$Bs[[2]], data$Vars$B[[1]] - data$Vars$B[[2]])
```

`multiFSSEMiPALM2` *multiFSSEMiPALM2*

Description

Implementing FSSELM algorithm for network inference. If Xs is identify for different conditions, multiFSSEMiPALM will be use, otherwise, please use `multiFSSEMiPALM2` for general cases

Usage

```
multiFSSEMiPALM2(
  Xs,
  Ys,
  Bs,
  Fs,
  Sk,
  sigma2,
  lambda,
  rho,
  Wl,
  Wf,
  p,
```

```
  maxit = 100,
  inert = inert_opt("linear"),
  threshold = 1e-06,
  verbose = TRUE,
  sparse = TRUE,
  trans = FALSE,
  B2norm = NULL,
  strict = FALSE
)
```

Arguments

Xs	eQTL matrices
Ys	Gene expression matrices
Bs	initialized GRN-matrices
Fs	initialized eQTL effect matrices
Sk	eQTL index of genes
sigma2	initialized noise variance from ridge regression
lambda	Hyperparameter of lasso term in FSSEM
rho	Hyperparameter of fused-lasso term in FSSEM
Wl	weight matrices for adaptive lasso terms
Wf	weight matrix for adaptive fused lasso term
p	number of genes
maxit	maximum iteration number. Default 100
inert	inertial function for iPALM. Default as k-1/k+2
threshold	convergence threshold. Default 1e-6
verbose	Default TRUE
sparse	Sparse Matrix or not
trans	Fs matrix is transposed to k x p or not. If Fs from ridge regression, trans = TRUE, else, trans = FALSE
B2norm	B2norm matrices generated from ridge regression. Default NULL.
strict	Converge strictly or not. Default False

Value

fit List of FSSEM model

Bs coefficient matrices of gene regulatory networks

Fs coefficient matrices of eQTL-gene effect

mu Bias vector

sigma2 estimate of covariance in SEM

Examples

```
seed = 1234
N = 100                                                 # sample size
Ng = 5                                                  # gene number
Nk = 5 * 3                                              # eQTL number
Ns = 1                                                  # sparse ratio
sigma2 = 0.01                                           # sigma2
set.seed(seed)
library(fssemR)
data = randomFSSEMdata(n = N, p = Ng, k = Nk, sparse = Ns, df = 0.3, sigma2 = sigma2,
                       u = 5, type = "DG", nhub = 1, dag = TRUE)
## If we assume that different condition has different genetics perturbations (eQTLs)
data$Data$X = list(data$Data$X, data$Data$X)
## gamma = cv.multiRegression(data$Data$X, data$Data$Y, data$Data$Sk, ngamma = 20, nfold = 5,
##                            N, Ng, Nk)
gamma = 0.6784248     ## optimal gamma computed by cv.multiRegression
fit   = multiRegression(data$Data$X, data$Data$Y, data$Data$Sk, gamma, N, Ng, Nk,
                        trans = FALSE)
Xs    = data$Data$X
Ys    = data$Data$Y
Sk    = data$Data$Sk


cvfitc <- cv.multiFSSEMiPALM2(Xs = Xs, Ys = Ys, Bs = fit$Bs, Fs = fit$Fs, Sk = Sk,
                              sigma2 = fit$sigma2, nlambda = 5, nrho = 5,
                              nfold = 5, p = Ng, q = Nk, wt = TRUE)

fitc0 <- multiFSSEMiPALM2(Xs = Xs, Ys = Ys, Bs = fit$Bs, Fs = fit$Fs, Sk = Sk,
                          sigma2 = fit$sigma2, lambda = cvfitc$lambda, rho = cvfitc$rho,
                          W1 = inverseB(fit$Bs), Wf = flinvB(fit$Bs),
                          p = Ng, maxit = 100, threshold = 1e-5, sparse = TRUE,
                          verbose = TRUE, trans = TRUE, strict = TRUE)


