Package 'HIMA'

September 10, 2023

Type Package

Title High-Dimensional Mediation Analysis

Version 2.2.1

Date 2023-09-10

Description Allows to estimate and test high-dimensional mediation effects based on advanced mediator screening and penalized regression techniques. Methods used in the package refer to Zhang H, Zheng Y, Zhang Z, Gao T, Joyce B, Yoon G, Zhang W, Schwartz J, Just A, Colicino E, Vokonas P, Zhao L, Lv J, Baccarelli A, Hou L, Liu L. Estimating and Testing High-dimensional Mediation Effects in Epigenetic Studies. Bioinformatics. (2016) <doi:10.1093/bioinformatics/btw351>. PMID: 27357171.

License GPL-3

Depends R (>= 3.4.0), ncvreg, glmnet

Imports utils, stats, MASS, survival, HDMT, hdi, conquer, quantreg, hommel, iterators, parallel, foreach, doParallel

Collate utils.R hima.R survHIMA.R microHIMA.R dblassoHIMA.R qHIMA.R hima2.R himaDat.R onAttach.R HIMA-package.R

Encoding UTF-8

LazyData true

URL https://github.com/YinanZheng/HIMA/

BugReports https://github.com/YinanZheng/HIMA/issues/

RoxygenNote 7.2.3

NeedsCompilation no

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Repository CRAN

Date/Publication 2023-09-10 16:02:34 UTC

R topics documented:

`HIMA-package` *High-Dimensional Mediation Analysis for 'Omic' Data*

Description

HIMA is an R package for estimating and testing high-dimensional mediation effects in omic studies. HIMA can perform high-dimensional mediation analysis on a wide range of omic data types as potential mediators, including epigenetics, transcriptomics, proteomics, and metabolomics using function `hima` and microbiome data (function `microHIMA`). HIMA can also handle survival data (function `survHIMA`).

Package:	HIMA
Type:	Package
Version:	2.2.1
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License:	GPL-3

Details

If package "qvalue" is not found during installation, please first install "qvalue" package # through Bioconductor: https://www.bioconductor.org/packages/release/bioc/html/qvalue.html

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References

1. Zhang H, Zheng Y, Zhang Z, Gao T, Joyce B, Yoon G, Zhang W, Schwartz J, Just A, Colicino E, Vokonas P, Zhao L, Lv J, Baccarelli A, Hou L, Liu L. Estimating and Testing High-dimensional Mediation Effects in Epigenetic Studies. Bioinformatics. 2016. DOI: 10.1093/bioinformatics/btw351. PMID: 27357171. PMCID: PMC5048064

2. Perera C, Zhang H, Zheng Y, Hou L, Qu A, Zheng C, Xie K, Liu L. HIMA2: high-dimensional mediation analysis and its application in epigenome-wide DNA methylation data. BMC Bioinformatics. 2022. DOI: 10.1186/s12859-022-04748-1. PMID: 35879655. PMCID: PMC9310002

3. Zhang H, Zheng Y, Hou L, Zheng C, Liu L. Mediation Analysis for Survival Data with High-Dimensional Mediators. Bioinformatics. 2021. DOI: 10.1093/bioinformatics/btab564. PMID: 34343267. PMCID: PMC8570823

4. Zhang H, Chen J, Feng Y, Wang C, Li H, Liu L. Mediation effect selection in high-dimensional and compositional microbiome data. Stat Med. 2021. DOI: 10.1002/sim.8808. PMID: 33205470; PMCID: PMC7855955

5. Zhang H, Chen J, Li Z, Liu L. Testing for mediation effect with application to human microbiome data. Stat Biosci. 2021. DOI: 10.1007/s12561-019-09253-3. PMID: 34093887; PMCID: PMC8177450

6. Zhang H, Hong X, Zheng Y, Hou L, Zheng C, Wang X, Liu L. High-Dimensional Quantile Mediation Analysis with Application to a Birth Cohort Study of Mother–Newborn Pairs. Bioinformatics. 2023. (In press)

`dblassoHIMA` *This is the function for high-dimensional mediation analysis using de-biased lasso HIMA with de-biased lasso*

Description

`dblassoHIMA` is used to estimate and test high-dimensional mediation effects using de-biased lasso penalty.

