

Package ‘SMAHP’

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Type Package

Title Survival Mediation Analysis of High-Dimensional Proteogenomic Data

Version 0.0.5

Description

SMAHP (pronounced as SOO-MAP) is a novel multi-omics framework for causal mediation analysis of high-dimensional proteogenomic data with survival outcomes. The full methodological details can be found in our recent preprint by Ahn S et al. (2025) <[doi:10.48550/arXiv.2503.08606](https://doi.org/10.48550/arXiv.2503.08606)>.

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Encoding UTF-8

Imports data.table, fdrtool, ncvreg, penAFT, survival, stats, glmnet

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Suggests knitr, rmarkdown, testthat (>= 3.0.0)

Language en-US

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Depends R (>= 3.5.0)

NeedsCompilation no

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example_dat	<i>Example Dataset</i>
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Description

A example simulated dataset used in the SMAP package.

Usage

data(example_dat)

Format

example_dat

Examples

data(example_dat)

get_adjusted_p	<i>A function that returns adjusted p-values</i>
----------------	--

Description

A function that returns adjusted p-values.

Usage

get_adjusted_p(res_SMAHP)

Arguments

res_SMAHP Outputs from SMAHP

Value

A matrix of adjusted p-values.

Examples

```
data(example_dat)
surv_dat <- example_dat$urv_dat
res_SMAHP <- SMAHP(example_dat$X, example_dat$M, example_dat$C, time = surv_dat$time,
status = surv_dat$status)
get_adjusted_p(res_SMAHP)
```

get_coef

A function that extracts coefficients.

Description

A function that extracts coefficients from mediation and outcome model.

Usage

```
get_coef(res_SMAHP)
```

Arguments

res_SMAHP Outputs from SMAHP

Value

A data frame which includes the name of exposure and mediator with coefficients from mediation and outcome model.

beta1	The coefficient estimate of exposure in mediation model
beta2	The coefficient estimate of mediator in outcome model
beta3	The coefficient estimate of exposure in outcome model

Examples

```
data(example_dat)
surv_dat <- example_dat$urv_dat
res_SMAHP <- SMAHP(example_dat$X, example_dat$M, example_dat$C, time = surv_dat$time,
status = surv_dat$status)
get_coef(res_SMAHP)
```

get_pairs	<i>A function that returns mediation-exposure matrix</i>
-----------	--

Description

A function that returns final mediation-exposure matrix.

Usage

```
get_pairs(res_SMAHP)
```

Arguments

res_SMAHP Outputs from SMAHP

Value

Mediation-exposure matrix.

Examples

```
data(example_dat)
surv_dat <- example_dat$urv_dat
res_SMAHP <- SMAHP(example_dat$X, example_dat$M, example_dat$C, time = surv_dat$time,
status = surv_dat$status)
get_pairs(res_SMAHP)
```

get_raw_p	<i>A function that returns unadjusted p-values</i>
-----------	--

Description

A function that returns unadjusted p-values.

Usage

```
get_raw_p(res_SMAHP)
```

Arguments

res_SMAHP Outputs from SMAHP

Value

A matrix of unadjusted p-values.

Examples

```
data(example_dat)
surv_dat <- example_dat$surv_dat
res_SMAHP <- SMAHP(example_dat$X, example_dat$M, example_dat$C, time = surv_dat$time,
status = surv_dat$status)
get_raw_p(res_SMAHP)
```

get_sig_pathway	<i>A function that returns significant pathways.</i>
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Description

A function that returns significant pathways.

Usage

```
get_sig_pathway(res_SMAHP)
```

Arguments

res_SMAHP	Outputs from SMAHP
-----------	--------------------

Value

A data frame which includes the name of exposure and mediator with adjusted p-value from identified significant pathways.

Examples

```
data(example_dat)
surv_dat <- example_dat$surv_dat
res_SMAHP <- SMAHP(example_dat$X, example_dat$M, example_dat$C, time = surv_dat$time,
status = surv_dat$status)
get_sig_pathway(res_SMAHP)
```

SIS_combo

SIS combo

Description

A function for SIS + SIS combo.

Usage

```
SIS_combo(X, M, C, time, status, p_adjust_option = "BH", thres = 0.05)
```

Arguments

X	An n by p matrix of exposures.
M	An n by p matrix of mediators.
C	An n by p matrix of covariates.
time	A vector of survival time of samples.
status	A vector of status indicator: 0=alive, 1=dead.
p_adjust_option	The method for multiple correction. Option include q-value, holm, hochberg, hommel, bonferroni, BH, BY, and fdr. Default is BH.
thres	Threshold for determining significance.

Value

A list which includes the final p-value matrix (p_final_matrix), adjusted p-value matrix (p_adjusted_matrix) and mediation-exposure matrix (p_med_matrix).

Examples

```
data(example_dat)
surv_dat <- example_dat$surv_dat
SIS_combo(example_dat$X, example_dat$M, example_dat$C, time = surv_dat$time,
status = surv_dat$status)
```

Description

An approach for survival mediation analysis of high-dimensional proteogenomic data.