(TPR(fitc0$Bs[[1]], data$Vars$B[[1]]) + TPR(fitc0$Bs[[2]], data$Vars$B[[2]])) / 2
(FDR(fitc0$Bs[[1]], data$Vars$B[[1]]) + FDR(fitc0$Bs[[2]], data$Vars$B[[2]])) / 2
TPR(fitc0$Bs[[1]] - fitc0$Bs[[2]], data$Vars$B[[1]] - data$Vars$B[[2]])
FDR(fitc0$Bs[[1]] - fitc0$Bs[[2]], data$Vars$B[[1]] - data$Vars$B[[2]])
```

`multiNFSSEMiPALM2` *multiNFSSEMiPALM2*

Description

Implementing NFSSEM algorithm for network inference. If Xs is identify for different conditions, multiNFSSEMiPALM will be use, otherwise, please use `multiNFSSEMiPALM2` for general cases

Usage

```
multiNFSSEMiPALM2(
```

```
  Xs,
  Ys,
  Bs,
  Fs,
  Sk,
  sigma2,
  lambda,
  rho,
  Wl,
  Wf,
  p,
  maxit = 100,
  inert = inert_opt("linear"),
  threshold = 1e-06,
  verbose = TRUE,
  sparse = TRUE,
  trans = FALSE,
  B2norm = NULL,
  strict = FALSE
)
```

Arguments

Xs	eQTL matrices
Ys	Gene expression matrices
Bs	initialized GRN-matrices
Fs	initialized eQTL effect matrices
Sk	eQTL index of genes
sigma2	initialized noise variance from ridge regression
lambda	Hyperparameter of lasso term in NFSSEM
rho	Hyperparameter of fused-lasso term in NFSSEM
Wl	weight matrices for adaptive lasso terms
Wf	weight matrix for columnwise l2 norm adaptive group lasso
p	number of genes
maxit	maximum iteration number. Default 100
inert	inertial function for iPALM. Default as k-1/k+2
threshold	convergence threshold. Default 1e-6
verbose	Default TRUE
sparse	Sparse Matrix or not
trans	Fs matrix is transposed to k x p or not. If Fs from ridge regression, trans = TRUE, else, trans = FALSE
B2norm	B2norm matrices generated from ridge regression. Default NULL.
strict	Converge strictly or not. Default False

Value

fit List of NFSSEM model

Bs coefficient matrices of gene regulatory networks

Fs coefficient matrices of eQTL-gene effect

mu Bias vector

sigma2 estimate of covariance in SEM

`multiRegression` *multiRegression*

Description

Ridge regression on multiple conditions, initialization of FSSEM algorithm

Usage

```
multiRegression(Xs, Ys, Sk, gamma, n, p, k, trans = FALSE)
```

Arguments

`Xs`	eQTL matrices. eQTL matrix can be matrix/list of multiple conditions
`Ys`	Gene expression matrices
`Sk`	eQTL index of genes
`gamma`	Hyperparameter for ridge regression
`n`	number of observations
`p`	number of genes
`k`	number of eQTLs
`trans`	if rows for sample, trans = TRUE, otherwise, trans = FALSE. Default FALSE

Value

fit List of SEM model

Bs coefficient matrices of gene regulatory networks

fs eQTL's coefficients w.r.t each gene

Fs coefficient matrices of eQTL-gene effect

mu Bias vector

sigma2 estimate of covariance in SEM

Examples

```
seed = 1234
N = 100                                              # sample size
Ng = 5                                               # gene number
Nk = 5 * 3                                           # eQTL number
Ns = 1                                               # sparse ratio
sigma2 = 0.01                                        # sigma2
set.seed(seed)
data = randomFSSEMdata(n = N, p = Ng, k = Nk, sparse = Ns, df = 0.3, sigma2 = sigma2,
                       u = 5, type = "DG", nhub = 1, dag = TRUE)
## If we assume that different condition has different genetics perturbations (eQTLs)
## data$Data$X = list(data$Data$X, data$Data$X)
gamma = cv.multiRegression(data$Data$X, data$Data$Y, data$Data$Sk, ngamma = 20, nfold = 5,
                           N, Ng, Nk)
fit   = multiRegression(data$Data$X, data$Data$Y, data$Data$Sk, gamma, N, Ng, Nk,
                        trans = FALSE)
```

`obj.multiRegression` *obj.multiRegression*

Description

obj.multiRegression

Usage