Usage

```
dblassoHIMA(
  X,
  Y,
  M,
  Z,
  Y.family = c("gaussian", "binomial"),
  topN = NULL,
  scale = TRUE,
  FDRcut = 0.05,
  verbose = FALSE
)
```

Arguments

`X`	a vector of exposure.
`Y`	a vector of outcome. Can be either continuous or binary (0-1).
`M`	a `data.frame` or `matrix` of high-dimensional mediators. Rows represent samples, columns represent variables.

Z	a data.frame or matrix of covariates dataset for testing the association M ~ X and Y ~ M.
Y.family	either 'gaussian' (default) or 'binomial', depending on the data type of outcome (Y). This parameter is passed to function lasso.proj in R package hdi for debiased lasso penalization.
topN	an integer specifying the number of top markers from sure independent screening. Default = NULL. If NULL, topN will be either ceiling(n/log(n)) if Y.family = 'gaussian', or ceiling(n/(2*log(n))) if Y.family = 'binomial', where n is the sample size. If the sample size is greater than topN (pre-specified or calculated), all mediators will be included in the test (i.e. low-dimensional scenario).
scale	logical. Should the function scale the data? Default = TRUE.
FDRcut	FDR cutoff applied to define and select significant mediators. Default = 0.05.
verbose	logical. Should the function be verbose? Default = FALSE.

Value

A data.frame containing mediation testing results of selected mediators (FDR <FDPcut).

- alpha: coefficient estimates of exposure (X) –> mediators (M).
- beta: coefficient estimates of mediators (M) –> outcome (Y) (adjusted for exposure).
- gamma: coefficient estimates of exposure (X) –> outcome (Y) (total effect).
- alpha*beta: mediation effect.
- % total effect: alpha*beta / gamma. Percentage of the mediation effect out of the total effect.
- p.joint: joint raw p-value of selected significant mediator (based on FDR).

#' @references Perera C, Zhang H, Zheng Y, Hou L, Qu A, Zheng C, Xie K, Liu L. HIMA2: high-dimensional mediation analysis and its application in epigenome-wide DNA methylation data. BMC Bioinformatics. 2022. DOI: 10.1186/s12859-022-04748-1. PMID: 35879655. PMCID: PMC9310002

Examples

```
## Not run:
# Note: In the following examples, M1, M2, and M3 are true mediators.
data(himaDat)

# When Y is continuous and normally distributed
# Example 1 (continuous outcome):
head(himaDat$Example1$PhenoData)

dblassohima.fit <- dblassoHIMA(X = himaDat$Example1$PhenoData$Treatment,
                               Y = himaDat$Example1$PhenoData$Outcome,
                               M = himaDat$Example1$Mediator,
                               Z = himaDat$Example1$PhenoData[, c("Sex", "Age")],
                               Y.family = 'gaussian',
                               scale = FALSE,
                               verbose = TRUE)
```

```
dblassohima.fit

# When Y is binary (should specify Y.family)
# Example 2 (binary outcome):
head(himaDat$Example2$PhenoData)

dblassohima.logistic.fit <- dblassoHIMA(X = himaDat$Example2$PhenoData$Treatment,
                                        Y = himaDat$Example2$PhenoData$Disease,
                                        M = himaDat$Example2$Mediator,
                                       Z = himaDat$Example2$PhenoData[, c("Sex", "Age")],
                                        Y.family = 'binomial',
                                        scale = FALSE,
                                        verbose = TRUE)
dblassohima.logistic.fit

## End(Not run)
```

---

hima *High-dimensional Mediation Analysis*

Description

hima is used to estimate and test high-dimensional mediation effects.

Usage

```
hima(
  X,
  Y,
  M,
  COV.XM = NULL,
  COV.MY = COV.XM,
  Y.family = c("gaussian", "binomial"),
  M.family = c("gaussian", "negbin"),
  penalty = c("MCP", "SCAD", "lasso"),
  topN = NULL,
  parallel = FALSE,
  ncore = 1,
  scale = TRUE,
  verbose = FALSE,
  ...
)
```

Arguments

X	a vector of exposure. Do not use data.frame or matrix.
Y	a vector of outcome. Can be either continuous or binary (0-1). Do not use data.frame or matrix.

