

Package ‘ROCSI’

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Type Package

Title Receiver Operating Characteristic Based Signature Identification

Version 0.1.0

Description Optimal linear combination predictive signatures for maximizing the area between two Receiver Operating Characteristic (ROC) curves (treatment vs. control).

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Contents

AUC	2
beta2theta	2
C.index	3
cvfolds0	4
data.gen	4
grad.sub	6
gradsqr	6
hessAUC	7
hessAUC.sub	8
HIC	8
MClogit	9
pair.diff	11
pair.diff.surv	11
ROCSI	12
theta2beta	14

Index	15
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AUC	<i>AUC</i>
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Description

Empirical AUC estimate

Usage

AUC(outcome, predict)

Arguments

outcome	binary outcome (1: desired outcome; 0: otherwise)
predict	prediction score

Details

Function for AUC when input is X and Y.

Value

a numeric value of empirical estimation of area under the ROC curves

Examples

```
# no run
```

beta2theta	<i>beta2theta</i>
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Description

Function to translate beta into theta, the n-sphere constrain

Usage

beta2theta(beta)

Arguments

beta	estimates of coefficient beta
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Details

Function to translate beta into theta, the n-sphere constrain

Value

a numeric vector for theta (dimension-1)

Examples

```
# no run
```

C.index	<i>C.index</i>
---------	----------------

Description

Empirical c-index estimate

Usage

```
C.index(yvar, score, censorvar, data)
```

Arguments

- | | |
|-----------|--|
| yvar | column name for observed time |
| score | column name for marker value |
| censorvar | column name for censor (1 is event, 0 is censored) |
| data | input data matrix |

Details

Function for c-index when input is X and Y.

Value

a numeric value of empirical estimation of c-index

Examples

```
# no run
```

cvfolds0	<i>cvfolds0</i>
----------	-----------------

Description

internal function for generating CV fold index

Usage

```
cvfolds0(X, Y, idx, nfolds = 5)
```

Arguments

X	marker matrix for non-responders
Y	marker matrix for responders
idx	m*n by 2 matrix for row index of marker matrix, first column is row index in X; second column is for Y
nfolds	the cross-validation folds

Details

Function for generate CV fold index

Value

a vector containing CV fold index for each row in Z

Examples

```
# no run
```

data.gen	<i>data.gen</i>
----------	-----------------

Description

Function for simulated data generation

Usage

```
data.gen(
  n,
  k,
  prevalence = sqrt(0.5),
  prog.eff = 1,
  sig2,
  y.sig2,
  rho,
  rhos.bt.real,
  a.constant
)
```

Arguments

n	Total sample size
k	Number of markers
prevalence	prevalence of predictive biomarkers with values above the cutoff
prog.eff	effect size <i>beta</i> for prognostic biomarker
sig2	standard deviation of each marker
y.sig2	Standard Deviation of the error term in the linear component
rho	$\rho \cdot \text{sig2}$ is the entries for covariance matrix between pairs of different k markers
rhos.bt.real	correlation between each prognostic and predictive markers
a.constant	a constant is set such that there is no overall treatment effect

Details

Function for simulated data generation

Value

A list of simulated clinical trial data with heterogeneous prognostic and predictive biomarkers

Examples

```
n <- 500
k <- 10
prevalence <- sqrt(0.5)
rho <- 0.2
sig2 <- 2
rhos.bt.real <- c(0, rep(0.1, (k-3))) * sig2
y.sig2 <- 1
prog.eff <- 0.5
effect.size <- 1
a.constant <- effect.size / (2 * (1 - prevalence))
ObsData <- data.gen(n=n, k=k, prevalence=prevalence, prog.eff=prog.eff,
  sig2=sig2, y.sig2=y.sig2, rho=rho,
  rhos.bt.real=rhos.bt.real, a.constant=a.constant)
```

<code>grad.sub</code>	<i>grad.sub</i>
-----------------------	-----------------

Description

Internal function of `grad_square` in the GCV

Usage

`grad.sub(z, beta)`

Arguments

<code>z</code>	($m \times n$) $\times$ p data matrix as prepared for ROCSI
<code>beta</code>	estimates of coefficient <code>beta</code>

Details

Internal function of `grad_square` in the GCV

Value

`grad_square` in the GCV

Examples

```
# no run
```

<code>gradsqr</code>	<i>gradsqr</i>
----------------------	----------------

Description

Internal function for HIC calculation

Usage

`gradsqr(beta, Z0, index, w = 1)`

Arguments

<code>beta</code>	estimates of coefficient <code>beta</code>
<code>Z0</code>	($m \times n$) $\times$ p <code>Z</code> matrix as prepared for ROCSI
<code>index</code>	$m \times n$ by 2 matrix for the subindex for the pair difference in <code>Z</code>
<code>w</code>	a vector of weights <code>Z</code> (can be used for inverse probability weighting for missing data, default is 1)

Details

Internal function for HIC calculation

Value

gradient square for the GCV.