```
obj.multiRegression(Xs, Ys, fit, trans = F)
```

Arguments

`Xs`	eQTL matrices
`Ys`	gene expression matrices
`fit`	regression fit result object
`trans`	if rows for sample, trans = TRUE, otherwise, trans = FALSE. Default FALSE

Value

error squared norm of ||(I-B)Y - FX||_2^2

`opt.multiFSSEMiPALM` *opt.multiFSSEMiPALM*

Description

optimize multiFSSEMiPALM's parameters by minimize BIC, when feature size is large (> 300), BIC methods will be much faster than Cross-validation

Usage

```
opt.multiFSSEMiPALM(
  Xs,
  Ys,
  Bs,
  Fs,
  Sk,
  sigma2,
  nlambda = 20,
  nrho = 20,
  p,
  q,
  wt = TRUE
)
```

Arguments

`Xs`	eQTL matrices
`Ys`	Gene expression matrices
`Bs`	initialized GRN-matrices
`Fs`	initialized eQTL effect matrices
`Sk`	eQTL index of genes
`sigma2`	initialized noise variance
`nlambda`	number of hyper-parameter of lasso term in CV
`nrho`	number of hyper-parameter of fused-lasso term in CV
`p`	number of genes
`q`	number of eQTLs
`wt`	use adaptive lasso or not. Default TRUE.

Value

list of model selection result

Examples

```
seed = 1234
N = 100                                                 # sample size
Ng = 5                                                  # gene number
Nk = 5 * 3                                              # eQTL number
Ns = 1                                                  # sparse ratio
sigma2 = 0.01                                           # sigma2
set.seed(seed)
library(fssemR)
data = randomFSSEMdata(n = N, p = Ng, k = Nk, sparse = Ns, df = 0.3, sigma2 = sigma2,
                       u = 5, type = "DG", nhub = 1, dag = TRUE)
## If we assume that different condition has different genetics perturbations (eQTLs)
## data$Data$X = list(data$Data$X, data$Data$X)
## gamma = cv.multiRegression(data$Data$X, data$Data$Y, data$Data$Sk, ngamma = 20, nfold = 5,
##                            N, Ng, Nk)
gamma = 0.6784248     ## optimal gamma computed by cv.multiRegression
fit   = multiRegression(data$Data$X, data$Data$Y, data$Data$Sk, gamma, N, Ng, Nk,
                        trans = FALSE)
Xs    = data$Data$X
Ys    = data$Data$Y
Sk    = data$Data$Sk

fitm <- opt.multiFSSEMiPALM(Xs = Xs, Ys = Ys, Bs = fit$Bs, Fs = fit$Fs, Sk = Sk,
                            sigma2 = fit$sigma2, nlambda = 10, nrho = 10,
                            p = Ng, q = Nk, wt = TRUE)

fitc0 <- fitm$fit

(TPR(fitc0$Bs[[1]], data$Vars$B[[1]]) + TPR(fitc0$Bs[[2]], data$Vars$B[[2]])) / 2
(FDR(fitc0$Bs[[1]], data$Vars$B[[1]]) + FDR(fitc0$Bs[[2]], data$Vars$B[[2]])) / 2
TPR(fitc0$Bs[[1]] - fitc0$Bs[[2]], data$Vars$B[[1]] - data$Vars$B[[2]])
FDR(fitc0$Bs[[1]] - fitc0$Bs[[2]], data$Vars$B[[1]] - data$Vars$B[[2]])
```

`opt.multiFSSEMiPALM2` *opt.multiFSSEMiPALM2*

Description

optimize multiFSSEMiPALM's parameters by minimize BIC, when feature size is large (> 300), BIC methods will be much faster than Cross-validation

Usage

```
opt.multiFSSEMiPALM2(
  Xs,
  Ys,
  Bs,
  Fs,
  Sk,
```

```
  sigma2,
  nlambda = 20,
  nrho = 20,
  p,
  q,
  wt = TRUE
)
```

Arguments

Xs	eQTL matrices
Ys	Gene expression matrices
Bs	initialized GRN-matrices
Fs	initialized eQTL effect matrices
Sk	eQTL index of genes
sigma2	initialized noise variance
nlambda	number of hyper-parameter of lasso term in CV
nrho	number of hyper-parameter of fused-lasso term in CV
p	number of genes
q	number of eQTLs
wt	use adaptive lasso or not. Default TRUE.

Value

list of model selection result

Examples