M	a data.frame or matrix of high-dimensional mediators. Rows represent samples, columns represent variables.
COV.XM	a data.frame or matrix of covariates dataset for testing the association M ~ X. Covariates specified here will not participate penalization. Default = NULL. If the covariates contain mixed data types, please make sure all categorical variables are properly formatted as factor type.
COV.MY	a data.frame or matrix of covariates dataset for testing the association Y ~ M. Covariates specified here will not participate penalization. If not specified, the same set of covariates for M ~ X will be applied. Using different sets of covariates is allowed but this needs to be handled carefully.
Y.family	either 'gaussian' (default) or 'binomial', depending on the data type of outcome (Y). See ncvreg
M.family	either 'gaussian' (default) or 'negbin' (i.e., negative binomial), depending on the data type of mediator (M).
penalty	the penalty to be applied to the model. Either 'MCP' (the default), 'SCAD', or 'lasso'.
topN	an integer specifying the number of top markers from sure independent screening. Default = NULL. If NULL, topN will be either ceiling(n/log(n)) if Y.family = 'gaussian', or ceiling(n/(2*log(n))) if Y.family = 'binomial', where n is the sample size. If the sample size is greater than topN (pre-specified or calculated), all mediators will be included in the test (i.e. low-dimensional scenario).
parallel	logical. Enable parallel computing feature? Default = FALSE.
ncore	number of cores to run parallel computing Valid when parallel == TRUE. By default max number of cores available in the machine will be utilized.
scale	logical. Should the function scale the data? Default = TRUE.
verbose	logical. Should the function be verbose? Default = FALSE.
...	other arguments passed to ncvreg.

Value

A data.frame containing mediation testing results of selected mediators.

- alpha: coefficient estimates of exposure (X) –> mediators (M).
- beta: coefficient estimates of mediators (M) –> outcome (Y) (adjusted for exposure).
- gamma: coefficient estimates of exposure (X) –> outcome (Y) (total effect).
- alpha*beta: mediation effect.
- % total effect: alpha*beta / gamma. Percentage of the mediation effect out of the total effect.
- Bonferroni.p: statistical significance of the mediator (Bonferroni-corrected p value).
- BH.FDR: statistical significance of the mediator (Benjamini-Hochberg FDR).

References

Zhang H, Zheng Y, Zhang Z, Gao T, Joyce B, Yoon G, Zhang W, Schwartz J, Just A, Colicino E, Vokonas P, Zhao L, Lv J, Baccarelli A, Hou L, Liu L. Estimating and Testing High-dimensional Mediation Effects in Epigenetic Studies. Bioinformatics. 2016. DOI: 10.1093/bioinformatics/btw351. PMID: 27357171. PMCID: PMC5048064

Examples

```
## Not run:
# Note: In the following examples, M1, M2, and M3 are true mediators.
data(himaDat)

# When Y is continuous and normally distributed
# Example 1 (continuous outcome):
head(himaDat$Example1$PhenoData)

hima.fit <- hima(X = himaDat$Example1$PhenoData$Treatment,
                 Y = himaDat$Example1$PhenoData$Outcome,
                 M = himaDat$Example1$Mediator,
                 COV.XM = himaDat$Example1$PhenoData[, c("Sex", "Age")],
                 Y.family = 'gaussian',
                 scale = FALSE,
                 verbose = TRUE)
hima.fit

# When Y is binary (should specify Y.family)
# Example 2 (binary outcome):
head(himaDat$Example2$PhenoData)

hima.logistic.fit <- hima(X = himaDat$Example2$PhenoData$Treatment,
                          Y = himaDat$Example2$PhenoData$Disease,
                          M = himaDat$Example2$Mediator,
                          COV.XM = himaDat$Example2$PhenoData[, c("Sex", "Age")],
                          Y.family = 'binomial',
                          scale = FALSE,
                          verbose = TRUE)
hima.logistic.fit

## End(Not run)
```

---

hima2 *Advanced High-dimensional Mediation Analysis*

Description

hima2 is an upgraded version of hima for estimating and testing high-dimensional mediation effects.