Examples

```
# no run
```

<i>hessAUC</i>	<i>hessAUC</i>
----------------	----------------

Description

function for Hessian matrix of AUC

Usage

```
hessAUC(beta, Z, w = 1)
```

Arguments

- | | |
|------|--|
| beta | estimates of coefficient beta |
| Z | (m x n) x p data matrix as prepared for ROCSI |
| w | a vector of weights Z (can be used for inverse probability weighting for missing data, default is 1) |

Details

function for Hessian matrix of AUC

Value

Hessian matrix of AUC.

Examples

```
# no run
```

hessAUC.sub	<i>hessAUC.sub</i>
-------------	--------------------

Description

Internal function for hessAUC

Usage

hessAUC.sub(z, beta)

Arguments

z (m x n) x p data matrix as prepared for ROCSI
beta estimates of coefficient beta

Details

Internal function for hessAUC

Value

Hessian matrix components.

Examples

no run

HIC	<i>HIC</i>
-----	------------

Description

function for HIC calculation

Usage

HIC(beta, Z, index, w = 1)

Arguments

beta estimates of coefficient beta
Z matrix prepared for ROCSI
index m*n by 2 matrix for the subindex for the pair difference in Z
w a vector of weights Z (can be used for inverse probability weighting for missing data, default is 1)

Details

Function for HIC calculation

Value

A numeric value with corresponding HIC

Examples

```
# no run
```

MClogit	<i>MClogit</i>
---------	----------------

Description

function for modified covariate methods based on glmnet

Usage

```
MClogit(
  dataset,
  yvar,
  xvars,
  trtvar,
  cvar = NULL,
  nfolds = 5,
  type = "binary",
  newx = NULL,
  bestsub = "lambda.1se",
  type.measure = "auc"
)
```

Arguments

dataset	data matrix for training dataset
yvar	column name for outcome
xvars	a string vector of column names for input markers
trtvar	column name for treatment (the column should contain binary code with 1 being treatment and 0 being control)
cvar	column name for censor (the column should contain binary code with 1 being event and 0 being censored)
nfolds	n fold CV used for cv.glmnet
type	outcome type ("binary" for binary outcome and "survival" for time-to-event outcome)

<code>newx</code>	data matrix for testing dataset X
<code>bestsub</code>	criteria for best lambda, used by glmnet
<code>type.measure</code>	type of measure used by glmnet

Details

function for ROCSI

Value

A list with ROCSI output

x.logit final beta estimated from MClogit

predScore a data.frame of testing data and its predictive signature scores (based on beta.aABC) for each subjects

abc ABC in testing dataset based on optimal beta

fit.cv the fitted glmnet object

Examples

```
n <- 100
k <- 5
prevalence <- sqrt(0.5)
rho<-0.2
sig2 <- 2
rhos.bt.real <- c(0, rep(0.1, (k-3)))*sig2
y.sig2 <- 1
yvar="y.binary"
xvars=paste("x", c(1:k), sep="")
trtvar="treatment"
prog.eff <- 0.5
effect.size <- 1
a.constant <- effect.size/(2*(1-prevalence))
ObsData <- data.gen(n=n, k=k, prevalence=prevalence, prog.eff=prog.eff,
  sig2=sig2, y.sig2=y.sig2, rho=rho,
  rhos.bt.real=rhos.bt.real, a.constant=a.constant)
TestData <- data.gen(n=n, k=k, prevalence=prevalence, prog.eff=prog.eff,
  sig2=sig2, y.sig2=y.sig2, rho=rho,
  rhos.bt.real=rhos.bt.real, a.constant=a.constant)
bst.mod <- MClogit(dataset=ObsData$data, yvar=yvar, xvars=xvars,
  trtvar=trtvar, nfolds = 5, newx=TestData$data,
  type="binary", bestsub="lambda.1se")
bst.mod$abc
bst.mod$x.logit[-1,1]
```

pair.diff

pair.diff

Description

internal function for generating Z matrix (binary endpoint)