```
seed = 1234
N = 100                                                 # sample size
Ng = 5                                                  # gene number
Nk = 5 * 3                                              # eQTL number
Ns = 1                                                  # sparse ratio
sigma2 = 0.01                                           # sigma2
set.seed(seed)
library(fssemR)
data = randomFSSEMdata(n = N, p = Ng, k = Nk, sparse = Ns, df = 0.3, sigma2 = sigma2,
                       u = 5, type = "DG", nhub = 1, dag = TRUE)
## If we assume that different condition has different genetics perturbations (eQTLs)
data$Data$X = list(data$Data$X, data$Data$X)
## gamma = cv.multiRegression(data$Data$X, data$Data$Y, data$Data$Sk, ngamma = 20, nfold = 5,
##                            N, Ng, Nk)
gamma = 0.6784248     ## optimal gamma computed by cv.multiRegression
fit   = multiRegression(data$Data$X, data$Data$Y, data$Data$Sk, gamma, N, Ng, Nk,
                        trans = FALSE)
Xs    = data$Data$X
Ys    = data$Data$Y
Sk    = data$Data$Sk
```

```
fitm <- opt.multiFSSEMiPALM2(Xs = Xs, Ys = Ys, Bs = fit$Bs, Fs = fit$Fs, Sk = Sk,
                             sigma2 = fit$sigma2, nlambda = 10, nrho = 10,
                             p = Ng, q = Nk, wt = TRUE)

fitc0 <- fitm$fit

(TPR(fitc0$Bs[[1]], data$Vars$B[[1]]) + TPR(fitc0$Bs[[2]], data$Vars$B[[2]])) / 2
(FDR(fitc0$Bs[[1]], data$Vars$B[[1]]) + FDR(fitc0$Bs[[2]], data$Vars$B[[2]])) / 2
TPR(fitc0$Bs[[1]] - fitc0$Bs[[2]], data$Vars$B[[1]] - data$Vars$B[[2]])
FDR(fitc0$Bs[[1]] - fitc0$Bs[[2]], data$Vars$B[[1]] - data$Vars$B[[2]])
```

`opt.multiNFSSEMiPALM2` *opt.multiNFSSEMiPALM2*

Description

optimize multiNFSSEMiPALM's parameters by minimize BIC, when feature size is large (> 300), BIC methods will be much faster than Cross-validation

Usage

```
opt.multiNFSSEMiPALM2(
  Xs,
  Ys,
  Bs,
  Fs,
  Sk,
  sigma2,
  nlambda = 20,
  nrho = 20,
  p,
  q,
  wt = TRUE
)
```

Arguments

`Xs`	eQTL matrices
`Ys`	Gene expression matrices
`Bs`	initialized GRN-matrices
`Fs`	initialized eQTL effect matrices
`Sk`	eQTL index of genes
`sigma2`	initialized noise variance
`nlambda`	number of hyper-parameter of lasso term in CV
`nrho`	number of hyper-parameter of fused-lasso term in CV

p	number of genes
q	number of eQTLs
wt	use adaptive lasso or not. Default TRUE.

Value

list of model selection result

---

pninvB *pninvB*

Description

inversed column l2 norm for perturbed group lasso penalty

Usage

```
pninvB(Bs)
```

Arguments

Bs	list of network matrices

Value

inversed l2 norm of B2 - B1

---

pnoneB *pnoneB*

Description

if you do not want adaptive group lasso penalty, pnoneB replace pninvB

Usage

```
pnoneB(Bs)
```

Arguments

Bs	list of network matrices

Value

inversed l2 norm of B2 - B1 with all entries is 1

`proc.centerFSSEM` *proc.centerFSSEM*

Description

proc.centerFSSEM

Usage

```
proc.centerFSSEM(Xs, Ys)
```

Arguments

`Xs`	eQTL matrices
`Ys`	list of gene expression matrices

Value

centered Xs and Ys and mean vectors

`proc.centerFSSEM2` *proc.centerFSSEM2*

Description

proc.centerFSSEM2

Usage