Usage

```
hima2(
  formula,
  data.pheno,
  data.M,
  outcome.family = c("gaussian", "binomial", "survival", "quantile"),
  mediator.family = c("gaussian", "negbin", "compositional"),
```

```
  penalty = c("DBlasso", "MCP", "SCAD", "lasso"),
  topN = NULL,
  scale = TRUE,
  verbose = FALSE,
  ...
)
```

Arguments

formula	an object of class formula: a symbolic description of the overall effect model, i.e., outcome ~ exposure + covariates, to be fitted. Make sure the "exposure" is the variable of interest, which must be listed as the first variable in the right hand side of the formula. independent variable in the formula. The same covariates will be used in screening and penalized regression.
data.pheno	a data frame containing exposure and covariates that are listed in the right hand side of the formula. The variable names must match those listed in formula. By default hima2 will scale data.pheno.
data.M	a data.frame or matrix of high-dimensional mediators. Rows represent samples, columns represent variables. By default hima2 will scale data.M.
outcome.family	either 'gaussian' (default, for normally distributed continuous outcome), 'binomial' (for binay outcome), 'survival' (for time-to-event outcome), or 'quantile' (for quantile mediation analysis)
mediator.family	either 'gaussian' (default, for continuous mediators), 'negbin' (i.e., negative binomial, for RNA-seq data as mediators), or 'compositional' (for microbiome data as mediators), depending on the data type of high-dimensional mediators (data.M).
penalty	the penalty to be applied to the model. Either 'DBlasso' (De-biased LASSO, default), 'MCP', 'SCAD', or 'lasso'. Please note, survival HIMA and microbiome HIMA can be only performed with 'DBlasso'; Quantile HIMA cannot be performed with 'DBlasso'.
topN	an integer specifying the number of top markers from sure independent screening. Default = NULL. If NULL, topN will be ceiling(2 * n/log(n)), where n is the sample size. If the sample size is greater than topN (pre-specified or calculated), all mediators will be included in the test (i.e. a low-dimensional scenario).
scale	logical. Should the function scale the data (exposure, mediators, and covariates)? Default = TRUE.
verbose	logical. Should the function be verbose and shows the progression? Default = FALSE.
...	other arguments.

Value

A data.frame containing mediation testing results of selected mediators.

References

Zhang H, Zheng Y, Zhang Z, Gao T, Joyce B, Yoon G, Zhang W, Schwartz J, Just A, Colicino E, Vokonas P, Zhao L, Lv J, Baccarelli A, Hou L, Liu L. Estimating and Testing High-dimensional Mediation Effects in Epigenetic Studies. Bioinformatics. 2016. DOI: 10.1093/bioinformatics/btw351. PMID: 27357171. PMCID: PMC5048064

Perera C, Zhang H, Zheng Y, Hou L, Qu A, Zheng C, Xie K, Liu L. HIMA2: high-dimensional mediation analysis and its application in epigenome-wide DNA methylation data. BMC Bioinformatics. 2022. DOI: 10.1186/s12859-022-04748-1. PMID: 35879655. PMCID: PMC9310002

Zhang H, Zheng Y, Hou L, Zheng C, Liu L. Mediation Analysis for Survival Data with High-Dimensional Mediators. Bioinformatics. 2021. DOI: 10.1093/bioinformatics/btab564. PMID: 34343267. PMCID: PMC8570823

Zhang H, Chen J, Feng Y, Wang C, Li H, Liu L. Mediation effect selection in high-dimensional and compositional microbiome data. Stat Med. 2021. DOI: 10.1002/sim.8808. PMID: 33205470; PMCID: PMC7855955

Zhang H, Chen J, Li Z, Liu L. Testing for mediation effect with application to human microbiome data. Stat Biosci. 2021. DOI: 10.1007/s12561-019-09253-3. PMID: 34093887; PMCID: PMC8177450