Usage

```
pair.diff(X, Y, A)
```

Arguments

X	marker matrix for non-responders
Y	marker matrix for responders
A	Treatment arm indicator (1 is treatment, 0 is control)

Details

Function for generate Z matrix for binary endpoint

Value

A list of prepared data input for ROCSI

Examples

```
# no run
```

pair.diff.surv

pair.diff.surv

Description

internal function for generating Z matrix (time-to-event endpoint)

Usage

```
pair.diff.surv(X, Y, A, C)
```

Arguments

X	marker matrix
Y	a vector for observed time
A	a vector for Treatment arm indicator (1 is treatment, 0 is control)
C	a vector for censor (1 is event, 0 is censored)

Details

Function for generate Z matrix for time-to-event endpoint

Value

A list of prepared data input for ROCSI

Examples

```
# no run
```

ROCSI	<i>ROCSI</i>
-------	--------------

Description

function for ROCSI

Usage

```
ROCSI(  
  Dtrain,  
  Dtest = NULL,  
  yvar,  
  xvars,  
  trtvar,  
  cvar = NULL,  
  nfolds = 5,  
  type = "binary"  
)
```

Arguments

- | | |
|--------|--|
| Dtrain | data matrix for training dataset |
| Dtest | optional data matrix for testing dataset |
| yvar | column name for outcome |
| xvars | a string vector of column names for input markers |
| trtvar | column name for treatment (the column should contain binary code with 1 being treatment and 0 being control) |
| cvar | column name for censor (the column should contain binary code with 1 being event and 0 being censored) |
| nfolds | n fold CV used for cv.glmnet |
| type | outcome type ("binary" for binary outcome and "survival" for time-to-event outcome) |

Details

function for ROCSI

Value

A list with ROCSI output

beta.aABC final beta estimated from ROCSI based on $ABC^{(acv)}$

beta.1se final beta estimated from lambda.1se based on nfold CV

lambda.aABC optimal lambda selected by optimizing $ABC^{(acv)}$

fit.cv fitted cv.glmnet model

log log matrix of all lambdas and ABCs

abc.test ABC in testing dataset based on optimal beta

abc.test1se ABC in testing dataset based on 1se beta

predScore a data.frame of testing data and its predictive signature scores (based on beta.aABC)
for each subjects

predScore.1se a data.frame of testing data and its predictive signature scores (based on beta.1se)
for each subjects

Examples

```
n <- 100
k <- 5
prevalence <- sqrt(0.5)
rho<-0.2
sig2 <- 2
rhos.bt.real <- c(0, rep(0.1, (k-3)))*sig2
y.sig2 <- 1
yvar="y.binary"
xvars=paste("x", c(1:k), sep="")
trtvar="treatment"
prog.eff <- 0.5
effect.size <- 1
a.constant <- effect.size/(2*(1-prevalence))
ObsData <- data.gen(n=n, k=k, prevalence=prevalence, prog.eff=prog.eff,
                    sig2=sig2, y.sig2=y.sig2, rho=rho,
                    rhos.bt.real=rhos.bt.real, a.constant=a.constant)
TestData <- data.gen(n=n, k=k, prevalence=prevalence, prog.eff=prog.eff,
                    sig2=sig2, y.sig2=y.sig2, rho=rho,
                    rhos.bt.real=rhos.bt.real, a.constant=a.constant)
bst.aabc <- ROCSI(Dtrain=ObsData$data, Dtest = TestData$data, yvar=yvar,
xvars=xvars, trtvar=trtvar, cvar=NULL, nfolds=5, type="binary")
bst.aabc$beta.aABC
bst.aabc$log
bst.aabc$abc.test
bst.aabc$beta.1se
bst.aabc$abc.test1se
```

theta2beta	<i>theta2beta</i>
------------	-------------------

Description

Function to translate theta into beta

Usage

theta2beta(theta)

Arguments

theta n-sphere coordination

Details

Function to translate beta into theta, the n-sphere constrain

Value

a numeric vector for beta (dimension+1)

Examples

no run

Index

AUC, [2](#)

beta2theta, [2](#)

C.index, [3](#)
cvfolds0, [4](#)

data.gen, [4](#)

grad.sub, [6](#)
gradsqr, [6](#)

hessAUC, [7](#)
hessAUC.sub, [8](#)
HIC, [8](#)

MClogit, [9](#)

pair.diff, [11](#)
pair.diff.surv, [11](#)

ROCSI, [12](#)

theta2beta, [14](#)