```
proc.centerFSSEM2(Xs, Ys)
```

Arguments

`Xs`	list of eQTL matrices
`Ys`	list of gene expression matrices

Value

centered Xs and Ys and mean vectors

randomFSSEMdata *randomFSSEMdata*

Description

randomFSSEMdata

Usage

```
randomFSSEMdata(
  n,
  p,
  k,
  sparse = 0.1,
  df = 0.2,
  sigma2 = 0.01,
  u = 5,
  type = c("DG", "ER"),
  dag = TRUE,
  coef = c(0.2, 0.4),
  nhub = 2
)
```

Arguments

n	number of observations
p	number of genes
k	number of eQTLs
sparse	ratio of edges / gene_number
df	ratio of differential edges among two network
sigma2	noise variance of error
u	variance of bias in SEM model.
type	type of generated network, can be selected as DG, ER, Scale-free network
dag	network is directed-acyclic or not. Default TRUE
coef	Range of absolute value of coefficients in simulated network matrices. Default (0.2, 0.4), or (0.5, 1)
nhub	If you select to generate ER network, nhub is the number of pre-defined hub node number. Default 2

Value

list of generated data

Data List of observed, Xs, Ys, Sk

Vars List of model, Bs, Fs, mu, n, p, k

randomFSSEMdata2 *randomFSSEMdata2*

Description

randomFSSEMdata2

Usage

```
randomFSSEMdata2(
  n,
  p,
  k,
  sparse = 0.1,
  df = 0.2,
  sigma2 = 0.01,
  u = 5,
  type = c("DG", "ER"),
  dag = TRUE,
  coef = c(0.2, 0.4),
  nhub = 2
)
```

Arguments

n	number of observations. Vector for unbalance observations
p	number of genes
k	number of eQTLs
sparse	ratio of edges / gene_number
df	ratio of differential edges among two network
sigma2	noise variance of error
u	variance of bias in SEM model.
type	type of generated network, can be selected as DG, ER, Scale-free network
dag	network is directed-acyclic or not. Default TRUE
coef	Range of absolute value of coefficients in simulated network matrices. Default (0.2, 0.4), or (0.5, 1)
nhub	If you select to generate ER network, nhub is the number of pre-defined hub node number. Default 2

Value

list of generated data

Data List of observed, Xs, Ys, Sk

Vars List of model, Bs, Fs, mu, n, p, k

randomFSSEMdata4Cor *randomFSSEMdata4Cor*

Description

randomFSSEMdata4Cor

Usage

```
randomFSSEMdata4Cor(
  n,
  p,
  k,
  sparse = 0.1,
  df = 0.2,
  sigma2 = 0.01,
  u = 5,
  type = c("DG", "ER"),
  dag = TRUE,
  coef = c(0.2, 0.4),
  nhub = 2,
  r = 0.5
)
```

Arguments

n	number of observations. Vector for unbalance observations
p	number of genes
k	number of eQTLs
sparse	ratio of edges / gene_number
df	ratio of differential edges among two network
sigma2	noise variance of error
u	variance of bias in SEM model.
type	type of generated network, can be selected as DG, ER, Scale-free network
dag	network is directed-acyclic or not. Default TRUE
coef	Range of absolute value of coefficients in simulated network matrices. Default (0.2, 0.4), or (0.5, 1)
nhub	If you select to generate ER network, nhub is the number of pre-defined hub node number. Default 2
r	correlation between different observations

Value

list of generated data

Data List of observed, Xs, Ys, Sk

Vars List of model, Bs, Fs, mu, n, p, k

`TPR` *TPR*

Description

Power of detection for network prediction

Usage

```
TPR(X, B, PREC = 0)
```

Arguments

`X`	list of predicted network matrices
`B`	list of true network matrices
`PREC`	precision threshold for FDR test. Default 0.

`transx` *transx*

Description

transx

Usage

```
transx(data)
```

Arguments

`data`	Collecting data structure generated by randomFSSEMdata function

Value

transformed list of eQTL matrices

Index