Zhang H, Hong X, Zheng Y, Hou L, Zheng C, Wang X, Liu L. High-Dimensional Quantile Mediation Analysis with Application to a Birth Cohort Study of Mother–Newborn Pairs. Bioinformatics. 2023. (In press)

Examples

```
## Not run:
# Note: In the following examples, M1, M2, and M3 are true mediators.
data(himaDat)

# Example 1 (continous outcome):
head(himaDat$Example1$PhenoData)

e1 <- hima2(Outcome ~ Treatment + Sex + Age,
      data.pheno = himaDat$Example1$PhenoData,
      data.M = himaDat$Example1$Mediator,
      outcome.family = "gaussian",
      mediator.family = "gaussian",
      penalty = "DBlasso",
      scale = FALSE) # Disabled only for example data
e1
attributes(e1)$variable.labels

# Example 2 (binary outcome):
head(himaDat$Example2$PhenoData)

e2 <- hima2(Disease ~ Treatment + Sex + Age,
      data.pheno = himaDat$Example2$PhenoData,
      data.M = himaDat$Example2$Mediator,
      outcome.family = "binomial",
      mediator.family = "gaussian",
      penalty = "DBlasso",
```

```
      scale = FALSE) # Disabled only for example data
e2
attributes(e2)$variable.labels

# Example 3 (time-to-event outcome):
head(himaDat$Example3$PhenoData)

e3 <- hima2(Surv(Status, Time) ~ Treatment + Sex + Age,
      data.pheno = himaDat$Example3$PhenoData,
      data.M = himaDat$Example3$Mediator,
      outcome.family = "survival",
      mediator.family = "gaussian",
      penalty = "DBlasso",
      scale = FALSE) # Disabled only for example data
e3
attributes(e3)$variable.labels

# Example 4 (compositional data as mediator, e.g., microbiome):
head(himaDat$Example4$PhenoData)

e4 <- hima2(Outcome ~ Treatment + Sex + Age,
      data.pheno = himaDat$Example4$PhenoData,
      data.M = himaDat$Example4$Mediator,
      outcome.family = "gaussian",
      mediator.family = "compositional",
      penalty = "DBlasso",
      scale = FALSE) # Disabled only for example data
e4
attributes(e4)$variable.labels

#' # Example 5 (quantile mediation anlaysis):
head(himaDat$Example5$PhenoData)

# Note that the function will prompt input for quantile level.
e5 <- hima2(Outcome ~ Treatment + Sex + Age,
      data.pheno = himaDat$Example5$PhenoData,
      data.M = himaDat$Example5$Mediator,
      outcome.family = "quantile",
      mediator.family = "gaussian",
      penalty = "MCP", # Quantile HIMA does not support DBlasso
      scale = FALSE, # Disabled only for example data
      tau = c(0.3, 0.5, 0.7)) # Specify multiple quantile level
e5
attributes(e5)$variable.labels

## End(Not run)
```

---

himaDat *Example datasets for HIMA demo*

Description

A `list` dataset containing datasets for various scenarios of HIMA. Each dataset contains a phenotype data frame and a high-dimension mediator data matrix. The datasets are simulated using parameters generated from real datasets. The code used to generate the data can be found in /inst/script folder of the package.

Usage

```
himaDat
```

Format

An object of class `list` of length 5.

Details

Example dataset 1 for HIMA: Continuous outcome

- Treatment: treated (value = 1) or not treated (value = 0)
- Outcome: outcome of the treatment- a normally distributed continuous variable
- Sex: female (value = 1) or male (value = 0)
- Age: Age of the participant

Example dataset 2 for HIMA: Binary outcome

- Treatment: treated (value = 1) or not treated (value = 0)
- Disease: diseased (value = 1) or healthy (value = 0)
- Sex: female (value = 1) or male (value = 0)
- Age: Age of the participant

Example dataset 3 for HIMA: Survival data outcome

- Treatment: treated (value = 1) or not treated (value = 0)
- Status: Status indicator: dead (value = 1) or alive (value = 0)
- Time: time to event
- Sex: female (value = 1) or male (value = 0)
- Age: Age of the participant