Usage

```
SMAHP(
  X,
  M,
  C,
  time,
  status,
  model_option = "MCP",
  SIS_thres = "n/log(n)",
  p_adjust_option = "BH",
  p_thres = 0.05
)
```

Arguments

X	An n by p matrix of exposures.
M	An n by p matrix of mediators.
C	An n by p matrix of covariates. If there are no covariates, set C = NULL.
time	A vector of survival time of samples.
status	A vector of status indicator: 0=alive, 1=dead.
model_option	The penalization method used when selecting X for M. Options include MCP, elastic net and lasso. Default is MCP.
SIS_thres	SIS thresholds. Default is "n/log(n)". Other options include "n-1", "n/2log(n)", "2n/log(n)", "3n/log(n)".
p_adjust_option	The method for multiple correction. Option include q-value, holm, hochberg, hommel, bonferroni, BH, BY, and fdr. Default is BH.
p_thres	Threshold for determining significance.

Value

A list with the following components:

p_final_matrix	raw p-value matrix before adjustment
p_adjusted_matrix	adjusted p-value matrix
p_med_matrix	mediation-exposure matrix
outcome_model	coefficient estimates from outcome model
med_results	coefficient estimates from mediation model

Examples

```
data(example_dat)
surv_dat <- example_dat$surv_dat
SMAHP(example_dat$X, example_dat$M, example_dat$C, time = surv_dat$time, status = surv_dat$status)
```

StepOne

*Penalized mediation and outcome models***Description**

An auxiliary function which conducts variable selection of X for Y using penAFT, X for M using the selected penalized model and M for Y using penAFT.

Usage

```
StepOne(X, M, time, status, model_option = "MCP")
```

Arguments

X	An n by p matrix of exposures.
M	An n by p matrix of mediators.
time	A vector of survival time of samples.
status	A vector of status indicator: 0=alive, 1=dead.
model_option	The penalization method used when selecting X for M. The options include MCP, elastic net and lasso. Default is MCP.

Value

A list with the following components:

X_sel_Y_s1	X selected for Y using penAFT
M_X_s1	X selected for M using the selected penalized model
M_sel_Y_s1	M selected for Y using penAFT

Examples

```
data(example_dat)
surv_dat <- example_dat$surv_dat
res_step1 <- StepOne(X = example_dat$X, M = example_dat$M, time = surv_dat$time,
status = surv_dat$status, model_option = "MCP")
```

StepThree

*Post-hoc model***Description**

An auxiliary function which generates p-value based on outcome and mediation model.

Usage

```
StepThree(X, M, C, time, status, X_sel_Y_s1, M_X_sel_s2)
```

Arguments

X	An n by p matrix of exposures.
M	An n by p matrix of mediators.
C	An n by p matrix of covariates. If there are no covariates, set C = NULL.
time	A vector of survival time of samples.
status	A vector of status indicator: 0=alive, 1=dead.
X_sel_Y_s1	Outputs from StepOne: A vector of selected X for Y.
M_X_sel_s2	Outputs from StepTwo: A data table with selected M, X pairs and related effect size.

Value

A list with the following components:

p_beta_m	p-values generated from outcome model
p_alpha_x	p-values generated from mediation model
outcome_model	coefficient estimates from outcome model
med_results	coefficient estimates from mediation model

Examples

```
data(example_dat)
surv_dat <- example_dat$surv_dat
res_step1 <- StepOne(X = example_dat$X, M = example_dat$M, time = surv_dat$time,
  status = surv_dat$status, model_option = "MCP")
M_X_sel_s2 <- StepTwo(X = example_dat$X, M = example_dat$M, time = surv_dat$time,
  status = surv_dat$status, X_sel_Y_s1 = res_step1$X_sel_Y_s1, M_X_s1 = res_step1$M_X_s1,
  M_sel_Y_s1 = res_step1$M_sel_Y_s1)
res_step3 <- StepThree(X = example_dat$X, M = example_dat$M, C = example_dat$C,
  time = surv_dat$time, status = surv_dat$status, X_sel_Y_s1 = res_step1$X_sel_Y_s1,
  M_X_sel_s2 = M_X_sel_s2)
```

StepTwo

*Select M-X pairs via SIS***Description**

An auxiliary function which selects M-X paris using SIS.

Usage

```
StepTwo(
  X,
  M,
  time,
  status,
  X_sel_Y_s1,
  M_X_s1,
  M_sel_Y_s1,
  SIS_thres = "n/log(n)"
)
```

Arguments

X	An n by p matrix of exposures.
M	An n by p matrix of mediators.
time	A vector of survival time of samples.
status	A vector of status indicator: 0=alive, 1=dead.
X_sel_Y_s1	Outputs from StepOne: A vector of selected X for Y.
M_X_s1	Outputs from StepOne: A list of selected X for M.
M_sel_Y_s1	Outputs from StepOne: A vector of selected M for Y.
SIS_thres	SIS thresholds. Default is "n/log(n)". Other options include "n-1", "n/2log(n)", "2n/log(n)", "3n/log(n)".

Value

A data table with selected M, X pairs and related effect size.

Examples

```
data(example_dat)
surv_dat <- example_dat$surv_dat
res_step1 <- StepOne(X = example_dat$X, M = example_dat$M, time = surv_dat$time,
  status = surv_dat$status, model_option = "MCP")
M_X_sel_s2 <- StepTwo(X = example_dat$X, M = example_dat$M, time = surv_dat$time,
  status = surv_dat$status, X_sel_Y_s1 = res_step1$X_sel_Y_s1, M_X_s1 = res_step1$M_X_s1,
  M_sel_Y_s1 = res_step1$M_sel_Y_s1)
```

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