Example dataset 4 for HIMA: Compositional mediator (e.g., microbiome)

- Treatment: treated (value = 1) or not treated (value = 0)
- Outcome: outcome of the treatment- a normally distributed continuous variable
- Sex: female (value = 1) or male (value = 0)
- Age: Age of the participant

Example dataset 5 for HIMA: High-dimensional quantile mediation analysis

- Treatment: treated (value = 1) or not treated (value = 0)
- Outcome: outcome of the treatment- abnormally distributed continuous variable
- Sex: female (value = 1) or male (value = 0)
- Age: Age of the participant

Value

A list of example datasets for HIMA demo and testing.

`microHIMA` *High-dimensional mediation analysis for compositional microbiome data*

Description

`microHIMA` is used to estimate and test high-dimensional mediation effects for compositional microbiome data.

Usage

```
microHIMA(X, Y, OTU, COV = NULL, FDRcut = 0.05, scale = TRUE, verbose = FALSE)
```

Arguments

`X`	a vector of exposure.
`Y`	a vector of outcome.
`OTU`	a `data.frame` or `matrix` of high-dimensional compositional OTUs (mediators). Rows represent samples, columns represent variables.
`COV`	a `data.frame` or `matrix` of adjusting covariates. Rows represent samples, columns represent microbiome variables. Can be `NULL`.
`FDRcut`	FDR cutoff applied to define and select significant mediators. Default = `0.05`.
`scale`	logical. Should the function scale the data? Default = `TRUE`.
`verbose`	logical. Should the function be verbose? Default = `FALSE`.

Value

A data.frame containing mediation testing results of selected mediators (FDR < `FDRcut`).

- ID: index of selected significant mediator.
- alpha: coefficient estimates of exposure (X) –> mediators (M).
- alpha_se: standard error for alpha.
- beta: coefficient estimates of mediators (M) –> outcome (Y) (adjusted for exposure).
- beta_se: standard error for beta.
- FDR: false discovery rate of selected significant mediator.

References

Zhang H, Chen J, Feng Y, Wang C, Li H, Liu L. Mediation effect selection in high-dimensional and compositional microbiome data. Stat Med. 2021. DOI: 10.1002/sim.8808. PMID: 33205470; PMCID: PMC7855955.

Zhang H, Chen J, Li Z, Liu L. Testing for mediation effect with application to human microbiome data. Stat Biosci. 2021. DOI: 10.1007/s12561-019-09253-3. PMID: 34093887; PMCID: PMC8177450.

Examples

```
## Not run:
# Note: In the following example, M1, M2, and M3 are true mediators.
data(himaDat)

head(himaDat$Example4$PhenoData)

microHIMA.fit <- microHIMA(X = himaDat$Example4$PhenoData$Treatment,
                           Y = himaDat$Example4$PhenoData$Outcome,
                           OTU = himaDat$Example4$Mediator,
                           COV = himaDat$Example4$PhenoData[, c("Sex", "Age")],
                           scale = FALSE)
microHIMA.fit

## End(Not run)
```

---

qHIMA *High-dimensional quantile mediation analysis*

Description

qHIMA is used to estimate and test high-dimensional quantile mediation effects.

Usage

```
qHIMA(
  X,
  M,
  Y,
  Z,
  penalty = c("MCP", "SCAD", "lasso"),
  topN = NULL,
  tau = 0.5,
  scale = TRUE,
  Bonfcut = 0.05,
  verbose = FALSE,
  ...
)
```

Arguments

X	a vector of exposure.
M	a data.frame or matrix of high-dimensional mediators. Rows represent samples, columns represent mediator variables.
Y	a vector of continuous outcome. Do not use data.frame or matrix.
Z	a matrix of adjusting covariates. Rows represent samples, columns represent variables. Can be NULL.
penalty	the penalty to be applied to the model (a parameter passed to function conquer.cv.reg in package conquer. Either 'MCP' (the default), 'SCAD', or 'lasso'.
topN	an integer specifying the number of top markers from sure independent screening. Default = NULL. If NULL, topN will be 2*ceiling(n/log(n)), where n is the sample size. If the sample size is greater than topN (pre-specified or calculated), all mediators will be included in the test (i.e. low-dimensional scenario).
tau	quantile level of outcome. Default = 0.5. A vector of tau is accepted.
scale	logical. Should the function scale the data? Default = TRUE.
Bonfcut	Bonferroni-corrected p value cutoff applied to define and select significant mediators. Default = 0.05.
verbose	logical. Should the function be verbose? Default = FALSE.
...	other arguments.

Value

A data.frame containing mediation testing results of selected mediators (Bonferroni-adjusted p value <Bonfcut).

- ID: index of selected significant mediator.
- alpha: coefficient estimates of exposure (X) –> mediators (M).
- alpha_se: standard error for alpha.
- beta: coefficient estimates of mediators (M) –> outcome (Y) (adjusted for exposure).
- beta_se: standard error for beta.
- Bonferroni.p: statistical significance of the mediator (Bonferroni-corrected p value).

References

Zhang H, Hong X, Zheng Y, Hou L, Zheng C, Wang X, Liu L. High-Dimensional Quantile Mediation Analysis with Application to a Birth Cohort Study of Mother–Newborn Pairs. Bioinformatics. 2023. (In press)

Examples

```
## Not run:
# Note: In the following example, M1, M2, and M3 are true mediators.
data(himaDat)

head(himaDat$Example5$PhenoData)
```

```
qHIMA.fit <- qHIMA(X = himaDat$Example5$PhenoData$Treatment,
                M = himaDat$Example5$Mediator,
                Y = himaDat$Example5$PhenoData$Outcome,
                Z = himaDat$Example5$PhenoData[, c("Sex", "Age")],
                Bonfcut = 0.05,
                tau = c(0.3, 0.5, 0.7),
                scale = FALSE,
                verbose = TRUE)
qHIMA.fit

## End(Not run)
```

---

survHIMA *High-dimensional mediation analysis for survival data*

Description

survHIMA is used to estimate and test high-dimensional mediation effects for survival data.

Usage

```
survHIMA(X, Z, M, OT, status, FDRcut = 0.05, scale = TRUE, verbose = FALSE)
```

Arguments

X	a vector of exposure.
Z	a matrix of adjusting covariates. Rows represent samples, columns represent variables. Can be NULL.
M	a data.frame or matrix of high-dimensional mediators. Rows represent samples, columns represent mediator variables.
OT	a vector of observed failure times.
status	a vector of censoring indicator (status = 1: uncensored; status = 0: censored)
FDRcut	FDR cutoff applied to define and select significant mediators. Default = 0.05.
scale	logical. Should the function scale the data? Default = TRUE.
verbose	logical. Should the function be verbose? Default = FALSE.

Value

A data.frame containing mediation testing results of selected mediators (FDR <FDPcut).

- ID: index of selected significant mediator.
- alpha: coefficient estimates of exposure (X) –> mediators (M).
- alpha_se: standard error for alpha.
- beta: coefficient estimates of mediators (M) –> outcome (Y) (adjusted for exposure).
- beta_se: standard error for beta.
- p.joint: joint raw p-value of selected significant mediator (based on FDR).

References

Zhang H, Zheng Y, Hou L, Zheng C, Liu L. Mediation Analysis for Survival Data with High-Dimensional Mediators. Bioinformatics. 2021. DOI: 10.1093/bioinformatics/btab564. PMID: 34343267. PMCID: PMC8570823

Examples

```
## Not run:
# Note: In the following example, M1, M2, and M3 are true mediators.
data(himaDat)

head(himaDat$Example3$PhenoData)

survHIMA.fit <- survHIMA(X = himaDat$Example3$PhenoData$Treatment,
                Z = himaDat$Example3$PhenoData[, c("Sex", "Age")],
                M = himaDat$Example3$Mediator,
                OT = himaDat$Example3$PhenoData$Time,
                status = himaDat$Example3$PhenoData$Status,
                FDRcut = 0.05,
                scale = FALSE,
                verbose = TRUE)
survHIMA.fit

## End(Not run)
```

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